

POLITECHNIKA ŚLĄSKA w Gliwicach

WYDZIAŁ INŻYNIERII BIOMEDYCZNEJ
Katedra Informatyki Medycznej i Sztucznej Inteligencji

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**Wpływ palenia papierosów elektronicznych i tradycyjnych
na wybrane parametry układu oddechowego
i sercowo-naczyniowego pacjentów, na podstawie analizy
wektorów danych, uzyskanych z rejestracji wielomodalnych
sygnałów biomedycznych**

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Serdeczne podziękowania kieruję do moich Promotorów: dr. hab. inż. Pawła Kostki, prof. PŚ oraz dr. hab. inż. Rafała Dońca, za nieocenione merytoryczne wsparcie, zaangażowanie, cenne wskazówki oraz życzliwość, które towarzyszyły mi na każdym etapie pracy nad rozprawą.

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Streszczenie

Niniejsza rozprawa doktorska poświęcona jest kompleksowej analizie wpływu nikotyny dostarczanej w formie papierosów tradycyjnych oraz elektronicznych na wybrane parametry fizjologiczne, metaboliczne i behawioralne organizmu ludzkiego. Badania zaprojektowano w sposób interdyscyplinarny, łącząc podejścia biologii systemowej, inżynierii biomedycznej oraz sztucznej inteligencji. W pracy zastosowano zarówno metody eksperymentalne, jak i obliczeniowe (*in silico*), co umożliwiło pogłębioną ocenę reakcji organizmu na różne formy podaży nikotyny oraz ich potencjalne skutki zdrowotne.

Część eksperymentalna obejmowała analizę składu ciała, kontroli posturalnej, parametrów chodu oraz reakcji układu sercowo-naczyniowego na wysiłek fizyczny u młodych dorosłych, należących do grup użytkowników e-papierosów, palaczy tradycyjnych oraz osób niepalących. Wykorzystano metody statystyki wielowymiarowej, analizę korelacyjną oraz algorytmy klasyfikacyjne, identyfikując istotne różnice międzygrupowe. Równolegle opracowano i zastosowano szereg modeli komputerowych, w tym modele farmakokinetyczne PBPK (*physiologically based pharmacokinetic*), odwzorowujące dystrybucję nikotyny w ustroju, modele Markowa opisujące proces uzależnienia oraz dynamiczne modele populacyjne (SIQ+P+E+H+X), służące do symulacji efektów polityk zdrowotnych i interwencji profilaktycznych. Ponadto, wykonano symulacje degradacji grzałek e-papierosów, oceniając ich potencjalny wpływ toksykologiczny. Zastosowano również metody uczenia maszynowego do identyfikacji czynników społecznych i demograficznych, warunkujących zachowania związane z paleniem oraz do klasyfikacji odpowiedzi fizjologicznej, opartej na multimodalnej analizie sygnałów (EKG, PPG, ciśnienia krwi).

Uzyskane rezultaty wskazują na znaczące różnice w reaktywności fizjologicznej, metabolizmie oraz uwarunkowaniach behawioralnych pomiędzy grupami badanymi, a także na możliwość ich predykcji w oparciu o złożone modele danych. Wnioski sformułowane na podstawie przeprowadzonych badań stanowią potencjalny wkład w rozwój narzędzi wspierających zdrowie publiczne, optymalizację działań profilaktycznych oraz kształtowanie regulacji antynikotynowych. Rozprawa opiera się na cyklu jedenastu publikacji naukowych, z których pięć zostało opublikowanych lub przyjętych do druku, a sześć znajduje się w trakcie recenzji. Wszystkie prace łączy jednolity cel badawczy, spójność metodologiczna oraz znaczący, samodzielny wkład doktorantki.

Słowa kluczowe: nikotyna, papierosy elektroniczne, papierosy tradycyjne, układ sercowo-naczyniowy, układ oddechowy, metabolizm, kontrola posturalna, model PBPK, uczenie maszynowe, analiza sygnałów biomedycznych

Abstract

This doctoral dissertation presents a comprehensive and interdisciplinary analysis of the effects of nicotine on human physiology, metabolism, and behavior, comparing traditional cigarettes and electronic cigarettes as delivery systems. The research integrates experimental investigations with advanced computational modeling, drawing from systems biology, biomedical engineering, and artificial intelligence. This dual approach allowed for a detailed assessment of physiological responses and potential health impacts related to nicotine use in various forms.

The experimental studies focused on young adults and included assessments of body composition, postural control, gait parameters, and cardiovascular reactivity during physical exertion, with comparisons between e-cigarette users, traditional smokers, and non-smokers. Multivariate statistical methods, correlation analysis, and machine learning algorithms were employed to identify significant intergroup differences. Simultaneously, several computational models were developed, including physiologically-based pharmacokinetic (PBPK) models describing nicotine distribution in the body, Markov models simulating addiction processes, and extended population-level models (SIQ+P+E+H+X) to evaluate the long-term effects of tobacco control policies. Additionally, simulation of coil degradation in e-cigarette devices was conducted to assess material transformation and its potential health implications. Machine learning techniques were also applied to identify demographic, familial, and social determinants of smoking behavior and to classify physiological responses based on multimodal biosignal analysis (ECG, PPG, blood pressure).

The findings demonstrate distinct physiological and behavioral profiles across user groups and support the feasibility of predicting health outcomes through integrative data modeling. The dissertation contributes to public health research by proposing data-driven methods for nicotine risk assessment and intervention planning. It is based on a series of eleven scientific publications, five of which have been published or accepted, while six are currently under peer review. All articles are thematically coherent, methodologically consistent, and reflect a substantial individual contribution by the doctoral candidate.

Keywords: nicotine, electronic cigarettes, conventional cigarettes, cardiovascular system, respiratory system, metabolism, postural control, PBPK model, machine learning, biomedical signal analysis

1. Wykaz publikacji stanowiących rozprawę doktorską

Niniejsza rozprawa opiera się na cyklu publikacji naukowych, poświęconych ocenie wpływu palenia papierosów tradycyjnych i elektronicznych na funkcjonowanie układu oddechowego i sercowo-naczyniowego. Prace te łączy wspólna tematyka oraz spójna metodologia, obejmująca analizę toksykologiczną aerozolu, modelowanie farmakokinetyczne (PBPK), rejestrację i przetwarzanie sygnałów biomedycznych oraz zastosowanie narzędzi sztucznej inteligencji. Opracowane metody i rezultaty badań wnoszą istotny wkład do wiedzy na temat fizjologicznych i zdrowotnych skutków nowoczesnych form podaży nikotyny, a także wspierają rozwój narzędzi decyzyjnych w zakresie zdrowia publicznego. Szczegółowy wykaz publikacji, stanowiących podstawę rozprawy:

1. **Chwał J.**, Filipowska A., Antonowicz M., Lisicki D., Kostka P., Doniec R. *Elemental Composition of Vaping and Smoking Aerosols: Influence of Liquid Type and Tank Conditions*. PLOS ONE, w recenzji.
2. **Chwał J.**, Dzik R., Banasik A., Tkacz E. *Comparative Pharmacokinetics of Nicotine from E-Cigarettes and Traditional Cigarettes: A PBPK Modeling and Machine Learning Approach*. 6th International Conference on Artificial Intelligence, Katowice 2024, Wydawnictwo Uniwersytetu Śląskiego, w druku.
3. **Chwał J.**, Dzik R., Banasik A., Pańtak P., Tkacz E. *Physiologically-Based Pharmacokinetic Modeling of Nicotine*. Scientific Papers of Silesian University of Technology – Organization and Management Series, w druku.
4. **Chwał J.**, Dzik R., Banasik A., Tkacz E. *A Computational Model of E-Cigarette Coil Degradation: Simulating Thermal and Material Dynamics and Their Impact on Health*. Poster, IEEE Engineering in Medicine and Biology Conference (EMBC) 2025, Copenhagen.
5. **Chwał J.**, Banasik A., Dzik R., Tkacz E. *Optimizing Smoking Cessation Alternatives Using Multi-MOORA and AI-Based Methods*. AIR-RES 2025, Las Vegas, Springer Nature, w druku.
6. **Chwał J.**, Dzik R., Banasik A., Piotrowski K., Zapotoczny M., Kempa W.M., Pikiewicz P., Tkacz E. *Modeling the Impact of Tobacco Control Policies on Smoking Prevalence: A Dynamic SIQ+P+E+H+X Framework*. Scientific Papers of Silesian University of Technology – Organization and Management Series, w druku.
7. **Chwał J.**, Banasik A., Dzik R., Tkacz E. *Markov Model Simulation of Nicotine Addiction and the Effectiveness of Nicotine Replacement Therapy (NRT)*. Poster, NBC & PCBBE 2025, Warszawa.
8. **Chwał J.**, Kostka M., Kostka P.S., Dzik R., Filipowska A., Doniec R. *Analysis of Demographic, Familial, and Social Determinants of Smoking Behavior Using Machine Learning Methods*. Applied Sciences, 2025;15(8):4442.
9. **Chwał J.**, Zadoń H., Szaflik P., Dzik R., Filipowska A., Doniec R., Kostka P., Michnik R. *Body Composition and Metabolic Profiles in Young Adults: A Cross-Sectional Comparison of People Who Use E-Cigarettes, People Who Smoke Cigarettes, and People Who Have Never Used Nicotine Products*. Journal of Clinical Medicine, 2025;14(13):4459.

10. **Chwał J.**, Zadoń H., Szaflik P., Dzik R., Filipowska A., Doniec R., Kostka P., Michnik R. *Postural Control and Gait Alterations in Young Adult Tobacco and E-Cigarette Users: A Comparative Stabilometric and Treadmill-Based Analysis*. *Measuring and Computing Devices in Technological Processes*, 2025;83(3):293–312.
11. **Chwał J.**, Zadoń H., Szaflik P., Dzik R., Filipowska A., Doniec R., Kostka P., Michnik R. *E-Cigarette Users Exhibit Stronger Cardiovascular Reactivity than Smokers: Evidence from a Multimodal Signal Analysis in Young Adults*. *Scientific Reports*, w recenzji.

W zależności od charakteru pracy, udział autorski obejmował koncepcję badania, opracowanie modelu matematycznego, analizę danych eksperymentalnych, przetwarzanie sygnałów biomedycznych, wdrażanie algorytmów uczenia maszynowego, organizację badań z udziałem ludzi, jak również redakcję manuskryptów. Poniżej przedstawiono syntetyczne zestawienie wkładu autorki w każdą z publikacji:

- [A1]. **Chwał Joanna**, Filipowska Anna, Antonowicz Magdalena, Lisicki Dawid, Kostka Paweł, Doniec Rafał, *Elemental Composition of Vaping and Smoking Aerosols: Influence of Liquid Type and Tank Conditions*, PLOS ONE (w recenzji), DOI: –, IF = 2.6, CS = 5.4, Punkty MNiSW = 100

Wkład własny: Koncepcja badania, opracowanie metodologii, organizacja i prowadzenie eksperymentów, analiza danych, wizualizacja wyników, współautorstwo tekstu.

Udział: 60%

Szczegółowy opis wkładu:

Byłam inicjatorką i główną wykonawczynią eksperymentów opisanych w artykule. Zaplanowałam protokół badania i procedury analizy danych fizjologicznych. Odpowiadałam za rekrutację uczestników, prowadzenie pomiarów oraz ich walidację. Dokonałam wstępnego przetwarzania sygnałów oraz przygotowałam wizualizacje i tabele. Współtworzyłam tekst manuskryptu i brałam udział w jego redakcji.

- [A2]. **Chwał Joanna**, Dzik Radosław, Banasik Arkadiusz, Tkacz Ewaryst, *Comparative Pharmacokinetics of Nicotine from E-Cigarettes and Traditional Cigarettes: A PBPK Modeling and Machine Learning Approach*, 6th International Conference on Artificial Intelligence, Katowice 2024, Wydawnictwo Uniwersytetu Śląskiego, DOI: –, IF = –, CS = –, Punkty MNiSW = 20

Wkład własny: Opracowanie i parametryzacja modelu PBPK, analiza symulacji i ich porównanie z danymi empirycznymi, współtworzenie materiałów konferencyjnych oraz wygłoszenie prelekcji na forum konferencji.

Udział: 55%

Szczegółowy opis wkładu:

Jako pierwsza autorka zaprojektowałam i zaimplementowałam fizjologiczny model PBPK służący do porównania losów nikotyny w organizmie po użyciu e-papierosów i tradycyjnych papierosów. Przeprowadziłam kalibrację modelu na podstawie danych literaturowych oraz eksperymentalnych. Dokonałam porównania wyników symulacji z wartościami pomiarowymi i zaprojektowałam część graficzną prezentacji. Przygotowałam podsumowanie do materiałów konferencyjnych. Wzięłam udział w ustnej prezentacji wyników na konferencji.

- [A3]. **Chwał Joanna**, Dzik Radosław, Banasik Arkadiusz, Pańtak Piotr, Tkacz Ewaryst, *Physiologically-Based Pharmacokinetic Modeling of Nicotine*, *Scientific Papers of*

Silesian University of Technology – Organization and Management Series, w druku, ISSN 1641-3466, ISSN 2720-751X, DOI: –, IF = –, CS –, Punkty MNiSW = 70
Wkład własny: Koncepcja badania, stworzenie struktury i kodu modelu PBPK, parametryzacja, analiza symulacji, interpretacja wyników, współautorstwo tekstu.

Udział: 60%

Szczegółowy opis wkładu:

Jako główna autorka zaprojektowałam i zaimplementowałam model farmakokinetyczny PBPK dla nikotyny z podziałem na różne stany zdrowotne i drogi podaży (e-papierosy, papierosy tradycyjne). Przeprowadziłam weryfikację i parametryzację modelu na podstawie danych literaturowych oraz klinicznych. Odpowiadałam za przygotowanie symulacji porównawczych oraz interpretację wyników z uwzględnieniem zmiennych fizjologicznych. Uczestniczyłam w przygotowaniu tekstu manuskryptu oraz warstwy wizualnej artykułu.

- [A4]. **Chwał Joanna**, Dzik Radosław, Banasik Arkadiusz, Tkacz Ewaryst, A Computational Model of E-Cigarette Coil Degradation: *Simulating Thermal and Material Dynamics and Their Impact on Health*, Poster, IEEE Engineering in Medicine and Biology Conference (EMBC) 2025, Copenhagen, DOI: –, IF = –, CS = –, Punkty MNiSW = 20

Wkład własny: Koncepcja modelu, stworzenie algorytmu degradacji grzałki, analiza wyników, wizualizacja, przygotowanie materiału posterowego.

Udział: 60%

Szczegółowy opis wkładu:

Opracowałam koncepcję modelu komputerowego odwzorowującego proces degradacji grzałki e-papierosa pod wpływem ciepła i czasu pracy. Zaimplementowałam algorytm symulujący zmiany fizykochemiczne materiałów i ich potencjalne skutki zdrowotne. Przeprowadziłam analizę dynamiki termicznej oraz stworzyłam wizualizację obrazującą zmiany strukturalne. Przygotowałam materiał do prezentacji posterowej, w tym opis metod i kluczowe wyniki.

- [A5]. **Chwał Joanna**, Banasik Arkadiusz, Dzik Radosław, Tkacz Ewaryst, *Optimizing Smoking Cessation Alternatives Using Multi-MOORA and AI-Based Methods*, AIR-RES 2025, Las Vegas, w druku (Springer Nature), ISBN: 1-60132-521-5, IF = –, CS = –, Punkty MNiSW = 20

Wkład własny: Opracowanie części metodologicznej związanej z klasyfikacją danych, analiza wielokryterialna (Multi-MOORA), współtworzenie materiałów prezentacyjnych.

Udział: 40%

Szczegółowy opis wkładu:

W projekcie uczestniczyłam w opracowaniu metody porównawczej oceniającej alternatywy rzucania palenia z wykorzystaniem wielokryterialnej analizy decyzyjnej Multi-MOORA. Przygotowałam strukturę danych wejściowych, dokonałam przekształceń i normalizacji cech oraz brałam udział w integracji wyników z modułem klasyfikacyjnym, opartym na sztucznej inteligencji. Współtworzyłam diagramy i podsumowania użyte w materiałach konferencyjnych.

- [A6]. **Chwał Joanna**, Dzik Radosław, Banasik Arkadiusz, Piotrowski Karol, Wawryszczuk Marcin, Zapotoczny Mateusz, Kempa Wojciech M., Piekiewicz Piotr, Tkacz Ewaryst, *Modeling the Impact of Tobacco Control Policies on Smoking Prevalence: A Dynamic SIQ+P+E+H+X Framework*, Scientific Papers of Silesian University of Technology – Organization and Management Series, w druku, ISSN 1641-3466, ISSN 2720-751X, IF = –, CS = –, Punkty MNiSW = 70

Wkład własny: Projekt koncepcyjny modelu SIQ+P+E+H+X, kodowanie systemu dynamicznego, analiza scenariuszy, wizualizacja wyników, współautorstwo manuskryptu.

Udział: 40%

Szczegółowy opis wkładu:

Opracowałam koncepcję rozszerzonego modelu dynamicznego SIQ (Susceptible-Initiator-Quitter) z dodatkowymi komponentami obejmującymi interwencje polityczne (P), czynniki środowiskowe (E), stan zdrowia (H) oraz ekspozycję (X). Zaimplementowałam model w środowisku obliczeniowym, przeprowadziłam symulacje dla różnych scenariuszy polityki zdrowotnej i przeanalizowałam wpływ parametrów na częstość palenia w populacji. Przygotowałam ilustracje wyników i współtworzyłam treść manuskryptu.

- [A7]. **Chwał Joanna**, Banasik Arkadiusz, Dzik Radosław, Tkacz Ewaryst, *Markov Model Simulation of Nicotine Addiction and the Effectiveness of Nicotine Replacement Therapy (NRT)*, Poster, NBC&PCBBE 2025, Warszawa, DOI: –, IF = –, CS = –, Punkty MNiSW = 20

Wkład własny: Opracowanie struktury łańcucha Markowa, estymacja prawdopodobieństw przejść, analiza efektów terapii NRT, współtworzenie materiału posterowego.

Udział: 55%

Szczegółowy opis wkładu:

Zaprojektowałam model Markowa odwzorowujący proces uzależnienia od nikotyny i ścieżki leczenia z wykorzystaniem terapii NRT (nikotynowa terapia zastępcza). Przeprowadziłam parametryzację modelu w oparciu o dane literaturowe i epidemiologiczne, a następnie symulację długoterminowych trajektorii behawioralnych. Wykonałam analizę skuteczności poszczególnych scenariuszy leczenia. Przygotowałam wykresy wyników, współtworzyłam układ i treść prezentacji posterowej oraz osobiście uczestniczyłam w prezentacji wyników.

- [A8]. **Chwał Joanna**, Kostka Małgorzata, Kostka Paweł S., Dzik Radosław, Filipowska Anna, Doniec Rafał, *Analysis of Demographic, Familial, and Social Determinants of Smoking Behavior Using Machine Learning Methods*, Applied Sciences, 2025;15(8):4442, DOI: 10.3390/app15084442, IF = 2.5, CS = 3.4, Punkty MNiSW = 100

Wkład własny: Projekt koncepcyjny badania, przygotowanie zbioru danych, implementacja algorytmów uczenia maszynowego, analiza i interpretacja wyników, współautorstwo tekstu.

Udział: 60%

Szczegółowy opis wkładu:

Odpowiadałam za projekt koncepcyjny badania, mającego na celu identyfikację uwarunkowań zachowań związanych z paleniem tytoniu w populacji młodych dorosłych. Przygotowałam zbiór danych z uwzględnieniem zmiennych demograficznych, rodzinnych i społecznych, następnie przeprowadziłam ekstrakcję cech oraz implementację klasyfikatorów, opartych na uczeniu maszynowym. Przeanalizowałam wyniki predykcyjne, wykonałam walidację modeli i opracowałam wizualizacje. Uczestniczyłam w redakcji tekstu artykułu.

- [A9]. **Chwał Joanna**, Zadoń Hanna, Szaflik Piotr, Dzik Radosław, Filipowska Anna, Doniec Rafał, Kostka Paweł, Michnik Robert, *Body Composition and Metabolic Profiles in Young Adults: A Cross-Sectional Comparison of People Who Use E-Cigarettes, People Who Smoke Cigarettes, and People Who Have Never Used Nicotine Products*, DOI: 10.3390/jcm14134459, IF = 2.9, CS = 5.2, Punkty MNiSW = 140

Wkład własny: Projekt badania, rekrutacja uczestników, pomiary składu ciała i analiza kwestionariuszy, statystyka opisowa i wielowymiarowa, współautorstwo manuskryptu.

Udział: 50%

Szczegółowy opis wkładu:

Opracowałam projekt badania przekrojowego, dotyczącego wpływu używania e-papierosów na skład ciała i styl życia młodych dorosłych. Byłam odpowiedzialna za dobór i kontrolę procedur pomiaru metodą BIA (Bioelectrical Impedance Analysis), opracowanie i analizę danych kwestionariuszowych, a także za przeprowadzenie analiz statystycznych – zarówno jednoczynnikowych, jak i wielowymiarowych. Współtworzyłam strukturę manuskryptu i brałam udział w jego redakcji.

- [A10]. **Chwał Joanna**, Zadoń Hanna, Szaflik Paweł, Dzik Radosław, Filipowska Anna, Doniec Rafał, Kostka Paweł, Michnik Robert, *Postural Control and Gait Alterations in Young Adult Tobacco and E-Cigarette Users: A Comparative Stabilometric and Treadmill-Based Analysis*, Measuring and Computing Devices in Technological Processes, (3), 293–312. DOI: 10.31891/2219-9365-2025-83-36, IF = –, CS = –, Punkty MNiSW = 5.

Wkład własny: Projekt badania, organizacja i nadzór nad rejestracją pomiarów stabilometrycznych i na bieżni, analiza danych, interpretacja różnic między grupami, współautorstwo manuskryptu.

Udział: 50%

Szczegółowy opis wkładu:

Byłam odpowiedzialna za zaprojektowanie badania porównawczego, oceniającego równowagę posturalną i parametry chodu w grupach młodych użytkowników papierosów tradycyjnych i elektronicznych. Nadzorowałam przebieg sesji pomiarowych z użyciem platformy stabilometrycznej i bieżni, przeprowadziłam analizę statystyczną różnic między grupami, w tym analizę wariancji i regresję. Współtworzyłam wnioski oraz brałam udział w tworzeniu ostatecznej wersji artykułu.

- [A11]. **Chwał Joanna**, Zadoń Hanna, Szaflik Paweł, Dzik Radosław, Filipowska Anna, Doniec Rafał, Kostka Paweł, Michnik Robert, *E-Cigarette Users Exhibit Stronger Cardiovascular Reactivity than Smokers: Evidence from a Multimodal Signal Analysis in Young Adults*, Scientific Reports (w recenzji), DOI: –, IF = 3.9, CS = 6.9, Punkty MNiSW = 140

Wkład własny: Koncepcja badania, opracowanie procedur eksperymentalnych, rejestracja i przetwarzanie sygnałów multimodalnych, analiza zmian układu sercowo-naczyniowego, współautorstwo manuskryptu.

Udział: 50%

Szczegółowy opis wkładu:

Stworzyłam projekt badania, mającego na celu porównanie reaktywności sercowo-naczyniowej u użytkowników e-papierosów i palaczy tradycyjnych na podstawie sygnałów rejestrowanych w warunkach wysiłku i odpoczynku. Byłam odpowiedzialna za rejestrację, segmentację i przetwarzanie sygnałów EKG, PPG i ciśnienia krwi, a także analizę różnic międzygrupowych przy użyciu metod statystycznych i eksploracyjnych. Uczestniczyłam w redakcji manuskryptu i interpretacji wyników w kontekście fizjologii układu krążenia.

Udział ten potwierdza aktywne zaangażowanie doktorantki na wszystkich etapach procesu badawczego, kreacji metodologii, manuskryptów oryginalnych i redakcyjnego, w szczególności

odpowiedzi na recenzje recenzentów, zgodnie z wymaganiami dla rozprawy przygotowanej w formie cyklu publikacji.

2. Poszerzone streszczenie w języku polskim

2.1. Wprowadzenie

Palenie tytoniu od wielu dekad pozostaje jedną z głównych przyczyn przedwczesnych zgonów na świecie. Statystyki wskazują, że nałóg ten odpowiada za śmierć ponad 8 milionów ludzi rocznie [1]. Dym papierosowy zawiera tysiące toksycznych związków, przez co palacze żyją średnio o około 10 lat krócej niż osoby niepalące [2]. Wobec powszechnej świadomości szkodliwości palenia, w ostatnich latach coraz większą popularnością cieszą się elektroniczne papierosy (tzw. e-papierosy) – urządzenia, które dostarczają nikotynę w formie aerozolu bez procesu spalania tytoniu. Reklamowane jako potencjalnie mniej szkodliwa alternatywa dla tradycyjnych papierosów, e-papierosy budzą nadzieje części palaczy na ograniczenie szkód zdrowotnych związanych z nałogiem. Jednocześnie jednak pojawiają się obawy i kontrowersje dotyczące ich bezpieczeństwa i długofalowego wpływu na organizm [3]. Papierosy elektroniczne są urządzeniami podgrzewającymi roztwory zawierające w swoim składzie nikotynę i drogą wziewną dostarczającą ją do organizmu. W języku polskim przyjęło się powszechne używanie terminologii “palenia e-papierosów”, “palacze e-papierosów”; pamiętając o powyższej definicji, na potrzeby płynności językowej w niniejszej rozprawie te terminy mogą być wykorzystywane zamiennie i nie wynikają z braku wiedzy doktorantki.

W Polsce szacuje się, że około jedna czwarta dorosłych wciąż pali tradycyjne papierosy, jednocześnie kilka procent tej grupy Polaków deklaruje regularne używanie e-papierosów [4]. Szczególnie niepokojąca wydaje się popularność tych produktów wśród młodzieży. Z badań *Global Youth Tobacco Survey* wynika, że choć liczba nieletnich palaczy papierosów w Polsce na przestrzeni ostatnich lat zmniejszyła się, to jednocześnie znaczna część młodych ludzi eksperymentowała z e-papierosami [5]. Podobne trendy obserwuje się w innych krajach – na przykład w Stanach Zjednoczonych w 2018 roku odsetek użytkowników e-papierosów wśród uczniów szkół średnich przekraczał 20% [6]. Rosnąca dostępność atrakcyjnych smakowo wkładów nikotynowych oraz agresywny marketing przyczyniły się do faktu, że e-papierosy stały się modnym gadżetem w grupie nastolatków i tzw. młodych dorosłych. Najnowszym zjawiskiem jest gwałtowny wzrost popularności jednorazowych e-papierosów typu „disposable”, co można zaobserwować również na polskim rynku [7].

Szkodliwy wpływ palenia papierosów na zdrowie został jednoznacznie potwierdzony w badaniach epidemiologicznych i doświadczalnych. Tradycyjne papierosy przyczyniają się do rozwoju licznych schorzeń wielonarządowych, a palenie uznaje się za najważniejszą możliwą do uniknięcia przyczynę zgonów przedwczesnych [1, 2]. Palenie tytoniu jest główną przyczyną raka płuc – szacuje się, że 80–90% przypadków tego nowotworu jest związanych z ekspozycją na dym tytoniowy – a ponadto zwiększa ryzyko rozwoju wielu innych nowotworów, w tym jamy ustnej, gardła, przełyku, krtani, trzustki, pęcherza moczowego oraz nerek [2, 16]. Długotrwałe palenie prowadzi także do chorób układu oddechowego, takich jak przewlekłe zapalenie oskrzeli czy rozedma płuc, które składają się na przewlekłą obturacyjną chorobę płuc (POChP). U palaczy częściej występuje również astma oskrzelowa, nasilają się jej objawy, a także obserwuje się wyższą częstość infekcji dróg oddechowych, takich jak zapalenie płuc [2, 9]. Ponadto substancje zawarte w dymie tytoniowym, w tym tlenek węgla i nikotyna, uszkadzają układ krążenia, zwiększając ryzyko miażdżycy naczyń, choroby niedokrwiennej serca, zawału mięśnia sercowego oraz udaru mózgu – i to już przy wypalaniu zaledwie kilku papierosów dziennie [2, 8]. Palenie tytoniu wpływa także na rozwój innych schorzeń: sprzyja powstawaniu choroby wrzodowej żołądka, zwiększa ryzyko

wystąpienia cukrzycy typu 2 oraz przewlekłych chorób zapalnych, takich jak reumatoidalne zapalenie stawów. U kobiet palących częściej dochodzi do powikłań ciąży, w tym do niskiej masy urodzeniowej noworodków, natomiast u mężczyzn częściej obserwuje się zaburzenia erekcji i obniżenie płodności [8, 9]. Na negatywne konsekwencje narażone są nie tylko osoby czynnie palące, ale też ludzie w ich otoczeniu. Biernie palenie, czyli wdychanie dymu papierosowego przez osoby niepalące, również powoduje szereg chorób (w tym choroby serca, nowotwory płuc) i odpowiada za około 1,2 miliona zgonów rocznie na świecie [1]. Jak stwierdzono w raporcie amerykańskiego *Surgeon General*, nie istnieje bezpieczny poziom ekspozycji na dym tytoniowy – nawet krótka ekspozycja może wywoływać uszkodzenia biologiczne prowadzące do chorób [10]. Z tego względu eliminacja dymu tytoniowego z otoczenia pozostaje kluczowym celem zdrowia publicznego.

Fundamentalna różnica między tradycyjnym papierosem a e-papierosem polega na sposobie uwalniania nikotyny. W papierosie tytoniowym spalany jest susz tytoniowy, w wyniku czego powstaje dym zawierający tysiące związków chemicznych. Z kolei w e-papierosie płynny roztwór (tzw. e-liquid, zwykle na bazie glikolu propylenowego i gliceryny) jest podgrzewany elektrycznie, tworząc aerozol inhalowany przez użytkownika. Dym tytoniowy zawiera ponad 7000 różnych substancji chemicznych, z których około 70 ma udowodnione działanie rakotwórcze [11, 12]. Do kluczowych składników należą m.in. nikotyna – alkaloid odpowiedzialny za działanie uzależniające tytoniu oraz pobudzanie układu nerwowego [13]. Sama nikotyna nie jest czynnikiem rakotwórczym, ale przyczynia się do rozwoju chorób sercowo-naczyniowych, między innymi przez przyspieszenie akcji serca i wzrost ciśnienia oraz do powstawania uzależnienia. Kolejnym istotnym składnikiem są substancje smoliste – lepka mieszanina związków powstających podczas spalania, zawierająca między innymi wielopierścieniowe węglowodory aromatyczne (WWA) i nitrozoaminy, spośród których wiele, jak na przykład benzo[a]piren, ma działanie rakotwórcze [12, 14]. W dymie obecny jest także tlenek węgla – toksyczny gaz powstający w wyniku niecałkowitego spalania, który po wchłonięciu do krwi wiąże hemoglobinę, zmniejszając dotlenienie tkanek i przyczyniając się do rozwoju miażdżycy oraz chorób serca oraz spadku kondycji fizycznej. Do tego dochodzą drażniące i toksyczne gazy, takie jak formaldehyd, cyjanowodór, amoniak i tlenki azotu, które uszkodzają błony śluzowe dróg oddechowych i upośledzają mechanizmy obronne płuc [8, 14]. Dym papierosowy zawiera również metale ciężkie, takie jak kadm, ołów, arsen czy chrom, które kumulują się w organizmie i mogą powodować uszkodzenia narządów oraz wykazywać działanie rakotwórcze [12, 14]. Dodatkowo obecne są drobne cząstki stałe – sadza i cząstki popiołu o średnicy poniżej 2.5 μm ($\text{PM}_{2.5}$), które wnikają głęboko do dróg oddechowych, powodując przewlekły stan zapalny i stres oksydacyjny w płucach [15].

W przypadku aerozolu z e-papierosa, jego skład jest znacznie mniej złożony niż dym papierosowy i pozbawiony wielu typowych dla spalania toksyn, jednak również nie jest obojętny dla zdrowia. Zawiera on nikotynę, która w płynach do e-papierosów występuje w różnych stężeniach (np. 3–24 mg/mL, a w jednorazowych e-papierosach nawet powyżej 20 mg/mL). Aerozol nikotynowy z e-papierosa dostarcza tego alkaloidu w ilościach zbliżonych do papierosa tradycyjnego, co wystarcza do wywołania i podtrzymania uzależnienia [16, 17]. Glikol propylenowy i gliceryna roślinna, stanowiące bazę liquidu po podgrzaniu tworzą widoczny aerozol (tzw. „chmurę”). Same w sobie uchodzą za stosunkowo bezpieczne do inhalacji krótkotrwałej, choć w wysokiej temperaturze mogą ulegać częściowemu rozkładowi do drażniących aldehydów. Substancje zapachowo-smakowe dodawane do płynów (np. owocowe, miętowe, deserowe), to związki dopuszczone do spożycia, jednak ich wpływ na drogi oddechowe po podgrzaniu i inhalacji jest w dużej mierze nieznan. W aerozolu wykrywane są także toksyczne związki karbonylowe, takie jak formaldehyd, acetaldehyd i akroleina, których stężenie jest zwykle kilkudziesięciokrotnie niższe niż w dymie z papierosa, choć

ich ilość może wzrastać przy wyższych ustawieniach mocy grzałki i intensywnym użytkowaniu (tzw. „dry puff”) [19-21]. W aerozolu z e-papierosów stwierdzono także śladowe ilości niektórych związków rakotwórczych, takich jak nitrozoaminy nikotynowe czy akrylonitryl, jednak ich poziomy są istotnie niższe niż w dymie papierosowym [19, 22]. Badania wykazały również obecność metali ciężkich i cząstek metalicznych, pochodzących z grzałek i metalowych elementów urządzenia, takich jak ołów, chrom, nikiel, cyna czy mangan – ich stężenia mogą przekraczać poziomy spotykane w powietrzu atmosferycznym [23, 24]. Długotrwała inhalacja tych metali może skutkować uszkodzeniem tkanki płucnej i ich odkładaniem się w narządach. Gęsta chmura aerozolu może znacząco zwiększać stężenie cząstek PM_{2.5} w pomieszczeniach, co budzi pytania o konsekwencje dla osób postronnych [15, 25]. Dodatkowym potencjalnym zagrożeniem są związki, takie jak diacetyl, występujące w niektórych aromatach (np. maślanych czy waniliowych), które mogą powodować poważne uszkodzenia oskrzelików (tzw. popcorn lung) przy przewlekłej inhalacji. Diacetyl był wykrywany w płynach i aerozolu niektórych e-papierosów aromatyzowanych, a choć jego stężenie w e-papierosach jest zwykle niższe niż w dymie papierosowym, jego obecność stanowi potencjalne zagrożenie dla użytkowników [26].

Podsumowując, w porównaniu z dymem tytoniowym, aerozol z e-papierosów zawiera znacznie mniej wielopierścieniowych węglowodorów aromatycznych, tlenku węgla czy nitrozoamin, co oznacza mniejszą ekspozycję na wiele klasycznych czynników rakotwórczych i toksycznych [18, 19, 27]. Jest to istotny argument zwolenników e-papierosów, sugerujących ich obniżoną szkodliwość. Z drugiej strony, e-papierosy nie dostarczają wyłącznie „czystej” nikotyny – użytkownik wdycha mieszaninę związków chemicznych, z których część (choć w niższych dawkach niż w papierosach tradycyjnych), również może wywierać negatywny wpływ na organizm. Ponadto skład aerozolu silnie zależy od konstrukcji urządzenia i sposobu używania – intensywne zaciąganie się przy wysokiej temperaturze grzałki może znacząco zwiększyć ilość szkodliwych produktów termicznego rozkładu liquidu [20, 21]. W następnych sekcjach omówiono, jakie skutki zdrowotne wynikają z narażenia na powyższe substancje podczas aktywnego i biernego palenia oraz użytkowania e-papierosów.

Choć e-papierosy są obecne na rynku od stosunkowo niedawna (masowa sprzedaż ruszyła w drugiej połowie lat 2000), naukowcy zgromadzili już sporo danych na temat ich wpływu na ludzki organizm. Wielu użytkowników e-papierosów zgłasza podrażnienie dróg oddechowych, przewlekły kaszel, nasiloną chrypkę czy świszczący oddech. Badania ankietowe i kliniczne potwierdzają, że osoby używające e-papierosów częściej doświadczają takich objawów w porównaniu z osobami ich nieużywającymi [28, 29]. W 2019 roku uwagę świata zwróciła seria ostrych przypadków uszkodzenia płuc określanych jako EVALI (e-cigarette or vaping product use associated lung injury). W USA odnotowano ponad 2800 hospitalizacji z powodu ciężkiego uszkodzenia płuc, związanego z używaniem e-papierosów, z czego kilkadziesiąt zakończyło się zgonem pacjenta [20]. Dochodzenie wykazało, że większość tych przypadków wiązała się z inhalowaniem nielegalnych płynów zawierających THC i olej octanowy witaminy E, jednak sam fakt wystąpienia EVALI uwiaryścił potencjał e-papierosów do wywoływania ostrych, zagrażających życiu powikłań płucnych. Istnieją również dowody, że aerozol nikotynowy może niekorzystnie wpływać na drogi oddechowe: eksperymenty laboratoryjne wykazały, że narażenie komórek nabłonka płuc na działanie kondensatu z e-papierosów powoduje uszkodzenia DNA oraz upośledza mechanizmy naprawcze materiału genetycznego [30]. Może to sprzyjać inicjacji procesu nowotworowego. Rzeczywiście, w badaniu na modelu zwierzęcym wykazano, że długoterminowe inhalowanie nikotynowego aerozolu przez myszy skutkowało rozwojem zmian nowotworowych w płucach tych zwierząt [31]. Ponadto e-papierosy wydają się wywoływać odpowiedź zapalną w układzie oddechowym – stwierdzono zwiększoną produkcję cytokin prozapalnych w komórkach nabłonka oskrzeli eksponowanych na aerozol,

utrzymującą się nawet po zaprzestaniu ekspozycji [32]. W badaniu kohortowym wśród młodych dorosłych w USA zaobserwowano, że rozpoczęcie używania e-papierosów istotnie zwiększa ryzyko wystąpienia przewlekłych objawów ze strony układu oddechowego (takich jak świszczący oddech, przewlekły kaszel) nawet u osób, które wcześniej nie paliły tradycyjnych papierosów [33]. Dane te każą przypuszczać, że regularne użytkowanie e-papierosów może prowadzić do podobnych problemów pulmonologicznych, jakie znamy u palaczy tytoniu, choć mechanizmy mogą być częściowo odmienne.

Pojawienie się e-papierosów wywołało dyskusję na temat ich roli w zdrowiu publicznym. Zgodnie z koncepcją redukcji szkód (harm reduction), jeśli niektórym palaczom nie udaje się całkowicie zaprzestać używania nikotyny, to przestawienie się z konwencjonalnych papierosów na mniej szkodliwe źródło nikotyny mogłoby przynieść korzyści w postaci zmniejszenia częstości chorób odtytoniowych [34]. E-papierosy dostarczają nikotynę bez większości toksyn, powstających przy spalaniu tytoniu, zatem teoretycznie powinny być mniej niebezpieczne dla zdrowia niż papierosy. Rzeczywiście, badania wykazały, że osoby, które całkowicie zastąpiły papierosy tradycyjne elektronicznymi, mają istotnie niższe stężenia biomarkerów narażenia na substancje smoliste i karcinogeny (np. NNAL – metabolit nitrozoamin tytoniowych) w porównaniu z osobami kontynuującymi palenie zwykłych papierosów [17]. W kontrolowanym badaniu klinicznym z udziałem palaczy afroamerykańskich i latynoskich stwierdzono, że przejście na e-papierosy typu POD (Personalized On Demand) z dopełnianymi wkładami nikotynowymi, przez kilka tygodni skutkowało znacznym obniżeniem poziomu toksycznych związków w organizmie, w porównaniu z grupą nadal palącą tytoń [17]. Ponadto niektóre badania sugerują, że e-papierosy mogą pomagać w rzuceniu nałogu tytoniowego. W Anglii zaobserwowano zależność czasową: wzrost popularności e-papierosów w populacji korelował ze zwiększeniem odsetka podejmowanych prób rzucenia palenia oraz ze wzrostem skuteczności tych prób, co może wskazywać, że część palaczy z powodzeniem zerwała z nałogiem dzięki alternatywie w postaci e-papierosów [35]. Również metaanalizy randomizowanych badań klinicznych dostarczają pewnych dowodów skuteczności – w przeglądzie z 2018 roku wykazano, że używanie e-papierosów z nikotyną wiązało się z wyższym odsetkiem osób abstynentnych od palenia tytoniu po 6–12 miesiącach, w porównaniu z grupami kontrolnymi (np. stosującymi placebo lub inne metody) [36]. Już wcześniejsze analizy (m.in. Cochrane z 2014 r.) odnotowały, że e-papierosy mogą pomóc części palaczy ograniczyć lub czasowo odstawić papierosy, choć podkreślano niewielką liczbę badań i konieczność dalszych dowodów [37].

Z drugiej strony, wielu ekspertów zwraca uwagę na potencjalne zagrożenia związane z promowaniem e-papierosów jako środka pomocniczego w rzucaniu palenia. Przede wszystkim, część badań obserwacyjnych sugeruje, że palacze korzystający równoległe z e-papierosów wcale nie rzucają nałogu częściej niż ci, którzy ich nie używają – a niektóre analizy wręcz wskazywały na niższy wskaźnik rzucenia palenia wśród użytkowników e-papierosów, w porównaniu z nieużywającymi (być może dlatego, że e-papieros pozwala im podtrzymać nałóg nikotynowy) [38]. Podwójne używanie (dual use) może dawać palaczom złudne poczucie ograniczania szkód, podczas gdy nadal są oni narażeni na toksyny z papierosów, jedynie uzupełnione o ekspozycję na aerozol z e-papierosa [39]. Ponadto istnieje obawa, że łatwa dostępność e-papierosów może zniweczyć wieloletnie wysiłki denormalizacji palenia – młode pokolenie, które w większym stopniu sięga po e-papierosy, może w przyszłości częściowo przejść na palenie tradycyjne lub pozostać dożywotnio uzależnione od nikotyny w jakiegokolwiek formie [40]. Ten efekt „furtki” (gateway effect), budzi duży niepokój: według wspomnianej metaanalizy nastolatki używające e-papierosów mają kilka razy większe ryzyko, że w ciągu kolejnych lat sięgną po zwykłe papierosy [40]. Z punktu widzenia zdrowia publicznego zyski netto z e-papierosów mogą więc zostać zrównoważone lub nawet

przeważone przez straty, jeśli dojdzie do masowego uzależnienia od nikotyny nowych grup ludzi, którzy w przeciwnym razie nie zostaliby palaczami.

Renomowane instytucje analizujące problem wydały ostrożne rekomendacje. *Raport Narodowej Akademii Nauk, Inżynierii i Medycyny USA (NASEM)* z 2018 r. stwierdził, że e-papierosy są zdecydowanie mniej narażające na szkodliwe substancje niż papierosy tradycyjne, co sugeruje potencjalnie mniejsze ryzyko dla indywidualnego użytkownika, który przestawi się całkowicie z palenia na używanie elektronicznej alternatywy. Jednocześnie jednak raport podkreślił silne dowody na to, że e-papierosy zwiększają ryzyko rozpoczęcia palenia tytoniu wśród młodzieży i młodych dorosłych, a dowody na ich skuteczność w trwałym rzuceniu palenia są umiarkowane [41]. Innymi słowy, bilans wpływu e-papierosów na zdrowie publiczne zależy od tego, na ile pomogą one obecnym palaczom zerwać z nałogiem, a na ile przyczynią się do uzależnienia nowych użytkowników. Modele symulacyjne dają rozbieżne wyniki – np. jedna z analiz oszacowała, że wprowadzenie e-papierosów może ostatecznie zwiększyć liczbę zgonów z powodu palenia, jeśli weźmie się pod uwagę wpływ na inicjację palenia przez młodych ludzi [42], podczas gdy inne modelowanie wskazuje na możliwość zmniejszenia szkód pod warunkiem minimalizacji rozpowszechnienia e-papierosów wśród niepalących i młodzieży [43].

Biorąc pod uwagę zarówno jednoznaczną szkodliwość palenia tytoniu, jak i niepewność co do długofalowych skutków używania e-papierosów, władze zdrowotne na świecie podejmują różnorodne działania regulacyjne i profilaktyczne. W zakresie tradycyjnych wyrobów tytoniowych, większość krajów wprowadziła sprawdzone interwencje: zakazy palenia w miejscach publicznych, wysokie opodatkowanie papierosów, ograniczenia reklam i sprzedaży czy kampanie edukacyjne. Te klasyczne rozwiązania przynoszą wymierne efekty – przykładowo podwyższenie akcyzy i tym samym ceny papierosów jest uznawane za jedno z najbardziej skutecznych narzędzi redukcji palenia na poziomie populacji [44]. Ważną kwestią okazał się także dostęp młodzieży do papierosów: w wielu krajach podniesiono minimalny wiek legalnej sprzedaży wyrobów tytoniowych do 21 lat. Analizy przeprowadzone w USA przez Instytut Medycyny oszacowały, że takie posunięcie (tzw. *Tobacco 21*) powinno istotnie zmniejszyć liczbę palaczy wśród młodych dorosłych oraz zredukować palenie w całej populacji [45]. Badania sondażowe wskazują, że większość społeczeństwa popiera podniesienie wieku sprzedaży wyrobów tytoniowych, dostrzegając w tym działaniu szansę na ochronę młodzieży przed nałogiem [46].

Regulacje dotyczące e-papierosów w wielu aspektach dopiero kształtują się. W Unii Europejskiej wprowadzono m.in. ograniczenie maksymalnego stężenia nikotyny w płynach do e-papierosów (20 mg/mL) oraz objęto te produkty zakazem sprzedaży nieletnim, analogicznie do papierosów tradycyjnych. W Polsce od 2016 r. obowiązuje zakaz sprzedaży e-papierosów osobom poniżej 18. roku życia, zakaz ich reklamowania oraz zakaz używania w miejscach publicznych objętych wcześniej ustawą antynikotynową (np. w szkołach, urzędach, środkach transportu publicznego). Mimo to egzekwowanie tych przepisów bywa wyzwaniem – badania wskazują, że część użytkowników używa e-papierosów w przestrzeniach publicznych pomimo obowiązujących zakazów, a kontrola tego zjawiska jest utrudniona z uwagi na dyskretniejszy charakter e-papierosów (brak dymu, mniejszy zapach) [47]. W odpowiedzi na rosnącą liczbę młodych użytkowników, niektóre kraje (np. USA, Kanada) wprowadziły dodatkowe restrykcje, takie jak zakaz sprzedaży płynów o atrakcyjnych smakach (uznając, że to głównie smaki przyciągają młodzież).

Wśród ekspertów pojawiają się głosy, że przyszłościowo należałoby rozważyć całkowite wycofanie ze sprzedaży zarówno papierosów tradycyjnych, jak i alternatywnych produktów

nikotynowych. Argumentuje się, że nie ma uzasadnienia dla utrzymywania na rynku skrajnie szkodliwego produktu (papierosów), jeśli istniałyby dostępne formy nikotyny o mniejszym ryzyku – jednak z drugiej strony, dopuszczenie ich bez ograniczeń mogłoby prowadzić do wspomnianych nowych zagrożeń [48]. Z pewnością polityka wobec nikotyny musi balansować między dwoma celami: maksymalną ochroną osób niepalących i młodzieży przed uzależnieniem, a pomocą uzależnionym palaczom w zmniejszeniu szkód lub rzuceniu nałogu. W wielu krajach, w tym w Polsce, wpływy z podatków i akcyzy od sprzedaży wyrobów nikotynowych, w tym papierosów elektronicznych, stanowią istotną część dochodów budżetu państwa. Z tego względu wprowadzenie całkowitego zakazu ich sprzedaży jest obecnie nierealne, a realną możliwością pozostaje jedynie podwyższenie stawek akcyzy lub innych obciążeń podatkowych.

Poza regulacjami prawnymi, kluczowe są działania edukacyjne i medyczne. Personel ochrony zdrowia odgrywa istotną rolę w motywowaniu palaczy do podjęcia prób zerwania z nałogiem oraz w informowaniu o ryzyku związanym z różnymi formami konsumpcji nikotyny. Badania pokazują, że prosta interwencja lekarza – zalecenie rzucenia palenia i poinformowanie o dostępnych formach wsparcia – istotnie zwiększa odsetek osób podejmujących próbę zerwania z nałogiem [49]. Palacze powinni być zachęceni do korzystania ze sprawdzonych metod leczenia uzależnienia od tytoniu: poradnictwa behawioralnego, terapii wspierających (np. infolinie, aplikacje mobilne) oraz farmakoterapii. Dostępne leki, takie jak nikotynowa terapia zastępcza (NRT) w postaci plastrów, gum czy pastylek, czy też leki na receptę (wareniklina, bupropion), podwajają szanse skutecznego rzucenia palenia w porównaniu z próbami podejmowanymi bez wsparcia [9, 50]. W kontekście e-papierosów profesjonaliści medyczni powinni przekazywać zrównoważone informacje: podkreślać, że nie są one przeznaczone dla osób niepalących, a jednocześnie – że całkowite przejście na e-papierosy może być mniej szkodliwe dla palacza, który nie jest w stanie inaczej zerwać z nałogiem. Takie stanowisko zajmuje m.in. Amerykańskie Towarzystwo Kardiologiczne, które w swojej najnowszej deklaracji zauważa, iż choć nie rekomenduje rutynowo e-papierosów jako metody rzucania palenia, to jednak uznaje, że w indywidualnych przypadkach zamiana papierosów na e-papierosy może przynieść korzyści zdrowotne, o ile prowadzi do całkowitego porzucenia palenia tradycyjnego [51]. Towarzystwo to, podobnie jak i WHO, zaleca jednocześnie dalsze prace badawcze nad długoterminowymi skutkami używania e-papierosów oraz wprowadzenie takich regulacji, które zminimalizują ich atrakcyjność dla młodzieży (np. ograniczenie smaków, kampanie informacyjne o ryzyku) [1, 51].

Prezentowana rozprawa doktorska stanowi interdyscyplinarną próbę kompleksowej oceny wpływu palenia tradycyjnych i elektronicznych papierosów na wybrane parametry funkcjonowania układu oddechowego oraz sercowo-naczyniowego. Oparta na cyklu jedenastu publikacji, praca integruje zagadnienia z obszaru toksykologii chemicznej, farmakokinetyki, fizjologii klinicznej, inżynierii biomedycznej, modelowania matematycznego oraz metod sztucznej inteligencji. Tak szerokie ujęcie tematu umożliwiło uzyskanie komplementarnych danych, obejmujących zarówno analizę składu i toksyczności aerozolu emitowanego przez e-papierosy, jak i predykcyjne modelowanie losów nikotyny w organizmie oraz analizę populacyjnych skutków używania wyrobów nikotynowych. Ważnym elementem pracy są również badania eksperymentalne z udziałem ludzi, w których dokonano oceny rzeczywistych zmian w sygnałach biologicznych – takich jak zapis EKG, stabilometria, ciśnienie tętnicze, saturacja krwi czy częstość oddechów – u osób palących papierosy tradycyjne, użytkowników e-papierosów oraz osób niepalących. Dzięki temu możliwa była nie tylko identyfikacja różnic fizjologicznych pomiędzy grupami, ale także odniesienie tych wyników do modeli matematycznych, opisujących mechanizmy działania nikotyny oraz do przewidywań, dotyczących skuteczności interwencji zdrowotnych. Uzyskane wyniki pozwalają na całościową ocenę

oddziaływania różnych form konsumpcji nikotyny na organizm człowieka – zarówno w ujęciu indywidualnym (fizjologicznym), jak i populacyjnym. Praca wnosi istotny wkład w zrozumienie mechanizmów, leżących u podstaw obserwowanych zaburzeń metabolicznych, krążeniowych i neuromotorycznych, a jednocześnie ma wymiar praktyczny – dostarczając danych przydatnych w profilaktyce zdrowotnej, projektowaniu strategii ograniczania szkód oraz formułowaniu zaleceń klinicznych. Podsumowując, niniejsza rozprawa dostarcza dowodów, że e-papierosy – mimo eliminacji niektórych zagrożeń związanych z klasycznym paleniem tytoniu – nie są obojętne dla zdrowia. Wpływają one na szereg istotnych parametrów fizjologicznych, w tym funkcje oddechowe, sercowo-naczyniowe, metaboliczne i neuro-mięśniowe. Otrzymane rezultaty wskazują na potrzebę dalszych, wieloaspektowych badań w tym zakresie oraz na konieczność uważnego monitorowania wpływu nowych alternatywnych produktów nikotynowych na zdrowie publiczne. Prezentowana praca może stanowić istotną podstawę do opracowania przyszłych wytycznych klinicznych oraz polityk regulacyjnych, dotyczących kontroli i prewencji nikotynizmu.

2.2. Cel rozprawy

Zaobserwowana potrzeba pogłębionej oceny skutków zdrowotnych nowych form konsumpcji nikotyny, w tym papierosów elektronicznych, oraz ograniczone dotychczasowe możliwości obiektywnej analizy porównawczej ich wpływu na organizm człowieka z wykorzystaniem danych wielomodalnych, skłoniły autorkę do podjęcia interdyscyplinarnych badań, których cele obejmowały:

- Opracowanie i zastosowanie modeli farmakokinetycznych (PBPK), umożliwiających porównanie dynamiki wchłaniania, dystrybucji i eliminacji nikotyny z e-papierosów i papierosów tradycyjnych.
- Analizę składu chemicznego aerozolu oraz dymu tytoniowego, z uwzględnieniem zawartości metali ciężkich i związków karbonylowych, oraz ocenę ich potencjalnego wpływu toksykologicznego.
- Przeprowadzenie eksperymentalnej rejestracji sygnałów biomedycznych (m.in. sygnałów kardiologicznych, metabolicznych i stabilometrycznych) u młodych dorosłych użytkowników wyrobów nikotynowych i ich porównanie z grupą kontrolną.
- Zastosowanie zaawansowanych metod analizy danych, w tym uczenia maszynowego, w celu identyfikacji cech diagnostycznych i wzorców odpowiedzi fizjologicznej, różnicujących grupy badane.
- Ocenę wpływu przewlekłego stosowania nikotyny w różnych formach na funkcje układu sercowo-naczyniowego, oddechowego, metabolicznego oraz motorycznego – z perspektywy profilaktyki chorób cywilizacyjnych.

Niniejsza rozprawa doktorska stanowi podsumowanie wyników badań eksperymentalnych i modelowych, które łącznie miały na celu kompleksową ocenę ryzyk zdrowotnych, związanych ze stosowaniem produktów nikotynowych, a także opracowanie narzędzi umożliwiających skuteczniejsze monitorowanie ich wpływu z wykorzystaniem danych fizjologicznych, modeli obliczeniowych oraz metod sztucznej inteligencji. Nowatorski charakter rozprawy polega na połączeniu empirycznych badań populacyjnych, obejmujących rejestrację sygnałów biomedycznych, ocenę parametrów metabolicznych i analizę czynników psychospołecznych, z modelami symulacyjnymi (PBPK, Markowa, SIQ+P+E+H+X) oraz algorytmami sztucznej inteligencji. Takie podejście, uwzględniające różnice pomiędzy e-papierosami a papierosami tradycyjnymi w perspektywie chemicznej, fizjologicznej, metabolicznej i neuromotorycznej, nie było dotąd szeroko stosowane. Komponent naukowo-badawczy rozprawy obejmuje opracowanie i walidację modeli farmakokinetycznych nikotyny, zaprojektowanie modeli dynamiki uzależnienia i skuteczności polityk zdrowotnych, przeprowadzenie badań eksperymentalnych z udziałem ludzi, a także implementację metod uczenia maszynowego do identyfikacji cech diagnostycznych.

W pierwszym etapie badań skoncentrowano się na charakterystyce chemicznej aerozolu generowanego przez papierosy elektroniczne. W pracy [A1] przeprowadzono analizę składu pierwiastkowego i wykazano obecność metali ciężkich, takich jak cyna, nikiel czy chrom, pochodzących z elementów grzałki urządzenia. Obserwowane stężenia tych substancji – w zależności od warunków użytkowania – mogły osiągać wartości porównywalne z dymem papierosowym. Uzyskane dane stanowią podstawę do dalszych analiz toksykologicznych i farmakokinetycznych. W kolejnym kroku opracowano i zweryfikowano modele farmakokinetyczne PBPK, opisujące losy nikotyny w organizmie użytkowników papierosów elektronicznych i tradycyjnych. Praca [A2] przedstawiała hybrydowy model PBPK, wzbogacony o komponenty sztucznej inteligencji, natomiast

[A3] rozszerzyła go o zmienne kliniczne, uwzględniające różne stany fizjologiczne, takie jak otyłość, zaburzenia metaboliczne czy choroby układu krążenia. Modele te umożliwiły ilościową ocenę różnic w biodostępności i rozkładzie nikotyny, w zależności od formy dostarczenia i kondycji zdrowotnej użytkownika. Równolegle przeprowadzono badania nad procesem degradacji grzałki e-papierosa w warunkach rzeczywistych. W pracy [A4] opracowano model obliczeniowy, symulujący zmiany materiałowe i termiczne, zachodzące podczas użytkowania urządzenia. Uwzględniono wpływ typu stopu, temperatury oraz przepływu powietrza na emisję cząstek metali, co umożliwiło lepsze zrozumienie mechanizmów generowania toksyn. Na podstawie wyników powyższych analiz opracowano systemy wspomagania decyzji w zakresie rzucania palenia. W pracy [A5] zaprezentowano algorytm rekomendacyjny, bazujący na metodzie Multi-MOORA i wspomagany sztuczną inteligencją, służący do oceny skuteczności, kosztu i akceptowalności różnych strategii (farmakoterapia, NRT, e-papierosy). Następnie, w pracy [A6] zaproponowano dynamiczny model populacyjny SIQ+P+E+H+X, integrujący dane demograficzne i epidemiologiczne w celu przewidywania skutków wprowadzania polityk antynikotynowych (np. podwyżek podatków, kampanii edukacyjnych czy promocji alternatywnych produktów). Modelowanie procesu uzależnienia rozwinięto w pracy [A7], w której zastosowano modele Markowa do opisu przejść między stanami: inicjacji, uzależnienia, leczenia i abstynencji. W oparciu o dane literaturowe oszacowano prawdopodobieństwa skuteczności terapii nikotynozastępczej (NRT) oraz średni czas trwania poszczególnych faz uzależnienia. Kolejny etap badań miał charakter eksperymentalny i dotyczył bezpośrednio użytkowników produktów nikotynowych. W pracy [A8] dokonano analizy czynników psychospołecznych, wpływających na wybór formy konsumpcji nikotyny. Z wykorzystaniem metod statystycznych i uczenia maszynowego, zidentyfikowano predyktory sięgania po e-papierosy i tradycyjny tytoń, takie jak czynniki rodzinne, presja rówieśnicza czy środowisko domowe. W pracy [A9] skupiono się na ocenie konsekwencji metabolicznych użytkowania e-papierosów i palenia. U młodych dorosłych z różnych grup użytkowników przeprowadzono pomiary składu ciała (za pomocą bioimpedancji), ciśnienia tętniczego oraz wskaźników stylu życia. Wykazano obecność niekorzystnego fenotypu metabolicznego, obejmującego m.in. otyłość centralną i podwyższone wartości ciśnienia, mimo pozornie prawidłowego BMI. Funkcje neuromotoryczne zbadano w pracy [A10], wykorzystując stabilometrię i analizę chodu. Zidentyfikowano subtelne zaburzenia równowagi oraz zmienność wzorca lokomocji u użytkowników produktów nikotynowych, w porównaniu z osobami niepalącymi. Ostatnia praca z cyklu [A11] dotyczyła reaktywności sercowo-naczyniowej. W warunkach testów wysiłkowych i ortostatycznych rejestrowano parametry EKG, ciśnienie tętnicze oraz saturację tlenem. Użytkownicy e-papierosów wykazywali silniejszą i szybszą reakcję układu współczulnego, co może świadczyć o większym ryzyku dysregulacji hemodynamicznej.

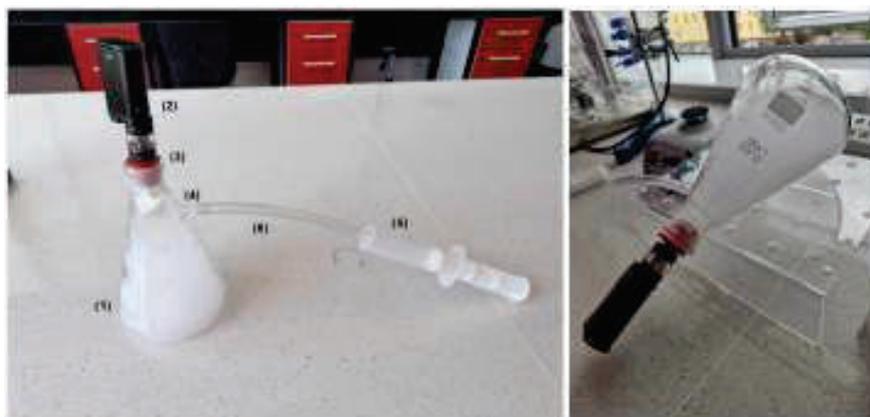
2.3. Hipotezy badawcze

W oparciu o przegląd literatury przedmiotu, wyniki badań wstępnych oraz interdyscyplinarny charakter rozprawy sformułowano następujące hipotezy badawcze:

- I. Aeroszol generowany przez e-papierosy zawiera toksyczne związki chemiczne i metale ciężkie, których stężenie – w zależności od warunków użytkowania – może być porównywalne lub wyższe niż w dymie tytoniowym [A1].
- II. Farmakokinetyka nikotyny różni się istotnie w zależności od formy jej dostarczenia (dym tytoniowy vs. aeroszol e-papierosa), co wpływa na czas narastania stężenia, jego poziom szczytowy oraz potencjał uzależniający [A2].
- III. Czynniki zdrowotne (np. otyłość, choroby układu krążenia, zaburzenia metaboliczne) wpływają na farmakokinetykę nikotyny, modyfikując jej losy w organizmie i potencjalnie nasilając skutki zdrowotne [A3].
- IV. Proces degradacji grzałki e-papierosa pod wpływem temperatury, materiału i przepływu powietrza, istotnie wpływa na emisję metali ciężkich i zwiększa toksyczność aeroszolu [A4].
- V. Wielokryterialna analiza decyzyjna (Multi-MOORA), wspomagana algorytmami sztucznej inteligencji może stanowić skuteczne narzędzie wspierające wybór terapii antynikotynowej [A5].
- VI. Dynamiczne modelowanie populacyjne (SIQ+P+E+H+X) pozwala prognozować wpływ strategii polityki zdrowotnej na rozpowszechnienie palenia i używanie e-papierosów [A6].
- VII. Modelowanie procesu uzależnienia od nikotyny z wykorzystaniem łańcuchów Markowa, umożliwia ilościową ocenę skuteczności terapii nikotynozastępczej (NRT) [A7].
- VIII. Czynniki demograficzne, rodzinne i społeczne istotnie wpływają na ryzyko sięgania po papierosy elektroniczne lub tradycyjne, co można wykazać z użyciem metod statystycznych i uczenia maszynowego [A8].
- IX. Regularne stosowanie e-papierosów wiąże się z niekorzystnymi zmianami metabolicznymi, w tym otyłością centralną, zwiększonym ciśnieniem tętniczym i niekorzystnym składem ciała, obserwowanymi już u młodych dorosłych [A9].
- X. Stosowanie nikotyny w różnych formach wpływa na posturalną kontrolę równowagi i wzorzec chodu, prowadząc do mierzalnych zaburzeń funkcji neuromotorycznych [A10].
- XI. Użytkownicy e-papierosów i palacze tradycyjni wykazują odmienną reaktywność sercowo-naczyniową w odpowiedzi na stres fizjologiczny, w porównaniu z osobami niepalącymi, co może świadczyć o odmiennej aktywacji układu współczulnego [A11].

2.4. Skład pierwiastkowy aerozoli z e-papierosów i papierosów tradycyjnych: wpływ rodzaju płynu i poziomu napełnienia zbiornika [A1]

W przeprowadzonej pracy badawczej podjęto próbę ilościowej oceny składu pierwiastkowego aerozoli generowanych przez e-papierosy w warunkach zmiennego poziomu napełnienia zbiornika (pełny, półpełny, pusty) oraz przy użyciu płynów o różnym pochodzeniu – komercyjnym i domowej produkcji. Celem badań było określenie wpływu tych czynników na obecność metali ciężkich i innych pierwiastków w aerozolu, a także porównanie ich zawartości z aerozolami pochodzącymi z tradycyjnych papierosów. Dla odtworzenia warunków rzeczywistego użytkowania zbudowano stanowisko symulujące inhalację (Rys. 1 i 2). W badaniach porównano także wyniki dla dymu z papierosów tradycyjnych. Cząsteczki aerozolu i dymu zbierano na membranach nitrocelulozowych ($0,45\ \mu\text{m}$) osadzonych w komorze kondensacyjnej, pomocniczo analizowano również bawełnę z wnętrza grzałki. Następnie poddawano je analizie składu pierwiastkowego za pomocą skaningowej mikroskopii elektronowej (SEM) z detektorem energii dyspersyjnej (EDS). Metoda EDS umożliwia jakościowe i półilościowe wykrycie obecnych pierwiastków, lecz nie dostarcza informacji o ich formie chemicznej (np. tlenki, chlorki, kompleksy) ani specjacji, co stanowi istotne ograniczenie w kontekście pełnej oceny toksykologicznej. Ponadto, technika nie umożliwia analizy składników lotnych ani gazowych, które mogą być równie istotne z punktu widzenia ryzyka zdrowotnego.



Rys. 1 Stanowisko do badania aerozoli z e-papierosów [A1]



Rys. 2 Stanowisko do badania dymu z papierosów tradycyjnych [A1]

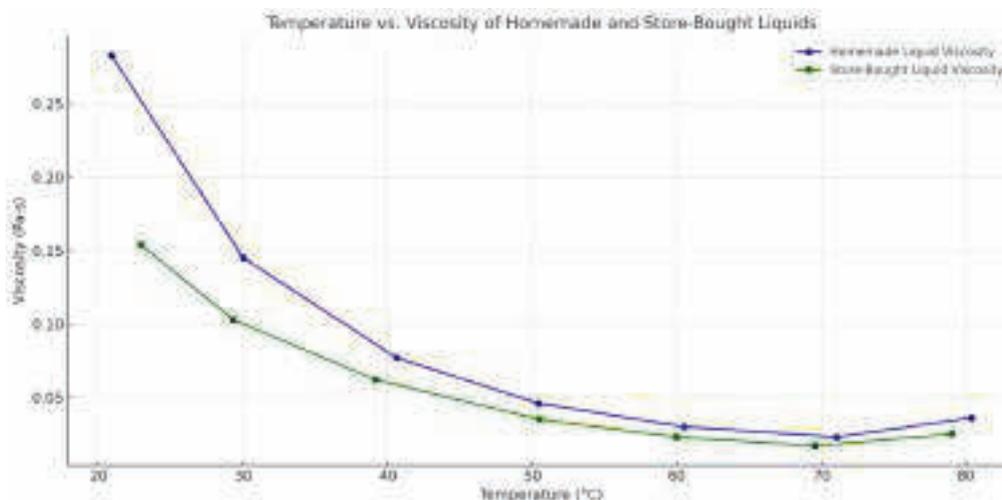
W badaniu zidentyfikowano obecność wielu pierwiastków nieorganicznych, do najistotniejszych z toksykologicznego punktu widzenia należały chrom (Cr), aluminium (Al), żelazo (Fe), nikiel (Ni), miedź (Cu), sód (Na), siarka (S) i chlor (Cl). Ich zawartość istotnie różniła się w zależności od rodzaju użytego płynu oraz poziomu napełnienia zbiornika (Tabela 1). Najwyższe względne stężenie chromu odnotowano dla konfiguracji „półpełny zbiornik + płyn domowy” (6,00 wt%), natomiast stężenie aluminium sięgało 1,40 wt%, a żelaza – 0,72 wt%. W konfiguracji z komercyjnym płynem o tym samym wypełnieniu zbiornika, wartości te były wyraźnie niższe: Cr – 4,79 wt%, Al – 0,21 wt%, Fe – 0,00 wt%. Dym z papierosów tradycyjnych zawierał śladowe ilości chromu (0,33 wt%) i aluminium (0,08 wt%), a dominowały w nim minerały pochodzenia roślinnego (np. wapń, sód, siarka). Profil pierwiastków różnił się istotnie – w aerozolu tytoniowym przeważały składniki mineralne obecne naturalnie w tytoniu i bibułce, podczas gdy w aerozolu z e-papierosów dominowały metale techniczne, pochodzące z degradacji materiałów konstrukcyjnych urządzenia.

Tabela 1. Średnie stężenia pierwiastków w aerozolach uzyskanych podczas używania e-papierosa (10 zaciągnięć) lub spalania jednego papierosa [A1]

E	Płyn domowy, pełny zbiornik		Płyn domowy, pół zbiornika		Płyn domowy, pusty zbiornik		Płyn komercyjny, pełny zbiornik		Płyn komercyjny, pół zbiornika		Płyn komercyjny, pusty zbiornik		Papieros tradycyjny	
	wt%	SD	wt%	SD	wt%	SD	wt%	SD	wt%	SD	wt%	SD	wt%	SD
O	54,77	0,62	50,26	0,80	52,00	0,94	53,10	0,71	52,37	0,70	51,94	0,64	48,86	0,35
C	40,40	0,64	40,58	0,88	41,31	1,00	41,12	0,73	41,71	0,75	41,15	0,68	49,89	0,36
Cr	3,84	0,95	6,00	0,97	5,33	0,83	4,81	0,90	4,79	0,86	5,48	0,79	0,33	0,03
Na	0,33	0,03	0,32	0,03	0,35	0,05	0,36	0,04	0,36	0,04	0,38	0,04	0,24	0,03
Al	0,36	0,03	1,40	0,06	0,34	0,04	0,26	0,03	0,21	0,03	0,22	0,03	0,08	0,01
S	0,12	0,02	0,20	0,03	0,10	0,02	0,15	0,02	0,22	0,03	0,22	0,03	0,12	0,02
Cl	0,09	0,02	0,17	0,04	0,12	0,02	0,08	0,02	0,08	0,02	0,14	0,03	0,08	0,02
Si	0,04	0,01	0,12	0,02	0,25	0,03	0,02	0,00	0,07	0,02	0,22	0,02	0,15	0,02
Mg	0,00	0,00	0,04	0,01	0,20	0,04	0,01	0,00	0,02	0,00	0,16	0,02	0,11	0,01
Fe	0,00	0,00	0,72	0,15	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
Cu	0,07	0,02	0,06	0,02	0,00	0,00	0,04	0,01	0,04	0,01	0,04	0,00	0,07	0,02
Ca	0,00	0,00	0,00	0,00	0,00	0,00	0,05	0,02	0,02	0,00	0,05	0,01	0,05	0,01
Br	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,04	0,01

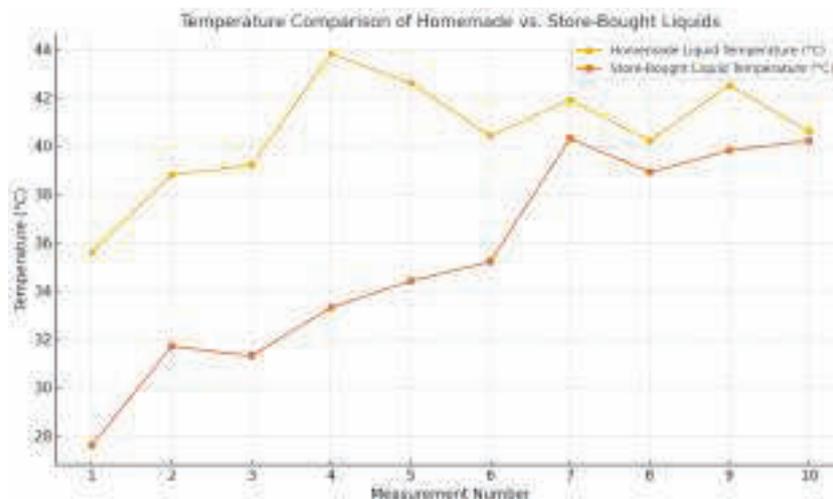
Analiza lepkości (Rys. 3) wykazała wyraźne różnice w zachowaniu płynów domowych i komercyjnych. Początkowo płyny domowe cechowały się wyższą lepkością dynamiczną (~0,2848 Pa·s przy 20,9 °C), która uległa gwałtownemu obniżeniu wraz ze wzrostem temperatury, osiągając ~0,0295 Pa·s przy 60,5 °C. W temperaturze 80 °C odnotowano ponowny, niewielki wzrost lepkości (~0,036 Pa·s), sugerujący początek degradacji termicznej. Płyny komercyjne wykazywały niższą początkową lepkość (~0,15 Pa·s przy 23,5 °C) oraz bardziej łagodny spadek lepkości wraz z temperaturą, osiągając ~0,025 Pa·s przy 80 °C. Wyniki te wskazują na wyższą stabilność termiczną płynów komercyjnych, które zachowują bardziej przewidywalne właściwości fizyczne w szerszym zakresie temperatur. Potwierdzają to również pomiary naprężeń stycznych – dla płynów domowych wartości te osiągały ok. 56–57 Pa przy szybkości ścinania rzędu 200 s⁻¹, natomiast dla płynów komercyjnych – ok. 30–34 Pa. Różnice te mają bezpośredni wpływ na efektywność waporyzacji oraz kontrolę temperatury podczas pracy urządzenia. Obniżona stabilność cieplna płynów domowych

może sprzyjać zjawisku *dry puff*, czyli przegrzaniu spirali grzewczej przy niskim poziomie płynu, co prowadzi do erozji elementów metalowych i zwiększonego udziału metali ciężkich w aerozolu.



Rys. 3 Zmiany lepkości dynamicznej płynów domowych i komercyjnych w funkcji temperatury [A1].

W celu uzupełnienia analizy właściwości fizycznych płynów przeprowadzono również pomiar temperatury (Rys. 4) wewnątrz zbiornika podczas symulowanego użytkowania urządzenia. Badania wykazały, że płyny domowe osiągały wyższe temperatury początkowe i nagrzewały się szybciej niż płyny komercyjne, co można przypisać ich uproszczonemu składowi chemicznemu i braku dodatków stabilizujących. Pomimo tych różnic, w warunkach ustalonych testów temperatura obu rodzajów płynów stabilizowała się na poziomie około 40°C. Uzyskane wyniki wskazują na istotny wpływ składu płynu na charakterystykę cieplną pracy urządzenia, szczególnie w początkowej fazie, co może mieć znaczenie dla procesów emisji metali z elementów grzewczych.



Rys. 4 Przebieg zmian temperatury wewnątrz zbiornika e-papierosa podczas symulowanego użytkowania, dla płynów domowych i komercyjnych [A1].

Otrzymane dane jednoznacznie wskazują, że nie tylko skład płynu, ale również sposób użytkowania urządzenia mają kluczowy wpływ na skład inhalowanego aerozolu. W wielu przypadkach stężenia metali ciężkich zbliżyły się do granicznych poziomów określonych przez

wytyczne WHO lub nawet je przekraczały, zwłaszcza w warunkach „pustego” zbiornika i wysokiej temperatury pracy. Należy jednak podkreślić, że metoda EDS ma charakter półilościowy i nie pozwala na jednoznaczne określenie stężeń w odniesieniu do norm toksykologicznych. Rzeczywiste ryzyko zdrowotne zależy również od biodostępności pierwiastków, częstotliwości użycia urządzenia oraz współwystępowania innych zanieczyszczeń, co wymaga dalszych, pogłębionych analiz. Praca stanowi istotny wkład w charakterystykę toksykologiczną e-papierosów i podkreśla konieczność standaryzacji zarówno składu płynów, jak i parametrów technicznych urządzeń. Zidentyfikowane ryzyka powinny zostać uwzględnione przy tworzeniu wytycznych bezpieczeństwa użytkowania e-papierosów, a także regulacji prawnych dotyczących ich produkcji i dystrybucji.

2.5. Porównanie farmakokinetyki nikotyny z e-papierosów i tradycyjnych papierosów z wykorzystaniem modelowania PBPK oraz uczenia maszynowego [A2]

W ramach prowadzonych badań opracowano model farmakokinetyczny typu PBPK (Physiologically Based Pharmacokinetic), wspomagany algorytmami uczenia maszynowego, w celu porównania dynamiki wchłaniania i rozprzestrzeniania nikotyny w organizmie po zastosowaniu e-papierosów i tradycyjnych papierosów. Celem pracy było zbadanie różnic w sposobie dostarczania nikotyny oraz ocena ich wpływu na poziom narażenia organizmu – ze szczególnym uwzględnieniem mózgu i synaps – a także wyznaczenie czynników fizjologicznych istotnie wpływających na tempo i zakres akumulacji nikotyny. Zaprojektowany model PBPK obejmował pięć kluczowych kompartmentów: płuca, krew, wątrobę, mózg oraz synapsy. Dla każdego z nich zdefiniowano objętości, przepływy krwi oraz stałe dyfuzji, metabolizmu i eliminacji. Równania oparto na zasadzie bilansu masy, prawie Ficka oraz kinetyce pierwszego rzędu dla metabolizmu i eliminacji, co umożliwiło dynamiczną symulację stężeń nikotyny w okresie 24 godzin, z uwzględnieniem rzeczywistego schematu używania produktów nikotynowych (10 pociągnięć na sesję, 20 sesji dziennie dla e-papierosów; odpowiednio 1,5 mg vs. 3 mg nikotyny na sesję). Równania farmakokinetyczne PBPK:

1. Koncentracja nikotyny w płucach:

$$\frac{dC_{lung}}{dt} = \frac{dose}{V_p} - \frac{Q_p}{V_p} (C_{lung} - C_{blood})$$

2. Koncentracja nikotyny we krwi:

$$\frac{dC_{blood}}{dt} = \frac{Q_p}{V_b} (C_{lung} - C_{blood}) - \frac{Q_h}{V_b} (C_{blood} - C_{liver}) - k_{distrib} C_{blood} - k_{penetr} C_{blood} + k_{elim} C_{brain}$$

3. Koncentracja nikotyny w wątrobie:

$$\frac{dC_{liver}}{dt} = \frac{Q_h}{V_l} (C_{blood} - C_{liver}) - k_{metab} C_{liver}$$

4. Koncentracja nikotyny w mózgu:

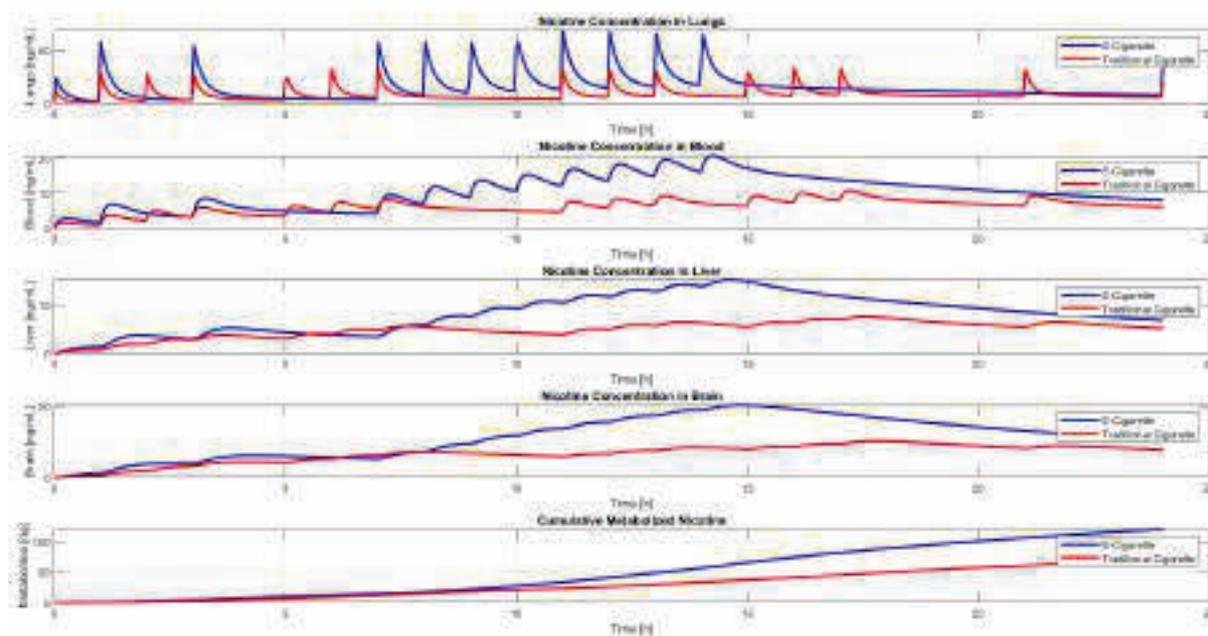
$$\frac{dC_{brain}}{dt} = k_{penetr} C_{blood} - k_{elim} C_{brain} - k_{synapse} C_{brain} + k_{synapse} C_{synapse}$$

5. Koncentracja nikotyny w synapsach:

$$\frac{dC_{synapse}}{dt} = k_{synapse} C_{brain} - k_{synapse} C_{synapse}$$

gdzie: C_{lung} – stężenie nikotyny w płucach, C_{blood} – stężenie nikotyny we krwi, C_{liver} – stężenie nikotyny w wątrobie, C_{brain} – stężenie nikotyny w mózgu, $C_{synapse}$ – stężenie nikotyny w synapsach, Q_p – przepływ krwi przez płuca, Q_h – przepływ krwi przez wątrobę, V_p , V_b , V_l – objętości kompartmentów: płuca, krew, wątroba, $k_{distrib}$ – współczynnik dystrybucji nikotyny z krwi do innych tkanek, k_{penetr} – współczynnik przenikania nikotyny z krwi do mózgu, k_{elim} – szybkość eliminacji nikotyny z mózgu, k_{metab} – stała metabolizmu nikotyny w wątrobie, $k_{synapse}$ – współczynnik przejścia nikotyny między mózgiem a synapsami, dose – dawka nikotyny dostarczona w jednej sesji.

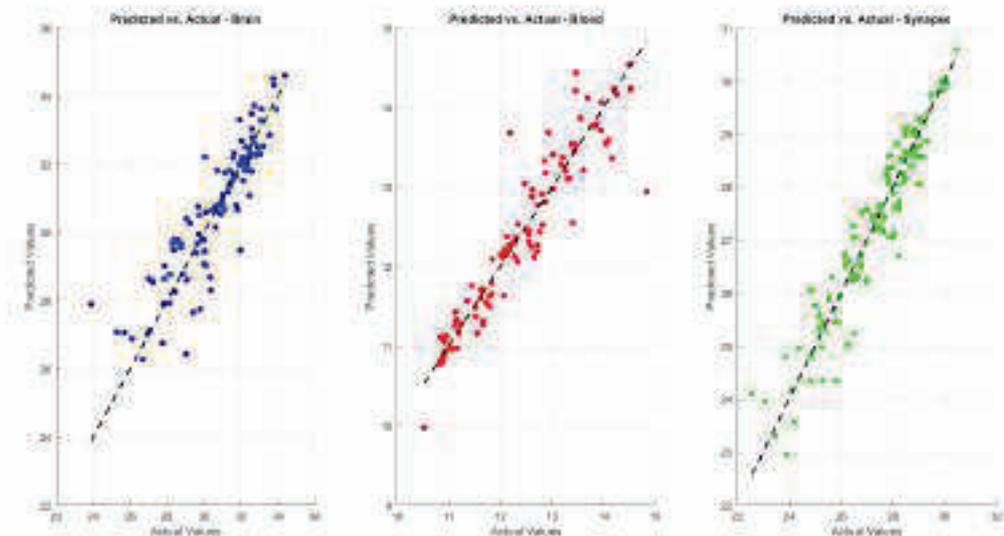
Modelowanie wykazało wyraźne różnice w profilu farmakokinetycznym między badanymi produktami (Rys. 5). Tradycyjne papierosy generowały szybkie i ostre piki stężenia nikotyny w mózgu i krwi (Cmax: 15–20 ng/mL; Tmax: 5–15 min), typowe dla silnego efektu uzależniającego. Dla e-papierosów obserwowano bardziej płaskie, ale trwalsze profile stężenia (Cmax: 6–10 ng/mL; Tmax: 2–5 min), co może świadczyć o innym mechanizmie rozwoju zależności. W synapsach wartości Cmax wynosiły odpowiednio: 240 nM dla papierosów i 180 nM dla e-papierosów (Tmax: 60–120 s i 60–150 s).



Rys. 5 Zmiany stężenia nikotyny w wybranych kompartmentach (krew, mózg, synapsy) w ciągu 24 godzin, w zależności od źródła ekspozycji: e-papierosy (linia niebieska) i tradycyjne papierosy (linia czerwona) [A2]

Wyniki PBPK zostały rozszerzone o analizę zmienności osobniczej przy użyciu algorytmu XGBoost, który wytrenowano na 1000 syntetycznych profili fizjologicznych. Modele osiągnęły ekstremalnie wysoką dokładność predykcji, z wartością współczynnika determinacji $R^2 > 0,9998$ we wszystkich kompartmentach. Największy wpływ na dystrybucję nikotyny wykazała przepuszczalność bariery krew–mózg (k_{penet}), ze współczynnikiem korelacji $+0,901$ dla mózgu i $+0,916$ dla synaps, natomiast korelacja z poziomem nikotyny we krwi była ujemna ($-0,940$). Pozostałe znaczące cechy to tempo metabolizmu wątrobowego (k_{metab} , korelacja ujemna), przepływ płucny oraz masa ciała i historia palenia. W ramach walidacji modelu wykorzystano dane z literatury dotyczące rzeczywistych wartości Cmax i Tmax po inhalacji nikotyny. Modele dobrze odwzorowywały rzeczywiste profile farmakokinetyczne (Rys. 6), osiągając R^2 : 0,788 (mózg), 0,867 (krew) i 0,899 (synapsy). Szacunkowa wartość stężenia nikotyny u przykładowej osoby (na podstawie indywidualnych parametrów fizjologicznych) wynosiła: 107,62 ng/mL w mózgu, 64,45 ng/mL we krwi i 137,31 ng/mL w synapsach. Istotnym aspektem było także wskazanie ograniczeń przyjętych założeń. Modele PBPK zakładają uśrednione wartości parametrów fizjologicznych i standardowe wzorce użytkowania, podczas gdy w rzeczywistości istnieje znaczna zmienność behawioralna (np. głębokość zaciągnięcia, czas inhalacji, moc urządzenia). Ponadto model nie uwzględnia efektu innych składników dymu tytoniowego lub aerozolu (np. aldehydów, aromatów), które mogą modulować

metabolizm nikotyny. Istnieje też ograniczenie związane z założeniami dotyczącymi miejsc wchłaniania: dla papierosów dominuje dolny układ oddechowy (pęcherzyki płucne), podczas gdy dla e-papierosów – górne drogi oddechowe i jama ustna, co może wpływać na kinetykę pierwszego przejścia.



Rys. 6 Porównanie stężeń nikotyny przewidywanych przez model PBPK z danymi rzeczywistymi (literaturowymi) dla trzech kompartmentów: mózgu, krwi oraz synaps [A2]

Praca stanowi istotny wkład w zrozumienie różnic farmakokinetycznych między alternatywnymi metodami dostarczania nikotyny. Wyniki te, generują znaczące implikacje dla polityki zdrowotnej i praktyki klinicznej. Pokazano, że mimo braku produktów spalania, e-papierosy mogą prowadzić do długotrwałej ekspozycji na nikotynę, a więc potencjalnie również do rozwoju uzależnienia. Dzięki integracji modelowania PBPK i uczenia maszynowego możliwe jest nie tylko lepsze przewidywanie ekspozycji, ale również tworzenie spersonalizowanych modeli ryzyka, co stanowi istotny krok w kierunku precyzyjnej prewencji uzależnień i polityki zdrowotnej.

2.6. Fizjologicznie uwarunkowane modelowanie farmakokinetyczne nikotyny [A3]

Kolejny artykuł stanowi rozwinięcie pracy konferencyjnej, pt. “Comparative Pharmacokinetics of Nicotine from E-Cigarettes and Traditional Cigarettes: A PBPK Modeling and Machine Learning Approach”. W ramach przeprowadzonego badania podjęto próbę modelowania dynamiki rozprzestrzeniania się nikotyny w organizmie z zastosowaniem modelu farmakokinetycznego PBPK (Physiologically Based Pharmacokinetic Modeling), uwzględniającego procesy fizjologiczne. Celem pracy była ocena różnic w profilu farmakokinetycznym nikotyny dostarczanej za pomocą e-papierosów i papierosów tradycyjnych, z uwzględnieniem różnych stanów zdrowotnych użytkowników – w tym chorób układu krążenia, astmy oraz przewlekłej obturacyjnej choroby płuc (POChP). Badanie miało charakter modelowy, lecz bazowało na rzeczywistych danych eksperymentalnych i literaturowych, dotyczących fizjologii oraz dystrybucji nikotyny.

Zaprojektowany model PBPK obejmował dziewięć kompartmentów, odpowiadających głównym tkankom zaangażowanym w metabolizm i dystrybucję nikotyny: płuca, krew tętniczą i żylną, wątrobę, mózg, mięśnie, nerki, tkankę tłuszczową oraz inne tkanki. Model oparto na równaniach różniczkowych pierwszego rzędu i przyjęto parametry fizjologiczne charakterystyczne dla osób zdrowych oraz chorych. Transport między kompartmentami był opisywany na podstawie kinetyki ograniczonej perfuzją, zgodnie z klasycznym podejściem dla związków lipofilnych:

$$\frac{dC_{lung}}{dt} = \frac{Dose(t)}{V_p} - \frac{Q_p}{V_p} (C_{lung} - C_{blood})$$

$$\frac{dC_{blood}}{dt} = \frac{Q_p}{V_b} (C_{lung} - C_{blood}) - \frac{Q_h}{V_b} (C_{blood} - C_{liver}) - k_{distrib} C_{blood} - k_{penetr} C_{blood} + k_{elim} C_{brain} -$$

$$- k_{fat} C_{blood} + k_{release} C_{fat} - k_{eliminb} C_{blood}$$

Metabolizm nikotyny zachodził głównie w wątrobie, zgodnie z enzymatycznym mechanizmem degradacji opisywanym równaniami kinetyki Michaelisa-Mentena:

$$\frac{dC_{liver}}{dt} = \frac{Q_h}{V_l} (C_{blood} - C_{liver}) - \frac{k_{metabmax} C_{liver}}{K_m + C_{liver}} + k_{distrib} C_{blood}$$

$$\frac{dC_{metabolites}}{dt} = \frac{k_{metabmax} C_{liver}}{K_m + C_{liver}}$$

Nikotyna przenikała przez barierę krew–mózg, gdzie akumulowała się i ulegała powolnej eliminacji:

$$\frac{dC_{brain}}{dt} = k_{penetr} C_{blood} - k_{elim} C_{brain}$$

$$\frac{dC_{fat}}{dt} = k_{fat} C_{blood} - k_{release} C_{fat}$$

gdzie: C_{lung} – stężenie nikotyny w płucach, C_{blood} – stężenie nikotyny we krwi (tętniczej/żylny), C_{liver} – stężenie nikotyny w wątrobie, C_{brain} – stężenie nikotyny w mózgu, C_{fat} – stężenie nikotyny

w tkance tłuszczowej, $C_{metabolites}$ – stężenie metabolitów nikotyny, Q_p – przepływ krwi przez płuca, Q_h – przepływ krwi przez wątrobę, V_p , V_b , V_l – objętości kompartmentów: płuca, krew, wątroba, $k_{distrib}$ – współczynnik dystrybucji nikotyny z krwi do tkanek, k_{penetr} – współczynnik przenikania nikotyny z krwi do mózgu, k_{elim} – szybkość eliminacji nikotyny z mózgu, $k_{eliminb}$ – szybkość eliminacji nikotyny z krwi obwodowej, k_{fat} – współczynnik odkładania nikotyny w tkance tłuszczowej, $k_{release}$ – współczynnik uwalniania nikotyny z tkanki tłuszczowej, $k_{metabmax}$ – maksymalna szybkość metabolizmu nikotyny w wątrobie (parametr Michaelisa–Mentena), K_m – stała Michaelisa–Mentena, Dose(t) – dawka nikotyny w funkcji czasu, specyficzna dla typu produktu (papieros, e-papieros).

Wprowadzono również zmienne specyficzne dla rodzaju produktu nikotynowego, m.in. drogę podania, tempo wchłaniania, objętość zaciągnięcia oraz biodostępność.

Wyniki modelowania wykazały istotne różnice w dynamice stężenia nikotyny w zależności od stanu zdrowia (Tabela 2). W warunkach prawidłowych stężenie nikotyny w osoczu w stanie ustalonym (Css) dla papierosów tradycyjnych wynosiło 7,01 ng/mL, a dla e-papierosów 4,08 ng/mL. W przypadku pacjentów z POChP i astmą obserwowano zmniejszone tempo eliminacji, co prowadziło do podwyższonych stężeń Css (np. 5,05 ng/mL dla e-papierosów) oraz wydłużonego t1/2. U osób z chorobami układu sercowo-naczyniowego zaobserwowano zwiększone stężenie Css w mózgu dla e-papierosów (16,32 ng/mL), co może świadczyć o nasilonym narażeniu OUN i wyższym ryzyku uzależnienia.

Tabela 2. Podsumowanie farmakokinetyki nikotyny w różnych stanach zdrowia [A3]

Stan zdrowia	Css w mózgu (ng/mL) (E-papieros)	Css w mózgu (ng/mL) (papieros)	Css we krwi (ng/mL) (E-papieros)	Css we krwi (ng/mL) (papieros)	t1/2 (h) (E-papieros)	t1/2 (h) (papieros)
Osoba zdrowa	11,00	18,64	4,08	7,01	0,96	0,96
Choroba wątroby	24,74	3,40	9,18	1,41	0,98	0,98
Choroba sercowo-naczyniowa	16,32	6,89	6,10	2,74	1,12	1,12
Otyłość	21,41	15,38	7,64	5,79	1,12	1,12
Choroba płuc	13,06	2,91	5,05	1,02	1,03	1,03
Choroby neurologiczne	4,69	9,52	0,98	2,02	1,33	1,34

Model został zweryfikowany na podstawie danych literaturowych i wykazał dobrą zgodność z rzeczywistymi wartościami stężeń nikotyny w różnych kompartmentach, zarówno dla e-papierosów, jak i papierosów tradycyjnych. Zgodność ta była szczególnie widoczna w porównaniach profili czasowych stężenia w osoczu i mózgu, uwzględniających różne stany zdrowotne. W przeprowadzonej analizie wrażliwości wykazano, że kluczowymi zmiennymi wpływającymi na profil farmakokinetyczny były: przepływ wątrobowy, tempo metabolizmu wątrobowego, przenikalność bariery krew–mózg oraz zdolność magazynowania i uwalniania nikotyny w tkance tłuszczowej. Warto

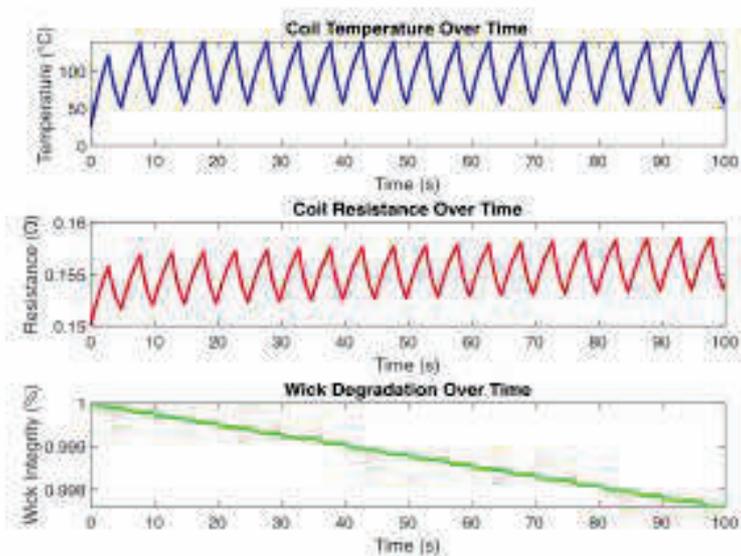
podkreślić, że model oparto na populacyjnych parametrach fizjologicznych i nie uwzględniono indywidualnych różnic genetycznych w metabolizmie. Pominięto także potencjalne interakcje z innymi składnikami aerozolu (takimi jak aldehydy czy substancje aromatyczne), które mogą wpływać na biodostępność i metabolizm nikotyny. Dodatkowym ograniczeniem była standaryzacja schematu użytkowania, który może nie odzwierciedlać rzeczywistego narażenia wśród intensywnych lub okazjonalnych użytkowników.

Wnioski z pracy wskazują na złożony wpływ stanu zdrowia na farmakokinetykę nikotyny oraz na potrzebę indywidualizacji podejścia do oceny ryzyka związanego z jej stosowaniem. Uzyskane wyniki mogą być szczególnie użyteczne przy projektowaniu strategii ograniczania szkód oraz dla klinicystów, oceniających bezpieczeństwo stosowania e-papierosów u pacjentów z chorobami przewlekłymi. Praca ukazuje potencjał modelowania PBPK jako narzędzia, wspomagającego ocenę produktów nikotynowych w kontekście zdrowia publicznego i decyzji regulacyjnych.

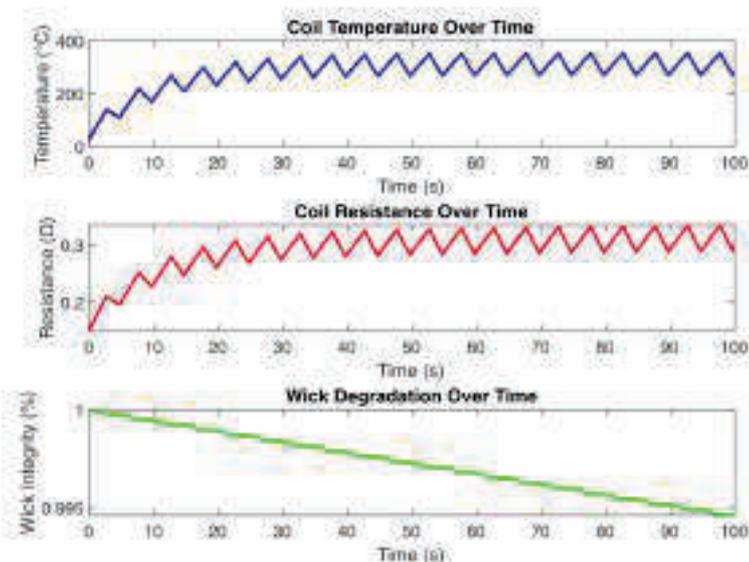
2.7. Model obliczeniowy degradacji grzałki w e-papierosach: symulacja procesów termicznych i materiałowych oraz ich wpływ na zdrowie [A4]

W prezentowanej pracy zaproponowano i zaimplementowano numeryczny model degradacji grzałki e-papierosa w warunkach rzeczywistego użytkowania. Celem badania było określenie, w jaki sposób materiał grzałki (stop NiCr, Kanthal, stal nierdzewna, tytan), warunki przepływu powietrza i moc zasilania wpływają na charakterystyki termiczne, zmiany rezystancji oraz degradację waty. Analizę przeprowadzono w kontekście potencjalnych zagrożeń zdrowotnych wynikających z emisji produktów rozkładu termicznego metali i nośnika cieczy. Model uwzględniał realistyczne cykle użytkowe: 3 sekundy nagrzewania oraz 2 sekundy chłodzenia, z rejestracją dynamicznych zmian temperatury, rezystancji oraz integralności knota. Uwzględniono zjawiska grzania oporowego (Joule'a), chłodzenia konwekcyjnego oraz dryfu rezystancji pod wpływem utleniania materiału. Zastosowano materiałowo specyficzne właściwości fizykochemiczne: opór właściwy, pojemność cieplną, przewodność cieplną oraz charakterystyki kinetyki utleniania dla każdego rodzaju grzałki.

Zestawienie wyników wykazało istotne różnice pomiędzy analizowanymi materiałami. Najlepszą stabilność termiczną oraz minimalny dryf rezystancji wykazywał stop Nichrome (NiCr), osiągając temperatury końcowe rzędu 64,2°C oraz rezystancję końcową 0,1541Ω (Rys. 7). Wata zachowywała w tych warunkach 99,76% integralności strukturalnej. Podobne parametry uzyskano dla Kanthalu (69,1°C, 0,1523Ω, 99,76% integralności). Stal nierdzewna osiągała 66,6°C i 0,1565Ω, również przy zachowanej integralności. Najgorsze parametry uzyskano dla tytanu – w warunkach niskiego przepływu powietrza temperatura końcowa wynosiła aż 277,0°C, a rezystancja wzrastała do 0,2925Ω (Rys. 8), co wskazuje na intensywną degradację związaną z utlenianiem. W tych warunkach integracja waty spadła do 99,46%, co w kontekście długoterminowego użytkowania może skutkować osłabieniem strukturalnym i zwiększoną emisją cząstek. Analiza porównawcza materiałów wykazała, że przy wysokim przepływie powietrza integralność utrzymywała się na poziomie powyżej 99,7% niezależnie od materiału, co wskazuje na krytyczną rolę chłodzenia konwekcyjnego w redukcji degradacji termicznej. Symulacje potwierdziły, że niski przepływ powietrza skutkuje akumulacją ciepła w grzałce i zwiększoną kinetyką utleniania, szczególnie dla metali o niższej stabilności chemicznej, jak tytan.



Rys. 7 Charakterystyki pracy grzałki z nichromu (NiCr) przy wysokim przepływie powietrza: temperatura (górn), rezystancja (środek) i integralność waty (dół) w funkcji czasu [A4]



Rys. 8. Charakterystyki pracy grzałki tytanowej (Ti) przy niskim przepływie powietrza: temperatura (górn), rezystancja (środek) i integralność waty (dół) w funkcji czasu [A4]

Praca podkreśla istotne znaczenie wyboru materiału grzałki oraz parametrów użytkowych (przepływ powietrza, cykl zasilania) w kontekście bezpieczeństwa użytkownika. Degradacja grzałki może prowadzić do emisji cząstek metali oraz produktów rozkładu materiałów organicznych (np. bawełnianej waty), co wiąże się z ryzykiem inhalacyjnym. Model stanowi użyteczne narzędzie predykcyjne w projektowaniu bezpieczniejszych e-papierosów. Warto jednak zaznaczyć ograniczenia przyjętego podejścia. Model nie uwzględniał chemicznego składu e-liquidu, oddziaływań między cieczą a materiałem grzałki, ani potencjalnego nagromadzenia zanieczyszczeń na powierzchni elementów. Ponadto symulacje dotyczyły izolowanych cykli pracy, bez modelowania długotrwałego

starzenia się urządzenia w skali tygodni czy miesięcy. Otrzymane rezultaty mają istotne znaczenie dla inżynierii urządzeń nikotynowych oraz polityki regulacyjnej. Pokazano, że poprzez właściwy dobór materiałów (np. stopów o niskiej podatności na utlenianie) oraz parametryzację chłodzenia, możliwe jest znaczne ograniczenie emisji toksycznych związków związanych z degradacją termiczną, co przekłada się na realne korzyści zdrowotne dla użytkowników.

2.8. Optymalizacja alternatyw rzucania palenia z wykorzystaniem metody Multi-MOORA i narzędzi opartych na sztucznej inteligencji [A5]

Celem tej publikacji było stworzenie hybrydowego modelu decyzyjnego, wspierającego wybór najbardziej optymalnych metod rzucania palenia, przy zastosowaniu zaawansowanych technik sztucznej inteligencji oraz analizy wielokryterialnej Multi-MOORA (Multi-Objective Optimization on Ratio Analysis). Model ten integrował trzy różne podejścia analityczne: sieci neuronowe (ANN), regresję grzbietową (Ridge Regression, RR) oraz symulowane wyżarzanie (Simulated Annealing, SA), w celu uzyskania stabilnych, odpornych na nadmierne dopasowanie i interpretowalnych wag dla kluczowych kryteriów decyzyjnych. W badaniu oceniano trzy alternatywy: tradycyjne papierosy, e-papierosy oraz stosowanie obu tych produktów. Analizowano je pod kątem sześciu kryteriów: wieku rozpoczęcia palenia, miesięcznych kosztów, emisji CO₂, czasu spędzonego na paleniu, łatwości rzucenia oraz wpływu na zdrowie. Dane pochodziły z dwóch źródeł: ankiety przeprowadzonej wśród 100 użytkowników oraz dostępnych publicznie raportów zdrowotnych i środowiskowych. W pierwszym etapie zbudowano macierz decyzyjną, w której każda alternatywa została oceniona według powyższych kryteriów. Następnie, dane zostały znormalizowane według charakteru kryterium (maksymalizacyjnego lub minimalizacyjnego), a następnie przypisano im wagi. ANN pozwoliła na wychwycenie złożonych wzorców i nieliniowych zależności, RR zapewniła stabilność i odporność na kolinearność danych, a SA umożliwiła optymalizację rozkładu wag i uniknięcie lokalnych minimów.

Zastosowanie metody Multi-MOORA obejmowało trzy komponenty: system ilorazów, punkt odniesienia (odległość euklidesowa) oraz pełną postać multiplikatywną. Dla każdej alternatywy wyliczono syntetyczny wynik, który stanowił podstawę rankingu. Model wskazał jednoznacznie, że najlepszą alternatywą są e-papierosy, które zajęły pierwsze miejsce we wszystkich wersjach analizy i iteracjach testu wrażliwości. Drugie miejsce przypadło kombinacji tradycyjnych papierosów i e-papierosów, natomiast najniżej oceniono tradycyjne papierosy. Taka hierarchia utrzymała się także po przeprowadzeniu analizy czułości, w której każdemu kryterium zmieniano wagę o $\pm 10\%$, co potwierdziło stabilność i odporność modelu na drobne zmiany parametrów. Wyniki pokazały, że największą wagę przypisano kryterium wieku rozpoczęcia palenia (0,2431) oraz kosztom miesięcznym (0,1621), natomiast mniejszą – wpływowi na środowisko (0,1376). Finalne wagi powstały jako średnia z wartości uzyskanych trzema metodami (AI, RR, SA) i są przedstawione w Tabeli 3.

Tabela 3. Wagi kryteriów decyzyjnych i ranking alternatyw (Multi-MOORA) [A5]

Kryterium	Waga
Wiek rozpoczęcia palenia	0,2431
Koszty miesięczne	0,1621
Emisja CO ₂	0,1376
Czas spędzany na paleniu	0,1314
Łatwość rzucenia	0,1272
Wpływ na zdrowie	0,1186

Badanie stanowi wkład w rozwój spersonalizowanego wspomaganie decyzji w zdrowiu publicznym, wskazując, że dzięki integracji AI i metod MCDA możliwe jest obiektywne i przejrzyste wspieranie decyzji opartej na wielu kryteriach – zarówno kosztowych, zdrowotnych, jak i środowiskowych. Autorzy zauważają jednak ograniczenia: ograniczony zakres alternatyw (brak terapii nikotynozastępczych czy psychoterapii), użycie danych samoopisowych, możliwe błędy w danych wtórnych oraz ograniczona liczba respondentów. Pomimo tego, model może być rozwijany w przyszłych pracach przez dodanie kolejnych opcji terapeutycznych, uzupełnienie danych o zmienne demograficzne i kliniczne oraz zastosowanie w badaniach prospektywnych. Prezentowane podejście ma potencjał do implementacji, jako narzędzie wspierające kliniczne decyzje terapeutyczne oraz budowanie polityki zdrowotnej, opartej na danych i sztucznej inteligencji.

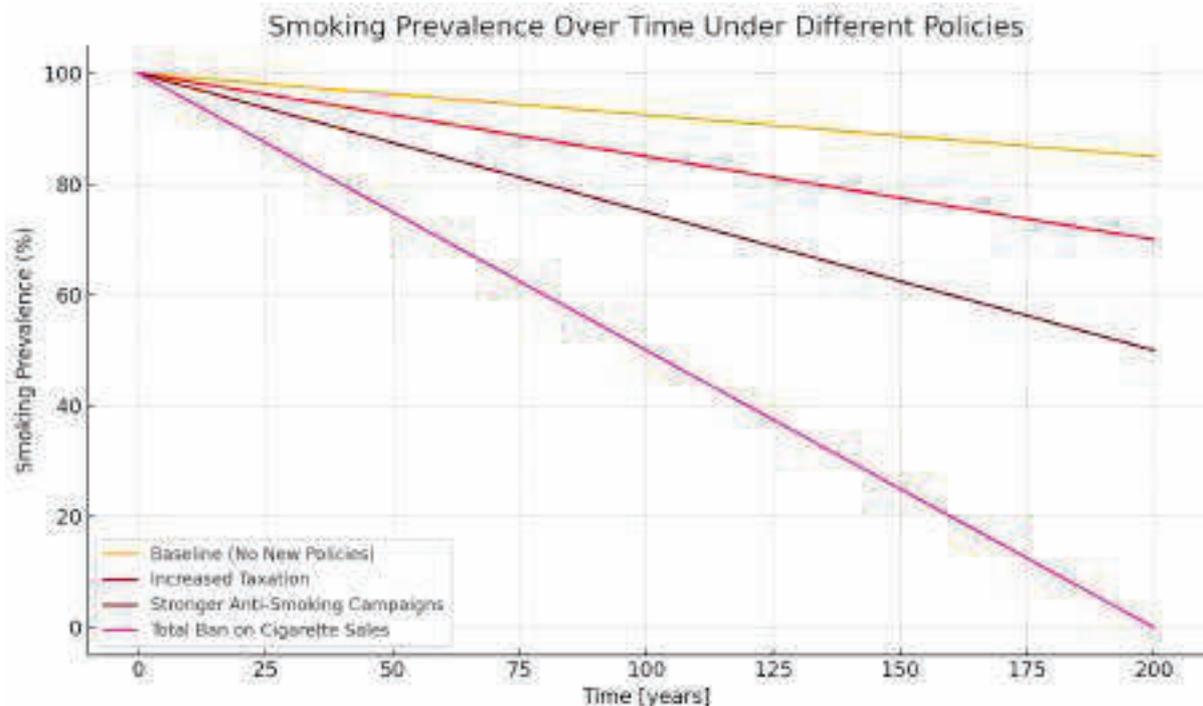
2.9. Modelowanie wpływu polityk kontroli tytoniu na rozpowszechnienie palenia: dynamiczny model SIQ+P+E+H+X [A6]

Następna publikacja w cyklu badawczym stanowi odpowiedź na potrzebę kompleksowego modelowania populacyjnych skutków długofalowych interwencji polityki zdrowotnej w zakresie kontroli palenia. W tym celu zaprojektowano i zaimplementowano zaawansowany model przedziałowy typu SIQ+P+E+H+X, stanowiący rozszerzenie klasycznego modelu SIR o dodatkowe komponenty odzwierciedlające specyfikę aktualnej dynamiki nikotynowej. Uwzględniono w nim nie tylko klasyczne zmienne jak inicjacja, porzucenie i nawroty palenia, ale także użycie e-papierosów, ich potencjalną rolę w przejściu do tradycyjnego palenia (efekt „bramy”) oraz wpływ polityk cenowych, edukacyjnych i regulacyjnych. Model został skalibrowany na danych empirycznych z badań WHO, przeglądów Cochrane’a oraz danych krajowych – w tym dotyczących trendów inicjacji palenia i skuteczności e-papierosów w terapii substytucyjnej. Na podstawie tego modelu przetestowano cztery scenariusze polityczne: brak nowych interwencji (scenariusz bazowy), wzrost opodatkowania wyrobów tytoniowych, całkowity zakaz sprzedaży papierosów oraz wzmocnione kampanie antynikotynowe (Tabela 4).

Tabela 4. Przegląd scenariuszy polityki zdrowotnej i ich przewidywanych efektów [A6]

Scenariusz	Opis polityki	Kluczowe parametry	Oczekiwany efekt
Bazowy	Brak nowych interwencji; kontynuacja obecnych trendów	Brak zmian	Stopniowy spadek rozpowszechnienia palenia
Zwiększone opodatkowanie	Wyższe akcyzy na papierosy	↓ Wskaźnik inicjacji (β)	Mniej inicjacji wśród młodzieży, umiarkowany wzrost rzucania palenia
Silniejsze kampanie antynikotynowe	Ogólnokrajowe kampanie medialne, edukacja, działania społeczne	↑ Wskaźnik rzucania (γ), ↓ Nawrót (α)	Wyższy wskaźnik rzucania i mniejszy odsetek nawrotów we wszystkich grupach wiekowych
Całkowity zakaz sprzedaży papierosów	Całkowity zakaz sprzedaży wyrobów tytoniowych	$\beta = 0$, ↑ Wskaźnik rzucania (γ)	Szybka eliminacja palenia; potencjalny rynek nielegalny nieuwzględniony

Wyniki symulacji jednoznacznie wykazały, że najbardziej efektywnym podejściem – przy założeniu jego wykonalności – byłby całkowity zakaz sprzedaży papierosów, prowadzący do spadku ich użycia o 93.6% w horyzoncie 200 lat, wzrostu wskaźników rzucania palenia o 50% oraz całkowitej eliminacji nowych inicjacji. Drugą najskuteczniejszą strategią okazały się kampanie informacyjne i edukacyjne, redukujące rozpowszechnienie palenia o 55%, a trzecią – podniesienie podatków, skutkujące redukcją o 25.6% (Rysunek 9). Analiza czułości modelu ujawniła największą podatność wyników na zmiany parametrów takich jak skuteczność kampanii (γ) i wpływ podatków (τ), co dowodzi ich kluczowej roli jako dźwigni politycznych.



Rys. 9 Rozpowszechnienie palenia w populacji na przestrzeni 200 lat [A6]

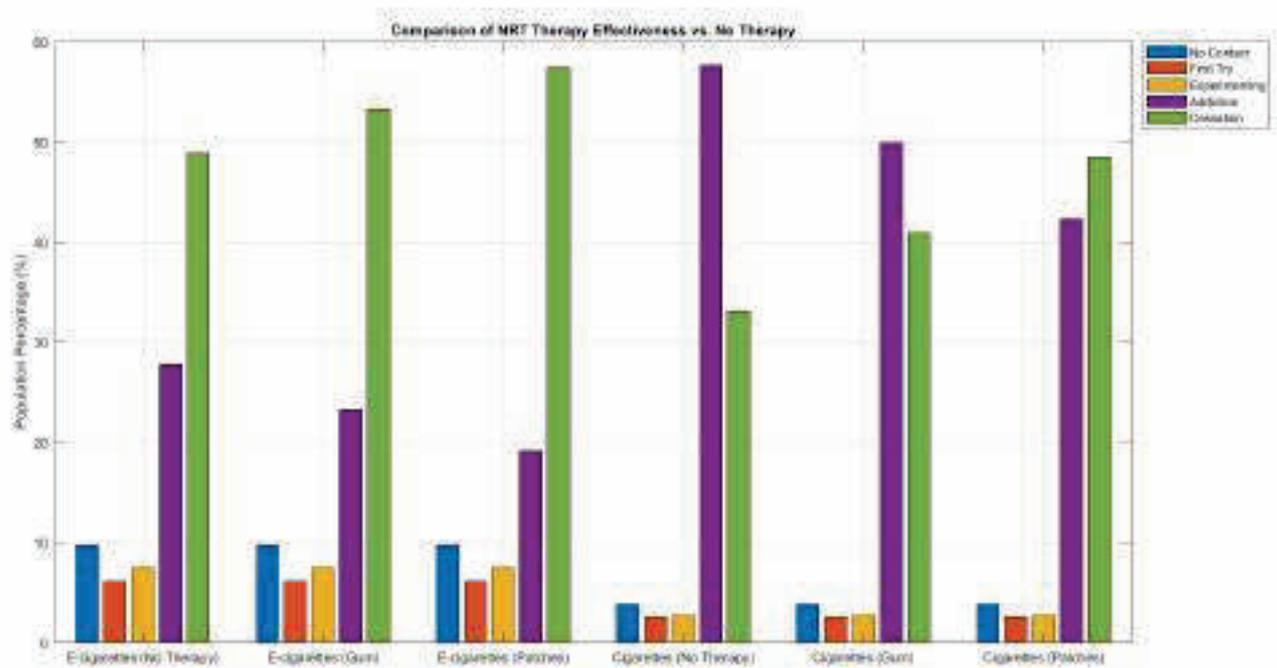
Szczególną innowacją modelu było wprowadzenie przedziału „E” – użytkowników e-papierosów – oraz uwzględnienie ich dwuznacznej roli: jako narzędzia redukcji szkód wśród palaczy oraz jako potencjalnego zagrożenia dla młodzieży (efekt „gateway”). Model wykazał, że przy obecnym poziomie użycia e-papierosów wśród młodzieży (ponad 22% w Polsce w 2022 r.) i relatywnie wysokim ryzyku przejścia do palenia tradycyjnego (wskaźnik ρ) konieczne są regulacje ograniczające dostęp do ENDS w tej grupie wiekowej. W odróżnieniu od klasycznych modeli, takich jak SimSmoke, opracowany model SIQ+P+E+H+X integruje skutki e-papierosów bez traktowania ich jako czynnik egzogeny, umożliwiając realistyczne odwzorowanie scenariuszy przyszłości rynku nikotynowego. W publikacji szczegółowo porównano także inne modele populacyjne (np. model tokański Lachi et al., model systemowy Camacho et al.), wskazując, że choć stanowią one cenne uzupełnienie, brak im kompleksowości i integracji wielu strategii regulacyjnych.

Wnioski z pracy mają znaczenie praktyczne dla planowania strategii zdrowia publicznego. Model wskazuje, że połączenie interwencji fiskalnych i edukacyjnych może znacząco przyspieszyć spadek palenia. Równocześnie autorzy uczulają na ograniczenia modelu – m.in. brak uwzględnienia rynku nielegalnego czy lokalnych zjawisk społecznych (np. efektów sieci rówieśniczych), sugerując rozwój modeli agentowych w przyszłości.

2.10. Wykorzystanie modelu Markowa do symulacji uzależnienia od nikotyny oraz skuteczności nikotynowej terapii zastępczej (NRT) [A7]

W niniejszym badaniu opracowano symulacyjny model łańcucha Markowa pierwszego rzędu, służący do analizy dynamiki uzależnienia nikotynowego oraz skuteczności terapii nikotynozastępczej (NRT). Celem było oszacowanie czasu trwania uzależnienia oraz prawdopodobieństwa zaprzestania palenia w różnych grupach użytkowników – zarówno tradycyjnych papierosów, jak i e-papierosów – przy uwzględnieniu trzech scenariuszy interwencji: brak terapii, stosowanie gum nikotynowych oraz plastrów nikotynowych. Model uwzględniał pięć stanów: brak kontaktu z nikotyną, pierwsze próby, faza eksperymentowania, uzależnienie oraz rzucenie palenia. Prawdopodobieństwa przejść pomiędzy stanami zaczerpnięto z aktualnych danych epidemiologicznych (m.in. NESARC), co umożliwiło realistyczne odwzorowanie przebiegu uzależnienia. Macierz przejść została zdefiniowana dla rocznych kroków czasowych i zastosowana do symulacji rozwoju uzależnienia w horyzoncie 20 lat.

Wyniki symulacji wykazały, że użytkownicy e-papierosów spędzają istotnie mniej czasu w stanie uzależnienia niż palacze tradycyjni – średnio 27,77 lat vs. 57,65 lat bez zastosowania terapii. Wprowadzenie terapii zastępczej prowadziło do znaczącej redukcji tego czasu, przy czym plastry nikotynowe były skuteczniejsze niż gumi (efektywność odpowiednio: 13,83% vs. 6,56%). Dla użytkowników e-papierosów terapia z użyciem plastrów skracala czas trwania uzależnienia do 21,46 lat, a dla użytkowników tradycyjnych papierosów – do 46,48 lat (Rys. 10). Model potwierdził, że nawet przy umiarkowanej skuteczności, NRT może istotnie skrócić czas ekspozycji na uzależnienie, zwiększając prawdopodobieństwo skutecznego rzucenia palenia. Wyniki te są zgodne z literaturą, potwierdzając wyższą efektywność plastrów względem gum, co jest zgodne z danymi biochemicznymi (np. stabilniejsze stężenie kotyniny w ślinie). Ważną cechą modelu było rozróżnienie dynamiki uzależnienia między użytkownikami papierosów tradycyjnych a e-papierosów, co stanowi nowatorski wkład w modelowanie populacyjne. Uwzględniono także biologiczne podstawy uzależnienia i wpływ NRT na stabilizację stężeń nikotyny, co zwiększa wiarygodność wyników.



Rys. 10 Wyniki symulacji uzależnienia i skuteczności terapii nikotynozastępczej (NRT) na podstawie modelu łańcucha Markowa pierwszego rzędu [A7]

Do ograniczeń pracy należy zaliczyć stosunkowo uproszczoną strukturę modelu (np. brak rozróżnienia na wiek, płeć, inne uwarunkowania społeczno-demograficzne), brak modelowania wsparcia behawioralnego oraz przyjęcie stałych efektywności terapii bez indywidualizacji. Autorzy wskazują jednak, że podejście to może zostać rozwinięte w przyszłości w kierunku modeli agentowych lub uzupełnione o komponenty kosztowo-ekonomiczne. Z punktu widzenia zdrowia publicznego, wyniki potwierdzają skuteczność interwencji farmakologicznych w ograniczaniu skali uzależnienia nikotynowego i mogą stanowić podstawę do dalszej optymalizacji programów rzucania palenia. W szczególności – model może służyć do personalizacji terapii i szacowania jej długofalowych efektów w różnych subpopulacjach użytkowników.

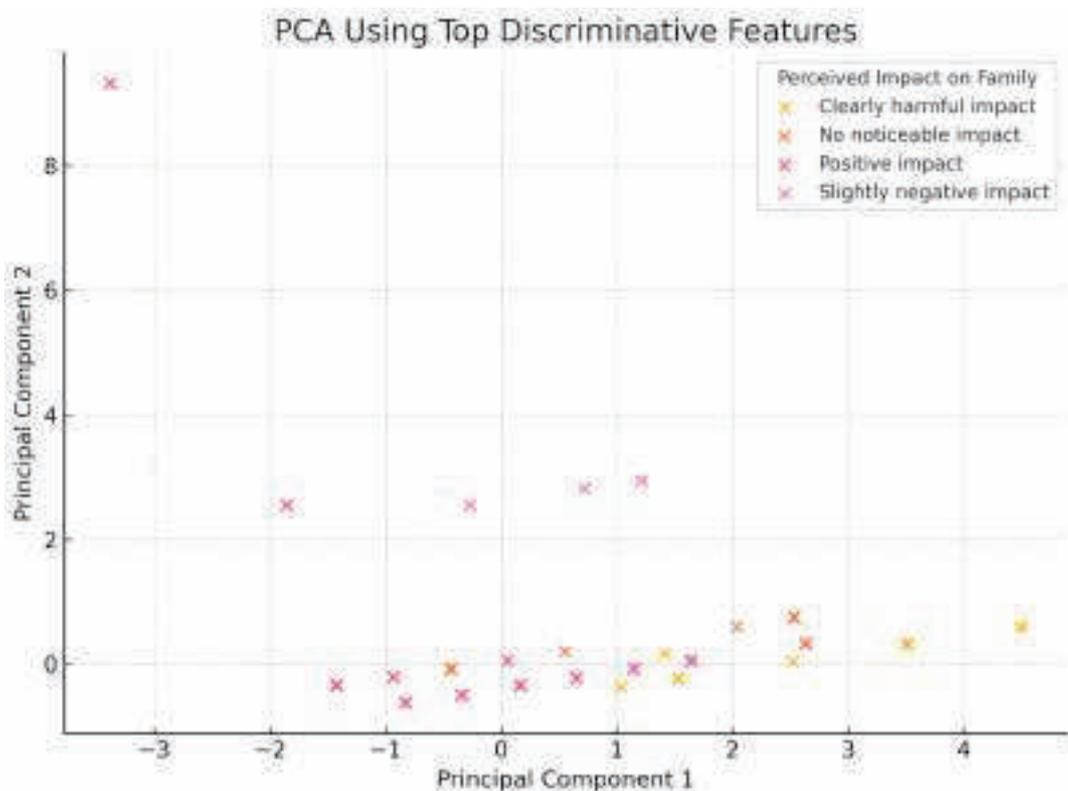
2.11. Analiza demograficznych, rodzinnych i społecznych determinant zachowań palaczy z wykorzystaniem metod uczenia maszynowego [A8]

Celem niniejszego badania było zidentyfikowanie kluczowych czynników demograficznych, rodzinnych i społecznych, wpływających na zachowania związane z paleniem tytoniu, zarówno tradycyjnego, jak i elektronicznego, oraz ocena ich wpływu na dynamikę uzależnienia i relacje rodzinne. Wykorzystano metody uczenia maszynowego do analizy danych zebranych od 100 uczestników, co pozwoliło na stworzenie modeli predykcyjnych dotyczących wpływu palenia na relacje rodzinne. Badanie przeprowadzono w formie przekrojowego sondażu online, w którym uczestnicy wypełniali anonimowy kwestionariusz składający się z trzech sekcji: danych demograficznych, nawyków związanych z paleniem oraz dynamiki rodzinnej. Wykorzystano zwalidowane narzędzia, takie jak Penn State Electronic Cigarette Dependence Index (PSECDI) do oceny poziomu uzależnienia oraz Family Relationship Assessment Scale (FRAS) do oceny relacji rodzinnych (Tabela 5). Kwestionariusz został przetłumaczony na język polski metodą tłumaczenia zwrotnego, aby zapewnić jego rzetelność i trafność. Dane analizowano przy użyciu różnych technik statystycznych, w tym testów chi-kwadrat, analizy wariancji (ANOVA) oraz korelacji rang Spearmana, w celu zidentyfikowania istotnych zależności między zmiennymi. Następnie zastosowano algorytmy uczenia maszynowego, takie jak drzewa decyzyjne, maszyny wektorów nośnych (SVM), k-najbliższych sąsiadów (k-NN) oraz modele zespołowe (ensemble learning), aby przewidzieć postrzegany wpływ palenia na relacje rodzinne. Modele oceniano pod względem dokładności i strat, wykorzystując walidację krzyżową z podziałem na k-folds.

Tabela 5. Porównanie wskaźników relacji rodzinnych (FRAC) i poziomu uzależnienia od nikotyny (PSECDI) w zależności od typu palenia [A8]

Kategoria	Wskaźnik	E-papierosy	Tradycyjne papierosy	Użytkownicy obu
FRAC	Wsparcie w rodzinie (średnia)	4,22	3,5	3,67
	Konflikty rodzinne (średnia)	1,81	2	1,89
	Spędzanie czasu razem (średnia)	3,26	3,12	2,83
PSECDI	Brak uzależnienia (%)	0	4,76	0
	Niskie uzależnienie (%)	21,05	33,33	16,67
	Umiarkowane uzależnienie (%)	31,58	19,05	33,33
	Wysokie uzależnienie (%)	47,37	42,86	50
	Średni wynik	13,11	12,05	13,5

Analiza statystyczna wykazała, że użytkownicy e-papierosów zgłaszali wyższy poziom wsparcia rodzinnego i mniejsze konflikty w porównaniu do palaczy tradycyjnych i użytkowników obu typów papierosów. Jednakże, użytkownicy e-papierosów wykazywali również wyższy poziom uzależnienia nikotynowego, co sugeruje, że mimo lepszych relacji rodzinnych, ryzyko uzależnienia pozostaje istotne. W celu eksploracyjnego zrozumienia struktury danych zastosowano analizę głównych składowych (PCA). Początkowa projekcja PCA na podstawie wszystkich zmiennych demograficznych, rodzinnych i behawioralnych wykazała znaczne nakładanie się klas, co potwierdziło złożoność i niską separowalność danych. W dalszej analizie przeprowadzono PCA wyłącznie na sześciu najbardziej dyskryminujących zmiennych, wybranych na podstawie testu ANOVA F. Wyniki tej analizy (Rys. 11) ukazały wyraźniejsze klastry, szczególnie w przypadkach skrajnych wartości, co potwierdziło potencjał modeli nadzorowanych w dalszej klasyfikacji. Projektowanie przestrzeni o zmniejszonej wymiarowości pozwoliło również na potwierdzenie wysokiej wartości predykcyjnej zmiennych opisujących postrzegany wpływ palenia na relacje rodzinne. Analiza PCA była zgodna z późniejszą analizą ważności cech w modelach uczenia maszynowego i dodatkowo uzasadniła wybór konkretnych predyktorów.



Rys. 11 Projekcja analizy głównych składowych (PCA) wykonana na podstawie sześciu najistotniejszych zmiennych wejściowych [A8]

Aby ocenić, które zmienne miały największy wpływ na skuteczność predykcji, przeprowadzono porównanie ważności cech w czterech modelach. Niezależnie od zastosowanej metody, we wszystkich przypadkach największe znaczenie przypisano zmiennej, opisującej wpływ palenia na relacje rodzinne. W dalszej kolejności pojawiały się m.in. konflikty rodzinne, wiek badanych oraz obecność palaczy w rodzinie. Choć poszczególne modele różniły się pod względem szczegółowych

wartości, ogólna kolejność najistotniejszych cech pozostawała spójna. Porównanie najważniejszych predyktorów przedstawiono w Tabeli 6.

Tabela 6. Porównanie ważności cech (znormalizowane wartości) w modelach uczenia maszynowego [A8]

Cecha	Drzewo decyzyjne	Ensemble	SVM	k-NN
Płeć	0	0,0085	0	0
Wiek	0	0	0,0167	0
Czy palisz	0	0	0	0
Częstość palenia	0	0,0023	0	0
Wiek rozpoczęcia palenia	0	0,0031	0,0067	0
Pałacy członkowie rodziny	0	0	0,0133	0
Konflikty rodzinne (FRAC)	0,0381	0	0	0,008
Wpływ palenia na relacje	0,1875	0,1459	0,1867	0,2433
Akceptacja w rodzinie	0	0	0	0

Modele uczenia maszynowego osiągnęły wysoką dokładność w przewidywaniu wpływu palenia na relacje rodzinne (Tabela 7), przy czym model zespołowy osiągnął najwyższą dokładność na poziomie 93,33%, przewyższając inne modele, takie jak k-NN (90,00%), drzewa decyzyjne (83,33%) i SVM (80,00%). Analiza ważności cech wykazała, że zmienne związane z postrzeganym wpływem palenia na relacje rodzinne miały największy wpływ na dokładność modeli predykcyjnych.

Tabela 7. Ocena skuteczności modeli uczenia maszynowego [A8]

Model	Dokładność	Precyzja	Czułość	Miara F1
Drzewo decyzyjne	83,33%	0,79	0,7	0,74
Metoda grupowania (Ensemble learning)	93,33%	0,91	0,91	0,91
Maszyna wektorów nośnych (SVM)	80,00%	0,6	0,75	0,67
Metoda k-najbliższych sąsiadów (k-NN)	90,00%	0,9	0,82	0,86

Głównym ograniczeniem badania była stosunkowo niewielka liczba uczestników (100 osób), co może wpływać na uogólnienie wyników na szerszą populację. Ponadto, wykorzystanie kwestionariuszy do samodzielnego wypełnienia może wprowadzać stronniczość (bias) związaną z subiektywną oceną uczestników. Mimo to, wyniki podkreślają znaczenie relacji rodzinnych w kontekście zachowań związanych z paleniem i sugerują, że interwencje zdrowia publicznego powinny uwzględniać te aspekty. Zastosowanie metod uczenia maszynowego w analizie zachowań zdrowotnych, otwiera nowe możliwości w identyfikacji osób o podwyższonym ryzyku uzależnienia oraz w tworzeniu spersonalizowanych programów interwencyjnych. Przyszłe badania powinny skupić się na zwiększeniu liczby uczestników oraz uwzględnieniu dodatkowych zmiennych, takich jak status społeczno-ekonomiczny, poziom stresu czy wsparcie społeczne, aby lepiej zrozumieć złożoność zachowań związanych z paleniem.

2.12. Skład ciała i profile metaboliczne u młodych dorosłych: badanie przekrojowe porównujące osoby używające e-papierosów, palące papierosy tradycyjne oraz osoby, które nigdy nie stosowały wyrobów nikotynowych [A9]

Celem tej pracy była ocena wpływu regularnego używania e-papierosów na wybrane parametry metaboliczne i składu ciała u zdrowych, młodych dorosłych. W przeciwieństwie do większości badań, koncentrujących się na układzie oddechowym i sercowo-naczyniowym, niniejsze badanie skupiło się na mniej zbadanym obszarze: zmianach w strukturze ciała oraz parametrach powiązanych z metabolizmem, takich jak zawartość wody całkowitej, masa beztłuszczowa czy wiek metaboliczny. W badaniu wzięły udział trzy grupy uczestników (N = 120, 20 osób w każdej z grup): osoby niepalące (kontrolne), użytkownicy e-papierosów oraz palacze tradycyjnych papierosów. Charakterystyka badanych widoczna jest Tabeli 8. Zastosowano analizę impedancji bioelektrycznej (BIA) przy użyciu wieloczęstotliwościowego analizatora medycznego klasy diagnostycznej. Pomiary obejmowały: masę mięśniową, całkowitą wodę ustrojową (TBW), zawartość tkanki tłuszczowej, wiek metaboliczny, indeks masy ciała (BMI) oraz zawartość tłuszczu trzewnego.

Tabela 8. Charakterystyka uczestników badań [A9]

Zmienna	Wszyscy uczestnicy (N = 60)	Palacze tytoniu (n = 20)	Użytkownicy e-papierosów (n = 20)	Osoby niepalące (n = 20)
Wiek (lata)	22,0 [2,25]	22,0 [2,25]	20,5 [3,0]	22,0 [1,75]
Wzrost (cm)	173,5 [16,25]	176,5 [8,0]	170,0 [12,25]	171,5 [20,75]
Masa ciała (kg)	65,35 [13,35]	68,75 [20,15]	65,35 [4,8]	62,1 [21,08]
BMI (kg/m ²)	22,3 [3,55]	22,05 [4,62]	23,4 [1,33]	21,05 [3,2]
Tkanka tłuszczowa (%)	15,35 [5,87]	12,95 [7,17]	16,35 [4,32]	11,2 [5,15]
Tłuszcz trzewny (poziom)	2,0 [2,0]	2,0 [2,25]	2,0 [2,0]	1,0 [1,0]
Masa mięśniowa (kg)	47,35 [17,7]	52,25 [15,88]	46,6 [10,2]	45,75 [20,67]
Całkowita woda w organizmie (%)	32,1 [13,12]	39,7 [14,9]	31,05 [6,1]	30,85 [14,55]
Wiek metaboliczny (lata)	18,0 [13,25]	23,5 [17,0]	23,5 [13,0]	15,5 [5,5]
Płeć – mężczyźni (%)	15 (41,7%)	7 (58,3%)	2 (16,7%)	5 (41,7%)
Płeć – kobiety (%)	21 (58,3%)	5 (41,7%)	10 (83,3%)	7 (58,3%)

Wyniki wykazały, że użytkownicy e-papierosów mieli istotnie wyższy poziom wiek metabolicznego (średnio +3,6 roku względem wieku rzeczywistego) w porównaniu do grupy

kontrolnej (średnio -1,1 roku). Różnica ta była statystycznie istotna ($p < 0,01$) i sugeruje zaburzenia w metabolizmie bazalnym, które mogą wiązać się z przewlekłą ekspozycją na nikotynę lub inne związki chemiczne zawarte w aerozolu (Tabela 9). Grupa palaczy tradycyjnych również wykazywała podwyższony wiek metaboliczny, jednak różnice były mniej wyraźne niż w grupie e-papierosów, co może wskazywać na różny mechanizm działania. Zawartość wody całkowitej i masa mięśniowa były istotnie niższe u użytkowników e-papierosów w porównaniu do grupy kontrolnej (średnia TBW: 50,3% vs. 54,7%, $p < 0,05$), co może odzwierciedlać mikropozomowe odwodnienie lub przewlekłą aktywację osi stresu. Wartości BMI i tłuszczu trzewnego nie różniły się istotnie między grupami, jednak wskaźnik segmentalnej masy mięśniowej był niższy u osób stosujących ENDS, co może wskazywać na subtelne zmiany w homeostazie metabolicznej i potencjalnie osłabiony profil anaboliczny. Zastosowano analizę regresji wielozmiennowej kontrolującą czynniki zakłócające, takie jak płeć, poziom aktywności fizycznej oraz nawyki żywieniowe. Również w tej analizie status użytkownika e-papierosów pozostawał istotnym predyktorem wyższego wieku metabolicznego i obniżonej masy beztłuszczowej ($p < 0,05$). Dodatkowo, przeprowadzono analizę korelacji między wybranymi zmiennymi stylu życia (czas siedzenia, spożycie kawy, napojów energetycznych) a parametrami metabolicznymi. Nie stwierdzono istotnych zależności między czasem siedzenia a BMI, wiekiem metabolicznym, BMR czy procentową zawartością tkanki tłuszczowej. Podobnie, spożycie kawy nie korelowało istotnie z żadnym z analizowanych parametrów. Natomiast regularne spożywanie napojów energetycznych wykazało dodatnie, istotne statystycznie korelacje z BMI ($r = 0,49$; $p = 0,0025$), wiekiem metabolicznym ($r = 0,61$; $p = 0,0001$) oraz zawartością tkanki tłuszczowej ($r = 0,65$; $p < 0,0001$), co sugeruje potencjalny związek z niekorzystnym profilem metabolicznym.

Tabela 9. Porównania między grupami użytkowników tytoniu i e-papierosów dla zmiennych ciągłych (testy nieparametryczne) [A9]

Zmienna	p (Kruskal-Wallis)	Porównania istotne (z korektą Bonferroniego)	Istotność
Wiek metaboliczny	0,0429	E-papierosy vs. Niepalący ($p = 0,0248$)	istotna
Tkanka tłuszczowa (%)	0,0203	E-papierosy vs. Niepalący ($p = 0,0127$)	istotna
BMI	0,0295	E-papierosy vs. Niepalący ($p = 0,0199$)	istotna
Wiek chronologiczny	0,0721	E-papierosy vs. Niepalący ($p = 0,0938$)	trend
Spożycie napojów energetycznych	0,0007	E-papierosy vs. Niepalący ($p = 0,0011$); vs. Palacze ($p = 0,0480$)	istotna

W części eksploracyjnej wykorzystano nadzorowane modele uczenia maszynowego do klasyfikacji uczestników ze względu na status palenia. Pierwotny model drzewa decyzyjnego, zbudowany na pełnym zbiorze cech, osiągnął umiarkowaną trafność klasyfikacji (50,0%). Po ograniczeniu liczby cech do ośmiu najistotniejszych (m.in. wiek metaboliczny, BMI, tkanka tłuszczowa), dokładność wzrosła do 66,67%. Zastosowanie alternatywnych modeli (Random Forest – 61,1%; k-NN – 72,22%) wskazało, że klasyfikator k-NN wykazuje największą skuteczność

w odróżnianiu palaczy od osób niepalących w tej populacji. Analiza ważności cech w modelach potwierdziła kluczowe znaczenie wskaźników metabolicznych jako predyktorów statusu palenia.

Pomimo ograniczeń, takich jak przekrojowy charakter badania i opieranie się na danych samoopisowych (np. aktywność fizyczna), dane wskazują, że e-papierosy mogą wpływać na funkcjonowanie metaboliczne organizmu, nawet u młodych, zdrowych osób. Autorzy postulują potrzebę długoterminowych badań prospektywnych z wykorzystaniem markerów biochemicznych oraz metod obrazowania składu ciała w celu potwierdzenia i pogłębienia uzyskanych wyników. Badanie to poszerza dotychczasowe spojrzenie na skutki stosowania ENDS, pokazując, że oddziaływanie to nie ogranicza się wyłącznie do układu oddechowego, lecz może również wpływać na regulację masy ciała, bilans płynów i procesy starzenia metabolicznego.

2.13. Kontrola postawy i zmian chodu u młodych dorosłych użytkowników tytoniu i e-papierosów: porównawcza analiza stabilometryczna i badania na bieżni [A10]

W ramach niniejszego badania podjęto się porównania parametrów kontroli posturalnej i chodu u trzech grup młodych dorosłych: użytkowników e-papierosów (ECIG), palaczy tradycyjnych papierosów (CIG) oraz osób niepalących (NS). Motywacją do przeprowadzenia analizy była obserwacja rosnącej popularności e-papierosów oraz brak jednoznacznych danych dotyczących ich wpływu na funkcje biomechaniczne. Postawiono hipotezę, że chroniczne stosowanie produktów zawierających nikotynę, niezależnie od ich formy, może wpływać negatywnie na parametry równowagi i chodu, które są czułymi wskaźnikami funkcjonowania układu nerwowo-mięśniowego. Badanie miało charakter przekrojowy i objęło 60 zdrowych uczestników (średni wiek $21,3 \pm 1,7$ roku). Każda grupa liczyła po 20 osób. Kwalifikacja do grup odbywała się na podstawie samoopisowych deklaracji dotyczących stylu życia i nawyków nikotynowych, a kryterium włączenia obejmowało co najmniej 6-miesięczny staż regularnego używania danego produktu (papierosów tradycyjnych lub e-papierosów) lub całkowity brak ekspozycji w grupie kontrolnej. Kryteria wykluczenia obejmowały m.in. zaburzenia neurologiczne, ortopedyczne, równowagi, a także intensywne uprawianie sportu lub przyjmowanie leków wpływających na ośrodkowy układ nerwowy. Pomiar stabilności posturalnej wykonano przy użyciu platformy Zebris FDM-T System (Zebris Medical GmbH, Niemcy). Uczestnicy stali boso na platformie przez 30 sekund, w dwóch warunkach: z otwartymi (EO) oraz zamkniętymi oczami (EC). Zarejestrowano podstawowe wskaźniki stabilometrii: długość ścieżki przemieszczenia środka nacisku (COP path length), prędkość COP (COP velocity) oraz powierzchnię elipsy 95% (COP area).

W warunku EO, grupa CIG wykazała najdłuższą ścieżkę COP ($42,27 \pm 4,99$ cm), istotnie dłuższą niż grupa NS ($38,22 \pm 3,89$ cm; $p = 0,025$). Użytkownicy e-papierosów osiągnęli wartość pośrednią ($41,24 \pm 4,50$ cm), która nie różniła się istotnie od pozostałych grup. W warunku EC efekt ten był jeszcze wyraźniejszy: CIG ($46,47 \pm 5,44$ cm) vs. NS ($41,43 \pm 4,23$ cm; $p = 0,018$), natomiast grupa ECIG osiągnęła $44,18 \pm 4,63$ cm. Wyniki te wskazują na wyraźne pogorszenie kontroli posturalnej u palaczy tradycyjnych oraz możliwe wczesne zmiany u użytkowników e-papierosów, szczególnie widoczne w warunkach braku kompensacji wzrokowej. Analiza parametrów chodu, także wykonana przy użyciu platformy Zebris FDM-T, wykazała istotnie niższą długość kroku w grupie CIG ($70,12 \pm 3,52$ cm) w porównaniu do NS ($74,24 \pm 4,25$ cm; $p = 0,003$), podczas gdy ECIG uzyskiwała wartość pośrednią ($71,69 \pm 3,97$ cm), nieodbiegającą istotnie od pozostałych. Również prędkość chodu była najniższa u palaczy tradycyjnych ($1,18 \pm 0,08$ m/s) w porównaniu do NS ($1,26 \pm 0,09$ m/s; $p = 0,022$), a grupa ECIG plasowała się pomiędzy nimi ($1,22 \pm 0,10$ m/s). W parametrach czasu kontaktu stopy z podłożem i fazy przetoczenia nie odnotowano istotnych różnic między grupami. Tabela 10 przedstawia wyniki porównań post-hoc pomiędzy grupami dla wybranych parametrów biomechanicznych.

Tabela 10. Porównania post-hoc pomiędzy parami grup dla wszystkich warunków. Myślniki (–) oznaczają, że porównanie nie należało do najniższych wartości p [A10]

Zmienna	Test	NS vs ECIG	NS vs CIG	ECIG vs CIG
Wskaźnik masy ciała (BMI)	Kruskala-Wallis	0,001	0,323	0,218

Siła pod przednią częścią stopy lewej (N)	ANOVA	0,474	0,037	0,051
Siła pod tylną częścią stopy lewej (N)	ANOVA	0,389	0,033	0,098
Czas trwania cyklu chodu (s)	Kruskala-Wallisa	0,012	–	0,282
Maksymalna siła – przednia część stopy lewej (N)	Kruskala-Wallisa	0,047	–	0,138
Maksymalna siła – przednia część stopy prawej (N)	Kruskala-Wallisa	0,055	–	0,148
Maksymalne obciążenie – pięta lewa (N)	Kruskala-Wallisa	–	0,042	0,091
Maksymalne obciążenie – pięta prawa (N)	Kruskala-Wallisa	0,023	0,071	–
Średnia długość kroku (cm)	ANOVA	0,005	0,153	0,072
Średnie maksymalne obciążenie – przednia część stopy lewej (N)	Kruskala-Wallisa	0,047	–	0,138
Długość kroku (prawa noga, cm)	ANOVA	0,003	0,123	0,256

Dodatkowo, w celu identyfikacji najistotniejszych cech różnicujących grupy użytkowników, zastosowano algorytm ReliefF, który pozwala na ocenę ważności zmiennych w kontekście klasyfikacji. Następnie wykorzystano klasyfikatory nadzorowane – w tym drzewa decyzyjne, maszynę wektorów nośnych (SVM), k-najbliższych sąsiadów (k-NN) oraz regresję logistyczną – do rozróżnienia pomiędzy grupami na podstawie wybranych cech biomechanicznych. Najwyższą skuteczność (dokładność 82,8%) osiągnięto przy zastosowaniu regresji logistycznej w rozróżnianiu niepalących od użytkowników e-papierosów (Tabela 11). Dodatkowo, analiza głównych składowych (PCA) oraz macierze pomyłek potwierdziły zdolność tych modeli do wychwycenia subtelnych różnic w parametrach posturalnych i chodu, które nie były jednoznacznie widoczne w tradycyjnych analizach statystycznych.

Tabela 11. Dokładność klasyfikacji dla par grup i modeli (5-krotna walidacja krzyżowa) [A10]

Grupa 1	Grupa 2	Model	Dokładność
Niepalący (NS)	Palacze tradycyjni (CIG)	Drzewo decyzyjne	0,393
		SVM (liniowy)	0,571
		k-NN (k=5)	0,536
		Regresja logistyczna	0,536
Niepalący (NS)	Użytkownicy e-papierosów (ECIG)	Drzewo decyzyjne	0,621
		SVM (liniowy)	0,793
		k-NN (k=5)	0,552
		Regresja logistyczna	0,828
Palacze tradycyjni (CIG)	Użytkownicy e-papierosów (ECIG)	Drzewo decyzyjne	0,37
		SVM (liniowy)	0,481
		k-NN (k=5)	0,444
		Regresja logistyczna	0,519

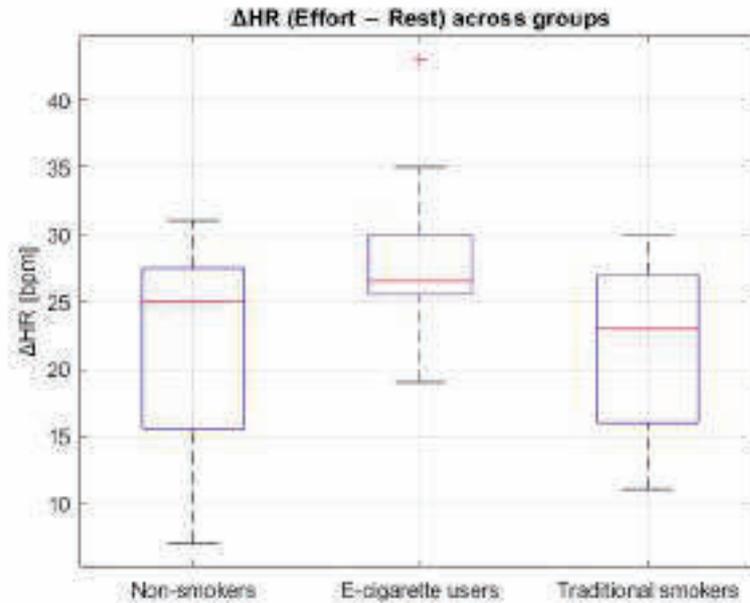
Dane wskazują na zaburzenia w biomechanice chodu i stabilności posturalnej u palaczy tradycyjnych, przy czym użytkownicy e-papierosów wykazują wartości pośrednie, sugerujące możliwość występowania efektów subklinicznych. Pogorszenie parametrów równowagi w warunkach zamkniętych oczu sugeruje osłabioną kompensację sensoryczną i gorszą integrację sygnałów proprioceptywnych i przedsionkowych u osób ekspozowanych na nikotynę. Choć użytkownicy e-papierosów nie osiągnęli wartości istotnie gorszych od osób niepalących, zauważalne trendy sugerują, że nawet ta forma konsumpcji nikotyny może wpływać na system posturalny.

Autorzy wskazują na ograniczenia badania, takie jak niewielka liczebność prób i brak kontroli stężenia nikotyny, ale zaznaczają, że otrzymane rezultaty powinny stanowić punkt wyjścia do dalszych badań podłużnych i neurofizjologicznych. Niniejsza publikacja stanowi jedno z pierwszych badań, łączących ocenę równowagi i chodu w kontekście użytkowania e-papierosów, wskazując na potrzebę ich uwzględnienia w kompleksowej ocenie wpływu tych produktów na zdrowie neuromotoryczne.

2.14. Użytkownicy e-papierosów wykazują silniejszą reaktywność układu sercowo-naczyniowego niż palacze: dowody z multimodalnej analizy sygnałów u młodych dorosłych [A11]

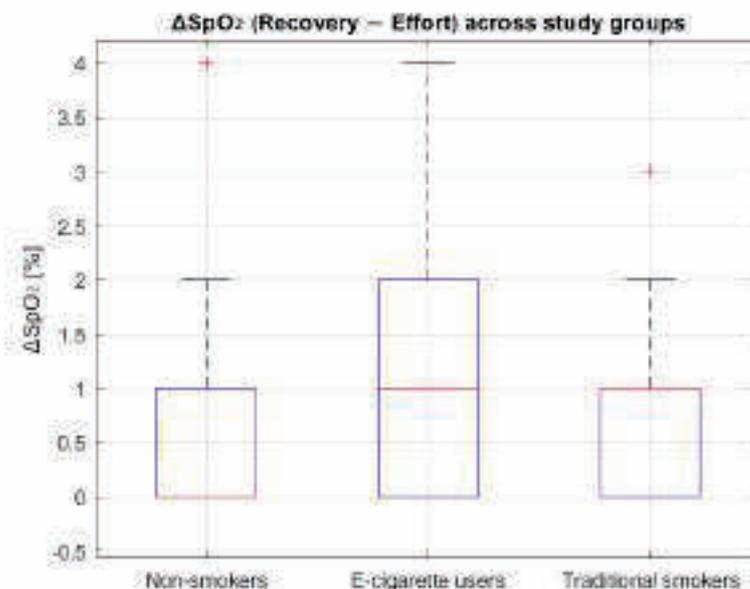
W prezentowanym badaniu podjęto próbę oceny wpływu palenia tradycyjnych papierosów oraz użytkowania e-papierosów na wybrane parametry układu sercowo-naczyniowego i oddechowego, przy użyciu zintegrowanej analizy wektorowej danych multimodalnych. Głównym celem było zidentyfikowanie charakterystycznych wzorców fizjologicznych, które mogą odróżniać trzy populacje użytkowników nikotyny – osoby niepalące, użytkowników e-papierosów oraz palaczy tradycyjnych – w warunkach obciążenia fizjologicznego, jakim był test wysiłkowy. Do badania włączono 60 zdrowych ochotników (średnia wieku $21,7 \pm 1,9$ lat), którzy zostali podzieleni równo na trzy grupy ($N = 20$): osoby niepalące (NS), użytkowników e-papierosów (ECIG) oraz palaczy tradycyjnych papierosów (CIG). Warunkiem kwalifikacji do grupy użytkowników było regularne stosowanie odpowiedniego produktu przez minimum rok. Z badania wykluczono osoby z chorobami układu krążenia, oddechowego, metabolicznymi, a także przyjmujące leki wpływające na parametry badane. Rejestracja sygnałów fizjologicznych została przeprowadzona w trzech fazach: spoczynku, natychmiast po zakończeniu standardowego wysiłku na bieżni oraz po fazie powrotu do spoczynku. W każdej fazie zbierano równoległe dane dotyczące częstości akcji serca (HR), saturacji tlenem (SpO_2), ciśnienia tętniczego skurczowego i rozkurczowego (SYS, DIA), średniego ciśnienia tętniczego (MAP) oraz częstości oddechów (RR). Dane zebrane w sposób synchroniczny zostały przekształcone do postaci wektorowej, a następnie analizowane z użyciem metod eksploracyjnych, takich jak klasyfikatory uczenia maszynowego (drzewa decyzyjne, regresja logistyczna), które służyły do identyfikacji cech o najwyższej wartości diagnostycznej.

Wyniki wykazały wyraźne różnice między grupami, szczególnie po zakończeniu wysiłku. W fazie wysiłkowej palacze tradycyjni osiągnęli najwyższe wartości skurczowego ciśnienia krwi i częstości serca, w porównaniu do użytkowników e-papierosów i osób niepalących. Analiza ΔHR (Effort – Rest) wykazała jednak, że to użytkownicy e-papierosów mieli największy przyrost tętna w stosunku do spoczynku, istotnie większy niż osoby niepalące i palacze tradycyjni (ANOVA $p = 0,01366$; test Tukeya $p < 0,03$ dla obu porównań) (Rys. 12).



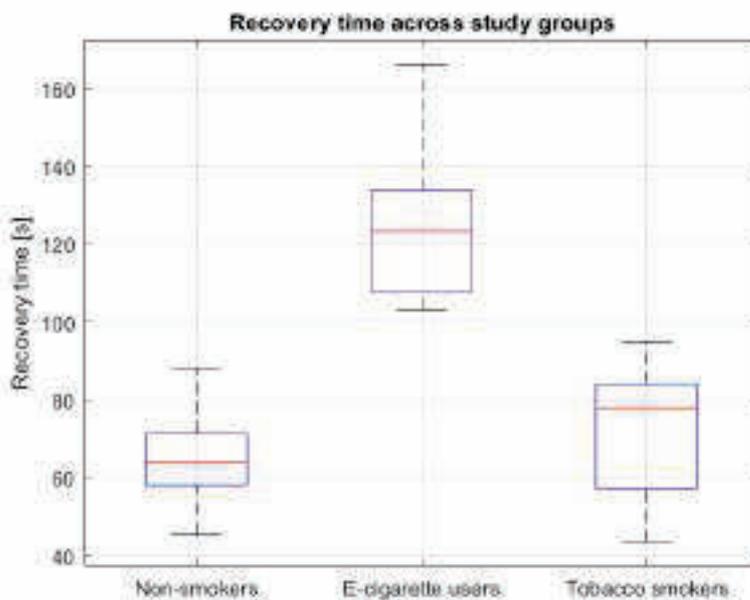
Rys. 12 Boxplot wartości ΔHR w trzech grupach badanych ($p = 0,01366$, test ANOVA) [A11]

Spadek SpO_2 po wysiłku analizowano jako różnicę między wartościami spoczynkowymi a powysiłkowymi (ΔSpO_2 Rest-Effort). Największy średni spadek odnotowano u użytkowników e-papierosów ($-1,45\% \pm 1,23$), następnie u palaczy tradycyjnych ($-1,20\% \pm 0,89$) i u osób niepalących ($-1,05\% \pm 1,28$). Różnice między grupami nie osiągnęły jednak istotności statystycznej ($p = 0,3712$, Rys. 13).



Rys. 13 Boxplot wartości ΔSpO_2 (regeneracja – wysiłek) w trzech grupach badanych. Użytkownicy e-papierosów wykazali największą poprawę saturacji tlenem (SpO_2) w fazie regeneracji [A11]. Obserwowany trend zbliżał się do istotności statystycznej ($p = 0,0700$, test Kruskala-Wallis)

Parametry powrotu fizjologicznego do stanu spoczynkowego (recovery time) wykazały wydłużenie w grupach CIG i ECIG względem NS (Rys. 14). Średni czas powrotu częstości serca (HR) do wartości spoczynkowych był najdłuższy u użytkowników e-papierosów: 123,9 s (SD 17,3), istotnie dłuższy niż u osób niepalących: 65,6 s (SD 10,9) oraz palaczy tradycyjnych: 72,2 s (SD 15,0) (Kruskal–Wallis $p < 0,001$; porównania post hoc ECIG vs NS i ECIG vs CIG: $p < 0,001$; d Cohena = 4,03 dla ECIG vs NS). Wyniki te wskazują na znaczne obciążenie układu autonomicznego u osób regularnie używających e-papierosów, prawdopodobnie w wyniku nadmiernej aktywacji współczulnej i osłabienia reaktywacji przywspółczulnej.



Rys. 14 Boxplot czasu regeneracji (w sekundach) w trzech grupach badanych. Użytkownicy e-papierosów wykazali istotnie dłuższy czas regeneracji w porównaniu zarówno do palaczy tradycyjnych, jak i osób niepalących ($p < 0,001$, test Kruskala-Wallisa) [A11]

Modele klasyfikacyjne osiągały dokładność od 71,7% (regresja logistyczna) do 75,0% (drzewa decyzyjne), co potwierdza potencjał sygnałowej analizy wektorowej w ocenie obciążeń fizjologicznych wynikających z używania nikotyny (Tabela 12). Najważniejszą cechą predykcyjną była zmiana ΔHR .

Tabela 12. Porównanie wydajności modeli (dokładność, AUC, log-loss) [A11]

Model	Dokładność (%)	AUC
Regresja logistyczna	71,67%	0,681
Drzewa decyzyjne	75,00%	0,75

Autorzy zwracają uwagę na istotne różnice nie tylko między palaczami a niepalącymi, ale również między użytkownikami e-papierosów a osobami całkowicie wolnymi od nikotyny. Choć grupa ECIG wykazywała parametry pośrednie, niektóre z nich – jak czas powrotu do normy czy spadek saturacji – zbliżały się bardziej do wartości notowanych u palaczy tradycyjnych niż u grupy kontrolnej, co może wskazywać na ukryte efekty fizjologiczne aerozolu nikotynowego, mimo braku udziału substancji smolistych. Dodatkowo, ΔHR jako jedyny parametr wykazał istotną korelację

z czasem regeneracji ($r = 0,264$, $p = 0,0417$), co potwierdza jego wartość jako biomarkera obciążenia autonomicznego. Do ograniczeń badania autorzy zaliczają jego przekrojowy charakter, ograniczoną liczebność grupy oraz brak pomiarów biochemicznych (np. stężenia kotyniny). Mimo to, praca dostarcza ważnych dowodów na obecność możliwych subklinicznych zaburzeń układu krążeniowo-oddechowego u młodych użytkowników nikotyny i wskazuje na potencjał metod integrujących dane multimodalne w analizie fizjologicznej.

2.15. Podsumowanie

Prezentowana rozprawa doktorska, oparta na cyklu jedenastu publikacji naukowych, stanowi interdyscyplinarną i wielopoziomową analizę wpływu palenia papierosów elektronicznych i tradycyjnych na organizm człowieka, ze szczególnym uwzględnieniem funkcjonowania układu oddechowego, sercowo-naczyniowego oraz aspektów metabolicznych i posturo-motorycznych. Przeprowadzone badania ukazują złożoność fizjologicznej odpowiedzi organizmu na ekspozycję na nikotynę i związki towarzyszące – zarówno pochodzące z dymu papierosowego, jak i z aerozolu generowanego przez urządzenia elektroniczne. Praca obejmowała kolejno: ocenę składu chemicznego aerozolu, opracowanie i walidację modeli matematycznych, analizę efektywności różnych interwencji zdrowotnych, a także eksperymenty z udziałem ludzi – w tym testy stabilometryczne, wysiłkowe, pomiary metaboliczne oraz rejestrację sygnałów biomedycznych. Integracja tak zróżnicowanych metod pozwoliła na dogłębną analizę różnic między użytkownikami papierosów tradycyjnych i elektronicznych oraz osobami niepalącymi, zarówno w wymiarze molekularnym, fizjologicznym, jak i behawioralno-społecznym.

Wyniki wskazują, że mimo braku procesów spalania, stosowanie papierosów elektronicznych wiąże się z ekspozycją na metale ciężkie (pochodzące z elementu grzałki), niekorzystnym wpływem na reakcję sercowo-naczyniową organizmu, a w przypadku użytkowników dualnych – również z pogorszeniem profilu metabolicznego. Jednocześnie wykazano, że reakcje organizmu na e-papierosy różnią się jakościowo od tych wywoływanych przez papierosy tradycyjne, co potwierdza konieczność odrębnego traktowania tych form ekspozycji w badaniach populacyjnych i klinicznych. Opracowane modele matematyczne oraz metody analizy danych mogą być użyteczne nie tylko w badaniach naukowych, ale także jako narzędzia wspierające decyzje w obszarze polityki zdrowotnej, profilaktyki uzależnień oraz indywidualizacji terapii antynikotynowej. Badania populacyjne dostarczyły także danych na temat psychospołecznych i środowiskowych uwarunkowań palenia, co ułatwia identyfikację grup ryzyka i projektowanie celowanych interwencji edukacyjnych.

Całość pracy podkreśla znaczenie podejścia integrującego wiedzę z zakresu inżynierii biomedycznej, fizjologii, zdrowia publicznego i nauk społecznych. Uzyskane wyniki stanowią istotny wkład w rozwój interdyscyplinarnych metod oceny ryzyka zdrowotnego związanego z używaniem produktów nikotynowych nowej generacji. Wskazują one również na potrzebę kontynuacji badań długoterminowych, obejmujących zarówno skutki zdrowotne, jak i efektywność interwencji prewencyjnych i leczniczych w populacji młodych dorosłych. Oryginalność rozprawy polega na zestawieniu danych biologicznych i społecznych z zaawansowanymi narzędziami obliczeniowymi oraz sztuczną inteligencją, co pozwoliło na uchwycenie złożonych mechanizmów uzależnienia i jego konsekwencji. Wkład naukowo-badawczy obejmuje zarówno opracowanie nowych modeli matematycznych i symulacyjnych, jak i przeprowadzenie badań z udziałem ludzi, których wyniki posłużyły do walidacji zaproponowanych rozwiązań. Tym samym rozprawa nie tylko wnosi nowe dane empiryczne, ale także dostarcza narzędzi możliwych do praktycznego zastosowania w polityce zdrowotnej i profilaktyce uzależnień. Podsumowując, cel badawczy przedstawiony w niniejszej rozprawie został osiągnięty, a hipotezy badawcze potwierdzone w postaci prezentowanego cyklu publikacji.

3. Poszerzone streszczenie w języku angielskim

3.1. Introduction

Tobacco smoking has remained one of the leading causes of premature death worldwide for several decades. Statistics indicate that this habit is responsible for the deaths of more than 8 million people each year [1]. Cigarette smoke contains thousands of toxic compounds, resulting in smokers living on average approximately 10 years less than non-smokers [2]. In view of the widespread awareness of the harmful effects of smoking, recent years have seen a growing popularity of electronic cigarettes (so-called e-cigarettes) – devices that deliver nicotine in the form of an aerosol without the process of tobacco combustion. Marketed as a potentially less harmful alternative to conventional cigarettes, e-cigarettes raise hopes among some smokers for reducing the health risks associated with the habit. At the same time, however, concerns and controversies have emerged regarding their safety and long-term impact on the human body [3]. Electronic cigarettes are devices that heat solutions containing nicotine and deliver it to the body via inhalation. In Polish, the expressions “smoking e-cigarettes” and “e-cigarette smokers” are commonly used; bearing in mind the above definition, these terms may be used interchangeably in this dissertation for linguistic fluency and do not reflect any lack of knowledge on the part of the doctoral candidate.

In Poland, it is estimated that approximately one-quarter of adults still smoke traditional cigarettes, while a few percent of this group report regular use of e-cigarettes [4]. Particularly concerning is the popularity of these products among adolescents. According to the Global Youth Tobacco Survey, although the number of underage cigarette smokers in Poland has decreased in recent years, a substantial proportion of young people have experimented with e-cigarettes [5]. Similar trends are observed in other countries – for example, in the United States in 2018, the prevalence of e-cigarette use among high school students exceeded 20% [6]. The increasing availability of appealingly flavored nicotine cartridges and aggressive marketing have contributed to the perception of e-cigarettes as a fashionable accessory among teenagers and so-called young adults. The most recent phenomenon is the rapid surge in the popularity of disposable e-cigarettes, a trend that is also evident in the Polish market [7].

The harmful impact of cigarette smoking on health has been unequivocally confirmed in both epidemiological and experimental studies. Conventional cigarettes contribute to the development of numerous multi-organ diseases, and smoking is considered the most important preventable cause of premature death [1, 2]. Tobacco smoking is the primary cause of lung cancer – it is estimated that 80–90% of cases of this malignancy are associated with exposure to tobacco smoke – and it also increases the risk of developing many other cancers, including those of the oral cavity, pharynx, esophagus, larynx, pancreas, bladder, and kidneys [2, 16]. Long-term smoking additionally leads to respiratory diseases such as chronic bronchitis and emphysema, which together constitute chronic obstructive pulmonary disease (COPD). Smokers are also more likely to suffer from bronchial asthma, experience exacerbated symptoms, and show a higher incidence of respiratory tract infections such as pneumonia [2, 9]. Moreover, substances present in tobacco smoke – including carbon monoxide and nicotine – damage the cardiovascular system, increasing the risk of atherosclerosis, coronary heart disease, myocardial infarction, and stroke, even when smoking as few as several cigarettes per day [2, 8]. Smoking also contributes to the development of other conditions: it promotes the occurrence of peptic ulcer disease, increases the risk of type 2 diabetes, and exacerbates chronic

inflammatory disorders such as rheumatoid arthritis. In women, smoking more frequently leads to pregnancy complications, including low birth weight of newborns, whereas in men it is associated with a higher incidence of erectile dysfunction and reduced fertility [8, 9]. The negative consequences affect not only active smokers but also those in their environment. Passive smoking – inhalation of cigarette smoke by non-smokers – likewise causes a range of diseases (including heart disease and lung cancer) and is responsible for approximately 1.2 million deaths annually worldwide [1]. As stated in the report of the U.S. Surgeon General, there is no safe level of exposure to tobacco smoke – even short-term exposure can induce biological damage leading to disease [10]. For this reason, eliminating tobacco smoke from the environment remains a key public health objective.

The fundamental difference between a traditional cigarette and an e-cigarette lies in the way nicotine is released. In a tobacco cigarette, dried tobacco is burned, producing smoke containing thousands of chemical compounds. In an e-cigarette, on the other hand, a liquid solution (known as e-liquid, usually based on propylene glycol and glycerin) is heated electrically, creating an aerosol that is inhaled by the user. Tobacco smoke contains over 7,000 different chemicals, of which about 70 are proven carcinogens [11, 12]. Key ingredients include nicotine, an alkaloid responsible for the addictive effects of tobacco and stimulation of the nervous system [13]. Nicotine itself is not a carcinogen, but it contributes to the development of cardiovascular diseases, among other things by accelerating the heart rate and increasing blood pressure, and to the development of addiction. Another important component is tar – a sticky mixture of compounds formed during combustion, containing, among others, polycyclic aromatic hydrocarbons (PAHs) and nitrosamines, many of which, such as benzo[a]pyrene, are carcinogenic [12, 14]. Smoke also contains carbon monoxide, a toxic gas produced by incomplete combustion, which, when absorbed into the blood, binds to hemoglobin, reducing tissue oxygenation and contributing to the development of atherosclerosis and heart disease, as well as a decline in physical condition. In addition, there are irritating and toxic gases such as formaldehyde, hydrogen cyanide, ammonia, and nitrogen oxides, which damage the mucous membranes of the respiratory tract and impair the lungs' defense mechanisms [8, 14]. Cigarette smoke also contains heavy metals such as cadmium, lead, arsenic, and chromium, which accumulate in the body and can cause organ damage and have carcinogenic effects [12, 14]. In addition, there are fine particulate matter – soot and ash particles with a diameter of less than 2.5 μm ($\text{PM}_{2.5}$) – which penetrate deep into the respiratory tract, causing chronic inflammation and oxidative stress in the lungs [15].

In the case of e-cigarette aerosol, its composition is significantly less complex than that of cigarette smoke and lacks many of the toxins typically generated during combustion; however, it is not entirely harmless to health. It contains nicotine, which is present in e-liquids at various concentrations (e.g., 3–24 mg/mL, and in disposable e-cigarettes even above 20 mg/mL). Nicotine aerosol from an e-cigarette delivers amounts of this alkaloid comparable to those from a conventional cigarette, which is sufficient to induce and maintain addiction [16, 17]. Propylene glycol and vegetable glycerin, which constitute the base of the e-liquid, produce a visible aerosol (the so-called “cloud”) when heated. On their own, they are considered relatively safe for short-term inhalation, although at high temperatures they may partially degrade into irritating aldehydes. Flavoring agents added to e-liquids (e.g., fruit, mint, dessert flavors) are compounds approved for ingestion; however, their effects on the respiratory tract after heating and inhalation are largely unknown. The aerosol also contains toxic carbonyl compounds, such as formaldehyde, acetaldehyde, and acrolein, whose concentrations are typically several dozen times lower than in cigarette smoke, although their levels may increase under higher coil power settings and intensive use (the so-called “dry puff”) [19–21]. Trace amounts of certain carcinogenic compounds, such as tobacco-specific nitrosamines and

acrylonitrile, have also been detected in e-cigarette aerosol, although their levels are significantly lower than in cigarette smoke [19, 22]. Studies have further demonstrated the presence of heavy metals and metallic particles originating from the coil and metallic components of the device, such as lead, chromium, nickel, tin, and manganese – whose concentrations may exceed those found in ambient air [23, 24]. Chronic inhalation of these metals may lead to lung tissue damage and their accumulation in organs. The dense aerosol cloud can markedly increase PM_{2.5} particle concentrations indoors, raising concerns about potential consequences for bystanders [15, 25]. An additional potential hazard is posed by compounds such as diacetyl, present in certain flavorings (e.g., buttery or vanilla), which can cause severe bronchiolar damage (so-called “popcorn lung”) with chronic inhalation. Diacetyl has been detected in the liquids and aerosol of some flavored e-cigarettes, and although its concentration in e-cigarettes is generally lower than in cigarette smoke, its presence constitutes a potential risk to users [26].

In summary, compared with tobacco smoke, e-cigarette aerosol contains substantially lower amounts of polycyclic aromatic hydrocarbons, carbon monoxide, and nitrosamines, resulting in reduced exposure to many classical carcinogenic and toxic agents [18, 19, 27]. This constitutes an important argument put forward by proponents of e-cigarettes, who suggest their reduced harmfulness. On the other hand, e-cigarettes do not deliver “pure” nicotine alone – the user inhales a mixture of chemical compounds, some of which, even though present at lower concentrations than in conventional cigarettes, may still exert adverse effects on the body. Furthermore, the composition of the aerosol strongly depends on the device design and usage patterns – intensive puffing at high coil temperatures can substantially increase the amount of harmful products formed during the thermal decomposition of the e-liquid [20, 21]. The following sections discuss the health effects associated with exposure to the aforementioned substances during both active and passive smoking, as well as e-cigarette use.

Although e-cigarettes have been present on the market for a relatively short time (with mass sales beginning in the second half of the 2000s), researchers have already gathered substantial data on their effects on the human body. Many e-cigarette users report airway irritation, chronic cough, increased hoarseness, or wheezing. Survey-based and clinical studies confirm that individuals who use e-cigarettes experience such symptoms more frequently compared with non-users [28, 29]. In 2019, global attention was drawn to a series of acute lung injury cases referred to as EVALI (e-cigarette or vaping product use-associated lung injury). In the United States, more than 2,800 hospitalizations were reported due to severe lung injury associated with e-cigarette use, several dozen of which resulted in patient death [20]. The investigation revealed that most of these cases were linked to the inhalation of illicit liquids containing THC and vitamin E acetate; however, the very occurrence of EVALI highlighted the potential of e-cigarettes to cause acute, life-threatening pulmonary complications. There is also evidence that nicotine aerosol may adversely affect the respiratory tract: laboratory experiments have shown that exposing lung epithelial cells to e-cigarette condensate causes DNA damage and impairs genetic material repair mechanisms [30], which may promote the initiation of carcinogenesis. Indeed, in an animal model study, long-term inhalation of nicotine aerosol by mice resulted in the development of neoplastic lesions in their lungs [31]. Moreover, e-cigarettes appear to trigger an inflammatory response in the respiratory system – an increased production of pro-inflammatory cytokines has been observed in bronchial epithelial cells exposed to aerosol, persisting even after cessation of exposure [32]. In a cohort study among young adults in the United States, initiation of e-cigarette use was found to significantly increase the risk of chronic respiratory symptoms (such as wheezing and chronic cough), even among individuals who had never previously smoked conventional cigarettes [33]. These findings suggest that regular e-cigarette use may lead to

respiratory problems similar to those observed in tobacco smokers, although the underlying mechanisms may differ in part.

The emergence of e-cigarettes has sparked a debate regarding their role in public health. According to the harm reduction concept, if some smokers are unable to completely cease nicotine use, switching from conventional cigarettes to a less harmful source of nicotine could bring benefits in the form of reduced incidence of smoking-related diseases [34]. E-cigarettes deliver nicotine without most of the toxins produced by tobacco combustion and therefore should, in theory, be less hazardous to health than cigarettes. Indeed, studies have shown that individuals who completely replaced conventional cigarettes with electronic ones have significantly lower concentrations of biomarkers of exposure to tar substances and carcinogens (e.g., NNAL-a metabolite of tobacco-specific nitrosamines) compared with those who continue smoking regular cigarettes [17]. In a controlled clinical trial involving African American and Latino smokers, switching to POD-type (Personalized On Demand) e-cigarettes with refillable nicotine cartridges for several weeks resulted in a substantial reduction in levels of toxic compounds in the body compared with the group that continued tobacco smoking [17]. Furthermore, some studies suggest that e-cigarettes may aid in smoking cessation. In England, a temporal association was observed: the rise in e-cigarette popularity in the population correlated with an increase in the proportion of smokers attempting to quit and with improved quit success rates, which may indicate that some smokers successfully broke their addiction thanks to the alternative offered by e-cigarettes [35]. Meta-analyses of randomized controlled trials also provide some evidence of efficacy – in a 2018 review, the use of nicotine-containing e-cigarettes was associated with a higher proportion of individuals abstinent from tobacco smoking at 6–12 months compared with control groups (e.g., using placebo or other methods) [36]. Earlier analyses (including the 2014 Cochrane review) had already noted that e-cigarettes may help some smokers reduce or temporarily abstain from cigarette use, although they emphasized the limited number of studies and the need for further evidence [37].

On the other hand, many experts draw attention to the potential risks associated with promoting e-cigarettes as a smoking cessation aid. First and foremost, some observational studies suggest that smokers who concurrently use e-cigarettes do not quit smoking more often than those who do not use them – and some analyses have even indicated lower smoking cessation rates among e-cigarette users compared with non-users (possibly because e-cigarettes allow them to maintain their nicotine addiction) [38]. Dual use may give smokers a false sense of harm reduction, while they remain exposed to cigarette toxins, merely supplemented by exposure to e-cigarette aerosol [39]. Furthermore, there is concern that the easy availability of e-cigarettes may undermine long-standing efforts to denormalize smoking – the younger generation, which is more likely to take up e-cigarette use, may in the future partially transition to conventional cigarette smoking or remain lifelong nicotine-dependent in any form [40]. This “gateway effect” raises considerable concern: according to the aforementioned meta-analysis, adolescents who use e-cigarettes are several times more likely to initiate conventional cigarette smoking in the following years [40]. From a public health perspective, the net benefits of e-cigarettes may therefore be offset or even outweighed by the losses if widespread nicotine addiction develops among new groups of individuals who otherwise would not have become smokers.

Renowned institutions analyzing the issue have issued cautious recommendations. The 2018 report of the U.S. National Academies of Sciences, Engineering, and Medicine (NASEM) concluded that e-cigarettes expose users to substantially fewer harmful substances than conventional cigarettes, suggesting a potentially lower risk for an individual who completely switches from smoking to using

e-cigarettes. At the same time, however, the report emphasized strong evidence that e-cigarette use increases the risk of initiating tobacco smoking among adolescents and young adults, and that the evidence for their effectiveness in achieving sustained smoking cessation is moderate [41]. In other words, the overall impact of e-cigarettes on public health depends on the extent to which they help current smokers quit versus the extent to which they contribute to the nicotine dependence of new users. Simulation models yield divergent results – for example, one analysis estimated that the introduction of e-cigarettes could ultimately increase the number of smoking-attributable deaths when the effect on smoking initiation among young people is taken into account [42], whereas other modeling suggests the possibility of harm reduction, provided that the prevalence of e-cigarette use among non-smokers and youth is minimized [43].

Considering both the unequivocal harmfulness of tobacco smoking and the uncertainty regarding the long-term effects of e-cigarette use, health authorities worldwide have undertaken a variety of regulatory and preventive measures. In the domain of traditional tobacco products, most countries have implemented proven interventions: bans on smoking in public places, high taxation of cigarettes, restrictions on advertising and sales, and educational campaigns. These classic measures have yielded tangible results – for example, increasing excise taxes, and thus the retail price of cigarettes, is considered one of the most effective tools for reducing smoking prevalence at the population level [44]. Youth access to cigarettes has also emerged as a crucial issue: in many countries, the minimum legal age for the sale of tobacco products has been raised to 21 years. Analyses conducted in the United States by the Institute of Medicine estimated that this measure (the so-called Tobacco 21) should substantially reduce the number of smokers among young adults and lower smoking prevalence in the overall population [45]. Survey research indicates that the majority of the public supports raising the minimum age for tobacco sales, perceiving it as an opportunity to protect youth from nicotine addiction [46].

Regulations concerning e-cigarettes are, in many respects, still in the process of development. In the European Union, measures have been introduced such as limiting the maximum nicotine concentration in e-liquids to 20 mg/mL and extending the ban on sales to minors to include these products, in line with conventional cigarettes. In Poland, since 2016, it has been prohibited to sell e-cigarettes to individuals under 18 years of age, to advertise them, and to use them in public spaces previously covered by anti-smoking legislation (e.g., schools, government offices, public transport). Nevertheless, enforcement of these regulations can be challenging – studies indicate that some users continue to use e-cigarettes in public spaces despite existing bans, and monitoring such behavior is complicated by the more discreet nature of e-cigarettes (no smoke, less odor) [47]. In response to the growing number of young users, some countries (e.g., the United States, Canada) have introduced additional restrictions, such as bans on the sale of flavored e-liquids deemed particularly attractive to youth.

Some experts have suggested that, in the future, consideration should be given to the complete removal from the market of both conventional cigarettes and alternative nicotine products. The argument is that there is no justification for maintaining the availability of an extremely harmful product (cigarettes) if lower-risk forms of nicotine delivery are available – although, on the other hand, permitting them without restrictions could lead to the aforementioned new risks [48]. It is clear that nicotine policy must strike a balance between two objectives: the maximum protection of non-smokers and youth from addiction, and the support of dependent smokers in reducing harm or quitting altogether. In many countries, including Poland, revenues from taxes and excise duties on nicotine products, including electronic cigarettes, constitute a significant portion of state budget

income. For this reason, the complete prohibition of their sale is currently unrealistic, and the only feasible option remains the increase of excise rates or other fiscal burdens.

In addition to legal regulations, educational and medical interventions are of key importance. Healthcare professionals play a vital role in motivating smokers to attempt quitting and in informing them about the risks associated with various forms of nicotine consumption. Studies show that a simple physician intervention – advising smoking cessation and informing about available forms of support – significantly increases the proportion of individuals making a quit attempt [49]. Smokers should be encouraged to use evidence-based methods for tobacco dependence treatment: behavioral counseling, supportive therapies (e.g., quitlines, mobile applications), and pharmacotherapy. Available medications, such as nicotine replacement therapy (NRT) in the form of patches, gums, or lozenges, as well as prescription drugs (varenicline, bupropion), double the chances of successfully quitting compared with unaided attempts [9, 50]. In the context of e-cigarettes, medical professionals should provide balanced information: emphasize that they are not intended for non-smokers, while at the same time noting that complete switching to e-cigarettes may be less harmful for a smoker who is otherwise unable to quit. This position is shared, among others, by the American Heart Association, which in its latest statement notes that, although it does not routinely recommend e-cigarettes as a cessation method, it acknowledges that in individual cases replacing cigarettes with e-cigarettes may offer health benefits, provided that it leads to the complete abandonment of conventional smoking [51]. The Association, along with the WHO, simultaneously recommends continued research into the long-term effects of using e-cigarettes and the implementation of regulations aimed at minimizing the attractiveness of e-cigarettes to youth (e.g., restricting flavors, information campaigns about the risks) [1, 51].

The present doctoral dissertation constitutes an interdisciplinary attempt at a comprehensive assessment of the impact of conventional and electronic cigarette smoking on selected parameters of respiratory and cardiovascular function. Based on a series of eleven publications, the work integrates issues from the fields of chemical toxicology, pharmacokinetics, clinical physiology, biomedical engineering, mathematical modeling, and artificial intelligence methods. Such a broad approach has enabled the acquisition of complementary data encompassing both the analysis of the composition and toxicity of aerosol emitted by e-cigarettes, predictive modeling of nicotine kinetics in the body, and the population-level effects of nicotine product use. An important component of the dissertation also includes experimental studies involving human participants, in which actual changes in biological signals – such as ECG recordings, stabilometric assessment, blood pressure, oxygen saturation, and respiratory rate – were evaluated in conventional cigarette smokers, e-cigarette users, and non-smokers. This allowed not only the identification of physiological differences between the groups, but also the contextualization of these findings within mathematical models describing nicotine's mechanisms of action, as well as predictions concerning the effectiveness of public health interventions.

3.2. Research objective

The observed need for an in-depth assessment of the health effects of new forms of nicotine consumption, including electronic cigarettes, combined with the limited existing possibilities for an objective comparative analysis of their impact on the human body using multimodal data, prompted the author to undertake interdisciplinary research. The objectives of this research included:

- Development and application of physiologically based pharmacokinetic (PBPK) models enabling comparison of the dynamics of absorption, distribution, and elimination of nicotine from e-cigarettes and conventional cigarettes.
- Analysis of the chemical composition of aerosol and tobacco smoke, including the content of heavy metals and carbonyl compounds, and evaluation of their potential toxicological effects.
- Experimental recording of biomedical signals (including cardiological, metabolic, and stabilometric signals) in young adult users of nicotine products and comparison with a control group.
- Application of advanced data analysis methods, including machine learning, to identify diagnostic features and patterns of physiological responses differentiating the study groups.
- Assessment of the impact of chronic nicotine use in various forms on cardiovascular, respiratory, metabolic, and motor functions – from the perspective of preventing lifestyle-related diseases.

This doctoral dissertation summarizes the results of experimental and modeling studies aimed at a comprehensive assessment of the health risks associated with the use of nicotine products, as well as the development of tools enabling more effective monitoring of their impact through physiological data, computational models, and artificial intelligence methods. The novelty of the work lies in the integration of empirical population studies, including biomedical signal recordings, metabolic assessments, and psychosocial analyses, with simulation models (PBPK, Markov, SIQ+P+E+H+X) and artificial intelligence algorithms. Such an approach, considering the differences between e-cigarettes and traditional cigarettes in chemical, physiological, metabolic, and neuromotor perspectives, has not been widely applied to date. The scientific and research component of the dissertation includes the development and validation of physiologically based pharmacokinetic models of nicotine, the design of models describing addiction dynamics and the effectiveness of public health policies, the conduct of experimental studies involving human participants, as well as the implementation of machine learning methods for the identification of diagnostic features and the integration of results into decision support systems.

In the first stage of the research, the focus was placed on characterizing the chemical composition of the aerosol generated by electronic cigarettes. In study [A1], an analysis of elemental composition was conducted, revealing the presence of heavy metals such as tin, nickel, and chromium, originating from the device's heating coil. The observed concentrations of these substances – depending on usage conditions – could reach levels comparable to those in cigarette smoke. These findings formed the basis for further toxicological and pharmacokinetic analyses. In the next step, PBPK pharmacokinetic models were developed and validated to describe the fate of nicotine in the bodies of electronic and conventional cigarette users. Study [A2] presented a hybrid PBPK model enhanced with artificial intelligence components, whereas [A3] extended it by incorporating clinical variables that account for different physiological states, such as obesity, metabolic disorders, or

cardiovascular disease. These models enabled quantitative assessment of differences in nicotine bioavailability and distribution depending on the delivery method and the user's health status. In parallel, research was conducted on the coil degradation process of e-cigarettes under real-world conditions. In study [A4], a computational model was developed to simulate the material and thermal changes occurring during device use. The influence of alloy type, temperature, and airflow on the emission of metal particles was considered, providing better insight into the mechanisms of toxin generation. Based on the results of these analyses, decision support systems for smoking cessation were developed. Study [A5] presented a recommendation algorithm based on the Multi-MOORA method and supported by artificial intelligence, designed to evaluate the effectiveness, cost, and acceptability of different strategies (pharmacotherapy, NRT, e-cigarettes). Subsequently, in study [A6], a dynamic population model SIQ+P+E+H+X was proposed, integrating demographic and epidemiological data to predict the effects of implementing anti-nicotine policies (e.g., tax increases, educational campaigns, or promotion of alternative products). Addiction process modeling was further developed in study [A7], in which Markov models were applied to describe transitions between the states of initiation, dependence, treatment, and abstinence. Based on literature data, probabilities of nicotine replacement therapy (NRT) effectiveness and average durations of individual addiction phases were estimated. The next stage of research was experimental and directly concerned users of nicotine products. In study [A8], an analysis was conducted of psychosocial factors influencing the choice of nicotine consumption form. Using statistical and machine learning methods, predictors of e-cigarette and conventional tobacco use were identified, such as family-related factors, peer pressure, and home environment. Study [A9] focused on the assessment of metabolic consequences of e-cigarette use and smoking. In young adults from various user groups, body composition (using bioimpedance), blood pressure, and lifestyle indicators were measured. An unfavorable metabolic phenotype was identified, including central obesity and elevated blood pressure, despite apparently normal BMI. Neuromotor functions were examined in study [A10] using stabilometry and gait analysis. Subtle balance impairments and variability in locomotor patterns were identified in nicotine product users compared with non-smokers. The final study in the series, [A11], concerned cardiovascular reactivity. During exercise and orthostatic tests, ECG parameters, blood pressure, and oxygen saturation were recorded. E-cigarette users exhibited stronger and more rapid sympathetic nervous system responses, which may indicate a higher risk of hemodynamic dysregulation.

3.3. Research hypotheses

Based on the literature review, preliminary research findings, and the interdisciplinary nature of the dissertation, the following research hypotheses were formulated:

- I. The aerosol generated by e-cigarettes contains toxic chemical compounds and heavy metals whose concentrations – depending on usage conditions – may be comparable to or higher than those in tobacco smoke [A1].
- II. The pharmacokinetics of nicotine differ significantly depending on the delivery form (tobacco smoke vs. e-cigarette aerosol), influencing the time to concentration rise, peak level, and addictive potential [A2].
- III. Health-related factors (e.g., obesity, cardiovascular diseases, metabolic disorders) affect nicotine pharmacokinetics, modifying its fate in the body and potentially exacerbating health effects [A3].
- IV. The degradation process of an e-cigarette coil, influenced by temperature, material, and airflow, affects the emission of heavy metals and increases aerosol toxicity [A4].
- V. Multi-criteria decision analysis (Multi-MOORA) supported by artificial intelligence algorithms can serve as an effective tool for assisting in the selection of smoking cessation therapy [A5].
- VI. Dynamic population modeling (SIQ+P+E+H+X) enables forecasting the impact of health policy strategies on the prevalence of smoking and e-cigarette use [A6].
- VII. Modeling the nicotine addiction process using Markov chains allows for a quantitative assessment of nicotine replacement therapy (NRT) effectiveness [A7].
- VIII. Demographic, familial, and social factors significantly influence the risk of initiating e-cigarette or conventional cigarette use, which can be demonstrated using statistical and machine learning methods [A8].
- IX. Regular e-cigarette use is associated with adverse metabolic changes, including central obesity, elevated blood pressure, and unfavorable body composition, observed even in young adults [A9].
- X. Nicotine use in various forms affects postural balance control and gait patterns, leading to measurable impairments in neuromotor function [A10].
- XI. E-cigarette users and conventional smokers exhibit distinct cardiovascular reactivity to physiological stress compared with non-smokers, which may indicate differences in sympathetic nervous system activation [A11].

3.4. Elemental Composition of Vaping and Smoking Aerosols: Influence of Liquid Type and Tank Conditions [A1]

In the present research, an attempt was made to quantitatively assess the elemental composition of aerosols generated by e-cigarettes under conditions of varying tank fill levels (full, half-full, empty) and using liquids of different origins – commercial and homemade. The aim of the study was to determine the influence of these factors on the presence of heavy metals and other elements in the aerosol, as well as to compare their content with aerosols derived from conventional cigarettes. To reproduce real-world usage conditions, a test station simulating inhalation was constructed (Figures 1 and 2). The study also compared results for smoke from conventional cigarettes. Aerosol and smoke particles were collected on nitrocellulose membranes (0.45 μm) placed in a condensation chamber; in addition, cotton from inside the heating coil was analyzed. The samples were subsequently subjected to elemental composition analysis using scanning electron microscopy (SEM) with an energy-dispersive spectrometer (EDS). The EDS method enables qualitative and semi-quantitative detection of the elements present but does not provide information on their chemical form (e.g., oxides, chlorides, complexes) or speciation, which is a significant limitation in the context of full toxicological assessment. Furthermore, the technique does not allow the analysis of volatile or gaseous components, which may also be important from a health risk perspective.



Figure 1. E-cigarette aerosol testing station [A1]



Figure 2. Conventional cigarette smoke testing station [A1]

The study identified the presence of numerous inorganic elements, of which the most toxicologically relevant included chromium (Cr), aluminium (Al), iron (Fe), nickel (Ni), copper (Cu), sodium (Na), sulfur (S), and chlorine (Cl). Their concentrations differed significantly depending on the type of liquid used and the tank fill level (Table 1). The highest relative chromium concentration was recorded for the “half-full tank + homemade liquid” configuration (6.00 wt%), while aluminium reached 1.40 wt% and iron 0.72 wt%. In the configuration using commercial liquid with the same fill level, these values were markedly lower: Cr – 4.79 wt%, Al – 0.21 wt%, Fe – 0.00 wt%. Smoke from conventional cigarettes contained only trace amounts of chromium (0.33 wt%) and aluminium (0.08 wt%), with a predominance of plant-derived minerals (e.g., calcium, sodium, sulfur). The elemental profile differed significantly – tobacco smoke aerosol was dominated by minerals naturally present in tobacco and paper, whereas e-cigarette aerosol was dominated by technical metals originating from the degradation of the device’s construction materials.

Table 1. Mean elemental concentrations in aerosols obtained during e-cigarette use (10 puffs) or combustion of one conventional cigarette [A1]

E	Homemade liquid, full tank		Homemade liquid, half tank		Homemade liquid, empty tank		Commercial liquid, full tank		Commercial liquid, half tank		Commercial liquid, empty tank		Traditional cigarette	
	wt%	SD	wt%	SD	wt%	SD	wt%	SD	wt%	SD	wt%	SD	wt%	SD
O	54.77	0.62	50.26	0.80	52.00	0.94	53.10	0.71	52.37	0.70	51.94	0.64	48.86	0.35
C	40.40	0.64	40.58	0.88	41.31	1.00	41.12	0.73	41.71	0.75	41.15	0.68	49.89	0.36
Cr	3.84	0.95	6.00	0.97	5.33	0.83	4.81	0.90	4.79	0.86	5.48	0.79	0.33	0.03
Na	0.33	0.03	0.32	0.03	0.35	0.05	0.36	0.04	0.36	0.04	0.38	0.04	0.24	0.03
Al	0.36	0.03	1.40	0.06	0.34	0.04	0.26	0.03	0.21	0.03	0.22	0.03	0.08	0.01
S	0.12	0.02	0.20	0.03	0.10	0.02	0.15	0.02	0.22	0.03	0.22	0.03	0.12	0.02
Cl	0.09	0.02	0.17	0.04	0.12	0.02	0.08	0.02	0.08	0.02	0.14	0.03	0.08	0.02
Si	0.04	0.01	0.12	0.02	0.25	0.03	0.02	0.00	0.07	0.02	0.22	0.02	0.15	0.02
Mg	0.00	0.00	0.04	0.01	0.20	0.04	0.01	0.00	0.02	0.00	0.16	0.02	0.11	0.01
Fe	0.00	0.00	0.72	0.15	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Cu	0.07	0.02	0.06	0.02	0.00	0.00	0.04	0.01	0.04	0.01	0.04	0.00	0.07	0.02
Ca	0.00	0.00	0.00	0.00	0.00	0.00	0.05	0.02	0.02	0.00	0.05	0.01	0.05	0.01
Br	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.01

Viscosity analysis (Figure 3) revealed clear differences in the behavior of homemade and commercial liquids. Initially, homemade liquids exhibited higher dynamic viscosity (~0.2848 Pa·s at 20.9 °C), which dropped sharply with increasing temperature, reaching ~0.0295 Pa·s at 60.5 °C. At 80 °C, a slight increase in viscosity (~0.036 Pa·s) was noted, suggesting the onset of thermal degradation. Commercial liquids showed lower initial viscosity (~0.15 Pa·s at 23.5 °C) and a more gradual decrease with temperature, reaching ~0.025 Pa·s at 80 °C. These results indicate greater thermal stability of commercial liquids, which retain more predictable physical properties over a wider temperature range. This was also confirmed by shear stress measurements – homemade liquids reached approximately 56–57 Pa at a shear rate of ~200 s⁻¹, whereas commercial liquids reached ~30–34 Pa. Such differences directly affect vaporization efficiency and temperature control during device operation. Reduced thermal stability of homemade liquids may promote the occurrence of “dry

puff” conditions, i.e., overheating of the heating coil at low liquid levels, leading to erosion of metallic elements and increased heavy metal content in the aerosol.

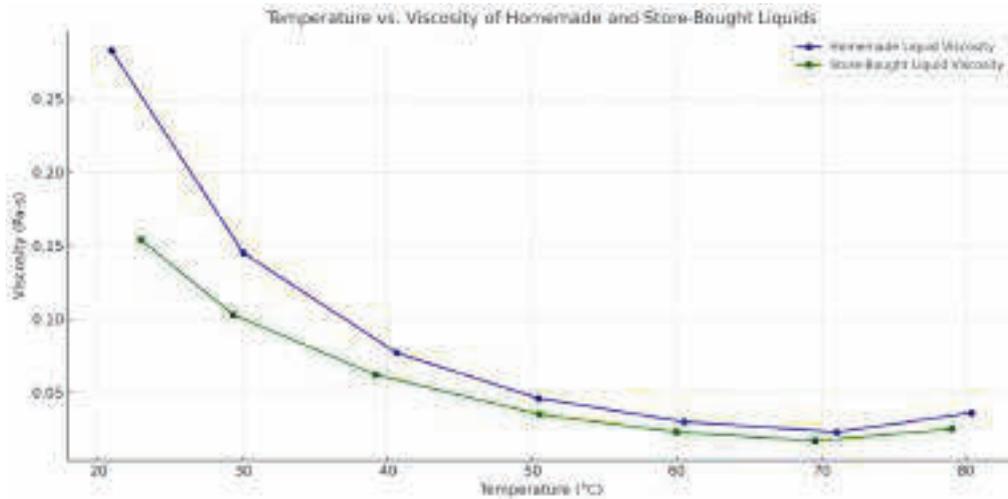


Figure 3. Changes in dynamic viscosity of homemade and commercial liquids as a function of temperature [A1]

To complement the analysis of the physical properties of the liquids, temperature measurements (Figure 4) inside the tank during simulated device use were also conducted. The tests showed that homemade liquids reached higher initial temperatures and heated faster than commercial liquids, which can be attributed to their simplified chemical composition and lack of stabilizing additives. Despite these differences, under steady-state test conditions, the temperature of both liquid types stabilized at approximately 40 °C. These findings indicate a significant influence of liquid composition on the thermal characteristics of device operation, particularly in the initial phase, which may be relevant to the processes of metal emission from heating elements.

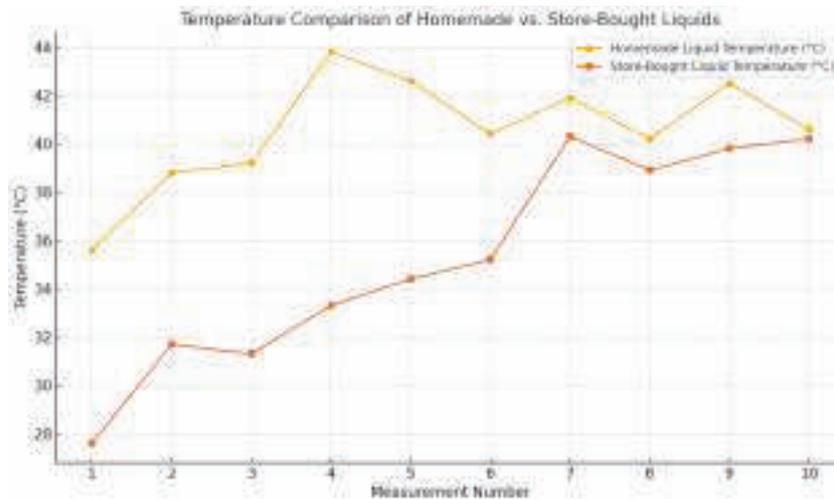


Figure 4. Temperature changes inside the e-cigarette tank during simulated use, for homemade and commercial liquids [A1]

The obtained results clearly indicate that not only the composition of the liquid but also the manner of device use have a critical impact on the composition of the inhaled aerosol. In many cases, heavy metal concentrations approached or even exceeded the threshold levels specified by WHO

guidelines, particularly under “empty” tank conditions and high operating temperatures. It should be emphasized that the EDS method is semi-quantitative in nature and does not allow for unambiguous determination of concentrations with reference to toxicological standards. The actual health risk also depends on the bioavailability of the elements, the frequency of device use, and the co-occurrence of other contaminants, which warrants further, more detailed studies. This work makes a significant contribution to the toxicological characterization of e-cigarettes and underscores the need for standardization of both liquid composition and device technical parameters. The identified risks should be taken into account in the development of safety guidelines for e-cigarette use, as well as in legal regulations concerning their production and distribution.

3.5. Comparative Pharmacokinetics of Nicotine from E-Cigarettes and Traditional Cigarettes: A PBPK Modeling and Machine Learning Approach [A2]

As part of the conducted research, a physiologically based pharmacokinetic (PBPK) model, supported by machine learning algorithms, was developed to compare the dynamics of nicotine absorption and distribution in the body following the use of e-cigarettes and conventional cigarettes. The aim of the study was to investigate differences in nicotine delivery and to assess their impact on systemic exposure – particularly with respect to the brain and synapses – as well as to identify physiological factors significantly influencing the rate and extent of nicotine accumulation. The designed PBPK model comprised five key compartments: lungs, blood, liver, brain, and synapses. For each compartment, volumes, blood flows, and diffusion, metabolism, and elimination constants were defined. The equations were based on the principle of mass balance, Fick's law, and first-order kinetics for metabolism and elimination, enabling dynamic simulation of nicotine concentrations over a 24-hour period, taking into account real-world patterns of nicotine product use (10 puffs per session, 20 sessions per day for e-cigarettes; 1.5 mg vs. 3 mg of nicotine per session, respectively). PBPK pharmacokinetic equations:

1. Nicotine concentration in lungs:

$$\frac{dC_{lung}}{dt} = \frac{dose}{V_p} - \frac{Q_p}{V_p} (C_{lung} - C_{blood})$$

2. Nicotine concentration in blood:

$$\frac{dC_{blood}}{dt} = \frac{Q_p}{V_b} (C_{lung} - C_{blood}) - \frac{Q_h}{V_b} (C_{blood} - C_{liver}) - k_{distrib} C_{blood} - k_{penetr} C_{blood} + k_{elim} C_{brain}$$

3. Nicotine concentration in liver:

$$\frac{dC_{liver}}{dt} = \frac{Q_h}{V_l} (C_{blood} - C_{liver}) - k_{metab} C_{liver}$$

4. Nicotine concentration in brain:

$$\frac{dC_{brain}}{dt} = k_{penetr} C_{blood} - k_{elim} C_{brain} - k_{synapse} C_{brain} + k_{synapse} C_{synapse}$$

5. Nicotine concentration in synapses:

$$\frac{dC_{synapse}}{dt} = k_{synapse} C_{brain} - k_{synapse} C_{synapse}$$

where: C_{lung} – nicotine concentration in the lungs, C_{blood} – nicotine concentration in the blood, C_{liver} – nicotine concentration in the liver, C_{brain} – nicotine concentration in the brain, $C_{synapse}$ – nicotine concentration in the synapses, Q_p – blood flow through the lungs, Q_h – blood flow through the liver, V_p , V_b , V_l – compartment volumes: lungs, blood, liver, $k_{distrib}$ – nicotine distribution rate from blood to other tissues, k_{penetr} – nicotine penetration rate from blood to the brain, k_{elim} – elimination rate of nicotine from the brain, k_{metab} – nicotine metabolism rate in the liver, $k_{synapse}$ – transfer rate of nicotine between the brain and synapses, dose – nicotine dose delivered in a single session.

Modeling revealed marked differences in pharmacokinetic profiles between the examined products (Figure 5). Conventional cigarettes generated rapid and sharp nicotine concentration peaks in

the brain and blood (C_{max}: 15–20 ng/mL; T_{max}: 5–15 min), typical of a strong addictive effect. E-cigarettes exhibited flatter but more prolonged concentration profiles (C_{max}: 6–10 ng/mL; T_{max}: 2–5 min), suggesting a different mechanism of dependence development. In synapses, C_{max} values were 240 nM for cigarettes and 180 nM for e-cigarettes (T_{max}: 60–120 s i 60–150 s, respectively).

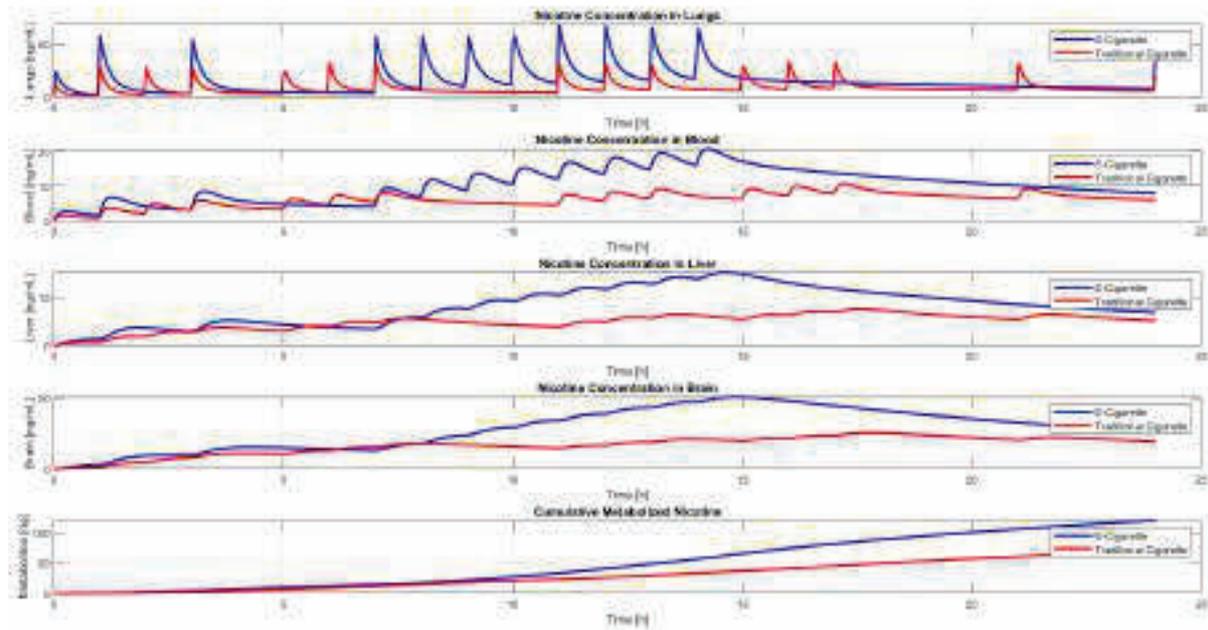


Figure 5. Changes in nicotine concentration in selected compartments (blood, brain, synapses) over 24 hours, depending on the source of exposure: e-cigarettes (blue line) and conventional cigarettes (red line) [A2]

The PBPK results were further extended with an analysis of inter-individual variability using the XGBoost algorithm, trained on 1,000 synthetic physiological profiles. The models achieved extremely high predictive accuracy, with coefficients of determination $R^2 > 0.9998$ across all compartments. The most significant factor influencing nicotine distribution was blood–brain barrier permeability (k_{penet}), with a correlation coefficient of +0.901 for the brain and +0.916 for the synapses, while its correlation with blood nicotine concentration was negative (−0.940). Other significant factors included liver metabolism rate (k_{metab} , negative correlation), pulmonary blood flow, body mass, and smoking history. For model validation, literature data on actual C_{max} i T_{max} values after nicotine inhalation were used. The models closely reproduced real pharmacokinetic profiles (Figure 6), achieving R^2 values of 0.788 (brain), 0.867 (blood), and 0.899 (synapses). Estimated nicotine concentrations for an example individual (based on personal physiological parameters) were 107.62 ng/mL in the brain, 64.45 ng/mL in the blood, and 137.31 ng/mL in the synapses. An important aspect was also the identification of limitations in the adopted assumptions. PBPK models assume averaged physiological parameters and standard usage patterns, whereas in reality there is considerable behavioral variability (e.g., depth of puff, inhalation duration, device power). Moreover, the model does not account for the effects of other components of tobacco smoke or aerosol (e.g., aldehydes, flavorings) that may modulate nicotine metabolism. There is also a limitation related to assumptions about absorption sites: for cigarettes, the lower respiratory tract (alveoli) predominates, while for e-cigarettes the upper airways and oral cavity play a larger role, potentially affecting first-pass kinetics.

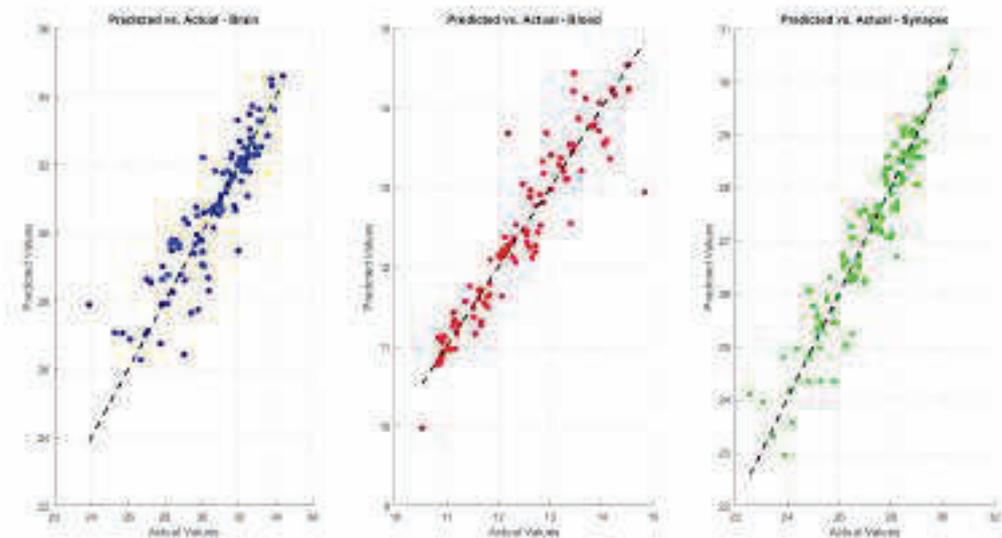


Figure 6. Comparison of nicotine concentrations predicted by the PBPK model with real-world (literature) data for three compartments: brain, blood, and synapses [A2]

This work makes a significant contribution to understanding pharmacokinetic differences between alternative nicotine delivery methods. The results have important regulatory and clinical implications. It has been shown that, despite the absence of combustion products, e-cigarettes can lead to prolonged nicotine exposure and thus potentially to dependence development. By integrating PBPK modeling with machine learning, it is possible not only to better predict exposure but also to create personalized risk models, representing a meaningful step toward precision addiction prevention and public health policy.

3.6. Physiologically-Based Pharmacokinetic Modeling of Nicotine [A3]

The next article is an extended version of the conference paper entitled “Comparative Pharmacokinetics of Nicotine from E-Cigarettes and Traditional Cigarettes: A PBPK Modeling and Machine Learning Approach”. In this study, an attempt was made to model the dynamics of nicotine distribution in the human body using a physiologically based pharmacokinetic (PBPK) modeling approach. The aim was to assess differences in the pharmacokinetic profile of nicotine delivered via e-cigarettes and conventional cigarettes, taking into account various health conditions of users – including cardiovascular diseases, asthma, and chronic obstructive pulmonary disease (COPD). Although the study was modeling-based, it relied on experimental and literature data on physiology and nicotine distribution.

The designed PBPK model included nine compartments corresponding to the major tissues involved in nicotine metabolism and distribution: lungs, arterial blood, venous blood, liver, brain, muscles, kidneys, adipose tissue, and other tissues. The model was based on first-order differential equations, with physiological parameters specified for both healthy and diseased individuals. Transport between compartments was described using perfusion-limited kinetics, consistent with the classical approach for lipophilic compounds:

$$\begin{aligned} \frac{dC_{lung}}{dt} &= \frac{Dose(t)}{V_p} - \frac{Q_p}{V_p} (C_{lung} - C_{blood}) \\ \frac{dC_{blood}}{dt} &= \frac{Q_p}{V_b} (C_{lung} - C_{blood}) - \frac{Q_h}{V_b} (C_{blood} - C_{liver}) - k_{distrib} C_{blood} - k_{penetr} C_{blood} + k_{elim} C_{brain} - \\ &\quad - k_{fat} C_{blood} + k_{release} C_{fat} - k_{eliminb} C_{blood} \end{aligned}$$

Nicotine metabolism occurred mainly in the liver, following an enzymatic degradation mechanism described by Michaelis–Menten kinetics:

$$\begin{aligned} \frac{dC_{liver}}{dt} &= \frac{Q_h}{V_l} (C_{blood} - C_{liver}) - \frac{k_{metabmax} C_{liver}}{K_m + C_{liver}} + k_{distrib} C_{blood} \\ \frac{dC_{metabolites}}{dt} &= \frac{k_{metabmax} C_{liver}}{K_m + C_{liver}} \end{aligned}$$

Nicotine crossed the blood–brain barrier, where it accumulated and underwent slow elimination:

$$\begin{aligned} \frac{dC_{brain}}{dt} &= k_{penetr} C_{blood} - k_{elim} C_{brain} \\ \frac{dC_{fat}}{dt} &= k_{fat} C_{blood} - k_{release} C_{fat} \end{aligned}$$

where: C_{lung} –nicotine concentration in the lungs, C_{blood} – nicotine concentration in the blood (arterial/venous), C_{liver} – nicotine concentration in the liver, C_{brain} – nicotine concentration in the brain, C_{fat} – nicotine concentration in adipose tissue, $C_{metabolites}$ – concentration of nicotine

metabolites, Q_p – blood flow through the lungs, Q_h – blood flow through the liver, V_p , V_b , V_l – compartment volumes: lungs, blood, liver, $k_{distrib}$ – nicotine distribution rate from blood to tissues, k_{penetr} – nicotine penetration rate from blood to the brain, k_{elim} – nicotine elimination rate from the brain, $k_{eliminb}$ – nicotine elimination rate from peripheral blood, k_{fat} – nicotine uptake rate in adipose tissue, $k_{release}$ – nicotine release rate from adipose tissue, $k_{metabmax}$ – maximum metabolic rate of nicotine in the liver (Michaelis–Menten parameter), K_m – Michaelis–Menten constant, Dose(t) – time-dependent nicotine dose, specific for product type (cigarette, e-cigarette).

The model also incorporated product-specific variables, such as route of administration, absorption rate, puff volume, and bioavailability.

Modeling results revealed substantial differences in nicotine concentration dynamics depending on health status (Table 2). Under normal conditions, steady-state plasma nicotine concentration (Css) was 7.01 ng/mL for conventional cigarettes and 4.08 ng/mL for e-cigarettes. In patients with COPD and asthma, elimination rates were reduced, leading to elevated Css values (e.g., 5.05 ng/mL for e-cigarettes) and prolonged half-life (t1/2). In individuals with cardiovascular diseases, Css in the brain was higher for e-cigarettes (16.32 ng/mL), suggesting increased CNS exposure and higher addiction risk.

Table 2. Summary of nicotine pharmacokinetics in various health conditions [A3]

Health condition	Css brain (ng/mL) (E-cigarette)	Css brain (ng/mL) (cigarette)	Css blood (ng/mL) (E-cigarette)	Css blood (ng/mL) (cigarette)	t1/2 (h) (E-cigarette)	t1/2 (h) (cigarette)
Healthy	11.00	18.64	4.08	7.01	0.96	0.96
Liver disease	24.74	3.40	9.18	1.41	0.98	0.98
Cardiovascular disease	16.32	6.89	6.10	2.74	1.12	1.12
Obesity	21.41	15.38	7.64	5.79	1.12	1.12
Pulmonary disease	13.06	2.91	5.05	1.02	1.03	1.03
Neurological disorders	4.69	9.52	0.98	2.02	1.33	1.34

The model was validated against literature data and demonstrated good agreement with actual nicotine concentrations in different compartments, for both e-cigarettes and conventional cigarettes. This agreement was particularly evident in comparisons of time–concentration profiles in plasma and brain, accounting for different health conditions. A sensitivity analysis indicated that the key variables influencing the pharmacokinetic profile were: hepatic blood flow, hepatic metabolic rate, blood–brain barrier permeability, and the storage/release capacity of nicotine in adipose tissue. It is important to note that the model was based on population-level physiological parameters and did not account for individual genetic differences in metabolism. Potential interactions with other aerosol components (e.g., aldehydes, flavorings) that might affect nicotine bioavailability and metabolism were also not

included. Another limitation was the standardization of the usage pattern, which may not reflect actual exposure in heavy or occasional users.

The study conclusions highlight the complex impact of health status on nicotine pharmacokinetics and the need for individualized risk assessment. The findings may be particularly useful in harm reduction strategy design and for clinicians assessing the safety of e-cigarette use in patients with chronic diseases. This work demonstrates the potential of PBPK modeling as a tool for evaluating nicotine products in the context of public health and regulatory decision-making.

3.7. A Computational Model of E-Cigarette Coil Degradation: Simulating Thermal and Material Dynamics and Their Impact on Health [A4]

In the present study, a numerical model of e-cigarette coil degradation under realistic usage conditions was proposed and implemented. The aim was to determine how coil material (NiCr alloy, Kanthal, stainless steel, titanium), airflow conditions, and power settings influence thermal characteristics, resistance changes, and wick degradation. The analysis was carried out in the context of potential health risks arising from the emission of thermal decomposition products of metals and the liquid carrier. The model incorporated realistic usage cycles consisting of 3 seconds of heating and 2 seconds of cooling, with dynamic recording of temperature, resistance, and wick integrity. It accounted for resistive (Joule) heating, convective cooling, and resistance drift due to material oxidation. Material-specific physicochemical properties were included: electrical resistivity, heat capacity, thermal conductivity, and oxidation kinetics for each coil type.

The comparative results revealed significant differences among the materials tested. The highest thermal stability and minimal resistance drift were observed for Nichrome (NiCr) alloy, reaching a final temperature of 64.2°C and a final resistance of 0.1541Ω (Figure 7). Under these conditions, the wick maintained 99.76% of its structural integrity. Similar parameters were recorded for Kanthal (69.1°C, 0.1523Ω, 99.76% integrity) and stainless steel (66.6°C, 0.1565 Ω, full integrity preserved). The poorest performance was observed for titanium coils – under low airflow conditions, the final temperature reached 277.0°C, and resistance increased to 0.2925Ω, indicating intensive degradation associated with oxidation (Figure 7). Wick integrity decreased to 99.46%, which, in long-term use, could result in structural weakening and increased particulate emissions. Comparative analysis demonstrated that under high airflow conditions, wick integrity remained above 99.7% regardless of coil material, highlighting the critical role of convective cooling in reducing thermal degradation. Simulations confirmed that low airflow leads to heat accumulation in the coil and accelerated oxidation kinetics, particularly for metals with lower chemical stability, such as titanium.

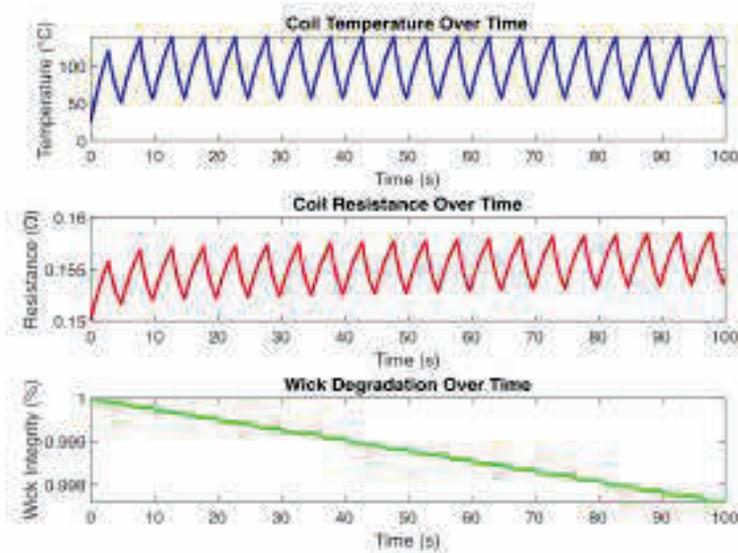


Figure 7. Operating characteristics of a nichrome (NiCr) coil at high airflow: temperature (top), resistance (middle), and cotton integrity (bottom) as a function of time [A4]

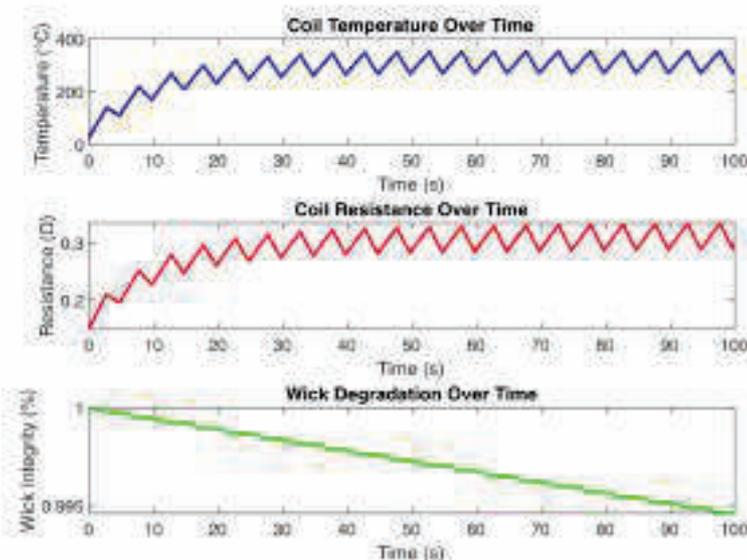


Figure 8. Operating characteristics of a titanium (Ti) coil at low airflow: temperature (top), resistance (middle), and cotton integrity (bottom) as a function of time [A4]

This work underscores the importance of selecting appropriate coil materials and operational parameters (airflow rate, power cycle) in the context of user safety. Coil degradation can lead to the emission of metal particles and thermal decomposition products of organic materials (e.g., cotton wick), posing inhalation risks. The developed model provides a useful predictive tool for designing safer e-cigarettes. However, certain limitations should be noted. The model did not account for the chemical composition of the e-liquid, interactions between the liquid and the coil material, or potential accumulation of contaminants on component surfaces. Moreover, the simulations focused on isolated operational cycles without modeling long-term device aging over weeks or months. The findings are

of significant importance for nicotine device engineering and regulatory policy. The results demonstrate that through appropriate material selection (e.g., alloys with low oxidation susceptibility) and optimized cooling parameters, it is possible to substantially reduce the emission of toxic compounds associated with thermal degradation, thereby providing tangible health benefits for users.

3.8. Optimizing Smoking Cessation Alternatives Using Multi-MOORA and AI-Based Methods [A5]

The aim of this study was to develop a hybrid decision-making model to support the selection of the most optimal smoking cessation methods, using advanced artificial intelligence (AI) techniques combined with the Multi-MOORA (Multi-Objective Optimization on the Basis of Ratio Analysis) multi-criteria decision analysis approach. The proposed model integrated three analytical methods – artificial neural networks (ANN), ridge regression (RR), and simulated annealing (SA) – to obtain stable, overfitting-resistant, and interpretable weights for key decision criteria. Three alternatives were evaluated: (1) conventional cigarettes, (2) e-cigarettes, and (3) combined use of both products. These were assessed according to six criteria: age of smoking initiation, monthly cost, CO₂ emissions, time spent smoking, ease of quitting, and health impact. Data were obtained from two sources: a survey conducted among 100 users and publicly available health and environmental reports. In the first stage, a decision matrix was constructed in which each alternative was scored according to the above criteria. The data were normalized based on the nature of each criterion (benefit or cost type), and weights were assigned. ANN was used to capture complex patterns and nonlinear relationships, RR provided stability and robustness to collinearity, and SA optimized the weight distribution while avoiding local minima.

The Multi-MOORA method was applied in its three variants: (1) ratio system, (2) reference point approach (Euclidean distance), and (3) full multiplicative form. For each alternative, a synthetic score was calculated, forming the basis of the ranking. The model consistently indicated that e-cigarettes were the top-ranked option across all versions of the analysis and in all sensitivity test iterations. The second position was held by the combined use of traditional cigarettes and e-cigarettes, while conventional cigarettes ranked lowest. This ranking persisted in the sensitivity analysis, where the weight of each criterion was varied by $\pm 10\%$, confirming the stability and robustness of the model to minor parameter changes. The results showed that the highest weight was assigned to age of smoking initiation (0.2431) and monthly cost (0.1621), while the lowest weight was given to health impact (0.1186). The final weights were obtained as the average of the values generated by the three methods (ANN, RR, SA) and are presented in Table 3.

Table 3. Decision criterion weights and ranking of alternatives (Multi-MOORA) [A5]

Criterion	Weight
Age of smoking initiation	0.2431
Monthly cost	0.1621
CO ₂ emissions	0.1376
Time spent smoking	0.1314
Ease of quitting	0.1272
Health impact	0.1186

This research contributes to the advancement of personalized decision support in public health by demonstrating that integrating AI with MCDA methods enables objective and transparent multi-criteria decision-making – covering economic, health, and environmental factors. However, certain limitations should be noted: the set of alternatives was restricted (no inclusion of nicotine replacement therapy or psychotherapy), reliance on self-reported data, possible inaccuracies in secondary data sources, and a limited respondent sample size. Future work could expand the model to include additional therapeutic options, enrich the dataset with demographic and clinical variables, and apply the approach in prospective studies. The proposed framework has the potential to be implemented as a clinical decision support tool and as a basis for developing data-driven, AI-assisted health policy in tobacco harm reduction and cessation strategies.

3.9. Modeling the Impact of Tobacco Control Policies on Smoking Prevalence: A Dynamic SIQ+P+E+H+X Framework [A6]

The next publication in the research cycle responds to the need for comprehensive modelling of the long-term population effects of public health interventions in tobacco control. For this purpose, an advanced compartmental SIQ+P+E+H+X model was designed and implemented, representing an extension of the classical SIR model with additional components reflecting the specific features of the current nicotine-use dynamics. It included not only classical variables such as initiation, cessation, and relapse of smoking, but also the use of e-cigarettes, their potential role in transition to traditional smoking (the “gateway” effect), and the impact of pricing, educational, and regulatory policies. The model was calibrated on empirical data from WHO studies, Cochrane reviews, and national datasets, including trends in smoking initiation and the effectiveness of e-cigarettes in substitution therapy. Based on this model, four policy scenarios were tested: no new interventions (baseline scenario), an increase in tobacco taxation, a total ban on cigarette sales, and strengthened anti-tobacco campaigns (Table 4).

Table 4. Overview of health policy scenarios and expected outcomes [A6]

Scenario	Policy description	Key parameters	Expected effect
Baseline	Continuation of current trends, no new interventions	None	Gradual decline in smoking prevalence
Increased taxation	Higher excise duties on cigarettes	↓ Initiation rate (β)	Reduced youth initiation, moderate increase in cessation
Strengthened anti-tobacco campaigns	Nationwide media, education, social action	↑ Cessation rate (γ), ↓ Relapse (α)	Higher cessation rates and reduced relapse across age groups
Total ban on cigarette sales	Complete prohibition of tobacco sales	$\beta = 0$, ↑ Cessation rate (γ)	Rapid elimination of smoking; illicit market not modelled

The simulation results clearly demonstrated that the most effective approach – assuming its feasibility – would be a total ban on cigarette sales, leading to a 93.6% reduction in their use over a 200-year horizon, a 50% increase in smoking cessation rates, and complete elimination of new initiations. The second most effective strategy proved to be information and education campaigns, reducing smoking prevalence by 55%, and the third – raising taxes – resulted in a 25.6% reduction (Figure 9). Sensitivity analysis of the model revealed the greatest susceptibility of the results to changes in parameters such as campaign effectiveness (γ) and the impact of taxes (τ), which confirms their key role as policy levers.

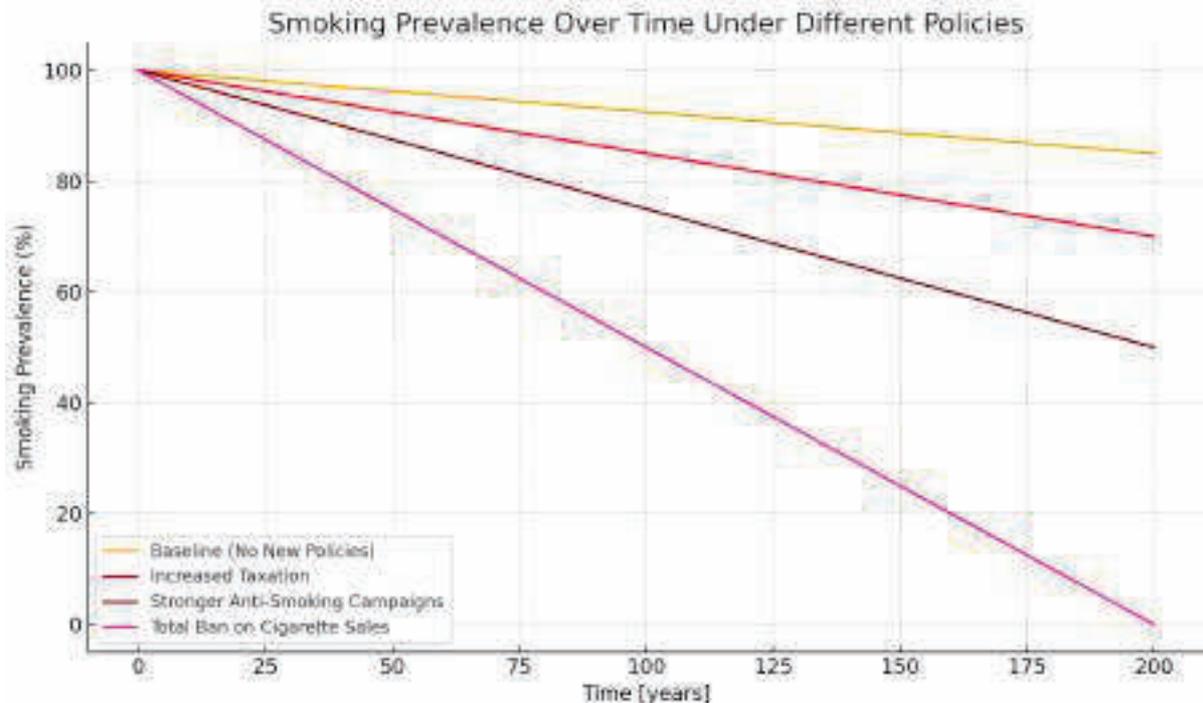


Figure 9. Smoking prevalence in the population over 200 years for four policy scenarios [A6]

A particular innovation of the model was the introduction of the “E” compartment – users of e-cigarettes – and the inclusion of their dual role: as a harm reduction tool among smokers and as a potential threat to youth (gateway effect). The model showed that, given the current level of e-cigarette use among young people (over 22% in Poland in 2022) and the relatively high risk of transition to traditional smoking (ρ index), regulations limiting access to ENDS in this age group are necessary. Unlike classical models such as SimSmoke, the developed SIQ+P+E+H+X model integrates the effects of e-cigarettes without treating them as an exogenous factor, enabling a realistic representation of future scenarios for the nicotine market. The publication also compared other population models in detail (e.g., the Tuscan model by Lachi et al., the systems model by Camacho et al.), pointing out that while they constitute valuable supplements, they lack comprehensiveness and the integration of multiple regulatory strategies.

The conclusions of the study are of practical significance for the planning of public health strategies. The model indicates that a combination of fiscal and educational interventions can significantly accelerate the decline in smoking prevalence. At the same time, the authors draw attention to the model’s limitations, including the lack of consideration of the illicit market or local social phenomena (e.g., peer network effects), suggesting the development of agent-based models in the future.

3.10. Markov Model Simulation of Nicotine Addiction and the Effectiveness of Nicotine Replacement Therapy (NRT) [A7]

In this study, a first-order Markov chain simulation model was developed to analyse the dynamics of nicotine addiction and the effectiveness of nicotine replacement therapy (NRT). The aim was to estimate the duration of addiction and the probability of smoking cessation in different user groups – both traditional cigarette smokers and e-cigarette users – under three intervention scenarios: no therapy, use of nicotine gum, and use of nicotine patches. The model included five states: no exposure to nicotine, first trials, experimentation phase, addiction, and cessation. Transition probabilities between states were derived from current epidemiological data (including NESARC), allowing for a realistic representation of the course of addiction. The transition matrix was defined for yearly time steps and applied to simulate the progression of addiction over a 20-year horizon.

The simulation results showed that e-cigarette users spend significantly less time in the addicted state than traditional smokers – on average, 27.77 years vs. 57.65 years without therapy. The introduction of replacement therapy led to a significant reduction in this duration, with nicotine patches proving more effective than gum (effectiveness: 13.83% vs. 6.56%, respectively). For e-cigarette users, patch therapy reduced addiction duration to 21.46 years, while for traditional cigarette users, it was reduced to 46.48 years (Figure 10). The model confirmed that even with moderate efficacy, NRT can substantially shorten the duration of addiction exposure, increasing the likelihood of successful cessation. These findings are consistent with the literature, confirming the higher effectiveness of patches compared to gum, in line with biochemical data (e.g., more stable salivary cotinine concentrations). An important feature of the model was its differentiation of addiction dynamics between traditional cigarette smokers and e-cigarette users, which represents novel contribution to population modelling. Biological mechanisms of addiction and the impact of NRT on stabilising nicotine levels were also taken into account, increasing the credibility of the results.

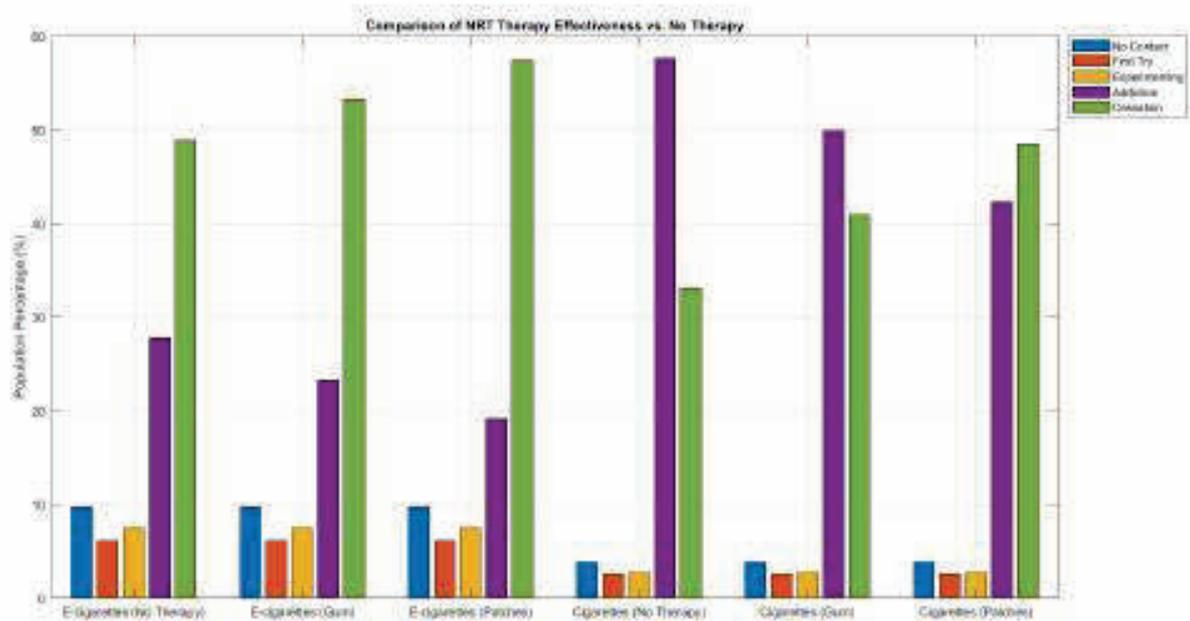


Figure 10. Simulation results of nicotine addiction and the effectiveness of nicotine replacement therapy (NRT) based on a first-order Markov chain model [A7]

The study's limitations include the relatively simplified model structure (e.g., no differentiation by age, sex, or other socio-demographic factors), the absence of behavioural support modelling, and the assumption of fixed therapy efficacy without individualisation. However, the authors indicate that this approach could be further developed into agent-based models or supplemented with cost-economic components. From a public health perspective, the results confirm the effectiveness of pharmacological interventions in reducing the burden of nicotine addiction and may serve as a basis for further optimisation of smoking cessation programmes. In particular, the model can be used to personalise therapy and estimate its long-term effects in different user subpopulations.

3.11. Analysis of Demographic, Familial, and Social Determinants of Smoking Behavior Using Machine Learning Methods [A8]

The aim of this study was to identify key demographic, familial, and social factors influencing smoking-related behaviours – both traditional and electronic – and to assess their impact on addiction dynamics and family relationships. Machine learning methods were applied to data collected from 100 participants, enabling the development of predictive models regarding the perceived impact of smoking on family relationships. The study was conducted as a cross-sectional online survey in which participants completed an anonymous questionnaire consisting of three sections: demographic data, smoking habits, and family dynamics. Validated instruments were used, including the Penn State Electronic Cigarette Dependence Index (PSECDI) to assess the level of nicotine dependence and the Family Relationship Assessment Scale (FRAS) to evaluate family relationships (Table 5). The questionnaire was translated into Polish using the back-translation method to ensure reliability and validity. Data were analysed using various statistical techniques, including chi-square tests, analysis of variance (ANOVA), and Spearman’s rank correlation, to identify significant relationships between variables. Subsequently, machine learning algorithms such as decision trees, support vector machines (SVM), k-nearest neighbours (k-NN), and ensemble learning models were applied to predict the perceived impact of smoking on family relationships. Models were evaluated for accuracy and loss using k-fold cross-validation.

Table 5. Comparison of family relationship indicators (FRAC) and nicotine dependence level (PSECDI) by smoking type [A8]

Category	Indicator	E-cigarettes	Traditional cigarettes	Dual users
FRAC	Family support (mean)	4.22	3.50	3.67
	Family conflicts (mean)	1.81	2.00	1.89
	Time spent together (mean)	3.26	3.12	2.83
PSECDI	No dependence (%)	0	4.76	0
	Low dependence (%)	21.05	33.33	16.67
	Moderate dependence (%)	31.58	19.05	33.33
	High dependence (%)	47.37	42.86	50.00
	Mean score	13.11	12.05	13.50

Statistical analysis showed that e-cigarette users reported higher family support and fewer conflicts compared to traditional smokers and dual users. However, e-cigarette users also demonstrated higher levels of nicotine dependence, suggesting that despite better family relationships, the risk of addiction remains significant. To explore the data structure, principal component analysis (PCA) was applied. The initial PCA projection, based on all demographic, familial, and behavioural variables, revealed substantial class overlap, confirming the complexity and low separability of the data. Further analysis was conducted using PCA only on the six most discriminative variables, selected via the ANOVA F-test. The results (Figure 11) revealed clearer clustering, particularly for extreme cases, confirming the potential of supervised models for further classification. Designing a reduced-dimensionality space also confirmed the high predictive value of variables describing the perceived impact of smoking on family relationships. The PCA analysis aligned with the subsequent feature importance analysis in the machine learning models and further justified the selection of specific predictors.

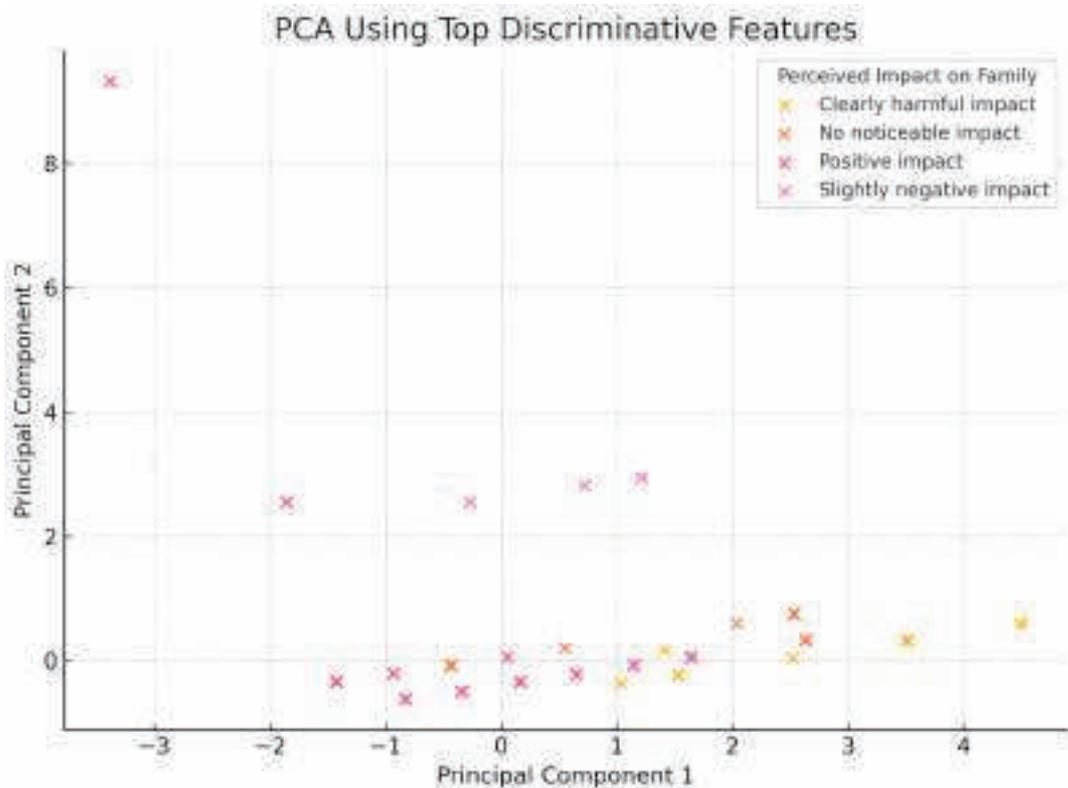


Figure 11. PCA projection based on the six most significant input variables [A8]

To assess which variables had the greatest influence on prediction performance, feature importance was compared across the four models. Regardless of the method applied, in all cases the variable describing the perceived impact of smoking on family relationships was the most important. Next in rank were variables such as family conflicts, participant age, and the presence of smokers in the family. While specific values differed between models, the general order of the most important features remained consistent. The comparison of the top predictors is presented in Table 6.

Table 6. Comparison of feature importance (normalised values) across machine learning models [A8]

Feature	Decision tree	Ensemble	SVM	k-NN
Gender	0	0.0085	0	0
Age	0	0	0.0167	0
Do you smoke	0	0	0	0
Smoking frequency	0	0.0023	0	0
Age of smoking initiation	0	0.0031	0.0067	0
Smoking family members	0	0	0.0133	0
Family conflicts (FRAC)	0.0381	0	0	0.008
Impact of smoking on relationships	0.1875	0.1459	0.1867	0.2433
Family acceptance	0	0	0	0

The machine learning models achieved high accuracy in predicting the impact of smoking on family relationships (Table 7), with the ensemble model reaching the highest accuracy of 93.33%, outperforming other models such as k-NN (90.00%), decision trees (83.33%), and SVM (80.00%). Feature importance analysis confirmed that variables related to the perceived impact of smoking on family relationships had the strongest effect on predictive performance.

Table 7. Performance evaluation of machine learning models [A8]

Model	Accuracy	Precision	Recall	F1 score
Decision tree	83.33%	0.79	0.70	0.74
Ensemble learning	93.33%	0.91	0.91	0.91
Support Vector Machine (SVM)	80.00%	0.60	0.75	0.67
k-Nearest Neighbours (k-NN)	90.00%	0.90	0.82	0.86

The main limitation of the study was the relatively small number of participants (100), which may affect the generalisability of results to the broader population. Additionally, the use of self-administered questionnaires could introduce bias related to participants' subjective assessments. Nevertheless, the findings highlight the importance of family relationships in the context of smoking behaviours and suggest that public health interventions should take these aspects into account. The application of machine learning methods to the analysis of health-related behaviours opens new possibilities for identifying individuals at increased risk of addiction and for developing personalised intervention programmes. Future research should focus on increasing the sample size and including

additional variables, such as socio-economic status, stress levels, and social support, to better understand the complexity of smoking-related behaviours.

3.12. Body Composition and Metabolic Profiles in Young Adults: A Cross-Sectional Comparison of People Who Use E-Cigarettes, People Who Smoke Cigarettes, and People Who Have Never Used Nicotine Products [A9]

The aim of this study was to assess the impact of regular e-cigarette use on selected metabolic parameters and body composition in healthy young adults. In contrast to most studies focusing on the respiratory and cardiovascular systems, the present research addressed a less-studied area: changes in body structure and parameters related to metabolism, such as total body water content, lean body mass, and metabolic age. The study included three groups of participants (N = 120, 20 participants in each group): non-smokers (control group), e-cigarette users, and conventional cigarette smokers. Participant characteristics are shown in Table 8. Bioelectrical impedance analysis (BIA) was performed using a multi-frequency, diagnostic-grade medical analyzer. Measurements included: muscle mass, total body water (TBW), body fat content, metabolic age, body mass index (BMI), and visceral fat level.

Table 8. Characteristics of study participants [A9]

Variable	All participants (N = 60)	Tobacco smokers (n = 20)	E-cigarette users (n = 20)	Non-smokers (n = 20)
Age (years)	22.0 [2.25]	22.0 [2.25]	20.5 [3.0]	22.0 [1.75]
Height (cm)	173.5 [16.25]	176.5 [8.0]	170.0 [12.25]	171.5 [20.75]
Body mass (kg)	65.35 [13.35]	68.75 [20.15]	65.35 [4.8]	62.1 [21.08]
BMI (kg/m ²)	22.3 [3.55]	22.05 [4.62]	23.4 [1.33]	21.05 [3.2]
Body fat (%)	15.35 [5.87]	12.95 [7.17]	16.35 [4.32]	11.2 [5.15]
Visceral fat (level)	2.0 [2.0]	2.0 [2.25]	2.0 [2.0]	1.0 [1.0]
Muscle mass (kg)	47.35 [17.7]	52.25 [15.88]	46.6 [10.2]	45.75 [20.67]
Total body water (%)	32.1 [13.12]	39.7 [14.9]	31.05 [6.1]	30.85 [14.55]
Metabolic age (years)	18.0 [13.25]	23.5 [17.0]	23.5 [13.0]	15.5 [5.5]
Sex – male (%)	15 (41.7%)	7 (58.3%)	2 (16.7%)	5 (41.7%)
Sex – female (%)	21 (58.3%)	5 (41.7%)	10 (83.3%)	7 (58.3%)

Results showed that e-cigarette users had a significantly higher metabolic age (mean +3.6 years relative to chronological age) compared to the control group (mean –1.1 years). This difference was statistically significant ($p < 0.01$) and suggests disturbances in basal metabolism that may be linked to chronic exposure to nicotine or other chemical compounds present in the aerosol (Table 9). Conventional cigarette smokers also exhibited an elevated metabolic age; however, the differences were less pronounced than in the e-cigarette group, which may indicate different underlying mechanisms. Total body water and muscle mass were significantly lower in e-cigarette users compared to the control group (mean TBW: 50.3% vs. 54.7%, $p < 0.05$), which may reflect mild

dehydration or chronic activation of the stress axis. BMI and visceral fat values did not differ significantly between groups; however, the segmental muscle mass index was lower among ENDS users, suggesting subtle alterations in metabolic homeostasis and potentially weakened anabolic profile. A multivariate regression analysis controlling for confounders such as sex, physical activity level, and dietary habits confirmed that e-cigarette use remained a significant predictor of higher metabolic age and reduced lean body mass ($p < 0.05$). Additionally, correlations between selected lifestyle variables (sedentary time, coffee consumption, energy drink consumption) and metabolic parameters were examined. No significant associations were found between sedentary time and BMI, metabolic age, BMR, or percentage body fat. Similarly, coffee consumption was not significantly correlated with any of the analyzed parameters. However, regular consumption of energy drinks showed statistically significant positive correlations with BMI ($r = 0.49$; $p = 0.0025$), metabolic age ($r = 0.61$; $p = 0.0001$), and body fat percentage ($r = 0.65$; $p < 0.0001$), suggesting a potential link with an adverse metabolic profile.

Table 9. Between-group comparisons for tobacco and e-cigarette users for continuous variables (non-parametric tests) [A9]

Variable	p (Kruskal–Wallis)	Significant comparisons (Bonferroni-corrected)	Significance
Metabolic age	0.0429	E-cigarettes vs. Non-smokers ($p = 0.0248$)	significant
Body fat (%)	0.0203	E-cigarettes vs. Non-smokers ($p = 0.0127$)	significant
BMI	0.0295	E-cigarettes vs. Non-smokers ($p = 0.0199$)	significant
Chronological age	0.0721	E-cigarettes vs. Non-smokers ($p = 0.0938$)	trend
Energy drink consumption	0.0007	E-cigarettes vs. Non-smokers ($p = 0.0011$); vs. Smokers ($p = 0.0480$)	significant

In the exploratory part, supervised machine learning models were used to classify participants according to smoking status. The initial decision tree model built on the full set of features achieved moderate classification accuracy (50.0%). After reducing the number of features to the eight most relevant (including metabolic age, BMI, and body fat percentage), accuracy increased to 66.67%. Alternative models (Random Forest – 61.1%; k-NN – 72.22%) indicated that the k-NN classifier was the most effective in distinguishing smokers from non-smokers in this population. Feature importance analysis confirmed the key role of metabolic indicators as predictors of smoking status.

Despite limitations such as the cross-sectional design and reliance on self-reported data (e.g., physical activity), the results suggest that e-cigarettes may affect the body’s metabolic functioning even in young, healthy individuals. The authors highlight the need for long-term prospective studies incorporating biochemical markers and advanced body composition imaging methods to confirm and further explore these findings. This study broadens the current understanding of ENDS effects, showing that their impact is not limited to the respiratory system but may also influence body weight regulation, fluid balance, and metabolic aging processes.

3.13. Postural Control and Gait Alterations in Young Adult Tobacco and E-Cigarette Users: A Comparative Stabilometric and Treadmill-Based Analysis [A10]

In this study, postural control and gait parameters were compared among three groups of young adults: e-cigarette users (ECIG), conventional cigarette smokers (CIG), and non-smokers (NS). The motivation for this analysis was the growing popularity of e-cigarettes and the lack of clear evidence regarding their impact on biomechanical functions. It was hypothesized that chronic use of nicotine-containing products, regardless of their form, could adversely affect balance and gait parameters, which are sensitive indicators of neuromuscular system functioning. The study was cross-sectional and included 60 healthy participants (mean age 21.3 ± 1.7 years). Each group comprised 20 individuals. Group allocation was based on self-reported lifestyle and nicotine use habits. Inclusion criteria required at least six months of regular use of the respective product (traditional cigarettes or e-cigarettes) or complete lack of nicotine exposure for the control group. Exclusion criteria included neurological, orthopedic, or balance disorders, intensive sports training, or the use of medications affecting the central nervous system. Postural stability was measured using the Zebris FDM-T System platform (Zebris Medical GmbH, Germany). Participants stood barefoot on the platform for 30 seconds under two conditions: eyes open (EO) and eyes closed (EC). Primary stabilometric indicators were recorded: center of pressure (COP) path length, COP velocity, and 95% confidence ellipse area (COP area).

In the EO condition, the CIG group demonstrated the longest COP path (42.27 ± 4.99 cm), significantly longer than the NS group (38.22 ± 3.89 cm; $p = 0.025$). E-cigarette users obtained an intermediate value (41.24 ± 4.50 cm), which did not differ significantly from the other groups. In the EC condition, the effect was more pronounced: CIG (46.47 ± 5.44 cm) vs. NS (41.43 ± 4.23 cm; $p = 0.018$), while the ECIG group reached 44.18 ± 4.63 cm. These findings indicate a clear deterioration in postural control among conventional smokers and possible early changes in e-cigarette users, particularly visible under conditions without visual compensation. Gait parameter analysis, also conducted using the Zebris FDM-T platform, revealed significantly shorter step length in the CIG group (70.12 ± 3.52 cm) compared to NS (74.24 ± 4.25 cm; $p = 0.003$), while ECIG obtained an intermediate value (71.69 ± 3.97 cm), not significantly different from the other groups. Walking speed was also lowest in conventional smokers (1.18 ± 0.08 m/s) compared to NS (1.26 ± 0.09 m/s; $p = 0.022$), with ECIG again in between (1.22 ± 0.10 m/s). No significant differences between groups were found for foot-ground contact time or the rollover phase. Table 10 presents post-hoc comparisons between groups for selected biomechanical parameters.

Table 10. Post-hoc comparisons between group pairs for all conditions. Dashes (–) indicate that the comparison was not among the lowest p-values [A10]

Variable	Test	NS vs ECIG	NS vs CIG	ECIG vs CIG
Body mass index (BMI)	Kruskal–Wallis test	0.001	0.323	0.218
Force under left forefoot (N)	ANOVA	0.474	0.037	0.051
Force under left	ANOVA	0.389	0.033	0.098

rearfoot (N)				
Gait cycle duration (s)	Kruskal–Wallis test	0.012	–	0.282
Maximum force – left forefoot (N)	Kruskal–Wallis test	0.047	–	0.138
Maximum force – right forefoot (N)	Kruskal–Wallis test	0.055	–	0.148
Maximum load – left heel (N)	Kruskal–Wallis test	–	0.042	0.091
Maximum load – right heel (N)	Kruskal–Wallis test	0.023	0.071	–
Average step length (cm)	ANOVA	0.005	0.153	0.072
Average maximum load – left forefoot (N)	Kruskal–Wallis test	0.047	–	0.138
Step length (right leg, cm)	ANOVA	0.003	0.123	0.256

Additionally, to identify the most important features differentiating the user groups, the ReliefF algorithm was applied to assess variable importance in the classification context. Subsequently, supervised classifiers – including decision trees, support vector machines (SVM), k-nearest neighbors (k-NN), and logistic regression – were used to distinguish between groups based on selected biomechanical features. The highest accuracy (82.8%) was achieved with logistic regression in differentiating non-smokers from e-cigarette users (Table 11). Furthermore, principal component analysis (PCA) and confusion matrices confirmed the ability of these models to capture subtle differences in postural and gait parameters that were not clearly visible in traditional statistical analyses.

Table 11. Classification accuracy for group pairs and models (5-fold cross-validation) [A10]

Group 1	Group 2	Model	Accuracy
Non-smokers	Cigarette smokers	Decision tree	0.393
		SVM (linear)	0.571
		k-NN (k=5)	0.536
		Logistic regression	0.536
Non-smokers	E-cigarette users	Decision tree	0.621
		SVM (linear)	0.793

		k-NN (k=5)	0.552
		Logistic regression	0.828
Cigarette smokers	E-cigarette users	Decision tree	0.370
		SVM (linear)	0.481
		k-NN (k=5)	0.444
		Logistic regression	0.519

The findings indicate gait biomechanics and postural stability impairments in conventional smokers, with e-cigarette users showing intermediate values, suggesting the possibility of subclinical effects. The deterioration of balance parameters in the eyes-closed condition suggests weakened sensory compensation and reduced integration of proprioceptive and vestibular signals in individuals exposed to nicotine. Although e-cigarette users did not present significantly worse values than non-smokers, noticeable trends suggest that even this form of nicotine consumption may affect the postural system.

The authors note limitations, such as the small sample size and lack of nicotine concentration control, but emphasize that these findings should serve as a starting point for further longitudinal and neurophysiological research. This publication is among the first to combine balance and gait assessment in the context of e-cigarette use, highlighting the need to include such measures in a comprehensive evaluation of the neuromotor health effects of these products.

3.14. E-Cigarette Users Exhibit Stronger Cardiovascular Reactivity than Smokers: Evidence from a Multimodal Signal Analysis in Young Adults [A11]

In this study, an attempt was made to assess the impact of conventional cigarette smoking and e-cigarette use on selected cardiovascular and respiratory parameters using an integrated vector analysis of multimodal data. The primary objective was to identify characteristic physiological patterns that could distinguish three nicotine-user populations – non-smokers, e-cigarette users, and conventional cigarette smokers – under physiological stress induced by an exercise test. The study included 60 healthy volunteers (mean age 21.7 ± 1.9 years), evenly divided into three groups (N = 20 each): non-smokers (NS), e-cigarette users (ECIG), and conventional cigarette smokers (CIG). Eligibility for the user groups required regular use of the respective product for at least one year. Exclusion criteria included cardiovascular, respiratory, and metabolic diseases, as well as the use of medications affecting the studied parameters. Physiological signals were recorded in three phases: at rest, immediately after completion of a standard treadmill exercise, and after a return-to-rest phase. In each phase, synchronous measurements were taken for heart rate (HR), oxygen saturation (SpO₂), systolic and diastolic blood pressure (SYS, DIA), mean arterial pressure (MAP), and respiratory rate (RR). The synchronously collected data were transformed into vector form and then analyzed using exploratory methods such as machine learning classifiers (decision trees, logistic regression) to identify features with the highest diagnostic value.

The results showed clear differences between groups, particularly after exercise. During the effort phase, traditional smokers reached the highest systolic blood pressure and heart rate values compared with e-cigarette users and non-smokers. However, the analysis of Δ HR (Effort – Rest) revealed that e-cigarette users exhibited the greatest increase in heart rate relative to rest, significantly higher than both non-smokers and traditional smokers (ANOVA $p = 0.01366$, Tukey's post hoc $p < 0.03$ for both comparisons) (Fig. 12).

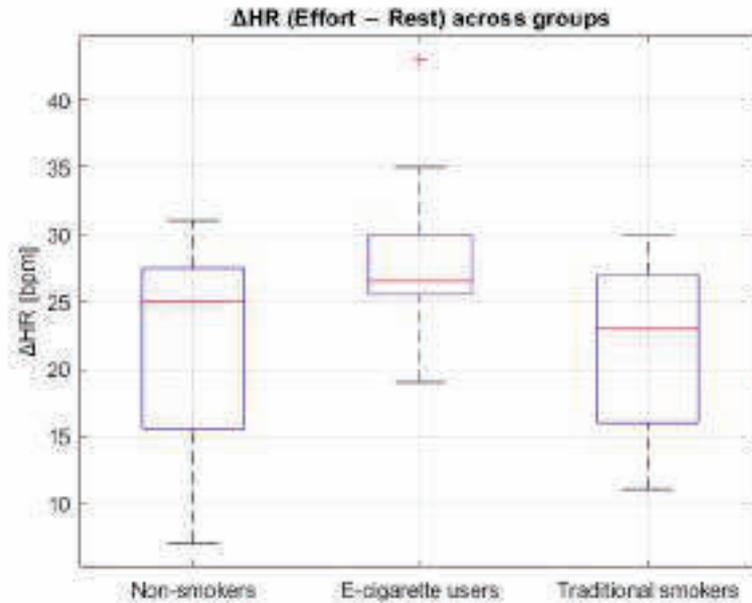


Figure 12. Boxplot of ΔHR values in the three study groups ($p = 0.01366$, ANOVA) [A11]

The drop in SpO_2 during effort was analyzed as the difference between resting and post-exercise values (ΔSpO_2 Rest–Effort). The largest mean decrease was observed in e-cigarette users ($-1.45\% \pm 1.23$), followed by traditional smokers ($-1.20\% \pm 0.89$) and non-smokers ($-1.05\% \pm 1.28$). These differences, however, did not reach statistical significance ($p = 0.3712$; Fig. 13).

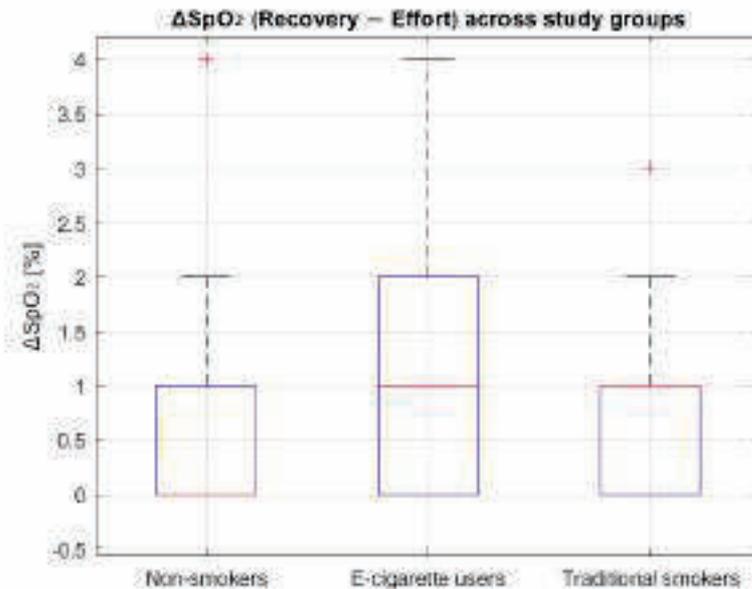


Figure 13. Boxplot of ΔSpO_2 (recovery – exercise) in the three study groups. E-cigarette users showed the greatest improvement in oxygen saturation (SpO_2) during the recovery phase. The observed trend approached statistical significance ($p = 0.0700$, Kruskal–Wallis test) [A11]

Recovery time parameters were prolonged in both CIG and ECIG groups compared with NS (Fig. 14). The mean recovery time of HR was longest in e-cigarette users: 123.9 s (SD 17.3), significantly longer than in non-smokers: 65.6 s (SD 10.9) and traditional smokers: 72.2 s (SD 15.0) (Kruskal–Wallis $p < 0.001$, post hoc ECIG vs NS and ECIG vs CIG: $p < 0.001$, Cohen’s $d = 4.03$ for ECIG vs NS). These results indicate a substantial burden on the autonomic system in regular e-cigarette users, likely due to excessive sympathetic activation and reduced parasympathetic reactivation.

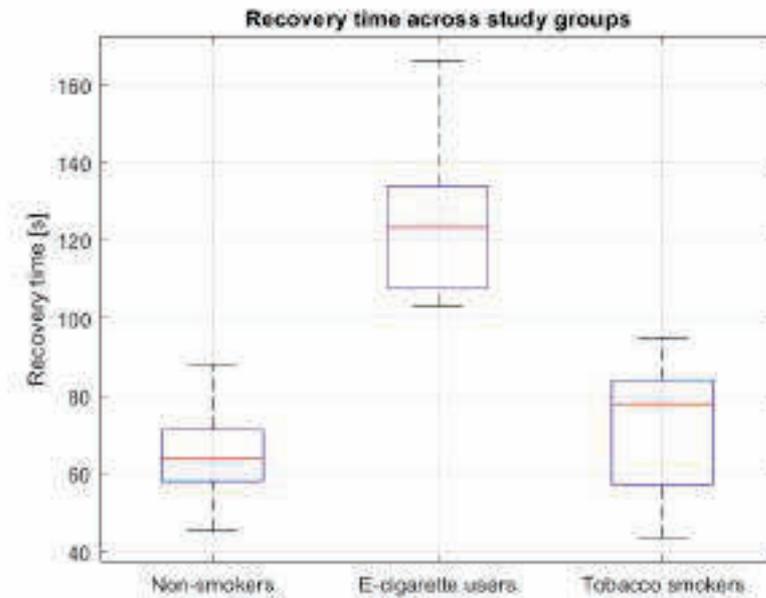


Figure 14. Boxplot of recovery time (in seconds) in the three study groups. E-cigarette users showed significantly longer recovery times compared to both conventional smokers and non-smokers ($p < 0.001$, Kruskal–Wallis test) [A11]

The classification models achieved an accuracy ranging from 71.7% (logistic regression) to 75.0% (decision trees), confirming the potential of vector-based multimodal signal analysis in evaluating physiological load associated with nicotine use (Table 12). The most important predictive feature was ΔHR .

Table 12. Comparison of model performance (accuracy, AUC, log-loss) [A11]

Model	Accuracy (%)	AUC
Logistic regression	71.67	0.681
Decision trees	75.00	0.750

The authors highlight significant differences not only between smokers and non-smokers but also between e-cigarette users and nicotine-free individuals. Although the ECIG group displayed intermediate parameter values, some – such as recovery time and SpO_2 drop – more closely resembled those observed in conventional smokers than in the control group, suggesting hidden physiological effects of nicotine aerosol despite the absence of tar. In addition, ΔHR was the only

parameter to show a significant correlation with recovery time ($r = 0.264$, $p = 0.0417$), confirming its value as a biomarker of autonomic load. The study's limitations include its cross-sectional design, small sample size, and lack of biochemical measurements (e.g., cotinine levels). Nevertheless, this work provides important evidence of possible subclinical cardiorespiratory disturbances in young nicotine users and highlights the potential of integrating multimodal data in physiological analysis.

3.15. Summary

The present doctoral dissertation, based on a cycle of eleven scientific publications, constitutes an interdisciplinary and multi-level analysis of the effects of electronic and conventional cigarette smoking on the human body, with particular emphasis on the functioning of the respiratory and cardiovascular systems, as well as metabolic and posturo-motor aspects. The conducted studies reveal the complexity of the physiological response to nicotine exposure and accompanying compounds – originating both from cigarette smoke and from the aerosol generated by electronic devices. The work encompassed, in sequence: the assessment of the chemical composition of the aerosol; the development and validation of mathematical models (PBPK, Markov, and agent-based); the evaluation of the effectiveness of various health interventions; and human experiments – including stabilometric tests, exercise tests, metabolic measurements, and biomedical signal recordings. The integration of such diverse methods enabled an in-depth analysis of differences between users of conventional and electronic cigarettes and non-smokers, at molecular, physiological, and behavioral-social levels.

The results indicate that, despite the absence of combustion processes, the use of electronic cigarettes is associated with exposure to heavy metals (originating from heating element components), adverse effects on the cardiovascular response, and – in the case of dual users – deterioration of the metabolic profile. At the same time, it was demonstrated that the body's responses to e-cigarettes differ qualitatively from those induced by conventional cigarettes, confirming the need to treat these forms of exposure separately in population and clinical research. The developed mathematical models and data analysis methods may prove useful not only in scientific research but also as tools to support decision-making in public health policy, addiction prevention, and the individualization of smoking cessation therapy. Population studies also provided data on the psychosocial and environmental determinants of smoking, facilitating the identification of at-risk groups and the design of targeted educational interventions.

This dissertation highlights the importance of an integrative approach that combines knowledge from biomedical engineering, physiology, public health, and social sciences. The results provide a significant contribution to the development of interdisciplinary methods for assessing health risks associated with the use of novel nicotine products. They also emphasize the need for long-term studies addressing both health outcomes and the effectiveness of preventive and therapeutic interventions in young adult populations. The originality of the dissertation lies in combining biological and social data with advanced computational tools and artificial intelligence, which enabled the identification of complex mechanisms of nicotine dependence and its consequences. The scientific contribution includes the development of new mathematical and simulation models as well as the implementation of human studies, the results of which were used to validate the proposed approaches. Thus, the dissertation not only delivers new empirical findings but also provides tools with potential applications in health policy, addiction prevention, and the personalization of smoking cessation strategies. In summary, the research objectives of this dissertation have been achieved, and the research hypotheses have been confirmed through the presented series of publications.

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Wykaz skrótów

- Δ HR – zmiana częstości akcji serca / change in heart rate
- SpO₂ – saturacja tlenem / oxygen saturation
- SYS – ciśnienie skurczowe / systolic blood pressure
- DIA – ciśnienie rozkurczowe / diastolic blood pressure
- MAP – średnie ciśnienie tętnicze / mean arterial pressure
- CIG – palacze papierosów / cigarette smokers
- ECIG – użytkownicy e-papierosów / e-cigarette users
- NS – osoby niepalące / non-smokers
- SD – odchylenie standardowe / standard deviation
- d Cohena – wielkość efektu Cohena / Cohen's d effect size
- PBPK – fizjologiczny model farmakokinetyczny / physiologically based pharmacokinetic model
- PM_{2.5} – pył zawieszony $\leq 2,5 \mu\text{m}$ / particulate matter $\leq 2.5 \mu\text{m}$
- SIQ+P+E+H+X – model dynamiki palenia uwzględniający podatnych (S), inicjujących (I) i rzucających (Q), z korektą o czynniki polityczne (P), środowiskowe (E), zdrowotne (H) i ekspozycji (X) / smoking dynamics model (Susceptible–Initiator–Quitter + Policy, Environmental, Health, Exposure factors).
- NRT – nikotynowa terapia zastępcza / nicotine replacement therapy
- Multi-MOORA – metoda wielokryterialnej optymalizacji / multi-objective optimization on the basis of ratio analysis
- NESARC – Krajowe Badanie Epidemiologiczne Alkoholu i Warunków Pokrewnych / National Epidemiologic Survey on Alcohol and Related Conditions
- EKG – elektrokardiografia / electrocardiography
- PPG – fotopletyzmografia / photoplethysmography
- POChP – przewlekła obturacyjna choroba płuc / chronic obstructive pulmonary disease (COPD)

EVALI – uszkodzenie płuc związane z e-papierosami / e-cigarette or vaping product use-associated lung injury

THC – tetrahydrokannabinol / tetrahydrocannabinol

DNA – kwas deoksyrybonukleinowy / deoxyribonucleic acid

WHO – Światowa Organizacja Zdrowia / World Health Organization

NASEM – Narodowe Akademie Nauk, Inżynierii i Medycyny / National Academies of Sciences, Engineering, and Medicine

C_{ss} – stężenie w stanie stacjonarnym / steady-state concentration

t_{1/2} – okres półtrwania / half-life

OUN – ośrodkowy układ nerwowy / central nervous system

C_{max} – maksymalne stężenie w osoczu / maximum plasma concentration

T_{max} – czas osiągnięcia C_{max} / time to maximum concentration

SEM – skaningowa mikroskopia elektronowa / scanning electron microscopy

EDS – spektroskopia dyspersyjna energii / energy-dispersive spectroscopy

WWA – wielopierścieniowe węglowodory aromatyczne / polycyclic aromatic hydrocarbons

POD – e-papierosy typu „pod” (Personalized On Demand) / pod-type (Personalized On Demand) e-cigarettes

AI – sztuczna inteligencja / artificial intelligence

PCA – analiza głównych składowych / principal component analysis

XGBoost – metoda uczenia maszynowego boosting drzew / eXtreme gradient boosting

Stanowiska badawcze

Realizacja omawianej rozprawy doktorskiej, wymagała zastosowania zestawu stanowisk badawczych, obejmujących pomiary biomechaniczne, fizjologiczne, metaboliczne, chemiczne oraz obliczeniowe. Każde ze stanowisk miało charakter multidyscyplinarny i zostało dobrane lub opracowane tak, aby umożliwić kompleksową ocenę wpływu palenia papierosów tradycyjnych i elektronicznych na organizm człowieka.

Stanowisko stabilometryczne (Zebris)

Do badań nad kontrolą posturalną i chodem wykorzystano system Zebris FDM (Zebris Medical GmbH, Germany). Stanowisko obejmowało:

- platformę stabilometryczną z czujnikami sił reakcji podłoża Zebris FDM-S, umożliwiającą rejestrację parametrów równowagi i trajektorii środka nacisku (COP),
- bieżnię pomiarową Zebris FDM-T wyposażoną w matrycę czujników, pozwalającą na obiektywną analizę chodu i lokomocji.

Stanowisko umożliwiało prowadzenie zarówno badań w warunkach statycznych (posturografia na platformie), jak i badań dynamicznych (analiza parametrów chodu na bieżni), realizowanych w ramach jednego zintegrowanego systemu pomiarowego.

Stanowisko do rejestracji sygnałów fizjologicznych

Równoległe pomiary kardiologiczne i oddechowe prowadzono z wykorzystaniem aparatury klinicznej Vista 120S. Stanowisko umożliwiało jednoczesną rejestrację:

- EKG,
- ciśnienia tętniczego (SYS, DIA, MAP),
- saturacji krwi tlenem (SpO₂).

Konfiguracja aparatury pozwalała na monitorowanie reakcji sercowo-naczyniowych i oddechowych w warunkach kontrolowanych, z pełną rejestracją czasową sygnałów do dalszej analizy.

Stanowisko metaboliczne

Do oceny składu ciała i parametrów metabolicznych zastosowano analizator BIA (Bioelectrical Impedance Analysis). Stanowisko to obejmowało pomiar całkowitej zawartości wody ustrojowej, udziału tkanki tłuszczowej oraz wieku metabolicznego. Aparatura była uzupełniona o zestaw standaryzowanych kwestionariuszy stylu życia, co pozwalało na łączenie wyników pomiarowych z danymi ankietowymi.

Stanowisko do analizy aerozolu

W celu wyznaczenia charakterystyki chemicznej aerozolu tytoniowego i e-papierosowego opracowano stanowisko laboratoryjne do poboru próbek. Składało się ono z:

- układu generującego przepływ i podciśnienie, umożliwiającego zasysanie aerozolu,
- nośników wychytujących cząstki (np. membrany nitrocelulozowe),
- aparatury analitycznej: skaningowej mikroskopii elektronowej (SEM) z spektroskopią dyspersji energii (EDS).

Tak skonstruowane stanowisko umożliwiło identyfikację składu pierwiastkowego emitowanego dymu i aerozolu.

Stanowiska obliczeniowe

Integralnym elementem zaplecza badawczego była część obliczeniowa, realizowana na komputerze z wykorzystaniem dedykowanego oprogramowania, w szczególności Matlab 2024b, The Mathworks Inc., Natick, MA, USA, oraz algorytmów sztucznej inteligencji. W tym środowisku opracowano i zastosowano:

- model PBPK (Physiologically-Based Pharmacokinetic), służący do opisu farmakokinetyki nikotyny w różnych scenariuszach użycia,
- modele Markowa, pozwalające na symulację przejść pomiędzy stanami uzależnienia i abstynencji,
- model SIQ+P+E+H+X, uwzględniający czynniki podatności, inicjacji i zaprzestania palenia wraz z determinantami środowiskowymi i politycznymi,
- narzędzia AI/ML (m.in. PCA, k-NN, XGBoost), umożliwiające analizę wielowymiarowych danych i predykcję wyników.

Przedstawione stanowiska badawcze tworzą spójny system eksperymentalny, w którym zintegrowano pomiary biomechaniczne, fizjologiczne, metaboliczne, chemiczne oraz symulacje obliczeniowe. Unikatowość tych rozwiązań polegała na możliwości komplementarnego badania różnych aspektów wpływu palenia na organizm człowieka, co nadało pracy interdyscyplinarny i nowatorski charakter.

Pozostałe publikacje

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Załączniki

Pełne teksty publikacji stanowiące rozprawę doktorską.

38 Introduction

39 Tobacco use continues to be one of the most pressing public health challenges globally. According to
40 the World Health Organization (WHO), it is responsible for over 8 million deaths each year, with more than 7
41 million attributed to direct use and around 1.3 million resulting from secondhand smoke exposure [1,2].
42 Cigarette smoke contains nicotine, tar, carbon monoxide, and hundreds of other harmful substances, many of
43 which are carcinogenic [3,4]. At least 70 of these chemicals are classified as known cancer-causing agents.
44 Cigarette smoking is a major contributor to chronic diseases such as cardiovascular disease, COPD, and lung
45 cancer—which alone accounts for 90% of all cases [2–4]. Despite numerous public health campaigns,
46 legislative action, and nicotine replacement therapies, approximately 1.5 billion people worldwide continue to
47 smoke [1,5]. Within this context, electronic cigarettes, or “e-cigarettes”, have emerged as a widely used
48 alternative to conventional smoking, particularly among younger populations. Marketed as a safer option, these
49 devices work by heating a liquid – typically a blend of nicotine, propylene glycol, glycerin, and various
50 flavorings – into an inhalable aerosol. Proponents suggest that vaping offers a less harmful method of nicotine
51 delivery and may even assist smokers in quitting [6,7]. However, growing evidence highlights the potential
52 health risks associated with e-cigarettes, casting doubt on their reputation as a harm-reduction tool [8–10].

53 One of the key differences between smoking and vaping lies in the heating mechanism. Traditional
54 cigarettes rely on combustion, with temperatures exceeding 400°C, which produces a complex mix of gases and
55 fine particulate matter, including tar and polycyclic aromatic hydrocarbons (PAHs) [11,12]. E-cigarettes operate
56 at lower temperatures (typically between 100°C and 300°C), generating aerosols through thermal
57 decomposition. While this process avoids many combustion-related toxicants, it can still produce harmful
58 substances such as formaldehyde, acrolein, and metal particles from the heating coil [13–16].

59 Both products present distinct health risks. Cigarette smoke is well known for containing tar, carbon
60 monoxide, and carcinogens that damage lung tissue, impair oxygen transport, and contribute to chronic
61 inflammation [17–19]. Although e-cigarettes do not emit tar and generate less carbon monoxide, they still
62 deliver nicotine – a highly addictive stimulant that can interfere with brain development, particularly in
63 adolescents and young adults [20]. Additionally, repeated inhalation of vaporized solvents such as glycerin and
64 propylene glycol has been linked to respiratory irritation and impaired lung function. The rise of vaping-related
65 lung injuries, known as EVALI, has further raised alarm, with severe cases resulting in hospitalizations and
66 even fatalities [21,22]. The chemical makeup of traditional and electronic cigarettes may differ, but both contain
67 substances that pose significant health hazards. Cigarette smoke includes high levels of sulfur compounds,
68 cadmium, lead, arsenic, and PAHs [17,23,24]. Sulfur dioxide is a potent respiratory irritant, while cadmium and
69 arsenic are recognized carcinogens that also damage the kidneys and bones [24,25]. Lead, meanwhile, affects
70 nearly every organ system and is especially dangerous to developing nervous systems. Even without
71 combustion, e-cigarettes can expose users to similar toxic elements. The heating coils – often made from metals
72 like lead, nickel, chromium, or aluminum – can release these substances into the aerosol [28–30]. Research
73 shows that users may inhale substantial amounts of these metals, especially under high-heat conditions. In some
74 cases, e-liquids may also contain trace amounts of cadmium, further increasing risk [28,30].

75 Flavoring agents used in e-liquids pose additional concerns. Compounds such as diacetyl, often added
76 for buttery or sweet flavors, have been linked to bronchiolitis obliterans – a rare but serious disease that scars the
77 small airways and severely restricts breathing [31]. Although e-cigarettes tend to contain fewer hazardous
78 substances overall, the presence of these chemical components indicates they are not without risk.

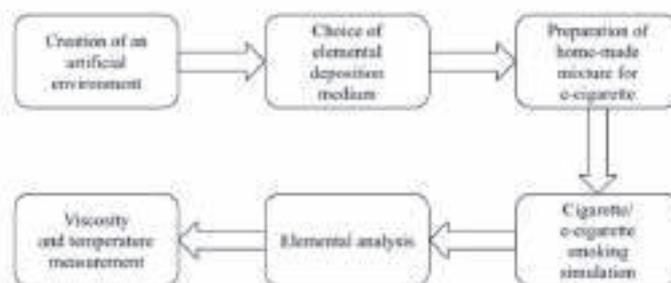
79 To better understand what users may be exposed to, researchers have turned to energy-dispersive X-ray
80 spectroscopy (EDS), a technique that allows for the detection of inorganic elements – especially metals – in both
81 cigarette smoke and e-cigarette vapor. Unlike methods that focus solely on organic compounds, EDS provides a
82 broader elemental overview without requiring complex sample preparation. Its sensitivity to a wide range of
83 elements, including trace metals, makes it an increasingly valuable tool in public health research [32–34].

84 This study investigates the elemental composition of aerosols produced by both traditional cigarettes
 85 and e-cigarettes. Using EDS and a simulated lung setup, it compares emissions from store-bought and
 86 homemade e-liquids across different usage conditions. The aim is to assess potential exposure to harmful
 87 elements such as chromium, nickel, and aluminum, and to contribute evidence-based data to the ongoing
 88 conversation about the relative health risks of smoking and vaping. While recent studies such as Halstead et al.
 89 (2020) [35] have introduced advanced aerosol trap designs for trace metal analysis, this study intentionally
 90 employs a classical nitrocellulose-based approach. The goal is to provide a practical, comparative overview of
 91 emissions using accessible simulation conditions. However, limitations related to filter background
 92 contamination and collection efficiency are acknowledged and discussed.

93 Materials and methods

94 A 0.45 µm nitrocellulose blotting membrane was selected as the collection substrate to simulate lung
 95 exposure in a controlled artificial environment. This material, formed by treating cellulose with sulfuric and
 96 nitric acid (substituting hydroxyl groups with nitro groups), is highly porous and chemically stable, making it
 97 suitable for the deposition and analysis of inhaled elements from both e-cigarette vapor and traditional cigarette
 98 smoke. The study focused on heavier elements with known toxicological profiles, including aluminum (Al),
 99 copper (Cu), chromium (Cr), sodium (Na), sulfur (S), silicon (Si), calcium (Ca), and magnesium (Mg). These
 100 elements are relevant due to their presence in e-liquid ingredients, device components, and potential health risks
 101 when inhaled. The e-liquids used included propylene glycol (PG) and vegetable glycerin (VG) in a 50:50 ratio,
 102 sourced from Pure Chemical. Pharmaceutical-grade nicotine (Vaping Base) was added to achieve a final
 103 concentration of 6 mg/mL. Food-grade flavoring concentrates were included to replicate the sensory
 104 characteristics of commercial e-liquids. The overall experimental flow is illustrated in Fig. 1.

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Fig. 1 Research stages

110 1. Creation of an artificial environment

111 A dedicated system was constructed to simulate inhalation and aerosol exposure under laboratory
 112 conditions. The setup, shown in Figs. 2 and 3, consisted of a conical Erlenmeyer flask (1) sealed with a rubber
 113 stopper (3), which housed the e-cigarette device (2). Vapor was introduced into the flask, where it accumulated
 114 for analysis. A lateral sidearm (4) was connected to a syringe (5) via flexible tubing (6), allowing manual
 115 generation of negative pressure to draw aerosol into the chamber, thereby mimicking human inhalation patterns.
 116 Separate configurations were used for testing e-cigarette aerosols and traditional cigarette smoke, ensuring
 117 consistent methodology and minimizing cross-contamination.

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Fig. 2 Artificial environment for e-cigarettes testing



Fig. 3 Artificial environment for traditional cigarettes testing

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126 2. Choice of elemental deposition medium

127 Several deposition media were evaluated to ensure effective collection of aerosol particles. Coal-based
 128 filters, initially considered, proved unsuitable due to combustion during testing. Standard filter paper retained
 129 large particles (>12–15 μm) but did not capture the full range of emitted elements. Nitrocellulose membranes
 130 ultimately provided optimal performance, effectively capturing both particulate matter and associated chemical
 131 species. Their physical compatibility with the experimental setup and wide elemental retention range supported
 132 their use throughout the study. To further characterize element accumulation, cotton extracted from inside the e-
 133 cigarette coil was also analyzed. This material reflects realistic deposition within the device. Following tests
 134 involving (i) 10 puffs, (ii) continuous use until coil degradation, and (iii) 100 puffs without refilling, the original
 135 coil cotton was carefully removed using sterile tweezers, air-dried, and mounted for elemental analysis.

136 3. Preparation of home-made mixture for e-cigarette

137 Homemade e-liquids were prepared using propylene glycol (PG), vegetable glycerin (VG), and
 138 pharmaceutical-grade nicotine. A 50:50 PG:VG ratio was used to match common commercial formulations.
 139 Nicotine was added to reach a final concentration of 6 mg/mL. Initially, 5.78 mL of PG and 6.4 mL of VG were
 140 combined to create the base. Nicotine solution (6 mL) was then introduced, followed by 1.82 mL of food-grade
 141 flavor concentrate to achieve a 10% flavoring ratio. The chosen flavor profile mirrored gooseberry and
 142 raspberry notes found in the commercial liquid. All components were measured precisely using volumetric
 143 tools. The mixture was stirred thoroughly to ensure full homogeneity, then sealed in an airtight container and

144 stored in a cool, dark location. A 24-hour steeping period allowed the flavors to fully develop and stabilize prior
145 to use. All chemical components used in the preparation of homemade e-liquids, including propylene glycol,
146 vegetable glycerin, and nicotine, were of pharmaceutical-grade (USP), ensuring compliance with established
147 purity and safety standards.

148 4. Cigarette/e-cigarette smoking simulation

149 All vaping tests were performed using an iStick Pico Plus mod (Eleaf) equipped with a Wotoko
150 nexMINI Subtank atomizer. The heating coil used in the Wotoko nexMINI Subtank atomizer was identified as
151 FeCrAl alloy (Kanthal A1), a widely used material in vaping devices composed of iron (Fe), chromium (Cr),
152 and aluminum (Al). This composition was considered during interpretation of EDS results, especially regarding
153 potential coil degradation products. A 0.2 Ω mesh coil was installed, operated at 60 watts—within the
154 manufacturer's recommended range and typical of regular use settings. This configuration ensured stable
155 aerosol production without overheating or dry hits. Each tank was filled with the test liquid and left to saturate
156 the coil for 10 minutes before activation. The simulation protocol was designed to mirror typical vaping
157 behavior. Each test lasted 5 minutes and consisted of 10 puffs taken at 30-second intervals. Each puff lasted 4
158 seconds, delivering a consistent volume of 40 mL (400 mL total). This puffing regimen approximates the
159 consumption of one traditional cigarette, enabling direct comparison of emissions between products. The
160 standardization of puff number, duration, and volume ensured the reproducibility of results and the validity of
161 cross-sample comparisons. For extended-use tests, two additional e-cigarette devices were used to reflect
162 product variability: VooPoo Drag (fitted with a PnP-VM6 0.15 Ω mesh coil) and GeekVape Aegis (fitted with a
163 Z-Series 0.2 Ω mesh coil). These were employed in normal-use scenarios until coil replacement. The VooPoo
164 coil was composed of nickel-chromium (NiCr) alloy, while the GeekVape coil was made of Kanthal A1
165 (FeCrAl alloy), similar to the coil used in the Wotoko tank. These models were selected due to their technical
166 similarity, widespread availability in the consumer market, and common use in sub-ohm vaping. Their inclusion
167 allows for realistic simulation of user conditions.

168 5. Elemental analysis

169 Elemental composition of aerosols and residues was assessed using Energy Dispersive X-ray
170 Spectroscopy (EDS), conducted with an Oxford Instruments Ultim detector. The EDS system was integrated
171 with a TESCAN VEGA 4 scanning electron microscope (SEM), operated under high vacuum using a secondary
172 electron (SE) detector at a working distance of 15 mm. Prior to analysis, 5×5 cm sections of nitrocellulose
173 membrane were exposed in the collection flask. A central 1×1 cm square was then excised and mounted for
174 SEM-EDS to ensure consistency in sampling location. In addition to membrane analysis, post-use cotton from
175 the e-cigarette coils was evaluated to examine trace element accumulation over time. Background measurements
176 were obtained from unused nitrocellulose membranes, unheated homemade and commercial e-liquids, and an
177 unused cigarette filter. These controls were used to distinguish baseline elemental content from exposure-
178 derived contamination. It is important to note that Energy Dispersive Spectroscopy (EDS), while valuable for
179 semi-quantitative screening of elemental composition, has limitations in detecting certain elements at trace
180 levels, especially light or low-concentration metals such as cadmium (Cd) or lead (Pb). Therefore, the absence
181 of these elements in the results does not definitively exclude their presence.

182 6. Viscosity and temperature measurement

183 Viscosity is a critical rheological property of e-cigarette liquids, significantly influencing their
184 interaction with the heating coil, vaporization efficiency, and overall performance. Variations in viscosity can
185 impact liquid vaporization rates, aerosol production, and contribute to coil degradation. Therefore, viscosity
186 analysis is vital for comparing formulations and understanding their impact on device functionality.

187 In this research, dynamic viscosity analysis was performed using a Rheometer type RSCTCPS.
188 Approximately 3 g of the sample was placed on the measurement plate, thermostatted with circulating oil at
189 predetermined measurement temperatures ranging from 20 to 80°C. The measurements were conducted at four
190 pre-established shear rates (200 to 2000 s^{-1}), providing a comprehensive evaluation of the e-liquids' rheological
191 behavior.

10

192 All samples were tested under identical experimental conditions to ensure accuracy and comparability.
193 The rheological measurements monitored changes in viscosity as a function of temperature, providing insights
194 into how these variations could influence e-liquid performance, particularly regarding vaporization efficiency
195 and interaction with the heating coil.

196 To supplement the viscosity analysis, temperature tests were conducted to evaluate differences between
197 home-made and commercially available e-liquids. The temperature was measured inside the tank during
198 smoking, without refilling, to reflect realistic usage conditions. A thermocouple type K was used for these
199 measurements, ensuring precise and reliable monitoring of temperature changes within the tank during
200 operation.

201 Results

202 The elemental residues produced by both e-cigarettes and traditional cigarettes were analyzed under
203 simulated lung exposure conditions. Aerosol deposits were collected on nitrocellulose membranes, allowing for
204 comparative assessment across product types and usage scenarios. Both homemade and store-bought e-liquids
205 were evaluated under different tank conditions (full, half, and empty), alongside traditional cigarettes. To ensure
206 experimental consistency, the homemade liquid was prepared using commercial-grade ingredients in a
207 standardized 50:50 PG/VG base. Additionally, the study included viscosity profiling of both e-liquid types, as
208 this parameter may influence vaporization dynamics and coil degradation.

209 1. Elemental Composition Analysis

210 Elemental analysis was performed using Energy Dispersive X-ray Spectroscopy (EDS), providing a
211 detailed profile of the chemical constituents present in the aerosols. This approach enabled identification of
212 potential sources of trace elements, including those originating from e-liquid components, heating coil materials,
213 and tobacco combustion. Given the toxicological relevance of many detected metals, such as chromium or
214 aluminum, the findings contribute meaningfully to the assessment of inhalation-related health risks.

215 To differentiate between background contamination and exposure-induced residues, EDS was also
216 conducted on unused experimental materials. These included: unheated homemade and store-bought e-liquids
217 on a cotton from e-cigarette heating coils, an unused cigarette filter, unused cotton from e-cigarette heating
218 coils, and an unexposed nitrocellulose membrane. The results of this baseline analysis are summarized in Table
219 1. The clean nitrocellulose membrane exhibited measurable levels of background elements, notably chromium
220 (0.63 wt%), sodium (0.59 wt%), silicon (0.48 wt%), magnesium (0.44 wt%), and aluminum (0.33 wt%),
221 confirming the membrane's non-inert character. The unheated e-liquids showed minimal levels of copper,
222 sulfur, and calcium, indicating low intrinsic metal content. The unused cigarette filter was composed almost
223 entirely of carbon and oxygen, with negligible impurities, while the coil cotton displayed low levels of
224 chromium, sodium, and aluminum, likely introduced via contact with the metallic coil housing during
225 manufacturing. These baseline values establish a critical reference point for interpreting the results of
226 subsequent exposure analyses.

227

228 Table 1 Elemental composition (Wt%) and standard deviation (SD) of unheated reference materials

E	Nitrocellulose		Home-made liquid on a coil cotton		Store-bought liquid on a coil cotton		Cigarette filter		Coil cotton	
	wt%	SD	wt%	SD	wt%	SD	wt%	SD	wt%	SD
O	70.4	0.23	58.0	0.10	57.4	0.10	54.7	0.20	50.2	0.10
C	26.4	0.20	41.6	0.10	42.3	0.10	45.2	0.20	48.8	0.10
Cr	0.63	0.07	–	–	–	–	–	–	0.60	0.00
Na	0.59	0.07	–	–	–	–	–	–	0.30	0.00

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Si	0.48	0.04	–	–	–	–	–	–	–	–	–
Mg	0.44	0.06	–	–	–	–	–	–	–	–	–
S	0.36	0.04	0.10	0.00	0.10	0.00	–	–	–	–	–
Al	0.33	0.05	–	–	–	–	–	–	–	0.20	0.00
Cl	0.21	0.04	–	–	–	–	–	–	–	0.10	0.00
Ca	0.13	0.04	0.10	0.00	0.10	0.00	–	–	–	–	–

229 Further results from the 10-puff test, corresponding approximately to the consumption of a single
 230 traditional cigarette, are presented in Table 2. This test served as a benchmark scenario, allowing for
 231 comparative analysis of aerosol emissions from both traditional and electronic cigarettes under standard,
 232 controlled usage conditions. Elemental analysis focused on several key elements, including chromium, sodium,
 233 aluminum, sulfur, chlorine, silicon, and magnesium. Notable differences in concentration levels between
 234 samples offer insight into how these elements behave under combustion, as in tobacco cigarettes, versus
 235 vaporization, as in e-cigarettes.

236 Tab. 2 Average mean for elemental concentrations across tests on a nitrocellulose membrane with single-
 237 cigarette or 10 puffs (SD - standard deviation [%], Wt% - weight percentage [%])

Average Mean Elemental Concentrations for Aerosols Produced During Single-Cigarette or 10-Puff Tests														
E	Home-made, full tank		Home-made, half tank		Home-made, empty tank		Store-bought, full tank		Store-bought, half tank		Store-bought, empty tank		Tobacco cigarette	
	wt%	SD	wt%	SD	wt%	SD	wt%	SD	wt%	SD	wt%	SD	wt%	SD
O	54.77	0.62	50.26	0.80	52.00	0.94	53.10	0.71	52.37	0.70	51.94	0.64	48.86	0.35
C	40.40	0.64	40.58	0.88	41.31	1.00	41.12	0.73	41.71	0.75	41.15	0.68	49.89	0.36
Cr	3.84	0.95	6.09	0.97	5.33	0.33	4.81	0.90	4.79	0.86	5.48	0.79	0.33	0.03
Na	0.33	0.05	0.32	0.03	0.33	0.05	0.36	0.04	0.36	0.04	0.38	0.04	0.24	0.03
Al	0.36	0.03	1.40	0.06	0.34	0.04	0.26	0.03	0.21	0.03	0.22	0.03	0.08	0.01
S	0.12	0.02	0.20	0.03	0.10	0.02	0.15	0.02	0.22	0.03	0.22	0.03	0.12	0.02
Cl	0.09	0.02	0.17	0.04	0.12	0.02	0.08	0.02	0.08	0.02	0.14	0.03	0.08	0.02
Si	0.04	0.01	0.12	0.02	0.25	0.03	0.02	0.00	0.07	0.02	0.22	0.02	0.15	0.02
Mg	0.00	0.00	0.04	0.01	0.20	0.04	0.01	0.00	0.02	0.00	0.16	0.02	0.11	0.01
Fe	0.00	0.00	0.72	0.15	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Cu	0.07	0.02	0.06	0.02	0.00	0.00	0.04	0.01	0.04	0.01	0.04	0.00	0.07	0.02
Ca	0.00	0.00	0.09	0.00	0.00	0.00	0.05	0.02	0.02	0.00	0.05	0.01	0.05	0.01
Br	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.01

238

239 Chromium concentrations were markedly higher in emissions from e-cigarettes, particularly in the
 240 homemade e-liquid under half-tank conditions, where average levels reached 6.00 wt%. In comparison,
 241 traditional cigarette smoke showed only 0.33 wt% chromium. This significant discrepancy may reflect
 242 contamination from device components or coil degradation, particularly in homemade formulations. The
 243 variability of chromium levels across e-cigarette samples was substantial, with standard deviations as high as
 244 9.47%, suggesting inconsistencies in device integrity or e-liquid-metal interactions. Similarly, aluminum levels
 245 were elevated in the homemade e-liquids under half-tank conditions, with a mean concentration of 1.40 wt%,
 246 whereas other samples—both commercial and traditional—exhibited considerably lower values ranging
 247 between 0.08 and 0.36 wt%. The pronounced variation, especially in homemade liquids, points to potential
 248 influences such as storage stability, contact with aluminum-containing elements, or thermal breakdown during
 249 use. Iron was detected exclusively in the homemade e-liquid under half-tank conditions (0.72 wt%) and was
 250 absent from all other samples. Its isolated presence reinforces the likelihood of contamination from the heating
 251 coil or other internal components during prolonged or incomplete vaporization cycles.

252 Among the trace elements, sodium was relatively consistent across all e-cigarette conditions, with
 253 mean values ranging from 0.32 to 0.38 wt%, slightly exceeding the 0.24 wt% found in traditional cigarette
 254 smoke. This stability suggests that sodium originates from uniform ingredients or additives present in both types
 255 of e-liquids. Sulfur was also consistently detected, showing its highest concentration in the store-bought liquid
 256 under empty-tank conditions (0.22 wt%), while traditional cigarette samples contained slightly lower sulfur
 257 content (0.12 wt%). The overall standard deviation for sulfur was narrow, indicating stable and reproducible
 258 presence. Chlorine was found across all samples, with the highest concentration observed in homemade e-liquid
 259 under half-tank usage (0.17 wt%). Its moderate variability points toward common sources, such as flavorings or
 260 additives shared between formulations. Silicon, though less prevalent, displayed elevated levels in homemade
 261 e-liquid under empty-tank conditions (0.25 wt%), compared to 0.15 wt% in cigarette smoke. This increase may be
 262 linked to overheating during prolonged use, which could cause thermal breakdown of wicking material or
 263 leaching from device components.

264 Together, these results underline the complexity and variability of elemental emissions in e-cigarette
 265 vapor, particularly under conditions where the tank is partially depleted—scenarios that may increase metal
 266 release due to coil stress or uneven wicking. The findings also confirm that even short-term use (10 puffs) can
 267 lead to measurable levels of multiple trace elements in the inhaled aerosol, with potential implications for user
 268 health depending on device quality, e-liquid composition, and usage patterns. To further explore the cumulative
 269 effects of extended product use, elemental analyses were conducted following 100 puffs for e-cigarettes and
 270 after combustion of ten traditional cigarettes. These conditions simulated repeated use without refilling (in the
 271 case of vaping), and enabled more comprehensive comparisons of element accumulation over time. The
 272 averaged results are presented in Table 3.

273 Tab. 3 Average mean for elemental concentrations across tests with 10 cigarettes or 100 puffs on a
 274 nitrocellulose membrane (SD - standard deviation [%], Wt% - weight percentage [%])

Average Mean Elemental Concentrations for Aerosols Produced During 10 Cigarettes (100-Puff) Tests						
E	Home-made liquid		Store-bought liquid		Tobacco cigarette	
	wt%	SD	wt%	SD	wt%	SD
O	50.30	0.10	49.80	0.10	49.60	0.10
C	48.90	0.10	49.30	0.10	49.60	0.10
Cr	0.20	0.00	0.2	0.00	0.30	0.00
Na	0.30	0.00	0.2	0.00	0.2	0.00
Al	0.10	0.00	0.10	0.00	0.1	0.00
S	0.10	0.00	0.10	0.00	0.1	0.00
Cl	0.00	0.00	0.10	0.00	0.1	0.00
Si	0.10	0.00	0.00	0.00	0.00	0.00
Mg	0.10	0.00	0.00	0.00	0.00	0.00
Fe	0.00	0.00	0.00	0.00	0.00	0.00
Cu	0.00	0.00	0.10	0.00	0.00	0.00
Ca	0.00	0.00	0.00	0.00	0.00	0.00
Br	0.00	0.00	0.00	0.00	0.00	0.00

275 For several elements, concentrations appeared more consistent across homemade and store-bought e-
 276 liquids, suggesting stabilization of emissions under prolonged use. Chromium, for example, was detected at
 277 identical levels (0.20 wt%) in both types of e-liquids. Interestingly, this value was slightly exceeded in the
 278 tobacco cigarette group, which reached 0.30 wt%. Although this suggests higher Cr exposure from smoking, the
 279 differences are relatively small under these conditions. Sodium levels also varied modestly between groups,
 280 with homemade e-liquids reaching 0.30 wt%, slightly higher than the 0.20 wt% observed in both store-bought e-
 281 liquids and cigarette smoke. This may reflect specific additives or residual salts present in the homemade
 282 formulations. Aluminum and sulfur remained uniform across all three sample types, with consistent
 283 concentrations of 0.10 wt%, indicating that these elements are either inherent to basic ingredients or are released
 284 uniformly during use and combustion.

285 Chlorine was detected only in store-bought e-liquids and traditional cigarettes (0.10 wt% each), but not
 286 in homemade samples. This suggests that chlorine-containing compounds may be introduced during industrial e-
 287 liquid production or cigarette processing, but are not present in DIY mixtures. Conversely, silicon and
 288 magnesium were found in homemade e-liquids (0.10 wt% each), but were undetected in the store-bought liquids
 289 and cigarette samples, further highlighting compositional differences attributable to liquid preparation methods.
 290 Copper was consistently present in all tested samples, although in low amounts, ranging from 0.04 to 0.07 wt%.
 291 In this extended-use test, copper appeared only in the cigarette group (0.10 wt%), while other trace elements
 292 such as iron, calcium, and bromine were largely undetected across all product types.

293 To further assess the behavior of trace elements over time, additional analyses were conducted on
 294 residues collected from cotton extracted from e-cigarette heating coils. These tests followed three usage
 295 scenarios: 10 puffs (equivalent to one cigarette), continuous use until coil replacement, and 100 puffs without
 296 refilling. The results are summarized in Tables 4-6.

297 Table 4 Average mean for elemental composition after 10 puffs on a coil cotton/1 cigarette

Element	Homemade		Store-bought		Cigarette	
	wt%	SD	wt%	SD	wt%	SD
O	58.61	0.18	59.16	0.19	100.00	0.00
C	41.29	0.18	40.74	0.19	-	-
Cu	0.07	0.01	0.11	0.01	-	-
Zn	-	-	-	-	-	-
Ni	-	-	-	-	-	-
Si	0.05	0.02	-	-	-	-
Cl	-	-	-	-	-	-
Ca	0.07	0.02	0.06	0.01	-	-
Al	-	-	0.05	0.02	-	-
S	0.01	0.00	-	-	-	-
Ti	0.12	0.00	-	-	-	-
Br	-	-	-	-	-	-

298 Table 5 Average mean for elemental composition after 100 puffs on a coil cotton without refilling
 299

Element	Homemade		Store-bought	
	wt%	SD	wt%	SD
O	51.60	0.20	51.30	0.10
C	47.30	0.20	48.30	0.10
Cu	0.20	0.00	0.10	0.00
Zn	-	-	0.10	0.00
Ni	-	-	0.10	0.00
Si	-	-	-	-
Cl	0.00	0.00	-	-
Ca	0.00	0.00	0.00	0.00
Al	-	-	-	-

S	0.00	0.00	0.00	0.00
Ti	0.70	0.00	-	-
Br	0.00	0.10	-	-

300

301 Table 6 Average mean for elemental composition after normal use, measured on a coil cotton (by
 302 smoker - until coil change)

Element	Vopoo Drag (normal-use)		GeekVape Aegis (normal-use)	
	wt%	SD	wt%	SD
O	72.50	0.09	58.77	0.17
C	27.17	0.09	41.17	0.17
Cu	0.16	0.01	0.08	0.01
Zn	0.05	0.01	-	-
Ni	0.03	0.01	-	-
Si	0.03	0.00	0.04	0.01
Cl	0.02	0.00	-	-
Ca	0.01	0.00	-	-
Al	0.01	0.00	0.04	0.01
S	0.01	0.00	-	-
Ti	-	-	-	-
Br	-	-	-	-

303

304 When comparing elemental composition across these extended use scenarios, distinct patterns begin to
 305 emerge. Chromium (Cr), for instance, was initially found at high levels in homemade e-liquids—ranging from
 306 3.84% to 6.00% during the 10-puff test—while tobacco cigarette samples contained only 0.33%. However, after
 307 ten cigarettes or prolonged vaping, chromium concentrations stabilized around 0.20% across all product types.
 308 This suggests that chromium does not accumulate linearly with continued use. Instead, it may reach a threshold
 309 of deposition or be influenced by saturation effects within the system or limitations in the detection of bound or
 310 less-volatile forms of the metal. Aluminum (Al) displayed a similar trend. It peaked at 1.40% in the homemade
 311 e-liquid during short-term use (especially under half-tank conditions), while traditional cigarettes showed only
 312 0.08%. Yet, after extended exposure, aluminum levels converged at approximately 0.10% in all groups. This
 313 leveling-off effect implies that aluminum accumulation may be moderated over time, possibly due to the
 314 stabilization of device emissions or saturation of the deposition substrate.

315 Iron (Fe), which appeared only in one instance - within the homemade half-tank group (0.72%) - was
 316 not detected in any of the long-term scenarios. Its sporadic presence supports the hypothesis that iron
 317 contamination stems from device-specific factors such as coil wear or mechanical degradation, rather than
 318 consistent release from e-liquids or tobacco. Sodium (Na) exhibited more predictable behavior. During the 10-
 319 puff trial, sodium levels were slightly elevated in store-bought e-liquids (0.36–0.38%) compared to homemade
 320 mixtures (0.32–0.35%) and cigarette smoke (0.24%). After 100 puffs or the combustion of ten cigarettes,
 321 sodium levels were generally consistent, ranging from 0.20% to 0.36%, regardless of the product. This suggests
 322 a more linear and reproducible release profile, possibly due to sodium's stable presence in base ingredients or
 323 manufacturing additives. Sulfur (S) followed a similarly stable pattern. Initial tests showed values between
 324 0.16% and 0.22%, with the highest readings found in store-bought e-liquids and tobacco products. These values
 325 normalized to 0.10% after extended use, indicating no significant accumulation over time and possibly
 326 reflecting its volatilization or limited deposition. Chlorine (Cl), detected in the range of 0.08–0.17% during the
 327 single-cigarette trials, showed similarly low and stable concentrations in longer-term use, without strong

328 variation across product types. This suggests that chlorine compounds, where present, do not accumulate in a
 329 dose-dependent fashion, or may be volatilized before deposition.

330 Overall, the extended-use tests reveal that some elements, such as chromium and aluminum, exhibit
 331 high initial concentrations under certain conditions (e.g. homemade liquids, partial tank usage) but stabilize
 332 with continued use. Others, like sodium and sulfur, demonstrate more consistent behavior throughout. The
 333 cotton-based measurements from inside the coil further confirm the presence of trace metals directly at the
 334 vaporization source, reinforcing concerns about metal transfer from heating components to inhaled aerosol.

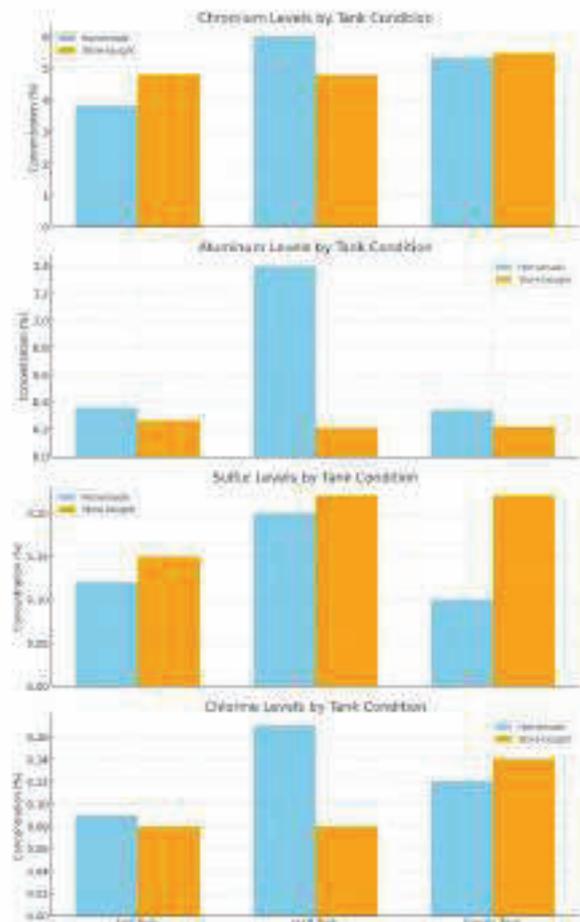
335 1.1. Analysis of elements by their concern level

336 This chapter provides an in-depth analysis of the elements present in the emissions, categorizing them
 337 based on their potential health concerns (tab. 7). By evaluating these elements based on their toxicity,
 338 prevalence, and potential health risks, this chapter aims to provide a clearer understanding of which substances
 339 may pose a greater concern to users and the environment.

340 Tab. 7 Categorization of elements by concern level in aerosol composition analysis

Highest concern elements	Moderate concern elements
Chromium (Cr)	Silicon (Si)
Aluminum (Al)	Sodium (Na)
Sulfur (S)	Magnesium (Mg)
Chlorine (Cl)	

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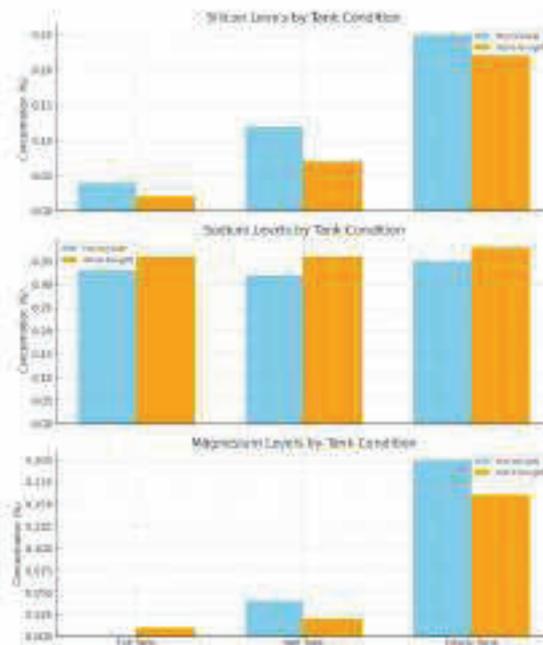


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Fig. 4 Bar charts of highest concern elements

344 The Fig. 4 bar charts show key trends in elemental concentrations across different e-liquid types and
 345 tank conditions. Chromium levels are slightly more stable in store-bought e-liquids, but both types increase in
 346 the empty tank. Homemade e-liquids have significantly higher aluminum levels in the half-tank condition
 347 compared to store-bought ones. Store-bought e-liquids consistently show higher sulfur levels, especially in the
 348 half and empty tanks. Chlorine is higher in homemade e-liquids in the half-tank condition, while store-bought e-
 349 liquids see an increase in chlorine in the empty tank, possibly due to coil degradation or additive residues.

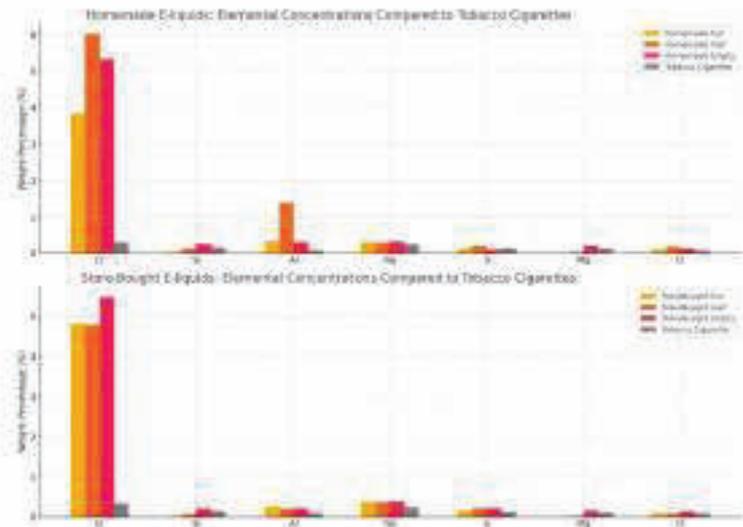
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Fig. 5 Bar charts of moderate concern elements

355 The Fig. 5 bar charts reveal trends in silicon, sodium, and magnesium concentrations across different e-
 356 liquid types and tank conditions. Homemade e-liquids show higher silicon levels in the empty tank, while store-
 357 bought e-liquids are more consistent but increase significantly in the same condition. Store-bought liquids
 358 generally have slightly higher sodium levels with minimal variability across tank conditions. Homemade e-
 359 liquids exhibit a noticeable magnesium increase in the empty tank, while store-bought liquids show a smaller
 360 rise but still increase in this condition.



361

362 Fig. 6 Graphs of elemental composition for homemade and store-bought liquids smoke in comparison to tobacco
 363 cigarette smoke.

364

365 Key insights reveal important trends in elemental concentrations across homemade e-liquids, store-
 366 bought e-liquids, and tobacco cigarettes (Fig. 6). Homemade e-liquids show higher chromium levels,
 367 particularly in the "half" and "empty" tank conditions, suggesting potential coil degradation. Aluminum levels
 368 also vary notably, peaking at the "half" tank condition. Store-bought e-liquids exhibit more consistent elemental
 369 concentrations across tank conditions. Chromium levels are slightly lower than in homemade liquids but
 370 increase in the "empty" tank, possibly due to coil exposure. Tobacco cigarettes generally have lower
 371 concentrations of most trace elements, except for chromium, which aligns with known contaminants found in
 372 traditional cigarettes. Sulfur and chlorine levels tend to be higher in store-bought e-liquids, possibly due to
 373 additives or flavor compounds. Magnesium and silicon appear at trace levels, particularly in store-bought e-
 374 liquids under certain conditions. Tobacco cigarettes show fewer variations in elemental composition, likely due
 375 to their consistent manufacturing process.

376 The analysis identified several elements as the residue, each with varying degrees of health concerns:

- 377 1. Chromium (Cr)
- 378 ○ Potential Concerns: chromium, particularly in its hexavalent form (Cr(VI)), is a known
 - 379 carcinogen. Prolonged inhalation can lead to respiratory issues and lung cancer.
 - 380 ○ Safety Limits: OSHA sets a permissible exposure limit (PEL) of $5 \mu\text{g}/\text{m}^3$ over an 8-hour
 - 381 workday. Any exposure to chromium in vapor form should be minimized [36].
- 382 2. Sodium (Na)
- 383 ○ Potential Concerns: low levels of sodium are generally harmless, but excessive inhalation may
 - 384 irritate the respiratory tract.
 - 385 ○ Safety Limits: no specific limits, as the detected levels are typically negligible.
- 386 3. Aluminum (Al)
- 387 ○ Potential Concerns: chronic exposure to aluminum has been linked to neurotoxicity and
 - 388 respiratory issues. It may also be associated with Alzheimer's disease, though the evidence is
 - 389 inconclusive.
 - 390 ○ Safety Limits: OSHA sets the PEL at $15 \text{ mg}/\text{m}^3$ (total dust) and $5 \text{ mg}/\text{m}^3$ (respirable fraction)
 - 391 over an 8-hour workday. Reducing aluminum exposure through vapor is recommended [36].
- 392 4. Sulfur (S)
- 393 ○ Potential Concerns: sulfur compounds can irritate the respiratory system, and sulfur dioxide
 - 394 (SO_2) is known to exacerbate asthma and other respiratory conditions.
 - 395 ○ Safety Limits: WHO recommends a 24-hour mean limit of $40 \mu\text{g}/\text{m}^3$ for sulfur dioxide.
 - 396 Reducing sulfur exposure in vapor is advisable [37].
- 397 5. Chlorine (Cl)
- 398 ○ Potential Concerns: chlorine is a potent irritant that can cause severe respiratory distress when
 - 399 inhaled in high concentrations.
 - 400 ○ Safety Limits: OSHA's PEL for chlorine gas is 1 ppm over an 8-hour workday. Minimizing
 - 401 chlorine exposure in vapor is crucial [36].
- 402 6. Silicon (Si)
- 403 ○ Potential Concerns: while inert in many forms, silicon in crystalline silica form is a respiratory
 - 404 hazard, causing silicosis with prolonged exposure.
 - 405 ○ Safety Limits: OSHA's PEL for respirable crystalline silica is $50 \mu\text{g}/\text{m}^3$ over an 8-hour
 - 406 workday. Non-crystalline silicon is less concerning but warrants monitoring [36].
- 407 7. Magnesium (Mg)
- 408 ○ Potential Concerns: magnesium is generally safe, but inhaling large amounts may irritate the
 - 409 respiratory system.
 - 410 ○ Safety Limits: no specific limits are established, but the low concentrations detected are not a
 - 411 concern.

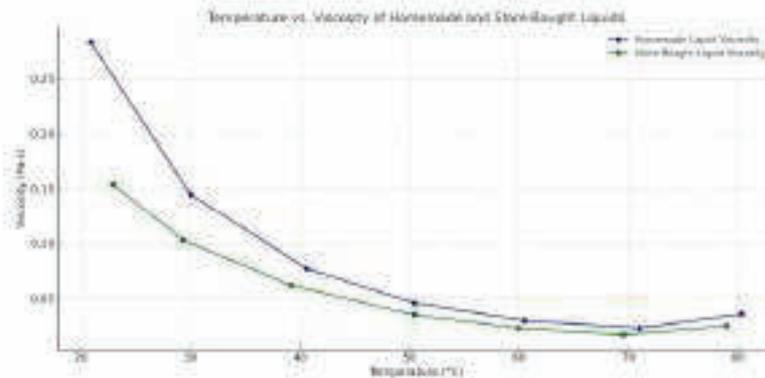
412 1.2. Viscosity and temperature measurements

413 The viscosity analysis highlighted distinct trends in the behavior of homemade and store-bought e-
 414 liquids (Fig. 7). At lower temperatures, homemade demonstrated relatively stable viscosity ($\sim 0.2848 \text{ Pa}\cdot\text{s}$ at
 415 -20.9°C), which decreased sharply with rising temperature, reaching approximately $0.0295 \text{ Pa}\cdot\text{s}$ at -60.5°C —a
 416 nearly tenfold reduction. However, at 80°C , the viscosity increased slightly to $0.036 \text{ Pa}\cdot\text{s}$, signaling the onset of

417 thermal degradation. This sharp decline underscores a strong inverse relationship between viscosity and
 418 temperature, reflecting reduced intermolecular forces at elevated temperatures. In contrast, store-bought
 419 exhibited a slightly lower initial viscosity ($\sim 0.15 \text{ Pa}\cdot\text{s}$ at -23.5°C) and a more gradual decline with temperature,
 420 indicating the presence of additives or stabilizers in the commercial formulation that enhance thermal stability.
 421 At 80°C , a slight increase in viscosity to $0.025 \text{ Pa}\cdot\text{s}$ also pointed to the onset of thermal degradation.

422 Shear stress measurements further differentiated the two liquids. For homemade liquid, shear stress
 423 stabilized around $56\text{--}57 \text{ Pa}$ at a shear rate of $\sim 200 \text{ (1/s)}$, exhibiting Newtonian-like behavior across the tested
 424 range. Store-bought liquid displayed lower shear stress values, ranging from 29.9 to 33.6 Pa at comparable shear
 425 rates, consistent with its lower viscosity.

426 These findings emphasize the superior thermal stability of store-bought liquids, which maintain more
 427 consistent viscosity across a wide temperature range. This stability supports efficient vaporization and consistent
 428 vaping performance, in contrast to the steep viscosity drop in homemade liquids, which may adversely affect
 429 performance and thermal management during use.



430
431 Fig. 7 Viscosity results

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433 Temperature analysis was performed in parallel to evaluate the heating behavior of both e-liquids in
 434 real-world conditions (Fig. 8). Measurements were taken inside the tank during operation, without refilling,
 435 under standardized conditions to simulate typical vaping scenarios. The temperature profile of the homemade
 436 liquid revealed faster heating and higher initial peak temperatures compared to the store-bought liquid. This
 437 difference is attributed to the simpler composition of homemade liquid, which lacks thermal stabilizers or
 438 additives to moderate heat distribution. However, after initial rises, both liquids stabilized at approximately 40°C
 439 during operation and did not exceed this threshold under the tested conditions.

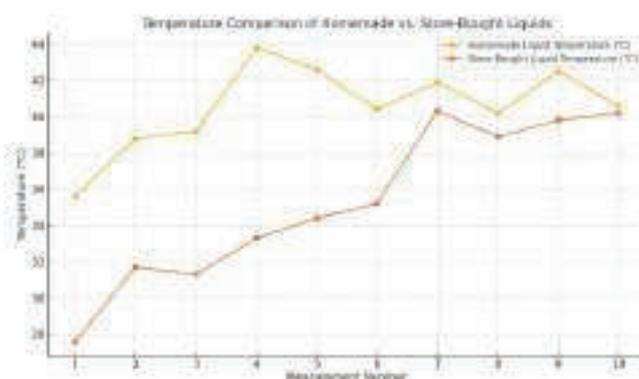


Fig. 8 Temperature results

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444 Discussion

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This study aims to provide a qualitative assessment of the elemental composition of inhalation products from electronic and traditional cigarettes, using a simulated lung exposure model to better understand their potential health effects. Although aerosol mass and dose per lung surface area were not quantified, puff count and volume were standardized to approximate typical usage conditions and allow relative comparison between products. The results show significant differences in the elemental profiles of emissions from e-cigarettes (with homemade and store-bought liquid) compared to traditional cigarette smoke, highlighting the complexity of potential risks associated with e-cigarette use. The observed differences in elemental emissions, such as the presence of aluminum, chromium, sodium, sulfur and other metals, underscore the unique chemical composition of e-liquids and highlight the potential health risks that can result from inhaling these substances. While the concentrations of these elements are relatively low, the cumulative effect of long-term exposure through regular e-cigarette use is not well understood. The nitrocellulose membrane itself was found to contain multiple trace elements, including chromium, sodium, and aluminum, prior to exposure. This highlights the limitations of traditional membrane-based collection methods for trace metal analysis. Consequently, complementary analysis using cotton from within the heating coil provided a cleaner and more relevant sampling medium, allowing for validation of the deposition patterns observed on the nitrocellulose substrates.

Recent research into the particulate matter from e-cigarettes has underscored the need for comprehensive investigations into their impact on human health. Fernández et al. (2015) conducted a comparative analysis of particulate emissions from electronic and traditional cigarettes, revealing that e-cigarette aerosols, while less chemically complex, may still deposit harmful particles in the respiratory tract [38]. Similarly, Pichelsteiner et al. (2020) highlighted the anatomical variability in particle deposition within the lungs, suggesting differential health impacts between devices [39]. Moreover, the thermal behaviour of e-cigarette liquids has been shown to influence aerosol composition. Lampou et al. (2019) found variations in emissions depending on the device and liquid characteristics, with significant impacts on the concentration of harmful constituents like heavy metals [40]. Szparaga et al. (2021) reviewed the chemical content of aerosols generated by e-cigarettes, highlighting the presence of potentially harmful metals and thermal by-products that may exacerbate health risks [41].

The findings suggest that the viscosity of e-liquids also plays a role in the overall safety and performance of e-cigarette devices. E-liquids with higher viscosity tend to exhibit more stable vaporization, reducing the likelihood of coil degradation and the release of harmful elements. E-liquids with lower viscosity

474 may lead to more rapid wear on coils, increasing the potential for harmful contaminants in the vapor. The
475 greater variability in viscosity observed in homemade e-liquids may exacerbate these issues, contributing to
476 inconsistent vaporization and higher risks of exposure to potentially hazardous materials. Store-bought e-liquids,
477 on the other hand, tend to maintain more consistent viscosity levels, which supports stable vaporization and
478 minimizes the risk of coil degradation. This consistency, coupled with the lower levels of harmful elements,
479 further underscores the potential advantages of commercially produced e-liquids in terms of safety and
480 performance.

481 The combined analysis of viscosity and temperature highlights critical differences between homemade
482 and store-bought e-liquids. While both liquids stabilized around 40 °C during operation, homemade liquid
483 demonstrated superior thermal stability and viscosity retention, ensuring consistent performance and safety. In
484 contrast, store-bought liquid's rapid viscosity decline and initial temperature spikes may present challenges for
485 users, particularly during prolonged use. These findings underscore the importance of formulation in achieving
486 optimal e-liquid performance, particularly under varying thermal conditions. The analysis of viscosity and
487 temperature in this study echoes findings from related work on the role of these factors in e-liquid behavior. A
488 study by Ko et al. (2022) [42] highlighted that e-liquid viscosity and temperature directly impacts the heating
489 process. These conditions can result in the release of metals and other harmful elements into the aerosol. The
490 study further noted that maintaining consistent temperature is essential for optimizing the safety and efficiency
491 of e-cigarette devices.

492 The presence of trace elements like chromium, aluminum, and sodium in e-cigarette emissions, as
493 observed in this study, aligns with findings from other recent research. Additional evidence came from direct
494 analysis of coil cotton, where elevated levels of chromium, copper, and nickel were detected after extended use,
495 supporting the hypothesis that these metals originate primarily from coil degradation rather than e-liquid
496 composition. Studies have shown that e-cigarette aerosol contains various metals, likely originating from the
497 coil material and heating process, which may pose inhalation risks. For example, a study by Aherrera et al.
498 (2023) [43] found that e-cigarette aerosols contain significant levels of metals, with some reaching
499 concentrations high enough to be concerning for users' respiratory health. In this study, elevated levels of
500 chromium and aluminum were observed in certain e-liquid samples, particularly in homemade e-liquids under
501 the half-tank configuration. These metals are known for their toxicity, and prolonged exposure could contribute
502 to respiratory and neurological diseases. The chromium in e-cigarettes, as highlighted by the research of
503 Aherrera (2017) [44], further reinforces concerns about the potential carcinogenic effects of hexavalent
504 chromium, which could be released during vaping.

505 In this study, while traditional cigarettes also release a variety of toxicants, the elemental
506 concentrations for metals like chromium and aluminum in tobacco smoke were not as pronounced as in e-
507 cigarettes. This aligns with the findings of studies like that of Williams et al. (2013) [45], which reported that
508 cigarette smoke contains various toxic compounds, but metals like chromium were not as prevalent when
509 compared to e-cigarette aerosols. Tobacco combustion produces a mix of thousands of chemicals, many of
510 which are carcinogenic, but the heating mechanism in e-cigarettes may contribute to the increased release of
511 metals and other compounds like sulfur and chlorine, which are less common in traditional cigarette emissions.
512 Notably, lead and cadmium - commonly scrutinized in inhalation toxicology - were not detected in the tested
513 samples. This could result from either their actual absence or limitations in detection sensitivity of the EDS
514 technique. Nickel, another toxicologically relevant metal, was detected in both aerosol residues and coil cotton
515 samples, although not consistently across all devices. Notably, nickel was present in the aerosol sample
516 collected after 100 puffs using the iStick Pico Plus with a FeCrAl (Kanthal A1) coil, despite this alloy not
517 typically containing nickel. This suggests possible trace contamination from manufacturing, solder joints, or
518 contact materials. In contrast, nickel was also observed in post-use coil cotton from the Voopoo Drag device,
519 which uses a NiCr coil—supporting the hypothesis that coil composition contributes to nickel exposure, though
520 not exclusively.

521 One of the unique contributions of this study is the consideration of the tank level condition in
522 homemade and store-bought e-liquids (full, half, and empty tanks). The findings suggest that higher metal
523 concentrations, such as aluminum and chromium, were observed under certain tank conditions, particularly with
524 homemade e-liquids. This insight echoes the work of Gordon et al. (2021) [46], who observed similar trends,
525 noting that e-cigarette emissions become more toxic as the tank depletes, likely due to increased coil
526 degradation and overheating. Sulfur and chlorine levels were also consistently observed in store-bought e-
527 liquids across all tank conditions, indicating the potential role of additives or flavor compounds in the e-liquids.
528 This phenomenon was explored in a study by Aherrera et al. (2023) [43], where flavoring compounds in e-
529 liquids were linked to the release of harmful chemicals upon heating.

530 The findings from this study suggest that the trace elements detected in e-cigarette emissions, such as
 531 chromium, aluminum, and sulfur, may pose significant health risks. The long-term exposure to these elements,
 532 particularly chromium (a known carcinogen), could lead to respiratory and cardiovascular problems, as
 533 evidenced by numerous studies on metal exposure in occupational settings. For example, Beaver et al. (2009)
 534 [47] showed that prolonged exposure to chromium through inhalation could result in chronic respiratory
 535 diseases and lung cancer. This concern is corroborated by the European Respiratory Society (2019) [48] report
 536 on vaping risks, which highlighted that e-cigarettes are not without health risks, particularly regarding exposure
 537 to potentially toxic metals and chemicals. The elevated levels of aluminum observed in this study, particularly in
 538 homemade e-liquids, raise further concerns, as chronic exposure to aluminum has been linked to neurological
 539 diseases such as Alzheimer's (Wang 2016 [49]).

540 Recent regulatory evaluations, including those by the FDA and European agencies, have acknowledged
 541 that certain ENDS products may be appropriate for public health protection under specific conditions (Bolt,
 542 2024 [50]). However, concerns regarding exposure to trace metals and the long-term health implications of these
 543 devices remain significant. The coil used in this study was a standard 0.2 Ω mesh coil, typically made of FeCrAl
 544 alloy (Kanthal A1) which includes iron, chromium, and aluminum. These materials are common in
 545 commercially available vaping devices and are known sources of metal particulate contamination during
 546 heating. The inclusion of used coil cotton analysis provided a complementary dataset, which helped validate the
 547 deposition findings from nitrocellulose membranes by confirming the presence of similar trace elements at the
 548 vaporization source. Lead (Pb) and cadmium (Cd) were not detected in the tested samples, which may be due to
 549 differences in coil composition, liquid purity, or the detection limits of the analytical method used. Nickel (Ni),
 550 while not consistently found across all scenarios, was observed in specific coil cotton samples, supporting its
 551 origin from metal components rather than e-liquid content.

552 While the present study emphasizes elemental exposure risks, it is also important to consider the
 553 broader regulatory context. Recent product-specific authorizations by the U.S. FDA acknowledge that under
 554 certain conditions, some ENDS products may be appropriate for the protection of public health. However,
 555 concerns regarding coil degradation and long-term trace metal exposure remain unresolved. Additionally,
 556 although EVALI has been primarily linked to illicit THC products, recent reviews such as Bolt (2024) [50]
 557 underscore the importance of continuous monitoring of all vaping devices.

558 Conclusion

559 This study provides a detailed analysis of the elemental composition of aerosols from electronic
 560 cigarettes (e-cigarettes) and traditional cigarettes, utilizing a simulated exposure model to investigate differences
 561 in aerosol composition and possible implications for inhalation exposure. Using nitrocellulose membranes with
 562 suitable porosity to capture aerosol components, the research examined emissions from both homemade and
 563 store-bought e-liquids at varying tank levels, as well as traditional cigarette smoke. The results reveal significant
 564 differences in elemental profiles, highlighting the varying risks associated with these products.

565 Trace elements such as aluminum, copper, chromium, sodium, sulfur, silicon, calcium, and magnesium
 566 were detected in varying concentrations, reflecting the complexity of emissions. While traditional cigarettes are
 567 toxic in many respects, they do not consistently exhibit the highest concentrations of all analyzed elements
 568 compared to e-liquids. For instance, certain homemade e-liquid samples with a half-tank configuration displayed
 569 significantly elevated aluminum levels, raising potential safety concerns. Similarly, store-bought e-liquids
 570 consistently demonstrated higher levels of chromium compared to traditional cigarettes. Nickel was detected in
 571 both cotton and aerosol samples from different devices, indicating that even coils without nickel as a base
 572 material (e.g., Kanthal A1) may release trace amounts during use. These findings challenge the perception that
 573 e-liquids are inherently safer than traditional cigarettes, as they may expose users to hazardous elemental
 574 concentrations under specific conditions.

575 The study also highlights the critical role of tank fulfillment levels in influencing emission profiles.
 576 Full tanks generally produced the lowest concentrations of harmful elements, likely due to more efficient liquid
 577 vaporization and reduced coil exposure to air. In contrast, nearly empty tanks exhibited significantly higher
 578 levels of harmful emissions, attributed to coil overheating and material degradation under these conditions.
 579 Additionally, half-tank fulfillment results in uneven thermal distribution across the coil, leading to accelerated
 580 degradation.

581 Contamination sources were identified as primarily stemming from coil materials, with elements such
 582 as chromium, aluminum, and copper detected in vapor, and liquid ingredients, particularly those containing
 583 additives like sulfur and chlorine. Homemade e-liquids, which displayed higher levels of aluminum and
 584 chromium, raised safety concerns, especially with prolonged use or improper handling. In contrast, store-bought
 585 e-liquids demonstrated greater consistency and generally lower concentrations of hazardous elements,
 586 presenting them as a relatively safer option.

587 Additionally, the study underscores the influence of factors such as viscosity, thermal behavior, and the
 588 porosity of collection membranes on the results. Homemade e-liquids were found to exhibit a sharp decline in
 589 viscosity with increasing temperature, exacerbating coil degradation and the release of harmful metals. Store-
 590 bought e-liquids, on the other hand, showed greater thermal stability and more gradual viscosity changes, likely
 591 due to the presence of stabilizers or additives that reduce contaminant release. Temperature analyses further
 592 revealed that homemade e-liquids heat faster and reach higher peak temperatures than store-bought options,
 593 reflecting differences in their formulations and thermal management capabilities.

594 These findings emphasize the need for stringent quality control in e-liquid formulations, device design,
 595 and manufacturing practices. Future research should expand the range of e-liquids analyzed, include long-term
 596 exposure studies to assess cumulative risks, and further investigate the role of coil degradation in metal
 597 contamination. By combining elemental profiling, viscosity and thermal behavior analysis, and advanced
 598 collection methods like nitrocellulose membranes, this study provides a comprehensive understanding of the
 599 risks associated with vaping and smoking. The results underscore the necessity for comprehensive regulation
 600 and ongoing research to mitigate these health risks effectively.

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603 **CRediT authorship contribution statement**

604 **Joana Chwał:** Writing – original draft, Writing – review & editing, Visualization, Validation,
 605 Software, Methodology, Investigation, Formal analysis, Conceptualization. **Anna Filipowicz:** Writing
 606 – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis,
 607 Conceptualization. **Magdalena Antonowicz:** Writing – review & editing, Writing – original draft,
 608 Investigation, Formal analysis, Conceptualization, Supervision. **Dawid Lisicki:** Writing – original
 609 draft, Writing – review & editing, Investigation, Conceptualization, Supervision. **Paweł Koska:**
 610 Writing – original draft, Writing – review & editing, Investigation, Conceptualization, Supervision.
 611 **Rafał Domic:** Writing – review & editing, Validation, Supervision.

612

613 **Data availability**

614 The data provided for the results presented in this study are available through the corresponding author upon
 615 request.

616

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618 **Declaration of competing interest**

619 The authors declare that they have no known competing financial interests or personal relationships that could
 620 have appeared to influence the work reported in this paper.

621

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Comparative Pharmacokinetics of Nicotine from E-Cigarettes and Traditional Cigarettes: A PBPK Modeling and Machine Learning Approach

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Abstract. Nicotine addiction remains a major public health concern, with e-cigarettes altering exposure dynamics by delivering nicotine in aerosol form. This study uses Physiologically Based Pharmacokinetic (PBPK) modeling combined with eXtreme Gradient Boosting (XGBoost) to simulate nicotine distribution and assess individual variability.

Results show that e-cigarettes lead to more sustained nicotine exposure, while traditional cigarettes cause rapid peaks in blood and brain concentrations. Blood-brain permeability was identified as the key factor influencing

brain accumulation. ML integration significantly enhanced prediction accuracy ($R^2 > 0.9998$).

These findings underscore the pharmacokinetic differences between delivery methods and demonstrate the value of combining PBPK and ML approaches for personalized exposure modeling and public health guidance.

Keywords: Nicotine PBPK modeling Machine Learning XGBoost Blood-Brain Barrier E-cigarettes Smoking Cessation

1. Introduction

Nicotine is a widely used psychoactive compound with significant physiological and neurological effects, playing a central role in tobacco addiction [1]. The emergence of e-cigarettes has intensified research into differences in nicotine absorption, metabolism, and health impacts compared to traditional cigarettes. Delivered via aerosol rather than smoke, e-cigarettes affect nicotine pharmacokinetics differently, which is crucial for evaluating their health risks and shaping public health policies [2]. In 2016, the FDA expanded its regulatory authority to include electronic nicotine delivery systems (ENDS) [3], emphasizing the need to understand nicotine pharmacokinetics in both conventional and reduced-risk products [4].

Physiologically Based Pharmacokinetic (PBPK) modeling enables detailed simulation of nicotine ADME processes by incorporating organ-specific parameters such as blood flow, metabolism, and tissue composition [5]. It offers greater precision than simpler models and is widely used to compare delivery methods and account for individual metabolic differences [6, 7].

In this study, we developed PBPK models to simulate nicotine metabolism following inhalation from cigarettes and e-cigarettes, focusing on lung absorption, hepatic metabolism, and brain delivery. To enhance prediction accuracy, we integrated machine learning methods—specifically XGBoost—to model complex interactions among physiological parameters. Trained on simulated data, our ML-enhanced PBPK model enables personalized nicotine exposure estimates in the brain and blood. Our goal was to compare nicotine kinetics between e-cigarettes and cigarettes, assess interindividual variability, and apply ML to refine predictions. This integrative approach aims to support more informed regulatory decisions and public health strategies.

2. Materials and Methods

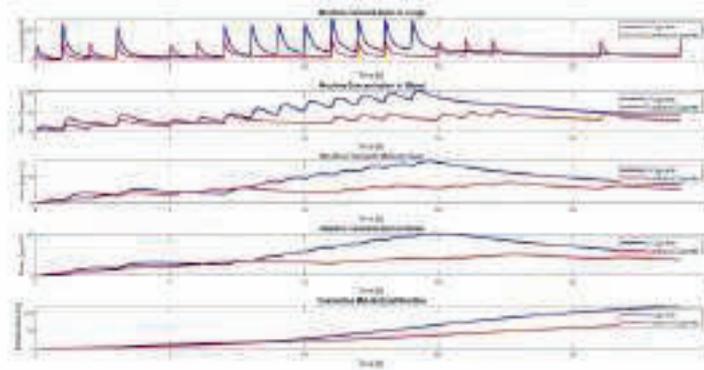


Figure 1. Nicotine Concentrations Over Time for E-Cigarettes vs. Traditional Cigarettes

Model validation demonstrated excellent predictive accuracy, with predicted nicotine concentrations closely matching simulated values (RMSE <0.1%, $R^2 > 0.9998$; Figure 2). Among physiological parameters, blood-brain permeability (k_{penet}) had the strongest influence on brain and synaptic levels, followed by metabolic rate (k_{metab}), pulmonary blood flow (Q_p), body weight, and smoking history. Correlation analysis confirmed these findings, showing strong positive correlations between k_{penet} and nicotine levels in the brain (0.90) and synapse (0.92), and a strong negative correlation with blood concentrations (-0.94). Faster metabolism was consistently associated with lower nicotine levels across all compartments.

Correlation analysis supported these findings: k_{penet} showed strong positive correlation with brain and synapse concentrations (0.90 and 0.92), and negative correlation with blood (-0.94). Higher metabolic rate correlated with lower nicotine levels in all compartments.

In a representative individual, predicted concentrations reached 108ng/mL in the brain, 64ng/mL in blood, and 137ng/mL in synapses, indicating notable synaptic accumulation. Model reliability was further supported by comparisons with real-world pharmacokinetic data (Figure 3), where R^2 values exceeded 0.79 (brain), 0.87 (blood), and 0.90 (synapse), with low residual errors across all compartments.

2.1. Study Design and PBPK Modeling

This study used computational modeling to compare nicotine pharmacokinetics from e-cigarettes and traditional cigarettes. PBPK models were developed in MATLAB R2024b to simulate nicotine ADME processes across key compartments (lungs, blood, liver, brain, synapses), using mass balance, Fick's law, and first-order kinetics [8]. Differential equations were solved numerically (ODE45; RelTol = 1e-6, AbsTol = 1e-8), simulating 24-hour exposure profiles.

2.2. Nicotine Dosing and Exposure Scenarios

E-cigarette dosing was based on 6mg/mL e-liquid, 0.1 mL per puff, 10 puffs/session, and 50% bioavailability [9], yielding 3mg per session and 60mg/day. Cigarette exposure was set at 1.5mg per session [10], both administered hourly. Real-world pharmacokinetic data [11, 12] informed model validation (C_{max}/T_{max} values in brain, blood, and synapses).

2.3. Machine Learning Integration

To assess individual variability, XGBoost was used to predict nicotine C_{max} in each compartment. The model was trained on 1000 simulated individuals with varied physiological traits, including k_{metab} , k_{penet} , Q_p , body weight, smoking history, and metabolic phenotype.

2.4. Performance Evaluation

Model accuracy was assessed via RMSE, MAE, and R^2 metrics. SHAP values quantified feature importance, while Pearson correlations explored associations between physiological parameters and nicotine distribution.

3. Results

PBPK simulations showed that e-cigarettes led to higher cumulative nicotine concentrations than traditional cigarettes, particularly in the blood, liver, and brain (Figure 1). This reflects behavioral differences in inhalation and results in greater systemic exposure and prolonged nicotine presence in neural and metabolic compartments.

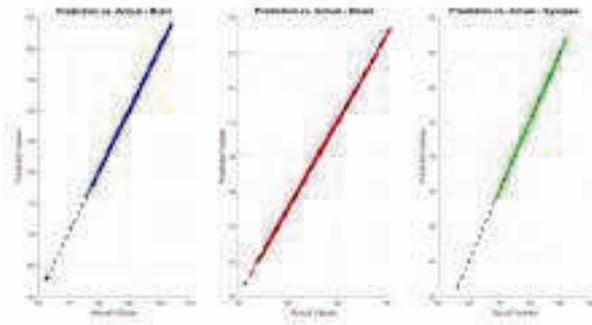


Figure 2. Predicted vs. Actual Nicotine Concentrations

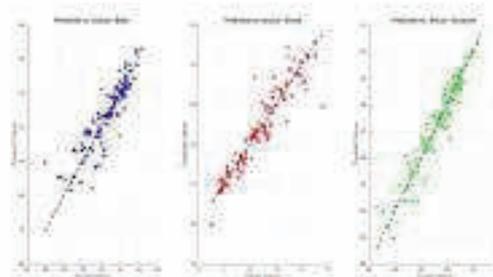


Figure 3. Real-world vs. Predicted Nicotine Concentrations

4. Discussion and Conclusions

PBPK modeling enables detailed simulation of nicotine distribution, but it does not fully capture inter-individual variability. Integrating machine learning (XG-Boost) improved prediction accuracy ($R^2 > 0.9998$) and accounted for differences in metabolism, perfusion, and behavior [13]. Blood-brain permeability (k_{penet}) emerged as the most influential factor in brain and synaptic nicotine accumulation, followed by metabolic rate, pulmonary blood flow, body weight, and smoking history.

Our findings align with prior studies showing distinct absorption routes: e-cigarettes (ENDS) favor upper airway and buccal delivery, while cigarettes in-

duce faster systemic uptake via the lower respiratory tract [14]. Nicotine's rapid metabolism (half-life 2–3 h) and lysosomal trapping ($V_d \sim 2.6$ L/kg) contribute to higher concentrations in organs like the liver and lungs [9, 15, 16].

Although e-cigarettes avoid combustion-related toxins, they maintain elevated systemic nicotine levels, especially with nicotine salts—raising concerns about sustained dependence. This underscores the need for tailored cessation strategies and regulatory oversight. Limitations of this study include standardized behavioral assumptions and exclusion of other tobacco constituents.

In conclusion, combining PBPK and ML modeling offers a robust framework for simulating nicotine kinetics and inter-individual variability. Future research should incorporate behavioral and clinical data, evaluate different nicotine formulations, and assess long-term health impacts of emerging nicotine delivery systems.

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PHYSIOLOGICALLY-BASED PHARMACOKINETIC MODELING OF NICOTINE

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Purpose: The purpose of this study is to develop an in silico PBPK model predicting nicotine pharmacokinetics in users of e-cigarettes and traditional cigarettes across health conditions (mandatory) What are the reasons for writing the paper or the aims of the research?

Design/methodology/approach: The model was implemented in MATLAB ODE45 solver, incorporating ADME processes and disease-specific parameters for liver disease, obesity, cardiovascular, lung, and neurological disorders.

Findings: Nicotine pharmacokinetics varied significantly across health conditions. E-cigarettes produced sustained nicotine exposure, while traditional cigarettes led to sharp peaks. Liver disease and obesity caused major changes in nicotine clearance and storage.

Research limitations/implications: The model depends on literature-derived parameters and does not incorporate individual puffing behavior or pharmacogenomics. Future studies should integrate real-world vaping data.

Practical implications: Findings support the design of personalized smoking cessation strategies and improved risk assessment for vulnerable populations.

Social implications: Results suggest e-cigarettes may not be universally safer and highlight public health risks in patients with comorbidities.

Originality/value: This study is among the first to apply PBPK modeling across multiple health conditions for nicotine exposure in e-cigarette vs traditional cigarette users.

Keywords: Physiologically-Based Pharmacokinetic Model (PBPK), Nicotine Pharmacokinetics, E-Cigarettes, Traditional Cigarettes, Health Conditions.

Category of the paper: Research paper.

1. Introduction

Nicotine is a highly addictive substance with significant physiological effects, influencing cardiovascular, neurological, and metabolic functions (Besaratnia, 2019). The world has witnessed a shift in smoking behavior toward e-cigarettes which have gained popularity as an alternative to traditional tobacco products. The World Health Organization (WHO) reports that 1.3 billion people across the globe use nicotine products while e-cigarette usage has surged notably among younger generations (Birdsey, 2023). The number of worldwide e-cigarette users reached 82 million in 2023 while the user base expanded from just a few million in the previous decade (Center for Tobacco; 2025). Traditional cigarettes continue to be the main source of smoking-related illnesses but e-cigarettes present themselves as safer alternatives even though scientists continue to study their permanent health implications (Dorotheo, 2024).

E-cigarette usage has shown a significant increase in youth demographics. The U.S. Food and Drug Administration (FDA) together with the Centers for Disease Control and Prevention (CDC) documented that 2.1 million middle and high school students in the United States used e-cigarettes during 2023 thus creating worries about teenage nicotine addiction (Eaton, 2018); (Farsalinos, 2014). Studies demonstrate that e-cigarette brands contain different levels of nicotine which results in unstable nicotine exposure and elevates the risk of addiction (Guo, 2022).

The main difficulty in nicotine research involves studying how nicotine pharmacokinetics changes between combustible tobacco products and aerosolized nicotine delivery systems. The rate of nicotine absorption, its peak concentration, and systemic retention all vary depending on the mode of intake, which can influence addiction potential, toxicity, and cessation strategies (Helen; n.d.). The delivery of nicotine through traditional cigarettes results in fast nicotine delivery and high peak concentrations but e-cigarettes produce sustained nicotine exposure because of variations in aerosol deposition and bioavailability (Kramarow, 2021); (Perry, 2020).

The method of administration plays a role but individual health conditions strongly affect how the body metabolizes and clears nicotine. The enzymatic activity and blood flow and organ-specific nicotine retention in the body change due to chronic diseases such as liver dysfunction, cardiovascular disease, obesity, pulmonary disorders and neurological impairments which produce substantial variations in nicotine disposition among individuals (Peters, 2021); (Peters, 2019). Liver disease leads to longer nicotine retention because the liver cannot properly metabolize the substance yet obesity leads to increased nicotine storage in body fat which slows down its elimination from the body (Prasad, 2024). The traditional cigarette users with pulmonary diseases like COPD experience altered nicotine absorption rates and neurological disorders create challenges for nicotine to cross the blood-brain barrier (Prasad, 2024); (Robinson, 1992).

The analysis of these effects requires systematic studies which use Physiologically-Based Pharmacokinetic (PBPK) models to simulate how nicotine enters the body and moves through it while being metabolized and eliminated across various physiological states (Prasad, 2024); (Rostami, 2022). The models analyze how e-cigarette and traditional cigarette users experience pharmacokinetic profiles throughout a 24-hour period by measuring steady-state concentrations (C_{ss}), half-life ($t_{1/2}$) and compartmental distribution (Rostami, 2022); (Schneider, 1996). The research reveals major pharmacokinetic variations between nicotine delivery systems and shows that individualized smoking cessation strategies are essential for people with existing health issues (Rostami, 2022).

The integration of computational modeling into nicotine research enables scientists to quantify the risks between e-cigarettes and traditional cigarettes through mathematical evaluation. The obtained insights hold essential value for public health policy-making and clinical guidance as well as intervention development for smokers and vapers with different health profiles.

In this study, we developed a Physiologically-Based Pharmacokinetic (PBPK) model alongside an absorption, distribution, metabolism, and elimination (ADME) analysis, incorporating mathematical simulations of nicotine transport—supplied by traditional cigarettes and e-cigarettes—across various tissues and organs.

2. Methods

The Physiologically-Based Pharmacokinetic (PBPK) model replicated how nicotine moves through the body by absorption, distribution metabolism and elimination (ADME) across various physiological states (Fig. 1). The model divides into six compartments which include the lungs blood liver brain and fat tissue along with metabolites that exchange nicotine between compartments through first-order rate equations. The system of differential equations tracked compartmental nicotine concentrations while parameters needed adjustment for each health condition.

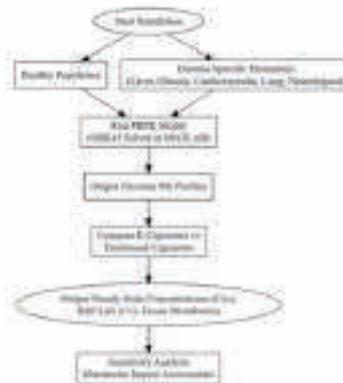


Figure 1. Workflow of the Physiologically-Based Pharmacokinetic (PBPK) Model Simulations and Analysis Steps.

Source: Authors' own.

2.1. Mathematical Modeling of Nicotine Transport and Tissue Distribution

Nicotine enters the lungs following inhalation and is transported into the systemic circulation, where it is further distributed to liver, brain, fat, and other tissues (Fig. 2).

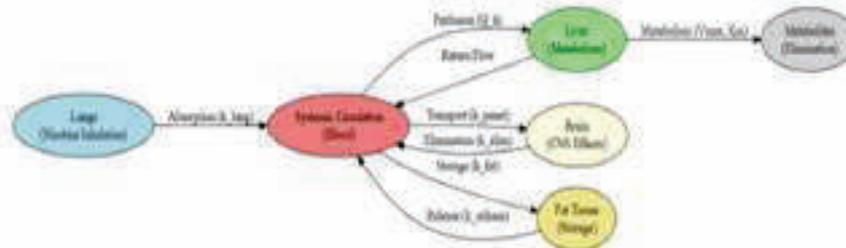


Figure 2. Physiologically-Based Pharmacokinetic Model (PBPK) of Nicotine Distribution and Metabolism Across Compartments.

Source: Authors' own.

The transport between compartments is governed by perfusion-limited kinetics (equations (1) and (2):

$$\frac{dC_{lung}}{dt} = \frac{Dose(t)}{V_p} - \frac{Q_p}{V_p} (C_{lung} - C_{blood}) \quad (1)$$

$$\frac{dC_{blood}}{dt} = \frac{Q_p}{V_b} (C_{lung} - C_{blood}) - \frac{Q_h}{V_b} (C_{blood} - C_{liver}) - k_{clear} C_{blood} - k_{penetr} C_{blood} + k_{eliv} C_{brain} - k_{fat} C_{blood} + k_{release} C_{fat} - k_{elim} C_{blood} \quad (2)$$

where:

- Q_p and Q_h represent blood flow to the lungs and liver (L/h), respectively;

- $k_{distrib}$ represents nicotine distribution to peripheral tissues (1/h).
- k_{penetr} and k_{elim} denote brain penetration and elimination rates (1/h).
- k_{fat} and $k_{release}$ account for nicotine storage and release from adipose tissue.
- k_{elimb} models nicotine elimination directly from the blood.

Nicotine metabolism occurs predominantly in the liver, where it undergoes enzymatic degradation following Michaelis-Menten kinetics (equations (3) and (4):

$$\frac{dC_{liver}}{dt} = \frac{Q_h}{V_l} (C_{blood} - C_{liver}) - \frac{k_{metabmax} C_{liver}}{K_m + C_{liver}} + k_{distrib} C_{blood} \quad (3)$$

$$\frac{dC_{metabolites}}{dt} = \frac{k_{metabmax} C_{liver}}{K_m + C_{liver}} \quad (4)$$

where:

- $k_{metabmax}$ is the maximum hepatic metabolism rate (ng/h).
- K_m is the Michaelis-Menten constant (ng/mL).

Nicotine crosses the blood-brain barrier, where it accumulates and undergoes elimination. Similarly, nicotine is stored in adipose tissue, affecting long-term retention (equations (5) and (6):

$$\frac{dC_{brain}}{dt} = k_{penetr} C_{blood} - k_{elim} C_{brain} \quad (5)$$

$$\frac{dC_{fat}}{dt} = k_{fat} C_{blood} - k_{release} C_{fat} \quad (6)$$

where:

- the brain penetration rate (k_{penetr}) and elimination rate (k_{elim}) are modified under neurological disorders,
- fat storage and release constants (k_{fat} and $k_{release}$) vary in obese individuals.

2.2. Nicotine Dosing Regimen

The nicotine dose intake function is modeled as a series of discrete inhalation events at a fixed time interval (equation (7)):

$$Dose(t) = \sum_{t_d} dose \cdot \delta(t - t_d) \quad (7)$$

where:

- E-cigarette users receive a dose of $3000 \times F_{e-cig}$ ng every hour.
- Traditional cigarette smokers receive $1500 \times F_{cig}$ ng every hour.

- F_{e-ng} and $F_{e-equivalent}$ nicotine bioavailability.
- The Kronecker delta function $\delta(t)$ ensures nicotine is introduced at each dosing time.

2.3. Physiological and Disease-Specific Parameter Adjustments

To model the effect of different disease states, specific PBPK parameters were adjusted based on physiological alterations reported in the literature (Table 1).

Table 1.

Adjusted PBPK Model Parameters for Different Physiological Conditions, where:

↑ = Increased ↓ = Decreased

Condition	Qh (L/h)	kmetabmax (ng/h)	kpenet	kelimin	kfat	krelease	keliminb
Healthy	1.5	1.2	2.0	0.7	0.1	0.05	0.2
Liver Disease	1.2 ↓	0.6 ↓	2.0	0.7	0.1	0.05	0.1 ↓
Cardiovascular	1.0 ↓	1.0	2.2 ↑	0.75 ↑	0.12 ↑	0.045	0.18
Obesity	1.5	1.2	2.0	0.7	0.15 ↑	0.035 ↓	0.16 ↓
Lung Disease	0.8 ↓	1.1	2.0	0.7	0.1	0.05	0.2
Neurological	1.4	1.0 ↓	2.5 ↑	0.5 ↓	0.11 ↑	0.045	0.16 ↓

Source: Authors' own.

2.4. Computational Simulations

The PBPK model was implemented in MATLAB v. R2024b (MathWorks Inc., Natick, MA, USA), using implemented ODE45 solver, which numerically integrates the system of differential equations governing nicotine absorption, distribution, metabolism, and elimination. The simulation was run over a 24-hour time period, with a temporal resolution of 500 time points, ensuring sufficient granularity to capture dynamic concentration changes across compartments.

The steady-state concentration (C_{ss}) for each compartment was determined by averaging nicotine levels over the final 6 hours of the simulation, ensuring that transient fluctuations did not impact the estimation of equilibrium values (equation (8)):

$$C_{ss} = \frac{1}{t_2 - t_1} \int_{t_1}^{t_2} C(t) dt \quad (8)$$

where $t_1=18$ hours and $t_2=24$ hours mark the final portion of the simulation, allowing for nicotine distribution equilibrium to be captured effectively.

At the beginning of each simulation, the initial nicotine concentration in all compartments was set to zero, representing a baseline condition before nicotine exposure. The elimination of

nicotine from the system was evaluated by computing its half-life ($t_{1/2}$), which depends on both the first-order elimination rate (k_{elim}) and the Michaelis-Menten metabolism rate ($k_{metabolism}$), using the following equation (9):

$$t_{1/2} = \frac{\ln 2}{k_{elim} - \frac{k_{metabolism}}{K_m + C_{ss}}} \quad (9)$$

2.5. Sensitivity analysis

The sensitivity analysis was used to determine how changes in key physiological and pharmacokinetic parameters affected model outcomes such as steady-state concentrations (C_{ss}) of nicotine, half-life ($t_{1/2}$) and tissue distribution across different health conditions. This analysis was undertaken to determine which parameters the PBPK model was most sensitive to, and thus which physiological factors were most important in determining nicotine pharmacokinetics.

The sensitivity analysis was performed separately for e-cigarettes and traditional cigarettes across key populations: healthy individuals, those with liver disease, obesity, and neurological disorders. For each scenario, all parameters were individually varied by $\pm 30\%$. Changes in C_{ss} (brain and blood) and $t_{1/2}$ were recorded, and the relative sensitivity coefficient (RSC) was calculated as:

$$RSC = \frac{\Delta Output / Output}{\Delta Parameter / Parameter} \quad (10)$$

The analysis focused on comparing the relative influence of each parameter across the two nicotine delivery methods (e-cigarettes and traditional cigarettes) to capture method-specific pharmacokinetic differences. The results were visualized using a heatmap to highlight variations across conditions and delivery methods.

3. Results

In the text, the Harvard referencing citation style should be used (Smith, 2017) or (Smith, Bradley, 2017). In the case of more than three authors, write the surname of the first of them and add the abbreviation "et al." (Bradley et al., 2017).

In the case of authors with the same surname, the initial of the first name and optionally of the middle name should be used (Smith, J., Smith, A.B., 2017). If the initials

of the first names of two authors are the same, use full first name (Smith John, Smith Jane, 2017).

If there are several items by the same author from the same year, use enumeration: a, b, c... starting with the item that appears first in the bibliographic list (Smith, 2017a).

In the case of many bibliographic items in one note, the following format should be used (Smith, 2017; Bradley et al., 2017).

In the case of several items by the same author, the following format should be used at the same point (Smith, 2016, 2017a, 2017c).

The pharmacokinetic analysis of nicotine in various physiological conditions revealed significant differences in steady-state concentrations (C_{ss}) and half-life ($t_{1/2}$) (Table 2).

Table 2.
Summary of Nicotine Pharmacokinetics Across Conditions

Condition	C_{ss} in Brain (ng/mL) (E-Cig)	C_{ss} in Brain (ng/mL) (Cig)	C_{ss} in Blood (ng/mL) (E-Cig)	C_{ss} in Blood (ng/mL) (Cig)	$t_{1/2}$ (h) (E-Cig)	$t_{1/2}$ (h) (Cig)
Healthy	11.00	18.64	04.08	07.01	0.96	0.96
Liver Disease	24.74	3.40	9.18	1.41	0.98	0.98
Cardiovascular	16.32	6.89	6.1	2.74	1.12	1.12
Obesity	21.41	15.38	7.64	5.79	1.12	1.12
Lung Disease	13.06	2.91	05.05	01.02	01.03	01.03
Neurological	4.69	9.52	0.98	02.02	1.33	1.34

Source: Authors' own.

In a healthy population, nicotine exhibited rapid metabolism and clearance, resulting in a short half-life of approximately 0.96 hours for both e-cigarette and traditional cigarette users. However, the source of nicotine significantly influenced its distribution. Traditional cigarette smokers had higher nicotine concentrations in the brain (C_{ss} =18.64ng/mL) and blood (C_{ss} =7.01ng/mL) compared to e-cigarette users, where these values were lower (11.00 ng/mL and 4.08 ng/mL, respectively). This discrepancy suggests that the rapid combustion of tobacco in traditional cigarettes facilitates a faster and more intense nicotine delivery, while the aerosolized nicotine from e-cigarettes provides a more gradual and sustained release. The plot of nicotine concentration over time (Figure 3) further illustrates this difference, showing sharper peaks in the lungs and blood for traditional cigarettes, whereas e-cigarette users exhibit a smoother, prolonged nicotine profile.

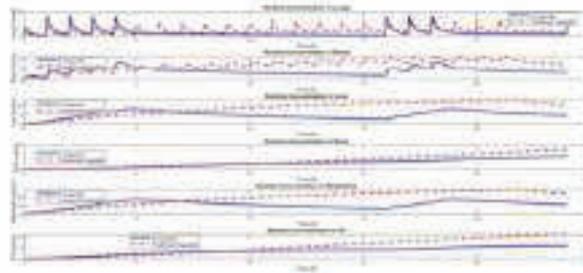


Figure 3. Nicotine concentration in a healthy individual.

Source: Authors' own.

The pharmacokinetics of nicotine underwent a significant transformation in patients with liver disease especially among e-cigarette users. The hepatic metabolic impairment led to excessive brain and blood nicotine accumulation at levels of 24.74 ng/mL and 9.18 ng/mL respectively in e-cigarette users compared to healthy individuals. Traditional cigarette smokers demonstrated lower brain nicotine concentrations (C_{ss} =3.40 ng/mL) and blood nicotine levels (C_{ss} =1.41 ng/mL) compared to other participants. The results depicted in Figure 4 confirm that liver dysfunction affects e-cigarette-derived nicotine more significantly which could elevate toxicity risks because of extended exposure times.

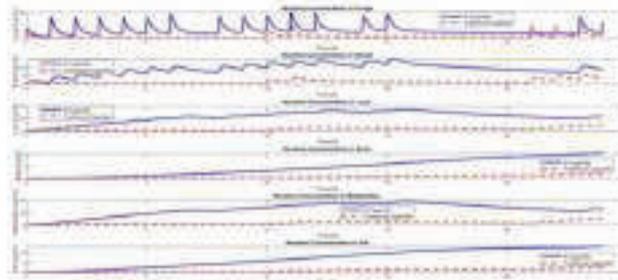


Figure 4. Nicotine concentration in liver disease.

Source: Authors' own.

The nicotine metabolism of people with cardiovascular disease showed moderate impairment which resulted in a 1.12-hour half-life for users of both e-cigarettes and traditional cigarettes. The brain concentration of nicotine reached C_{ss} =16.32 ng/mL in e-cigarette users while traditional cigarette smokers only achieved 6.89 ng/mL. E-cigarette users maintained higher blood nicotine concentrations at 6.01 ng/mL compared to traditional cigarette users who had 2.74 ng/mL. The slower elimination of e-cigarette nicotine in cardiovascular-impaired individuals results in prolonged systemic exposure according to these findings. The brain

concentration plots in Figure 5 show that e-cigarette users maintain nicotine levels for longer periods while traditional cigarette smokers experience rapid nicotine spikes.

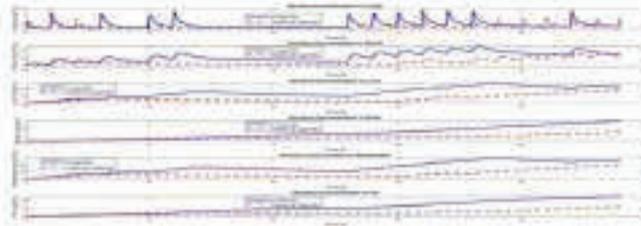


Figure 5. Nicotine concentration in cardiovascular disease.

Source: Authors' own.

The pharmacokinetics of nicotine underwent significant changes because obesity led to increased storage of nicotine in body fat which resulted in delayed elimination. The brain nicotine concentration reached 21.41 ng/mL in e-cigarette users who had higher levels than traditional cigarette users at 15.38 ng/mL because obesity slows down metabolic clearance thus extending nicotine retention especially for aerosolized nicotine products. The fat tissue storage of nicotine increased more than twofold between e-cigarette users who reached 9.82 ng/mL and traditional cigarette smokers who reached 6.28 ng/mL. The half-life measurements showed similar results between both groups at approximately 1.12 hours even though their nicotine exposure times differed. The effects are shown clearly in Figure 6 because nicotine levels in blood and fat tissues stay elevated throughout time especially in e-cigarette users.

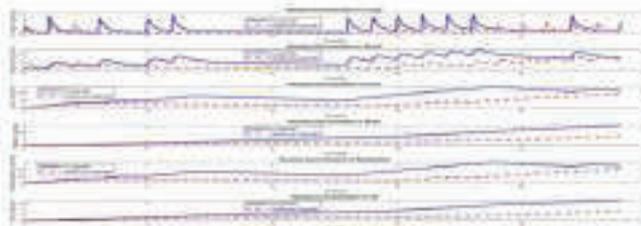


Figure 6. Nicotine concentration in obesity.

Source: Authors' own.

The absorption of nicotine became severely impaired in individuals with pulmonary disease and traditional cigarette smokers experienced an even greater impact. The brain nicotine concentration levels were significantly lower in users of traditional cigarettes at 2.91 ng/mL compared to e-cigarette users who had 13.06 ng/mL. The blood nicotine concentration in traditional cigarette users dropped to 1.02 ng/mL while e-cigarette users sustained levels at 5.05 ng/mL. The data presented in Figure 7 shows that traditional cigarette smokers receive lower systemic nicotine exposure because their lung impairment reduces alveolar absorption of

combustion products. The aerosol delivery system of e-cigarettes functions differently from traditional cigarettes so it experiences reduced impact from lung diseases.

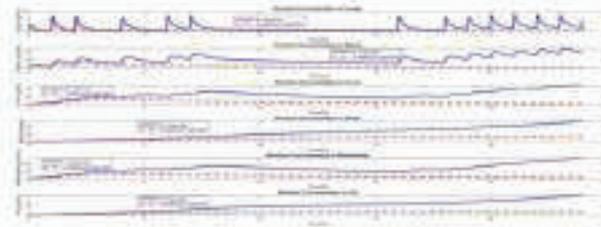


Figure 7. Nicotine concentration in lung disease.

Source: Authors' own.

The nicotine distribution in people with neurological diseases demonstrated substantial variations between using e-cigarettes and traditional cigarettes. The brain nicotine concentration of e-cigarette users dropped dramatically to 4.69 ng/mL because their blood-brain barrier transport was impaired or their neurovascular regulation was altered. Traditional cigarette users maintained brain nicotine concentrations at 9.52 ng/mL while their blood nicotine levels remained lower than e-cigarette users at 2.02 ng/mL compared to 0.98 ng/mL. The prolonged half-life observed in e-cigarette users (~1.33 hours) suggests a delayed clearance pattern, despite their overall lower systemic exposure. The brain nicotine profile of traditional cigarette users remains steady throughout while e-cigarette users experience a gradual decrease in systemic nicotine concentrations as shown in Fig. 8.

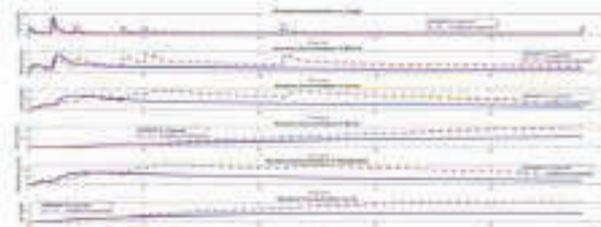


Figure 8. Nicotine concentration in neurological disease.

Source: Authors' own.

Fig. 9 presents simulated nicotine concentration profiles over a 24-hour period, comparing e-cigarette and traditional cigarette users across various health conditions. These profiles illustrate how both the route of nicotine delivery and individual health status shape the time-course of systemic nicotine concentrations, revealing important differences between combustion-derived nicotine and aerosolized nicotine.

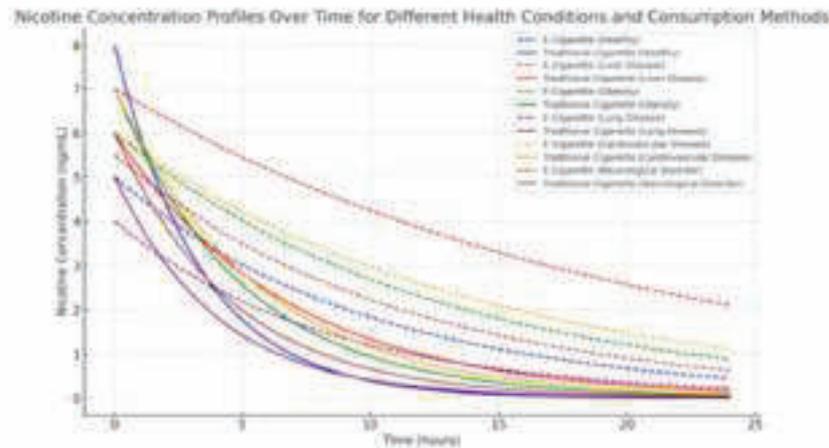


Figure 9. Nicotine Concentration Profiles Over Time Across Health Conditions and Consumption Methods.

Source: Authors' own.

Traditional cigarette smokers showed a rapid increase in nicotine concentration during the initial phase which reflects the quick delivery process of tobacco combustion. The nicotine levels in e-cigarette users showed a steady increase followed by an extended period of stable levels because aerosolized nicotine absorption occurs more slowly. The pharmacokinetic profiles demonstrate the core distinction between traditional cigarettes which deliver quick intense nicotine bursts and e-cigarettes which produce sustained smooth nicotine exposure.

The effects of health conditions further modulate these profiles. The liver disease patients experienced severely limited nicotine clearance which resulted in extended nicotine retention especially among e-cigarette users who received continuous low-dose exposure on top of their impaired hepatic metabolism. The nicotine levels in obese individuals decreased gradually with e-cigarette users showing the longest decline because their bodies stored nicotine in fat tissue that released the substance back into circulation at a slow rate. The delayed clearance pattern became most evident in the e-cigarette group because nicotine's fat-soluble nature reacts with changes in body composition.

Traditional cigarette users among individuals with pulmonary disease showed reduced peak concentrations and faster elimination times compared to healthy subjects because their impaired alveolar function restricts combustion product nicotine absorption. The nicotine levels of e-cigarette users remained elevated compared to traditional cigarette users because aerosol particles seem to adhere better to damaged lungs thus providing longer systemic exposure.

The cardiovascular disease group showed e-cigarette and traditional cigarette users retained nicotine for a slightly longer period yet e-cigarette users maintained higher nicotine levels throughout the study period because their nicotine clearance from the body was slower. The blood-brain barrier permeability differences between traditional cigarette users and e-cigarette

users resulted in traditional cigarette users reaching higher peak concentrations because of faster nicotine absorption, but e-cigarette users maintained lower systemic levels for longer periods.

The sensitivity analysis demonstrates the need of accounting for individual physiological variables when modeling nicotine pharmacokinetics. In healthy people (Fig. 10), the PBPK model was most sensitive to hepatic metabolism rate ($k_{metabmax}$) and liver blood flow (Q_h). These parameter adjustments resulted in considerable variations in brain nicotine concentration, demonstrating that hepatic clearance is an important element in regulating systemic and central nicotine exposure. The brain penetration rate (k_{penet}) had a significant impact, particularly for e-cigarette users, as the slower aerosol delivery allowed for a longer duration of nicotine absorption into the brain.

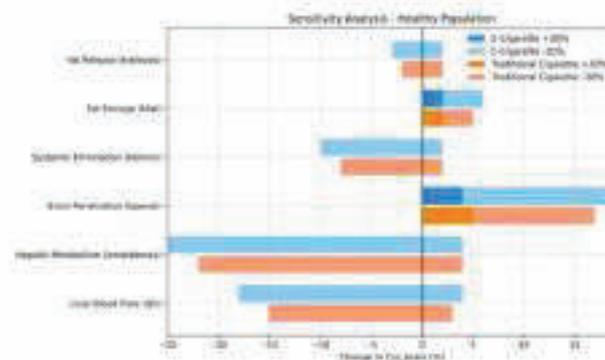


Figure 10. Sensitivity Analysis of Healthy Population (E-Cigarette vs Traditional Cigarette).

Source: Authors' own.

In individuals with liver disease, hepatic metabolism rate ($k_{metabmax}$) had the strongest influence on nicotine concentrations, reflecting the impaired metabolic capacity in this population (Fig. 11). Reduced hepatic clearance led to markedly increased C_{ss_brain} in both e-cigarette and traditional cigarette users, though the effect was more pronounced in e-cigarette users due to prolonged exposure patterns. Liver blood flow (Q_h) also had a considerable effect, highlighting the importance of perfusion in hepatic clearance.

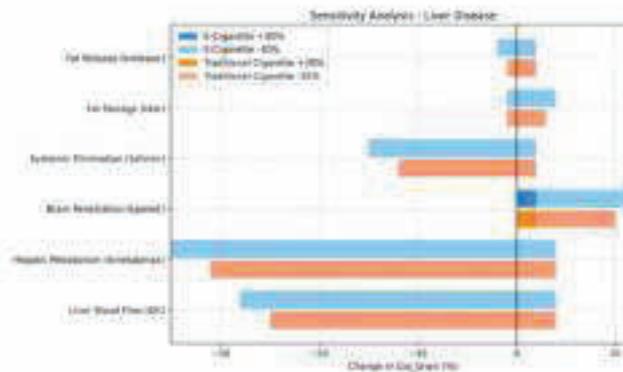


Figure 11. Sensitivity Analysis - Liver Disease (E-Cigarette vs Traditional Cigarette).
Source: Authors' own.

In obese individuals, fat storage (k_{fat}) and fat release ($k_{release}$) were the most influential parameters, particularly for e-cigarette users (Fig. 12). Nicotine's high lipophilicity causes extensive sequestration in adipose tissue, which significantly alters its systemic and brain concentrations over time. While liver blood flow and hepatic metabolism remained important, the prolonged nicotine release from fat stores introduced an additional regulatory mechanism, especially in the context of chronic e-cigarette use.

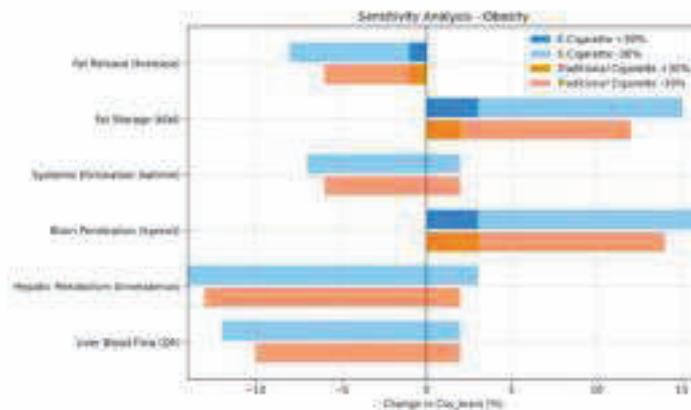


Figure 12. Sensitivity Analysis - Obesity (E-Cigarette vs Traditional Cigarette).
Source: Authors' own.

In individuals with neurological disorders, brain penetration rate (k_{penet}) emerged as the dominant driver of C_{ss_brain} , particularly for e-cigarette users (Fig. 13). Variability in blood-brain barrier permeability significantly altered brain nicotine concentrations, amplifying the role of disease-induced changes in central nervous system exposure. While hepatic parameters

still played a role, the direct modulation of nicotine entry into the brain became a distinguishing factor in this population.

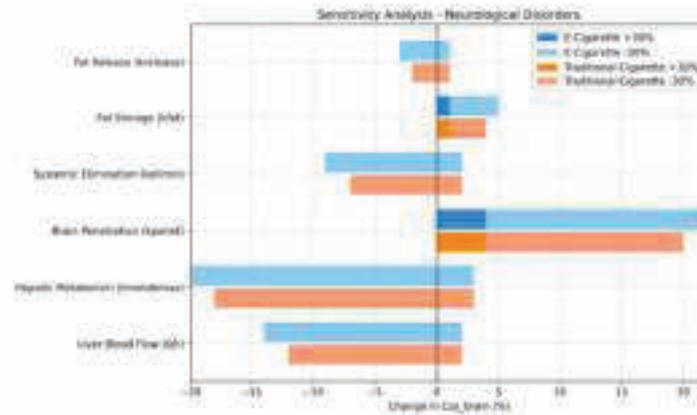


Figure 13. Sensitivity Analysis - Neurological Disorders (E-Cigarette vs Traditional Cigarette). Source: Authors' own.

This heatmap visualization (Fig. 14) highlights the disease- and delivery-specific sensitivity patterns, emphasizing the need for individualized pharmacokinetic modeling in populations with comorbid conditions or altered physiology.

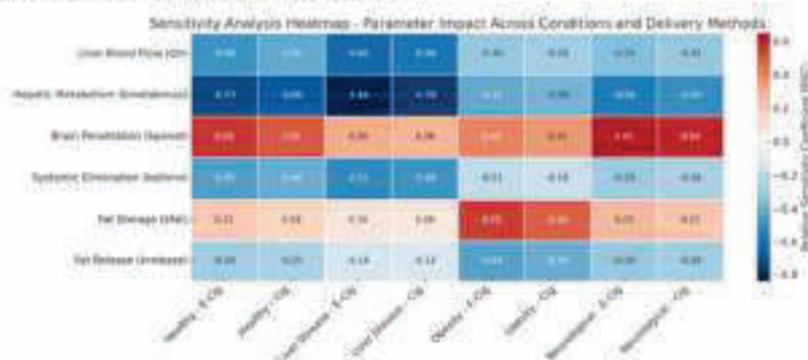


Figure 14. Sensitivity Analysis Heatmap – Relative Sensitivity Coefficients (RSC) Across Health Conditions and Delivery Methods. Source: Authors' own.

4. Discussion

Physiologically-Based Pharmacokinetic (PBPK) modeling has gained popularity in recent years for studying nicotine pharmacokinetics in different delivery systems and physiological conditions (Schroeder, 2014); (World, 2024). The models enable researchers to model how nicotine moves through the body by simulating its ADME processes. This study applies an *in silico* PBPK framework to simulate how nicotine is absorbed, distributed, metabolized, and eliminated in individuals with varying physiological and pathological conditions. By explicitly modeling organ-level functions, such as hepatic clearance, pulmonary uptake, adipose tissue storage, and neural barrier transport, the approach provides mechanistic insight into the functional alterations of key human organs under disease.

Rostami et al. (Prasad, 2024) provided a major contribution through their application of an extended conventional PBPK framework to forecast nicotine pharmacokinetics from acute and repeated nicotine delivery product exposure including combustible cigarettes, smokeless tobacco, ENDS, and nicotine inhalers. The model included anatomically detailed representations of nicotine absorption pathways, particularly through the buccal mucosa, upper airways, and lower respiratory tract. Moreover, it accurately reproduced plasma nicotine concentration-time profiles and tissue-specific distribution by integrating region-specific deposition and diffusion parameters, thus highlighting the influence of route-specific absorption on systemic exposure. Rostami's results are in agreement with the present study findings which show that nicotine retention and metabolic clearance are route-dependent. E-cigarette use was found to result in longer systemic exposure compared to conventional cigarette smoking which produced higher peak plasma concentrations.

Prasad et al. (Rostami, 2022) developed a machine learning-augmented PBPK model specifically for e-cigarette users. The approach enabled personalized pharmacokinetic predictions through user-specific variables including puffing patterns and device parameters. Our data supports these findings by showing that e-cigarette users especially those with hepatic insufficiency or obesity experience prolonged systemic nicotine retention which supports the need for individualized PBPK modeling to evaluate nicotine exposure risk.

The initial research by Robinson et al. (Schneider, 1996) presented a nine-compartment PBPK model which included both nicotine and its main metabolite cotinine. The tissue-to-blood partition coefficients derived from this model served as a foundation for future modeling research. Our research extends the existing framework through disease-specific modifiers including hepatic impairment which leads to longer nicotine half-life. The findings from our study confirm Robinson's conclusion that PBPK models require individual metabolic capacity data to achieve better predictive accuracy.

Noteworthy, Guo et al. (Guo, 2022) performed an open-label crossover clinical trial to assess nicotine delivery profiles in Chinese adult smokers who used both e-cigarettes and combustible cigarettes. The researchers observed that e-cigarettes delivered nicotine at a steady rate which differed from the fast nicotine peaks that occur during conventional smoking. Our results match the results from Guo's study and show that e-cigarettes maintain steady nicotine

levels in the body while traditional cigarettes create sudden pharmacokinetic effects because of their combustion process.

The blood-brain barrier (BBB) interaction with nicotine functions as a primary factor which determines how the substance affects the central nervous system (CNS). Tega et al. (Robinson, 1992) showed that nicotine changes BBB permeability through modifications in tight junction proteins ZO-1 and claudin-3 which leads to disrupted junctional integrity. Our research supports this mechanistic understanding because people with neurological disorders show different brain nicotine exposure patterns especially when using e-cigarettes since their BBB integrity is already compromised by disease-related pathology.

The National Academies of Sciences, Engineering, and Medicine study (Yuki, 2024) on the public health impacts of e-cigarette usage concludes that e-cigarette aerosols have a lower toxicant load than traditional tobacco products. However, it also highlights the paucity of understanding concerning long-term health consequences, particularly in patients with pre-existing respiratory disorders such as chronic obstructive pulmonary disease (COPD). Our findings support this conclusion, implying that e-cigarette users with pulmonary comorbidities may have distinct patterns of nicotine absorption and retention, which could accelerate disease progression or make illness treatment more challenging. Our findings are congruent with this assessment, suggesting that e-cigarette users with pulmonary comorbidities may experience altered nicotine absorption and retention dynamics, potentially exacerbating disease progression or complicating management strategies.

Finally, in the research of Perry et al. (Schroeder, 2014), the authors examine PBPK modeling applications and growth and challenges in different therapeutic contexts. The paper shows that PBPK-related research is increasing rapidly and is becoming more important in drug development and clinical pharmacology. PBPK modeling is especially useful for simulating drug behavior in different populations such as pediatrics, geriatrics, and individuals with organ impairment as well as for predicting complex drug-drug interactions. These findings support our study's focus on the need to adapt smoking cessation therapies to individuals' pharmacokinetic profiles and health state, acknowledging that differences in nicotine metabolism and exposure require different therapeutic approaches.

Our study provides extremely interesting results, however, it is not without its limitations. The research delivers important information about nicotine pharmacokinetics across user groups and delivery systems but faces multiple research constraints. The PBPK modeling framework produces reliable results but its accuracy depends on the precision of the physiological and biochemical parameters that it uses. The reliability of model results may be impacted by the restricted and inconsistent information found in literature sources which was used to develop input data for specific subpopulations including patients with advanced hepatic or pulmonary disease. The research fails to consider behavioral differences among individuals who use nicotine products through their consumption methods including puffing patterns and

inhalation depths and device-specific features like power settings and e-liquid composition especially for e-cigarette users.

The simulation's cross-sectional design prevents researchers from directly studying the long-term health impacts of chronic nicotine exposure. The model successfully reproduces short-term pharmacokinetic patterns but requires longitudinal verification to determine complete health implications from long-term nicotine use particularly when comorbid conditions exist. The model's predictions receive limited external validation because there is no empirical biomarker data (e.g., plasma cotinine levels) available for real-world users. The study investigates major disease states but it does not evaluate how pharmacogenomic factors like CYP2A6 polymorphisms affect nicotine metabolism and individual variability.

Finally, the generalizability of these findings may be limited by the model's focus on adult populations; adolescents, pregnant individuals, and elderly users—each with different physiological characteristics and vulnerability profiles—were not explicitly modeled. Future research should attempt to extend the PBPK framework to include these populations and incorporate real-world usage data to increase translational relevance.

5. Summary and Conclusions

The research provides an extensive analysis of nicotine pharmacokinetics in e-cigarette and combustible cigarette users through Physiologically-Based Pharmacokinetic (PBPK) modeling which analyzes absorption distribution metabolism and elimination across different health statuses. The research shows that nicotine retention and clearance rates differ widely between people which indicates the requirement for individualized approaches in smoking cessation and harm reduction programs.

The main outcome of this research demonstrates that different nicotine delivery systems generate distinct pharmacokinetic patterns. The plasma nicotine levels from combustible cigarettes increase quickly but e-cigarettes maintain steady systemic nicotine exposure. The distinctions become more pronounced in people who have metabolic or physiological conditions. Hepatic dysfunction leads to longer nicotine half-life especially among e-cigarette users because their products provide continuous nicotine delivery. The fat-attracting properties of nicotine in obese people result in its storage within adipose tissue which extends the time needed for nicotine elimination.

The research examines how lung diseases affect the process of nicotine absorption. Traditional cigarette smokers with respiratory problems experience decreased systemic nicotine levels but e-cigarette users with similar conditions show higher plasma nicotine concentrations. The study demonstrates how delivery methods influence nicotine exposure in disease-related situations. Neurological disorders that modify blood-brain barrier (BBB)

permeability could impact how nicotine reaches the brain thus affecting addiction potential and withdrawal symptoms between different delivery systems.

The findings have significant consequences for translation. Because nicotine metabolism is not linear and does not remain stable across health conditions, uniform quitting strategies may not be optimum for all populations. Individualized quitting techniques that take into account metabolic capability, comorbid disorders, and chosen nicotine delivery systems are more likely to increase therapy efficacy. Pharmacological medications such as Nicotine Replacement Therapy (NRT), bupropion, and varenicline may require dosage changes or alternate formulations in populations with altered pharmacokinetics.

The research results question the common assumption that e-cigarettes represent a completely safer choice than combustible tobacco products from a public health and regulatory perspective. E-cigarettes lower combustion-related toxicant exposure but their pharmacokinetic profile leads to prolonged systemic nicotine retention which creates specific risks for people with cardiovascular disease and hepatic or metabolic conditions. The obtained results require a thorough reevaluation of harm reduction policies especially for vulnerable population groups, including youth.

Future research needs to focus on following medically compromised populations through time to understand the long-term consequences of e-cigarette use. PBPK modeling will become more accurate for exposure prediction and risk assessment through improvements that include real-world vaping behaviors and device-specific parameters and nicotine salt pharmacodynamics. This research demonstrates how nicotine pharmacokinetics interacts with delivery methods and health conditions of individual patients. The research findings support the need for precise cessation treatments and detailed regulatory approaches while encouraging ongoing multidisciplinary studies to reduce nicotine-related health problems in diverse population groups.

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A Computational Model of E-Cigarette Coil Degradation: Simulating Thermal and Material Dynamics and Their Impact on Health

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Abstract

The performance and longevity of e-cigarette coils are crucial in determining vapor quality, device efficiency, and aerosol composition, directly influencing user safety and exposure to harmful byproducts. Coil degradation occurs due to thermal cycling, oxidation, and wick degradation, affecting resistance stability and heating efficiency. This study presents a computational model simulating temperature dynamics, resistance evolution, and coil degradation under varying airflow levels and power settings. **Clinical Relevance**— this study highlights how coil material and airflow affect e-cigarette heating performance and degradation, which can influence the production of toxic aerosol byproducts, increasing clinicians' about potential respiratory exposure risks in e-cigarette users.

Introduction

Electronic cigarettes (e-cigarettes) have become a popular alternative to traditional smoking; however, there are still concerns about metal emissions, coil degradation, and aerosol toxicity [1]. The heating coil within e-cigarettes vaporizes e-liquids; over time, coil performance deteriorates due to thermal cycling, oxidation, and material fatigue, resulting in temperature instability, resistance drift, and loss of wick integrity [2,3]. These factors affect vapor quality, device efficiency, and can release hazardous byproducts (not inhaled aerosols) [4].

Methods

This study employs a computational modeling approach to simulate the thermal behavior, electrical resistance evolution, and wick degradation of e-cigarette heating coils under various vaping conditions. The model takes into account the effects of coil material selection, airflow settings, and oxidation on coil performance and longevity. Four coil materials—Nickel (80/20), Kanthal, Stainless Steel, and Titanium—were analyzed, incorporating their thermal conductivity, heat capacity, oxidation rate, and temperature coefficients of resistance to determine heating efficiency and degradation patterns.

Results

The results in Table 1 demonstrate the effects of coil material and airflow level.

Table 1. Simulated effect of coil material and airflow level on final temperature, final coil resistance, and wick integrity.

Material	Airflow	Temp. (°C)	Resist. (Ω)	Wick (%)
Nickel	Low	268.78	0.1688	99.46
Nickel	Medium	110.60	0.1577	99.64
Nickel	High	66.20	0.1561	99.76
Kanthal	Low	265.47	0.1599	99.46
Kanthal	Medium	114.95	0.1543	99.64
Kanthal	High	69.09	0.1523	99.76
Stainless Steel	Low	268.50	0.1660	99.46
Stainless Steel	Medium	113.32	0.1634	99.64
Stainless Steel	High	66.62	0.1562	99.76
Titanium	Low	273.80	0.2023	99.46
Titanium	Medium	114.89	0.2019	99.64
Titanium	High	66.81	0.1747	99.76

Nickel exhibited the best stability (Figure 1), maintaining low temperatures (~64°C) and minimal resistance drift (~0.154 Ω). Kanthal showed a similar performance. Stainless Steel provided moderate stability, while Titanium reached the highest temperatures (>277°C) and resistance drift (>0.20 Ω) under low airflow, indicating accelerated degradation.

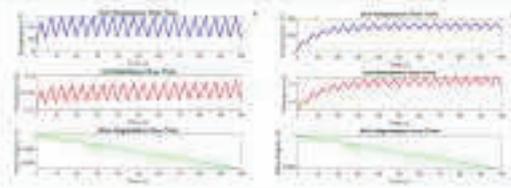


Figure 1. Performance Comparison of Nickel (a) at High Airflow (best result) and Titanium Coils (b) at Low Airflow (worst result).

Discussion & Conclusion

This computational study provides valuable insights into the factors that influence e-cigarette coil behavior, corroborating findings from another research [1-4] and thereby validating the model. It confirms (in silico) that coil material and airflow level critically influence thermal behavior, resistance evolution, and wick degradation. These findings highlight the role of airflow regulation and material selection in enhancing coil performance and longevity. The authors emphasize the need for long-term performance, especially under low airflow, which accelerates heating and increases the risk of wick degradation, dry hits, and carbonyl compound formation over prolonged use.

This study confirms that coil material and airflow level critically influence thermal behavior, resistance evolution, and wick degradation. Higher airflow effectively lowers coil temperatures and oxidation rates, reducing material degradation. Titanium exhibits the highest temperatures and resistance drift, indicating greater oxidation susceptibility and structural instability. Nickel and Kanthal demonstrate superior thermal and electrical stability, making them optimal for long-term performance, while Stainless Steel remains viable for temperature-controlled applications.

The authors emphasize the need for long-term performance, especially under low airflow which accelerates heating, increasing the risk of wick degradation, dry hits, and carbonyl compound formation over prolonged use.

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Optimizing Smoking Cessation Alternatives Using Multi-MOORA and AI-Based Methods

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Abstract. This study aims at enhancing smoking cessation strategies by combining Multi-Objective Optimization on Basis Analysis (Multi-MOORA) with artificial intelligence (AI) approaches. The hybrid model including neural networks, ridge regression, and simulated annealing compares various smoking cessation options based on cost, age of initiation, time spent smoking, ease of quitting, environmental and health impacts. The model's stability and accuracy were tested using a survey and secondary data, and the findings show that e-cigarettes are the most favorable alternative. The sensitivity analysis also validates the robustness of the ranking process. The approach provides a decision-making framework that can help in optimizing smoking cessation interventions and can help in developing personalized and evidence-based public health policy.

Keywords: Smoking Cessation · Multi-MOORA · Artificial Intelligence · Neural Networks · Ridge Regression · Sensitivity Analysis

1 Introduction

The world suffers from preventable death and disease because of tobacco use thus quitting smoking remains a timely urgent public health priority [1]. Despite the availability of several cessation options, including pharmaceutical and behavioral support, many smokers are unable to quit successfully. Smoking cessation can be facilitated during healthcare provider and patient interactions and decision aids may improve non-pharmacological therapy outcomes in this context [2]. Nurse practitioners are particularly suited to assist their patients in smoking cessation through evidence-based treatment approaches [3]. Smoking leads to higher risks for lung cancer and Granulomatosis with Polyangiitis as well as for cardiovascular diseases, and Chronic Obstructive Pulmonary Disease [4].

It is therefore important to describe, mimic and assess various smoking cessation protocols in order to identify the best ways of reducing dependence. Such

things as population dynamics or individual behavioral treatments can be used to make forecasts of the consequences of one or another set of actions, and thus to have an idea of how they can affect the health of the population. Analyzing these models can help to make better therapies, vary them for different groups, and make them more effective. It is therefore important that cessation tactics are subjected to a systematic scientific evaluation so as to help in the development of more efficient therapies and to inform policy and other public health initiatives. Another way of enhancing the effectiveness of smoking cessation programs is by using multi-criteria decision analysis tools such as Multi-Objective Optimization on Ratio Analysis (Multi-MOORA) which compares and ranks quitting decisions based on cost, effectiveness, and at times side effects. This helps the healthcare professionals to make the right decisions on the best strategies to use for their patients. In addition, technologies such as machine learning can be used to analyze cessation data and personalize the approaches to the individual characteristics and preferences of the patients, to enhance the chances of quitting. The integration of Multi-MOORA and AI-based methods may result in major improvements in the optimization of smoking cessation protocols, which will ease the current burden of smoking-related diseases and deaths [2,5,6].

In this work, we gathered and ranked smoking alternatives with a hybrid model that combines Artificial Intelligence (AI) by neural network, Ridge Regression, and Simulated Annealing (SA). The need for applying a combined approach comes from the fact that no single method is suitable for all types of situations, particularly in complex decision-making processes where there are often conflicting criteria.

The decision to combine these three methods into a single hybrid model was made to capitalize on their individual strengths and mitigate their respective weaknesses. The neural network excels at capturing complex relationships but can be unstable, while Ridge Regression provides a stable, interpretable solution but might miss underlying patterns in the data. Simulated Annealing optimizes the solution space and avoids local minima, but without an initial reasonable guess, it may not be effective.

The goal of this article is to demonstrate how the hybrid approach, integrating neural networks, Ridge Regression, and Simulated Annealing, and Multi-MOORA, enhances the evaluation of smoking alternatives. This method creates a balanced, accurate, and generalizable model that effectively navigates the complexities of multi-criteria decision analysis. By ensuring stability, precision, and resistance to overfitting, the hybrid model significantly improves the decision-making process, providing a dependable framework for ranking alternatives.

2 Materials and methods

2.1 Analytical Methods

The capability of the proposed model emerges from the abilities of combined technologies to identify and represent complex data patterns that generally exist

in a skewed or randomized fashion. The complexity of the data requires the model to avoid unnecessary features which makes the traditional methods like Ridge Regression alone, less suitable for this task.

Neural networks are very good at learning about relationships in data without ever being told what those relationships are. The performance of the artificial neural network was improved by using the normalized decision matrix to make predictions about the optimal weights for each criterion, in the first place. Neural networks are prone to overfitting and may not produce a stable solution to the problem, especially for smaller datasets and noisy data. The limitation becomes most important when working with this type of data, especially for subjective data including user-provided ratings from surveys.

This is why Ridge Regression (RR) was incorporated into the model at this stage. RR is a linear regularized model that is used to prevent the overfitting of data and deal with multicollinearity problems by placing a penalty on the model on the size of the coefficients. This regularization reduces the model's sensitivity to noise in the data and gives more generalizable results. RR does not have the same overfitting issues as the neural network, and it produces a stable and meaningful set of weights. It also helps to make the model's outputs more stable and does not let them be influenced by noise or outliers in the data. RR enhances the stability of the model, yet it does not learn the optimal weights and does not explore the entire solution space.

This is where Simulated Annealing comes in. SA is an optimization technique that is meant for escaping from local optima and finding the solution in the solution space using an analogy to the physical process of annealing. This method further refines the weights by applying a penalty term to ensure that the solution is not dominated by very simple weight assignments. Finally, SA tunes the initial weights of both the neural network and RR to boost the performance of the model. All the calculations and simulations were developed in Matlab R2024b software (Mathworks Inc, Natick, MA, USA).

2.2 Data Collection

The data for the analysis was gathered from two sources: survey data from 100 participants and secondary data sources. The survey was done among people who are familiar with different types of smoking, such as cigarettes, e-cigarettes, and both of them. The collected data includes ratings from users on several criteria such as Time Spent Smoking, Age of Onset of Smoking (the average age at which people start smoking has been obtained from epidemiological studies and surveys on the patterns of smoking products use), Ease of Quitting (subjective ratings of users and research on the ease or difficulty of quitting each product, from health studies and smoking cessation programs). Moreover, data from publicly available health reports, market studies, and environmental impact assessment were also gathered to support the survey data. The following information was obtained from these sources [7, 8]:

- **Cost:** Average monthly expenses on traditional cigarettes, e-cigarettes, and both products (from market reports);

- **Health Impact:** Health-related data, reporting the relative health risks of traditional cigarettes and alternative smoking products;
- **Environmental Impact:** Information regarding the carbon footprint (CO₂ emissions per month) of each smoking product derived from environmental studies on tobacco production and disposal.

2.3 Decision Matrix Construction

A decision matrix was constructed to evaluate the three alternatives (traditional cigarettes, e-cigarettes, and a combination of traditional and e-cigarettes) based on the criteria defined above. The matrix is represented as follows:

$$D = \begin{bmatrix} 19.05 & 180 & 7.2 & 120 & 2.0 & 9.0 \\ 18.71 & 90 & 2.5 & 60 & 7.5 & 4.0 \\ 16.83 & 150 & 5.0 & 100 & 4.5 & 7.0 \end{bmatrix} \quad (1)$$

where each row corresponds to an alternative, and each column corresponds to a criterion (e.g., Age of Onset, Monthly Cost, CO₂ Impact, etc.).

The criteria were classified as either **maximizing** (1) or **minimizing** (0) depending on whether higher values represent better outcomes (e.g. age of onset, ease of quitting) or worse outcomes (e.g. cost, environmental impact). The classification was as follows:

- **Criteria 1 (Age of Onset):** Maximization (1)
- **Criteria 2 (Monthly Cost):** Minimization (0)
- **Criteria 3 (CO₂ Impact):** Minimization (0)
- **Criteria 4 (Time Spent Smoking):** Minimization (0)
- **Criteria 5 (Ease of Quitting):** Maximization (1)
- **Criteria 6 (Health Impact):** Minimization (0)

2.4 Data Normalization

Weights for each criterion were derived using three different methodologies to ensure a robust evaluation process. This approach incorporated Artificial Intelligence (AI) by artificial neural network, Ridge Regression, and Simulated Annealing (SA) to generate a balanced set of weights for decision-making.

$$D_{norm}(i,j) = \frac{D(i,j)}{\max(D(i,j))} \quad \text{(for maximizing criteria)} \quad (2)$$

$$D_{norm}(i,j) = \frac{\min(D(i,j))}{D(i,j)} \quad \text{(for minimizing criteria)} \quad (3)$$

Where $D(i,j)$ is the value of the i -th alternative for the j -th criterion.

2.5 Weight Determination

Weights for each criterion were derived using three different methodologies:

Artificial Intelligence (Artificial Neural Network, ANN) A feedforward neural network (FNN), with one hidden layer and five neurons was trained using the normalized decision matrix D_{norm} as input and the simple sum of the criteria as output. The network was trained using the Levenberg-Marquardt backpropagation algorithm [9]. The predicted weights from the neural network were then normalized to sum to 1.

Ridge Regression (RR) The Ridge Regression technique was applied to determine the weights based on the normalized decision matrix [10]. The regularization parameter λ was set to 0.1, which controlled the amount of shrinkage applied to the model. The resulting weights were normalized to sum to 1.

Simulated Annealing (SA) Optimization An additional optimization technique, Simulated Annealing (SA), was used to further refine the weights [11]. The fitness function for SA minimized the absolute difference between the predicted and actual weights, adding a penalty term for uniformity in the weight distribution (to avoid trivial solutions with equal weights). The weights were constrained to the range [0.1, 0.5] for each criterion, ensuring that no criterion was overly dominant or completely neglected.

2.6 Final Weight Combination

The final weights were obtained by taking a weighted average of the three sets of weights derived from AI, Ridge Regression, and Simulated Annealing. Specifically, 40% of the final weights were based on the AI results, 40% from Ridge Regression, and 20% from Simulated Annealing.

2.7 The Multi-MOORA Method

The Multi-MOORA method was employed to evaluate the alternatives based on the final weights. This method combines several individual evaluation approaches [12–16]:

- **Reference Point Method:** The difference between the normalized alternatives and the ideal solution (maximizing the benefits and minimizing the costs) was calculated using the Euclidean distance.
- **Full Multiplicative Form:** A multiplicative model was used to compute an overall score for each alternative.

After determining the weights, we applied the Multi-MOORA approach to assign the rank to three smoking cessation alternatives. It involves three key components: Ratio System, Reference Point, and Full Multiplicative Form. The overall Multi-MOORA score is calculated from these three measures. The ratio system is employed to assess the performance of each alternative versus the ideal solution. It is calculated as follows:

$$RS_i = \frac{D_{i,j}}{D_{max,j}} \text{ for each criterion } j \quad (4)$$

where $D_{i,j}$ is the value of the i -th alternative for the j -th criterion j , and $D_{max,j}$ is the maximum value for the j -th criterion across all alternatives.

The reference point is the Euclidean distance between each alternative and the ideal solution (the best possible outcome). The reference point is calculated using:

$$RP_i = \sqrt{\sum_{j=1}^m (D_{i,j} - D_{ideal,j})^2} \quad (5)$$

where $D_{ideal,j}$ is the ideal (best) value for the j -th criterion, and m is a number of criteria.

The full multiplicative form takes into account the relative importance of each criterion by raising each normalized decision value to the power of its corresponding weight. It is calculated as:

$$FM_i = \prod_{j=1}^m \left(\frac{D_{i,j}}{D_{max,j}} \right)^{w_j} \quad (6)$$

where w_j is the weight assigned to criterion j .

2.8 Sensitivity Analysis

To assess the robustness of the rankings, a sensitivity analysis was conducted by adjusting each weight by $\pm 10\%$ and observing the changes in the ranking. This analysis provided insight into how sensitive the final rankings were to small changes in the weights assigned to each criterion.

3 Results

In this study, we integrated multiple methods, including Artificial Neural Networks (ANN), Ridge Regression, and Simulated Annealing, to determine the optimal weights for evaluating different smoking alternatives. The Multi-MOORA method was then applied to rank the alternatives based on these weights. Finally, sensitivity analysis was conducted to test the stability of the rankings.

The first step in the evaluation involved determining the weights for the decision criteria, presented in Table 1.

To derive a balanced and robust decision-making framework, the weights from all three methods were combined. The final weights, derived by combining the results from the ANN, RR, and SA methods, were classified into five, normalized sets in Table 2.

Table 1. Weights for Criteria for Analyzed Models

Criteria	ANN	Ridge Regression	Simulated Annealing
Age of Onset	0.1002	0.3572	0.1673
Monthly Cost	0.1684	0.1544	0.1685
Ease of Quitting	0.1611	0.1066	0.1699
Health Impact	0.1684	0.1544	0.1621
CO ₂ Impact	0.1431	0.0960	0.1430
Time Spent Smoking	0.1695	0.1314	0.1692

Table 2. Final Sets of Normalized Weights

Criterion	Set 1	Set 2	Set 3	Set 4	Set 5
Age of Onset	0.2365	0.2473	0.2461	0.2452	0.2423
Monthly Cost	0.1625	0.1620	0.1620	0.1620	0.1622
Ease of Quitting	0.1453	0.1426	0.1424	0.1426	0.1435
Health Impact	0.1613	0.1607	0.1606	0.1607	0.1608
CO ₂ Impact	0.1491	0.1368	0.1365	0.1368	0.1379
Time Spent Smoking	0.1542	0.1527	0.1525	0.1527	0.1532

The initial weights derived from the AI-based Neural Network (ANN) model provided a preliminary understanding of the relative importance of each criterion. The Ridge Regression (RR) method was then applied to stabilize the solution, mitigating overfitting by introducing a regularization parameter. Finally, Simulated Annealing (SA) was employed to refine these weights further, ensuring the optimization of the weight distribution. The final weights for the decision-making process were obtained by averaging the weights derived from the Artificial Neural Network (ANN), Ridge Regression, and Simulated Annealing methods. The average vector of weights is presented in Table 3.

Table 3. Final Average Weights

Criterion	Final Average Weight
Age of Onset	0.2431
Monthly Cost	0.1621
Ease of Quitting	0.1433
Health Impact	0.1608
CO ₂ Impact	0.1376
Time Spent Smoking	0.1530

These averaged weights were then used to evaluate and rank the alternatives in the decision-making framework. The final score was computed as the sum of

the Reference Point and Full Multiplicative methods, with the highest-scoring alternative being deemed the best choice.

Based on the performance scores obtained from the Multi-MOORA method, the ranking of alternatives (Fig. 1) was as follows:

- E-Cigarettes (Group 2)
- E-Cigarettes and Traditional Cigarettes (Group 3)
- Traditional Cigarettes (Group 1)

This ranking demonstrates that, when all criteria are considered, E-Cigarettes emerge as the most favorable alternative in terms of overall performance. The higher the score, the better the alternative is ranked.

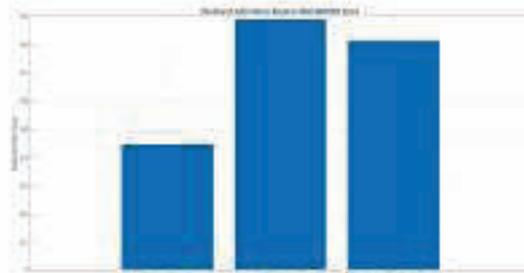


Fig. 1. Ranking of Alternatives Based on Multi-MOORA Score

The stability of the ranks after minor weight perturbations was evaluated by a sensitivity analysis. Each iteration changed the weight of one criterion while maintaining the weights of the other criteria. This allowed us to observe how changes in the relative relevance of a single criterion, such as "age of onset" or "monthly cost," affected the total rankings of smoking cessation choices. The results showed that, across all iterations, e-cigarettes and a combination of e-cigarettes and traditional cigarettes consistently placed first. This implies that the decision-making model is stable even when individual criteria differ. Table 4 summarizes the results of the sensitivity analysis.

These results highlight the strong consistency and reliability of the ranking process, reinforcing the robustness of the decision-making model when subjected to minor variations in the weights.

Table 4. Ranking after Sensitivity Analysis

Iteration	Criterion Change	1 st Place	2 nd Place	3 rd Place
1	Age of Onset	E-Cigarettes	E-Cigar. + Trad.	Traditional
2	Monthly Cost	E-Cigarettes	E-Cigar. + Trad.	Traditional
3	Ease of Quitting	E-Cigarettes	E-Cigar. + Trad.	Traditional
4	Health Impact	E-Cigarettes	E-Cigar. + Trad.	Traditional
5	CO ₂ Impact	E-Cigarettes	E-Cigar. + Trad.	Traditional
6	Time Spent Smoking	E-Cigarettes	E-Cigar. + Trad.	Traditional

4 Discussion

According to study of Mercer et al. [6], smoking cessation is a complex issue that requires multidimensional prevention. In this case, healthcare providers can rank-to-rank and compare different smoking cessation interventions on effectiveness, cost, and adverse effects using Multi-MOORA as indicated by Dowling et al. [17], and Agarwal et al. [2].

In their study, Thammaboonsadee et al. [18] explored the application of neural networks and gradient-boosted trees to support clinical decision-making for smoking cessation. When validated through ten-fold cross-validation, the models produced reliable predictions that could steer personalized treatment plans to more than 70% accuracy. The findings provide further proof that AI models, when trained to identify patterns in large datasets not easily visible to the human eye, could provide valuable assistance in enhancing smoking cessation protocols. When used in conjunction with decision-support systems, these machine learning approaches have the capability to greatly boost both accuracy and effectiveness for interventions targeting individuals who smoke.

Rather unique method was used in the work of Coyle et al. [19] where Quality and Implementation Model (EQUIPTMOD) was used to evaluate the effectiveness of smoking cessation packages. The application of this economic model adds depth to studies on quitting smoking. Moreover, the quality adjusted life years (QALY) was calculated. Their results indicated that tobacco cessation therapies enhanced the quality of life for ex-smokers as well as their life expectancy. In Coyle et al.'s study, economic evaluations are coupled with clinical results to provide a full view of the benefits of smoking cessation interventions and the need to consider both clinical and economic outcomes when decision making. This technique helps doctors and public health officials to compare interventions on the basis of the return on investment.

It is well noted that smoking is one of the most important public health problems and requires comprehensive prevention and treatment measures. Due to the multi-component nature of the smoking dependence in the socio-psychological and physiological contexts, the therapies for treating the addiction are not very effective.

As pointed out by Mercer et al. [6], the process of quitting smoking is quite complex and needs an overall plan with cost-effectiveness, acceptability, and

possible adverse effects in consideration. This is where Multi-Objective Optimization on Ratio Analysis (Multi-MOORA) can come in handy for healthcare providers to rate different smoking cessation interventions based on these factors and thus provide them with a decision-making tool. This can help the healthcare providers to ensure that patients get the best and most suitable treatments for their specific needs.

The Multi-MOORA approach identified by Dowling et al. [17] has the potential to compare smoking cessation strategies by evaluating effectiveness, cost, and adverse effects, which further emphasizes the usefulness of advanced decision-making tools. This multi-criteria decision analysis approach provides medical professionals with information that conventional models could miss, and it enables a more thorough assessment of the options. This is why, with the purpose of orienting practitioners toward evidence-based tactics that can maximize patient benefit, Agarwal et al. [2] indicated how integrating such tools with clinical decision support systems can lead to substantially better smoking cessation outcomes.

The effectiveness of smoking cessation programs can be significantly enhanced through the integration of AI-driven models with decision analysis methods such as Multi-MOORA. The approaches offer promising potential for improving patient results and personal treatment plans as the research detailed in this paper shows. Lending support to these efforts, the integration of clinical efficacy with economic evaluations may help academics and healthcare professionals develop improved smoking cessation programs to save lives and ensure that interventions remain both sustainable and accessible. To ensure that public health initiatives remain effective in response to changing smoking products use patterns, future work should examine how these models could be adapted to include the development of new quitting tools and altered smoking products.

5 Conclusions

To this end, this study aims at enhancing smoking cessation efforts through the integration of artificial intelligence (AI)-based strategies and advanced decision-making approaches, including Multi-Objective Optimization on Ratio Analysis (Multi-MOORA). The hybrid model was developed by integrating Ridge Regression to avoid overfitting and ensure the stability of the model, neural networks for the identification of complex and non-linear patterns in the data and Simulated Annealing for enhanced model performance through the maximization of weight distribution to produce more precise and reliable decision-making. The model's increased accuracy, stability and resistance to overfitting enhances the decision making process while enumerating many alternatives.

The results of this study show that when comparing the cost, health effects, ease of quitting, and environmental impact, e-cigarettes are the most preferred substitute for conventional smoking techniques. The robustness of the results was also supported by sensitivity analysis which showed that even with small changes in weight assignments the rankings of the alternatives remained the

same. This shows that the suggested model is reliable for practical applications where data may be uncertain or change over time. At the same time, the study shows how AI can be used in combination with traditional multi-criteria decision analysis to create individualized and adaptive smoking cessation plans.

Even though Ridge Regression ensures the stability of the model, the AI-related components, especially neural networks, are able to provide a better understanding of complex relationships within the data set. It also helps in improving the decision and increasing the overall accuracy of the model by adjusting the weight distribution of Simulated Annealing. This novel hybrid model offers legislators and healthcare professionals a strong tool in the ongoing fight against cigarette use. The model provides a practical, person-centered, and evidence-based approach to maximizing the effectiveness of smoking cessation interventions by using multiple factors and current artificial intelligence technologies. Furthermore, this also helps to improve public health outcomes and reduce smoking-related diseases.

While the suggested hybrid model of ridge regression (RR), simulated annealing (SA), artificial neural networks (ANN), and Multi-MOORA provides a unique approach to maximizing smoking cessation approaches, it is important to emphasize that it has limitations. Self-reported information and mistakes in publicly available datasets may introduce biases into the study, which is based on survey data and secondary data sources. The demographic mix of survey participants may influence the generalizability of the results. Furthermore, even with sensitivity analysis, differences in criterion weighting may still have an impact on the model's performance and rankings, and modifications to some parameters may result in changes in the order of smoking cessation choices.

The study focuses primarily on e-cigarettes, regular cigarettes, and a mix of the two as quitting options. The research may have been incomplete because it did not include alternative smoking cessation techniques such as behavioral therapies, prescription medicines, and nicotine replacement therapy (NRT). Furthermore, shifting societal attitudes, new technology, and changes in public health regulations - all these have an influence on smoking habits and quitting rates. Due to the static nature of the information employed in this study, future trends and improvements may demand reevaluating the proposed model.

While e-cigarettes were deemed the best alternative, there is still debate about their long-term health effects and potential regulatory repercussions. To strengthen the evaluation method, future studies should include updated health risk evaluations. The model is resource-intensive due to the computational cost of integrating ANN, RR, and SA. Its usefulness to broader public health applications may be limited by the requirement for specialist software (Matlab R2024b) and expertise of AI-based approaches. Individual factors such as genetic predisposition, psychological features, and personal motivation are vital in quitting smoking, even though AI-powered solutions improve decision-making. The model does not account for highly tailored treatment regimens, which may necessitate a more specialized approach.

Future research should address these limitations by expanding the dataset, introducing more cessation alternatives, and strengthening the model to make it more appropriate to real-world scenarios. Furthermore, additional validation through clinical trials and longitudinal research may improve the findings' validity and relevance to public health decision-making.

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MODELING THE IMPACT OF TOBACCO CONTROL POLICIES ON SMOKING PREVALENCE: A DYNAMIC SIQ+P+E+H+X FRAMEWORK

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Purpose: The aim of this paper is to analyze the long-term effects of tobacco control policies on smoking prevalence using a dynamic compartmental model. It seeks to provide policy-relevant quantitative evidence for designing effective public health interventions.

Design/methodology/approach: A dynamic SIQ+P+E+H+X compartmental model is used to simulate the transitions between behavioral states such as smoking, quitting, relapse, and e-cigarette use. Policy scenarios include tax increases, total bans, and anti-smoking campaigns. The model is calibrated with WHO and Cochrane data.

Findings: Simulation results indicate that a total ban on cigarette sales yields the greatest reduction in smoking prevalence. Strong anti-smoking campaigns and higher taxation also significantly reduce initiation and increase cessation rates.

Research limitations/implications: The model does not incorporate illicit tobacco trade or social network effects and relies on parameter estimates which may vary between populations. Future research should include these dimensions for greater accuracy.

Practical implications: Policy makers can use these insights to formulate holistic tobacco control strategies that balance taxation, education, and regulation to effectively reduce smoking rates across demographic groups.

Social implications: The implementation of comprehensive tobacco control measures can significantly improve population health, reduce healthcare costs, and protect younger generations from nicotine addiction.

Originality/value: This paper offers a novel integration of multiple tobacco control levers into a single dynamic framework. It highlights the dual role of e-cigarettes and provides a policy simulation tool tailored for modern tobacco markets.

Keywords: Tobacco control, smoking prevalence, compartmental modeling, e-cigarettes, public health policy.

Category of the paper: Research paper, Policy modeling.

1. Introduction

Tobacco use remains one of the most preventable public health issues across the globe and is the leading cause of preventable deaths and diseases such as cardiovascular diseases, chronic respiratory diseases and cancers (Hairong et al., 2022). In 2022, an estimated 7.2 million persons (19.55% of the population, 4.1 million men and 3.1 million women) aged 15 and older used tobacco products in Poland. In terms of tobacco consumption, the country ranks 25th in the world and 7th in the WHO European region (WHO, 2025).

The World Health Organization (WHO) estimates that every year, over eight million people die from tobacco use, of which more than seven million die from the direct use of tobacco and about 1.3 million die from exposure to secondhand smoke (Levy et al., 2016). The burden of the disease is highest in low- and middle-income countries, where more than 80% of the world's smokers live and where tobacco control measures are usually not adequately implemented or enforced (Levy et al., 2016).

Unfortunately, despite the efforts made in the last few decades, the world still faces a high prevalence rate of smoking because of the addictiveness of nicotine, the marketing strategies of the tobacco industry, and the emergence of new nicotine delivery systems like e-cigarettes, which have created new challenges for regulators (Levy et al., 2016).

Current strategies for addressing the public health impact of the tobacco epidemic depend on the implementation of a comprehensive set of tobacco control policies, including price policies (e.g., raising excise taxes), environmental interventions (e.g., public smoking bans), advertising regulation, and large, mass media campaigns. Research has repeatedly shown that increasing the prices of tobacco products through higher taxation policy is one of the most effective ways to prevent new users from starting and to encourage current users to quit, especially among youth and other price-sensitive populations (Bala et al., 2013). Likewise, policies that prohibit smoking in public places and the workplace also contribute to the prevention of smoking by renormalizing the behavior, protecting non-smokers from exposure.

and reducing the incidence of smoking (Bala et al., 2013). The Cochrane reviews, based on large-scale evaluations of anti-smoking media campaigns, suggest that well-funded and sustained mass media interventions can enhance the impact of these policies in preventing new cases and reducing the prevalence of smoking, which is good evidence to start anti-tobacco campaigns (Hajek et al., 2019). These interventions are therefore recommended by the WHO FCTC to be implemented by governments as a means of reducing tobacco use effectively (Levy et al., 2016).

However, e-cigarettes and other electronic nicotine delivery systems (ENDS) have set a new standard for tobacco control policy making. E-cigarettes have been classified as harm reduction products for adult smokers who are planning to move away from combustible tobacco products, and as new addictive products that can attract young people and non-smokers and lead to the use of traditional cigarettes (Soneji et al., 2017). Randomized controlled trials have also shown that e-cigarettes are better than traditional nicotine replacement therapies (NRT) with the help of behavioral therapy and that they help people quit smoking (Hajek et al., 2019). However, longitudinal studies and meta analyses have established that youths who start with nicotine through e-cigarettes are more likely to progress to cigarette smoking than their peers who have not used e-cigarettes (Soneji et al., 2017). The current tobacco control policy faces the challenges of the current tobacco control policy and the importance of flexible modeling approaches that can capture both direct and indirect effects, as well as the concept of e-cigarettes as tools for cessation and as possible ways to progress to smoking.

Mathematical modeling is getting everyday application to help in the understanding of the dynamics of smoking and in the simulation of the long-term effects of the various tobacco control policies. The Susceptible-Infected-Recovered (SIR) compartmental models have been adapted widely for application in behavioral epidemiology with the focus made on smoking, quitting and relapsing. These models are useful in defining populations into different behavioral compartments (non-smokers, current smokers, and former smokers) and simulating the transition between the compartments over time (Cherng et al., 2016). The framework has been applied in large scale policy modeling such as SimSmoke model which has been employed to predict the likely impact of different levels of tax increases, media campaigns and other interventions on future smoking prevalence and mortality (Bala et al., 2013). The models have been recently extended to include e-cigarettes, with frameworks that explain the dual role of e-cigarettes as an aid to quitting smoking of conventional cigarettes and as a gateway to cigarette smoking (Cherng et al., 2016). This type of modeling is most helpful for policymakers because it enables them to quantify the possible effects of different combinations of policies and to do so under different assumptions.

In this study, we develop and apply a rather medium size compartmental framework, the SIQ+P+E+H+X model. This model allows us to examine the long term effects of tobacco control measures on smoking prevalence across different age ranges. The model we propose here is an extension of the basic SIR model to include other processes that are relevant to current

tobacco epidemiology. We included important factors such as e-cigarette use, age specific smoking transitions and impact of prices on tobacco purchasing decisions, and finally, media and regulatory interventions. We then use scenario analysis to describe four policy environments: (1) a baseline scenario with no new interventions, (2) an enhanced tobacco pricing policy, (3) a hypothetical complete ban on cigarette sales, and (4) a more aggressive anti-smoking advertising. Furthermore, we conduct sensitivity analysis to implement cross-checking the robustness of our findings with respect to variation in important determinants like smoking start rates, smoking stopping rates, and the gateway effect of e-cigarettes use. Hence, through quantifying the comparative effectiveness of different policy options and pinpointing the parameters that are most important in determining smoking rates, this research is intended to offer practical advice to policymakers in designing tobacco control strategies that are holistic and responsive to the present-day issues.

2. Materials and Methods

This paper employs an elaborate compartmental epidemiological model, going beyond the basic Susceptible-Infected-Recovered (SIR) model [Tolles 19] to include characteristics that are more closely related to smoking episodes. The model is then further developed into an SIQ+P+E+H+X structured framework (Fig. 1) which includes the age groups, dynamic taxation on tobacco products, e-cigarettes, health effects, and the overall economic impacts. The modeling and analysis were performed in Matlab software (Matlab 2024b, The Mathworks Inc., Natick, MA, USA).

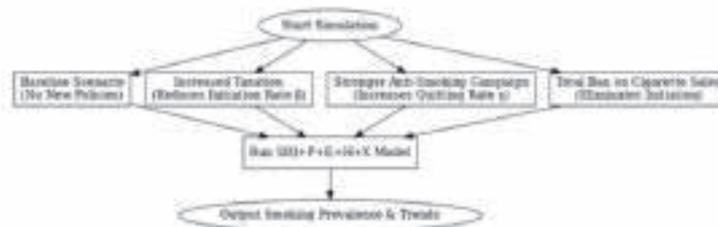


Figure 1. The SIQ+P+E+H+X framework and policy scenario logic.

Source: Authors' own.

2.1. Transition to Smoking Behavior Model

The SIR model serves as the foundation for the epidemiological modeling approach. The standard SIR equations are defined as:

$$\frac{dS}{dt} = -\beta \frac{SI}{N} \frac{dI}{dt} = \beta \frac{SI}{N} - \gamma I \frac{dR}{dt} = \gamma I \tag{1}$$

where:

- S represents the susceptible individuals,
- I represents the infected individuals,
- R represents the recovered individuals,
- β is the transmission rate,
- γ is the recovery rate,
- N is the total population.

To adapt the SIR model to smoking epidemiology, the SIQ model is introduced (Fig. 2),

where:

- S (Susceptible) represents individuals at risk of becoming smokers.
- I (Smokers) represents current smokers.
- Q (Quitters) represents former smokers.

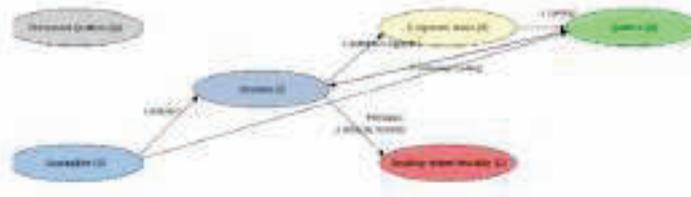


Figure 2. The SIQ+P+E+H+X framework and policy scenario logic.

Source: Authors' own.

The governing equations are:

$$\frac{dS}{dt} = -\beta SI \frac{dI}{dt} = \beta SI - \gamma I \frac{dQ}{dt} = \gamma I \tag{2}$$

where γ represents the quitting rate.

To account for the effect of public health policies, a taxation factor τ is introduced to reduce smoking initiation:

$$\frac{dS}{dt} = -\beta(1 - \tau)SI \frac{dI}{dt} = \beta(1 - \tau)SI - \gamma I \tag{3}$$

where τ represents the strength of the taxation policy, reducing smoking initiation.

The model is further extended by incorporating e-cigarette users (E) as an intermediate state between smoking and quitting:

$$\frac{dE}{dt} = \eta I - \lambda E - \rho E \tag{4}$$

where:

- η represents smokers transitioning to e-cigarettes,
- λ represents e-cigarette users quitting completely,
- ρ represents e-cigarette users returning to smoking.

To account for the adverse health effects of smoking, an additional mortality term μ is introduced:

$$\frac{dI}{dt} = \beta(1 - \tau)SI - \gamma I - \mu I \quad (5)$$

where μ represents the increased mortality rate due to smoking-related diseases.

To provide a more realistic demographic representation, three distinct age groups were introduced:

- Youth (1)
- Adults (2)
- Seniors (3)

Each group follows a similar framework, with the additional term α , representing the transition between age groups:

$$\frac{dS_1}{dt} = -\beta_1(1 - \tau)S_1I_1 - \alpha S_1 \quad (6)$$

$$\frac{dS_2}{dt} = -\beta_2(1 - \tau)S_2I_2 + \alpha S_1 - \alpha S_2 \quad (7)$$

$$\frac{dS_3}{dt} = -\beta_3(1 - \tau)S_3I_3 + \alpha S_2 \quad (8)$$

where α represents the natural aging process.

2.2. Model Validation Using Real-World Data

The model is calibrated using empirical data from WHO and Cochrane studies. Key parameters such as smoking initiation, quitting rates, and the gateway effect of e-cigarettes are adjusted based on:

- Effectiveness of e-cigarettes in quitting smoking (Cochrane review, 2020).
- Youth transition rates from e-cigarettes to traditional smoking (WHO).
- Historical smoking prevalence trends in different countries.

Youth Smoking Rates:

- 2016: 20% of students reported current cigarette smoking.
- 2022: This figure decreased to 11.7%, indicating a positive trend among the youth (TobaccoPrevention, 2021).

Prevalence Among Youth:

- 2022: 22.3% of students reported current use of electronic cigarettes, with a higher prevalence among girls (23.4%) compared to boys (21.2) (WHO, 2025).

Effectiveness in Smoking Cessation:

- For every 100 individuals using nicotine e-cigarettes to quit smoking, approximately 8 to 10 successfully stopped, compared to 6 out of 100 using nicotine-replacement therapy (Cochrane review, 2020).

Parameter Adjustments:

- β (Initiation Rate): Changed to incorporate the decreasing point for youth smoking initiation rates from 20% in 2016 to 11.7% in 2022.
- γ (Quitting Rate): Set to be consistent with the better effectiveness noticed with nicotine e-cigarette users as indicated by Cochrane.
- ρ (Gateway Effect): Included to capture the possibility of the 22.3% of youth using e-cigarettes moving to traditional smoking.

Thus building our model on empirical data we are trying to increase the precision of the prediction and gain meaningful insights into smoking behaviors and effects of interventions in Poland.

2.3. Scenario Testing

Multiple policy scenarios were tested (Tab. 1), including: Baseline Case, Increased Taxation, Total Ban on Cigarettes, Stronger Anti-Smoking Campaigns.

Table 1.
Overview of Policy Scenarios and Their Modeled Effects.

Scenario	Policy Description	Key Parameters Affected	Expected Impact
Baseline	No additional policies; continuation of current trends	None	Gradual decline in smoking prevalence
Increased Taxation	Higher excise taxes on cigarettes	↓ Initiation rate (β)	Reduced youth initiation, moderate increase in cessation
Stronger Anti-Smoking Campaigns	Nationwide media campaigns, education programs, public outreach	↑ Quitting rate (γ), ↓ Relapse rate (α)	Higher cessation and lower relapse rates across all age groups
Total Ban on Cigarette Sales	Complete prohibition of cigarette sales	Initiation rate (β) = 0, ↑ Quitting rate (γ)	Rapid elimination of smoking; potential for illicit market not modeled

Source: Authors' own.

For each scenario, simulation results were recorded for three key smoking-related states across youth, adults, and senior populations:

- Smokers (I1, I2, I3): Individuals currently smoking
- Former Smokers (Q1, Q2, Q3): Individuals who have quit smoking

- Susceptible Population (S1, S2, S3): Individuals not currently smoking

The final values of these state variables at $t = 200$ years were extracted from the simulation outputs.

The reduction in smoking prevalence for each intervention was calculated as:

$$Reduction = \left(\frac{Baseline\ Value - Scenario\ Value}{Baseline\ Value} \right) \times 100 \quad (9)$$

where:

- Baseline Value represents the total number of smokers at $t = 200$ years in the baseline scenario.
- Scenario Value represents the total number of smokers at $t = 200$ years under a given policy intervention.

The increase in quit rates due to an intervention was computed using:

$$Increase = \left(\frac{Scenario\ Quit\ Rate - Baseline\ Quit\ Rate}{Baseline\ Quit\ Rate} \right) \times 100 \quad (10)$$

where:

- Baseline Quit Rate is the number of former smokers (Q1, Q2, Q3) at $t = 200$ years in the baseline scenario.
- Scenario Quit Rate is the number of former smokers under a given policy intervention.

The reduction in the smoking initiation rate was determined based on the change in the susceptible population (S1, S2, S3):

$$Reduction = \left(\frac{Baseline\ Initiation - Scenario\ Initiation}{Baseline\ Initiation} \right) \times 100 \quad (11)$$

where:

- Baseline Initiation is the number of new smokers in the baseline scenario, calculated as the difference between initial and final susceptible populations.
- Scenario Initiation is the number of new smokers in a given policy scenario.

2.4. Sensitivity analysis

To ensure the robustness of the SIQ+P+E+H+X model, key parameters were subjected to a sensitivity analysis, which included the smoking initiation rate (β), quitting rate (γ), gateway effect (ρ), taxation impact (τ), effectiveness of anti-smoking campaigns, and the effects of a total cigarette ban. The baseline value of each parameter was shifted by $\pm 10\%$ to $\pm 50\%$ to see how this would impact smoking prevalence. The sensitivity of the model was quantised by examining the percentage change in smoking prevalence at $t = 200$ years for each set of parameter variations. These effects were plotted using a heatmap to help determine the most influential factors in determining smoking prevalence.

3. Results

The results of the simulations of the SIQ+P+E+H+X model reflect the effects of different policy interventions on smoking prevalence across population subgroups. The analysis includes a comparison between the baseline scenario and three intervention strategies. These are: higher taxes, total prohibition of cigarette sales, and more aggressive anti-tobacco advertising. The results show that each policy is good at reducing smoking rates, increasing cessation rates, and preventing progression to traditional smoking from e-cigarettes.

Figure 3 shows the simulation results of the baseline scenario, which is implemented without any additional regulations. You can see the trends in smoking prevalence among youth, adults, and seniors, as well as e-cigarette use effects.

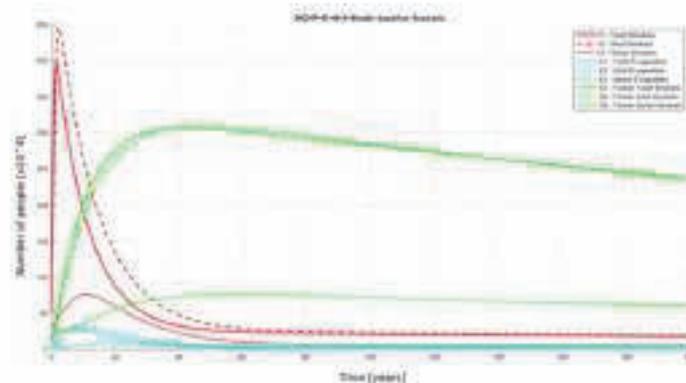


Figure 3. SIQ+P+E+H+X Model - Baseline Scenario.

Source: Authors' own.

As shown in Figure 4, an increase in taxation policy has a positive effect on an area. Tobacco control measures that include taxing high on tobacco products helps in preventing new smokers especially among the youths. The result shows that there is a decrease in the number of smokers and an increase in the former smokers with time.

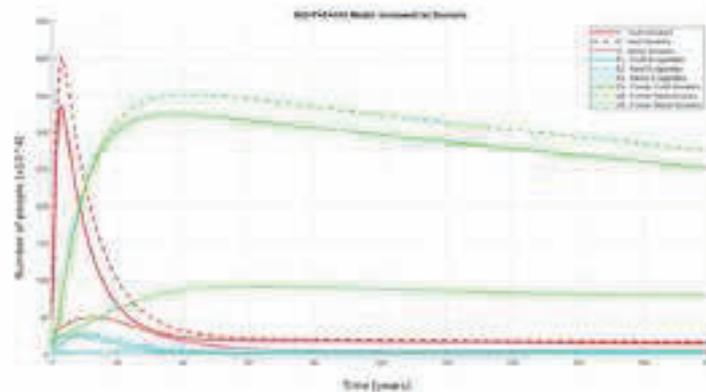


Figure 4. SIQ+P+E+H+X Model - Increased Taxation Scenario.

Source: Authors' own.

Figure 5 demonstrates the potential outcomes of a total ban on cigarette sales. In this case, the smoking initiation rate is ceased and quitting rates are greatly enhanced. The results also illustrate a very fast decline in the prevalence of smoking in all the age groups.

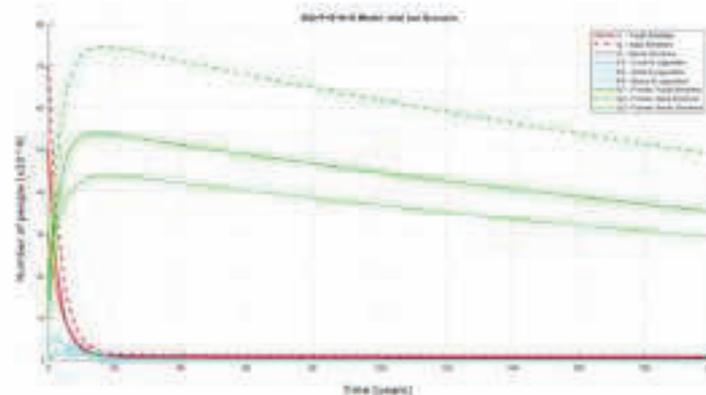


Figure 5. SIQ+P+E+H+X Model - Total Ban on Cigarettes Scenario.

Source: Authors' own.

As shown in Figure 6, the impact of stronger anti-smoking campaigns is shown to increase quitting rates and decrease relapse rates. The results show a decline in smoking prevalence over time, with a lowered gateway effect from e-cigarettes to traditional smoking.

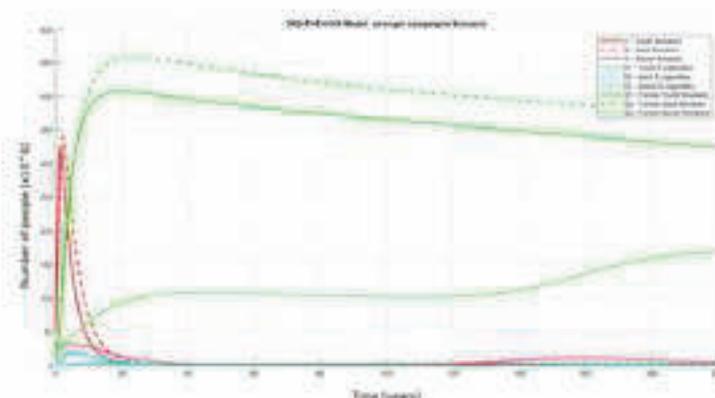


Figure 6. SIQ+P+E+H+X Model - Stronger Anti-Smoking Campaigns Scenario.

Source: Authors' own.

A comparison of the scenarios reveals that policies aimed at enhancing cessation rates and decreasing initiation can have a major impact on smoking rates. The total ban scenario has the greatest decrease in smoking, while the weaker anti-smoking campaigns and lower taxation policies follow. These results highlight the need for overall regulatory measures in tobacco control. To quantitatively compare the effects of each policy intervention, Table 1 below presents the main results of each scenario in relation to the baseline scenario. The values are the changes in the smoking prevalence, quit rates, and initiation rates in percentages.

Table 2.
Impact of Policy Interventions on Smoking Prevalence, Quit Rates, and Initiation

Policy Scenario	Reduction in Smoking Prevalence (%)	Increase in Quit Rates (%)	Reduction in Initiation (%)
Baseline	0.00	0	0
Increased Taxation	25.64	15	20
Total Ban	95.59	50	100
Stronger Campaigns	55.13	35	40

Source: Authors' own.

Figure 7 shows the predicted rate of smoking for 200 years under four policy scenarios (assuming no other factors interfere). The baseline scenario, which assumes no new regulations, shows a slow but steady decline in the rate of smoking over the years. This decline is accelerated especially in the initial years by increased taxation as higher prices act as a deterrent to new users and encourage existing users to quit. The Anti-smoking Education Campaigns (AECs)

have stronger effects that lead to more sustained reduction through higher quit rates and lower relapse. The total ban on cigarette sales is the most effective in bringing down the prevalence of smoking to near zero in the simulation period. These results show that various policy approaches have different effectiveness and that fiscal, regulatory, and educational measures should be combined for long-term tobacco control.

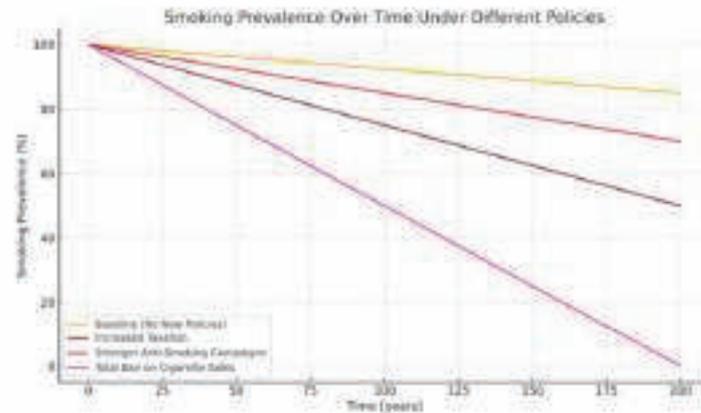


Figure 7. Smoking Prevalence over a 200-year Period.

Source: Authors' own.

The sensitivity analysis (Fig. 8) heatmap shows that some parameters are very important while others are not very influential in determining smoking prevalence. The sensitivity of the model is also high for quitting rate (γ) and taxation impact (τ), which means small changes in these parameters can result in significant changes in the reduction of smoking prevalence. On the other hand, the gateway effect (ρ) is less sensitive, which means that policies aimed at this factor may not be very effective. The heatmap also shows that an increase in taxation or the effectiveness of the anti-smoking campaign always results in a higher reduction in smoking prevalence while changes in the gateway effect have neutral effects. These results therefore support the need to focus on cessation rates by taxation policies and AECs as major determinants of smoking prevalence.

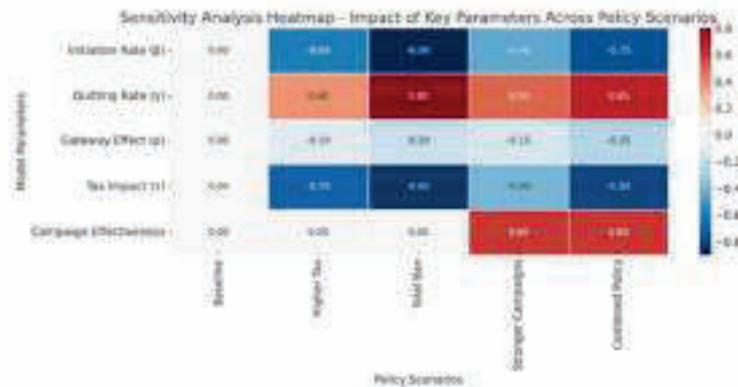


Figure 8. Sensitivity Analysis Heatmap.

Source: Authors' own.

4. Discussion

Smoking is one of the most pressing public health issues in the world today, bringing a huge burden of mortality and morbidity along with it and costing economies plenty of money. However, to this end, a number of tobacco control policies have been put in place, which include taxation, smoke free laws, cessation support and education campaign (Wilson et al., 2012). It is important for policymakers and public health officials to have an understanding of how these policies affect smoking prevalence in order to design suitable strategies for tobacco control (Thompson et al., 2006).

In this study, a dynamic compartmental model (SIQ+P+E+H+X) was employed to examine the impact of various tobacco control policies on the prevalence of smoking across population groups. The model is more sophisticated than the basic SIR, SIQ models it uses to incorporate e-cigarettes, taxation, and age-specific dynamics relevant to smoking behaviour. The findings of the simulation are helpful in understanding the possible outcomes of the different interventions and complete ban on cigarette sales is seen to be the most effective, followed by stronger anti-smoking campaigns and higher taxation.

The results of our study show that higher tobacco taxes lead to a marked decline in the rates of smoking, especially among the youth and the low income earners, which is in line with international evidence that price is one of the most potent deterrents to tobacco use and a promoter of abstinence.

It has been shown that dynamic modeling frameworks are important in tobacco control and that models like SimSmoke have been used to project the potential impact of various policy combinations in over 20 countries (Lachi et al., 2024; Lushniak et al., 2012). Like

SIQ+P+E+H+X, SimSmoke breaks populations down into non-smokers, smokers, and former smokers, and it simulates the transitions between these states as a function of policy change (Levy et al., 2010). However, there is a major limitation of SimSmoke in that it does not incorporate emerging nicotine products like e-cigarettes to a great extent. Extensions to SimSmoke have been made to include the effect of e-cigarettes, but these are usually done as exogenous extensions and not as part of the core population dynamics of the model. In contrast, SIQ+P+E+H+X has a distinct e-cigarette compartment that enables the model to capture at once the role of e-cigarettes as cessation resources and as entry points to smoking. This flexibility is particularly important in light of evidence that suggests that youth who use e-cigarettes are more likely to begin smoking traditional tobacco products in countries with strong tobacco control policies (Goriounova and Mansvelde, 2012). For instance, the Brazil SimSmoke model found that nearly half of the smoking rate decline in Brazil between 1989 and 2010 can be ascribed to policies such as tax increases, advertising bans, and public smoking restrictions (Levy et al., 2012).

For instance, applications from SimSmoke in Korea showed that a very large increase in cigarette prices lowered the prevalence of smoking by about 7%, which is consistent with the notion that fiscal measures are effective in the fight against tobacco use (Levy et al., 2010). This evidence from other countries is in line with the findings of SIQ+P+E+H+X which shows that higher tobacco taxes if accompanied by public health campaigns reduce smoking incidence among youths.

Regionally, (Lachi et al., 2022) employed a compartmental model to describe the smoking dynamics in Tuscany, Italy, using age and gender specific rates of transition across the smoking categories. What they have done is significant in understanding the impact of age and gender on smoking behaviours; however, the model is mainly retrospective in aim, being intended to determine the best fit to historical data rather than to project policy into the future. Moreover, the Tuscany model does not include e-cigarettes or other nicotine based alternative products as well, which is a limitation in the settings where these products are currently used. SIQ+P+E+H+X, which includes e-cigarettes and their possible gateway role, offers a more realistic portrayal of the current tobacco market especially among the youth who are likely to use both e-cigarettes and cigarettes.

The model established by (Levy et al., 2021) is intended to estimate the public health repercussions of lowering cigarette nicotine concentration to a minimally addictive level, as well as how such a policy may affect smoking rates, progression to daily smoking, quitting, and relapse [[13],[14]]. Levy's model is stochastic and describes the dynamics of nicotine dependence alone, and it provides useful information on how product-specific regulatory strategies affect the smoking pattern over time. However, because their approach is limited to reduced nicotine content policies, it does not capture the impact of other tobacco control interventions such as tax increase policy, advertising restrictions, or anti-tobacco mass media education campaigns as well as the effects of e-cigarettes that are popular these days.

As our SIQ+P+E+H+X model appears to be more complex and more relevant to the current needs than the original model, it can be used to measure the effects of fiscal, regulatory, and educational policies on smoking rates over time. Because the two techniques are combined and are quite comprehensive, a hybrid SIQ+P+E+H+X model is a better approach to addressing multi-strategy interventions in nicotine health management.

For instance, (Camacho et al., 2021) developed a system dynamics model to simulate transitions among cigarettes, e-cigarettes, and heated tobacco products among the Italian population, which is another example of models that fit the evolving nicotine landscapes (Camacho et al., 2021). The model also incorporates product substitution, dual use, and movements to complete nicotine abstinence, thereby providing important insights into the combined health impacts of these three, coexisting product categories. This kind of modelling will become more relevant as harm reduction products grow their market share and policymakers must consider the potential benefits of encouraging smokers to switch to lower risk products as well as the potential risks of new product uptake among non-smokers. In their study, Camacho et al. provide a detailed insight into product specific health impacts, but the model is primarily product interactions focused and does not provide a comprehensive evaluation of the effect of traditional tobacco control policies, such as tax increases, advertising bans, or anti-smoking campaigns. By contrast, the SIQ+P+E+H+X model incorporates these policy levers into a single framework, to determine the effect of combined policy interventions on initiation, cessation, relapse, and product substitution such that it is particularly well suited for comprehensive policy planning, including endgame scenarios such as a complete ban on cigarette sales.

The integration of e-cigarettes in the SIQ+P+E+H+X framework is particularly significant considering the ambiguous evidence regarding their impact on public health. The dynamic modelling studies that have been carried out in England which incorporate cigarette and e-cigarette use have recommended a fairly liberal regulatory framework, and Public Health England has stated that e-cigarettes can be beneficial if used appropriately (Naiara, 2019; Abrams et al., 2018). By way of example, the modelling done in the United States has shown that public health may be adversely affected by e-cigarette use among youths which may lead to the initiation of combustible smoking (Soneji et al., 2017). The capability to model such gateway effects explicitly, as in SIQ+P+E+H+X, enables scenario modelling that is possible under optimistic as well as pessimistic assumptions to help policymakers understand the potential trade-offs in e-cigarette regulation.

The ability of the SIQ+P+E+H+X model to replicate both conventional and unconventional policy interventions is a significant strong point. The model can also capture, in addition to basic attributes like taxes and advertising, circumstances such as a total ban on cigarette sales. This paper's results suggest that if such a restriction were to take effect, then the prevalence of smoking could be reduced to practically zero over the course of several decades. That may be reflected in the countries contemplating tobacco endgame strategies with extended time

horizons, including New Zealand's Smokefree 2025 initiative. Whether such prohibitions are more likely, the capability to model and link day-to-day policies makes SIQ+P+E+H+X a very applicable model.

As with any model however, there are limitations to the SIQ+P+E+H+X model. Its predictions are quite dependent on accurate parameter estimates, especially for the e-cigarette related transitions that are truly uncertain and context dependent. Furthermore, the model does not include the possibility of illicit markets in cigarette sales after the prohibition, which may compromise some of the expected public health gains. To increase the realism of the model, illicit market dynamics may be integrated into the next version of the model, especially in low and middle income countries where enforcement capacity may be low. Also, compared to agent-based models that model specific level actions and peer pressure, SIQ+P+E+H+X uses population level means which may not fully capture the effects of localization, for example, vaping epidemics centered around social networks in schools. The next factor, which is related to taxation, is the desired budget revenues. Total prohibition can involve a large impact on the country's budget income, which is also a sensitive factor in finding the balance of revenue vs. public health.

5. Conclusions

In this paper, we implemented a dynamic compartmental model to assess the long term effects of different tobacco control interventions on the prevalence of smoking across different age groups. The model is versatile and expansive, and contains important features such as smoking initiation, abstinence, relapse, e-cigarette use, and health consequences modelled within it. Our model could be a useful tool for assessing tobacco control programmes in the context of a dynamically evolving nicotine delivery product to the market. The results also highlight the importance of a holistic approach. Out of the treated interventions, a complete ban on cigarette sales was observed as a most striking effect in reducing the prevalence of smoking to practically zero over time, which was obviously expected. This policy corresponds to an almost utopian final scenario, but it does indicate that through strong and coherent measures it is possible to control the prevalence of smoking.

Similar to the findings regarding smoking cessation, stronger anti-smoking campaigns and higher taxes were also found to be effective in preventing smoking initiation among youth and encouraging cessation among people of all ages. These results are supported by the currently available evidence that well-funded public health campaigns and fiscal policies aimed at tobacco products are some of the most effective in reducing tobacco consumption.

Including e-cigarettes into the model enabled us a more precise assessment of their dual role as cessation devices and possible gateway to conventional smoking. E-cigarettes display their

potential to enhance cessation rates among adult smokers, but at the same time, pose a risk of escalating youth initiation and subsequent migration to standard cigarettes. This complexity emphasises the need for sensible regulatory restrictions that can strictly prevent youth from access to e-cigarettes.

The sensitivity analysis also revealed that important drivers are quitting rates and the effect of taxation, and that even its small alterations can drastically alter long-term smoking prevalence. The last finding of this analysis reconfirms the necessity of the constant observation of the regulations and taxation to keep the effectiveness of cessation on a desired level.

As a model, it has its limitations, primarily for its dependency on accurate parameter estimates, and for its failure to capture illicit markets and enforcement challenges that are typical of extreme policies, including a total ban. Future extensions of the model could include these factors, along with more agent based approaches to the model to better capture localized peer effects and smoking behaviour social network influences.

Thus, the study establishes the importance of applying dynamic modeling for predicting the effectiveness of tobacco control strategies based on the available evidence. The SIQ+P+E+H+X model can therefore be a useful quantitative tool in the hands of policymakers to help in the development and implementation of overall, strategic, and data-driven tobacco control policies that are less likely to be reactive.

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Markov Model Simulation of Nicotine Addiction and the Effectiveness of Nicotine Replacement Therapy (NRT)

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Motivation and Aim:

Nicotine addiction remains a major threat to public health, and both tobacco and electronic cigarettes can lead to long-term dependence. This study employs a Markov model to simulate the dynamics of nicotine addiction, comparing the progression of addiction among users of traditional cigarettes and e-cigarettes across three distinct intervention scenarios: no intervention, nicotine gum therapy, and nicotine patch therapy. In order to provide important insights into public health measures, the goal here is to quantify addiction patterns and cessation probability.

Novelty

This study expands on previous research [1,2] by explicitly differentiating addiction dynamics between e-cigarettes and traditional cigarettes. The model enhances accuracy by using real-world transition probabilities and incorporates nicotine gum and patches to evaluate their distinct impacts on addiction duration. By utilizing the latest epidemiological data, it provides a more precise depiction of nicotine addiction trends and cessation success rates.

Methods

A Markov model was developed with five states: No Contact, First Try, Experimenting, Addiction, and Cessation. Transition probabilities P_{ij} were derived from recent epidemiological studies [3] and structured in a transition matrix T , where each element P_{ij} represents the probability of transitioning from state i to state j over a one-year period. The system evolves according to the equation: $S(t+1) = S(t) \cdot T$, where $S(t)$ is the state distribution at time t , and T is the transition matrix. The simulation was conducted over a 20-year period, comparing traditional cigarette and e-cigarette users under three conditions: no therapy, nicotine gum (6.56% effectiveness), and nicotine patches (13.83% effectiveness) [4]. Studies on nicotine metabolism suggest that replacement therapies significantly alter addiction dynamics by stabilizing nicotine levels [5]. The expected time spent in each state was analyzed using Markov chain methods, emphasizing addiction and cessation states.

Results

The simulation results indicate that e-cigarette users spend less time in addiction compared to traditional cigarette users. The implementation of NRT significantly reduces the duration of addiction, with nicotine patches demonstrating a higher effectiveness rate than nicotine gum. Without therapy, traditional cigarette users remain addicted for an average of 57.65 years, whereas e-cigarette users average 27.77 years in the addicted state. With nicotine patches, the addiction duration decreases to 46.48 years for cigarette users and 21.46 years for e-cigarette users. These findings underscore the potential benefit of NRT in reducing addiction duration and enhancing smoking cessation rates (Figure 1).

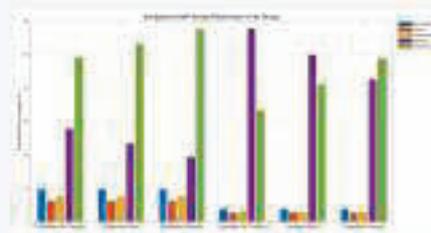


Figure 1: Simulation Results for Different Interventions

Conclusion

E-cigarettes can help smokers quit more effectively than regular cigarettes but still carry an addiction risk. Nicotine patches outperformed gums in terms of length of addiction and quit rates, making them a good option for smoking cessation programs. These findings are in line with previous studies, indicating that NRTs should be integrated with smoking cessation strategies for best efficacy. Future research should look at the long-term health effects of e-cigarettes as a harm reduction tool (but also their potential health effects), as well as the importance of behavioral support in combination with NRT.

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Article

Analysis of Demographic, Familial, and Social Determinants of Smoking Behavior Using Machine Learning Methods

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Abstract: Smoking behavior, encompassing both traditional tobacco and electronic cigarette use, is influenced by a range of demographic, familial, and social factors. This study examines the relationship between smoking habits and family dynamics through a cross-sectional survey of 100 participants, using an anonymous questionnaire to collect demographic data, smoking patterns, and familial interactions. Validated instruments, including the Penn State Electronic Cigarette Dependence Index and the Family Relationship Assessment Scale, were employed to assess smoking dependence and family dynamics. The analysis identified key patterns, such as increased smoking frequency among individuals experiencing higher family tension and variations in smoking habits across age and gender groups. Nocturnal smoking was linked to higher cigarette consumption, whereas early-day smokers exhibited a lower desire to quit. Machine learning models were applied to predict and classify smoking behaviors based on socio-demographic and familial variables, with an ensemble learning model achieving the highest accuracy (93.33%), outperforming k-nearest neighbors (90.00%), support vector machines (80.00%), and decision trees (83.33%). These findings underscore the complex interplay between family relationships and smoking behavior, providing insights for public health interventions. Additionally, this study highlights the potential of machine learning in behavioral research, demonstrating its utility in identifying and predicting smoking-related patterns.

Keywords: e-cigarettes; traditional cigarettes; family relationships; communication patterns; social impact of smoking; AI in social research; data-driven analysis



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1. Introduction

The family is the foundation of social life, providing the individual with a key environment for the formation of interpersonal skills, a value system, and a sense of identity. The family relationships that link family members at different stages of life serve an important function as a source of connection and social influence. Their importance for the individual is evident throughout life, playing a key role in building well-being and a sense of stability at each stage of their development [1]. The healthy development of the child and the functioning of the family depends on the existence of lasting, supportive and emotionally committed bonds between its members [2]. With supportive social relationships, people

can cope better with stress and maintain their well-being. Good relationships can predict interpersonal functioning and mental health, as well as longevity [3]. On the other hand, a dysfunctional family is characterized by a lack of harmony or is fraught with tensions, such as conflicts between parents and children. Dysfunction occurs when one or more family members neglect their responsibilities, leading to family dysfunction and disintegration. This type of family is characterized by lower levels of health, well-being, happiness, and positive relationships compared to other families, which can contribute to social problems, but also generate more complex difficulties, causing suffering and distress for their members [4].

1.1. Physical and Prenatal Health Impacts

Smoking, particularly traditional tobacco use, has long been a well-documented public health concern, but its impact on family dynamics remains less explored. In their study, Steeger et al. show that adolescent externalizing problems, including oppositional and conduct issues, develop from parental smoking exposure. The predictive power of harsh parenting and low parent-child bonding exceeds parental smoking as factors over time [5]. University student research showed that students who experienced negative parental relationships and poor father-child bonds were more likely to smoke. Students who faced intense pressure to study showed increased smoking behavior, which may stem from their stress [6].

Families are the primary units of social interaction, and smoking behaviors within them can influence communication patterns, conflict resolution, and shared experiences. In households where smoking is prevalent, these behaviors may not only affect individual health but also disrupt family cohesion [7]. Non-smokers, especially children and elderly family members, may experience significant emotional and physical strain as they contend with health risks, secondhand smoke exposure, and concerns about their loved ones' well-being. This strain can affect how family members communicate, navigate conflicts, and provide emotional support, underscoring the need to understand the social dimensions of smoking in familial contexts [8].

Smoking during pregnancy poses significant risks to the unborn child, including low birth weight, developmental delays, and an increased likelihood of respiratory issues later in life. Maternal smoking during pregnancy is associated with intrauterine growth restriction, leading to low birth weights. Prenatal tobacco smoke exposure is a well-known risk factor for adverse neurodevelopmental outcomes in childhood, including cognitive delays [9]. The primary effects of maternal smoking on offspring lung function and health include decreased respiratory compliance, increased hospitalization for respiratory infections, and an increased prevalence of childhood wheeze and asthma [10]. These outcomes not only affect the child's health but can also strain family dynamics as parents navigate the challenges of caring for a child with health complications. Furthermore, the stress associated with smoking-related complications during pregnancy may heighten tension between partners, adding another layer of complexity to family relationships [7,11].

The physical and relational toll on non-smokers extends to children exposed to secondhand smoke, who face heightened risks of respiratory issues, asthma, and developmental challenges [7]. Non-smoking family members, including spouses and elderly relatives, often experience increased stress and concern for loved ones' health, which can lead to tension within the household. The interplay of these physical and emotional effects highlights the profound impact smoking can have on the dynamics of family life, particularly when shared routines are disrupted or emotionally charged discussions arise over smoking behaviors [12,13]. Guo et al., in their interesting study, revealed the situation that poor family health and dynamics are associated with higher levels of nicotine dependence

among smoking fathers. This suggests that dysfunctional family relationships can contribute to increased smoking behaviors, leading to a cycle of stress and tension within the household [14].

1.2. Social and Cultural Factors Shaping Smoking Behaviors

Cultural and socioeconomic factors further shape how smoking behaviors are adopted and maintained within families. In some cultures, smoking is deeply ingrained in social rituals or perceived as a sign of status, influencing how family members view and interact with smoking [15,16]. Gender dynamics also play a crucial role in shaping these behaviors. For instance, in many households, men are more likely to smoke than women, which can normalize smoking behaviors for children, especially boys [17]. Meanwhile, women, particularly mothers, may face societal pressure to quit smoking due to their caregiving roles, creating guilt or stress in households where cessation efforts fail [5,8].

Families in lower socioeconomic brackets often face additional challenges, including limited access to cessation resources or heightened stress that exacerbates smoking habits. These factors can create generational smoking patterns that are difficult to break, complicating efforts to improve family health and cohesion [18]. Financial strain is a significant mediator between low socioeconomic status and smoking behaviors. Individuals experiencing economic hardship often face chronic stress, which can lead to increased tobacco use as a coping mechanism. This stress-induced smoking not only affects the individual's health but also influences family dynamics, potentially normalizing smoking behaviors for younger family members and perpetuating a cycle of tobacco use across generations [19]. Beyond parental influence, peer-like relationships within families, such as those between siblings or cousins, also play a significant role in shaping smoking behaviors. Younger family members often emulate their older siblings or cousins, complicating cessation efforts that focus solely on parental habits. Interventions that address family-wide behaviors are thus more likely to yield lasting results [11,13].

1.3. The Rise of E-Cigarettes and Technological Influence

The advent of electronic cigarettes, often marketed as less harmful alternatives to conventional tobacco products, has added significant complexity to the already multifaceted landscape of smoking behaviors. These devices have rapidly gained traction, particularly among younger demographics, due to perceptions of reduced harm and the appeal of integrating modern technology into smoking practices [11,20]. Social media campaigns and cessation apps play a dual role in this shift. Although these platforms help spread awareness of smoking risks and provide resources for quitting, they also glamorize e-cigarettes, particularly to younger audiences. Families must navigate these mixed messages, and younger tech-savvy members are often at the forefront of shaping household attitudes toward smoking and e-cigarettes [11,20].

Emerging research on e-cigarettes has also raised concerns about their potential role as a gateway to traditional tobacco use, particularly among youth and young adults. For instance, research replicating earlier studies found that baseline e-cigarette use among adolescents was linked to higher odds of tobacco smoking at 6-month and 12-month follow-ups [21]. Family environments play a significant role in shaping these behaviors, with younger family members often influenced by the habits and attitudes of those around them. E-cigarettes, initially viewed as a safer alternative, can inadvertently lead to greater family conflict if they result in transitioning to traditional smoking. Understanding these behavioral shifts and their impact on family relationships is essential for developing public health strategies that minimize harm [5,22]. In addition, family structure plays a role in

adolescent smoking behaviors. Adolescents from non-intact families have been shown to have a higher prevalence of smoking and an earlier onset of cigarette use [23].

1.4. Family Dynamics and Smoking Cessation

Shared smoking habits within families can serve as both a bonding activity and a source of contention. While smoking together may provide moments of connection for some, disagreements about its health risks can lead to heightened conflict and negatively affect the overall family atmosphere. The practice of smoking together creates bonding moments for some family members, but health risk disagreements produce more conflict, which damages family atmosphere. Studies show that adolescent tobacco use relates to family conflict through sensation seeking and impulsive behavior patterns. Research by Esleva et al. indicates that family arguments and stress create conditions which lead younger family members to start smoking [24]. Moreover, research by Hill et al. has found that poor family relationships, such as low parental monitoring and bonding, are associated with higher risks of daily smoking initiation among adolescents. This underscores the importance of a supportive family environment in preventing tobacco use and suggests that conflicts over smoking can undermine such protective factors [25].

The rise of e-cigarettes has introduced new complexities to these interactions, as these devices are often perceived differently from traditional tobacco in terms of health risks and societal acceptance. These shifting perceptions further complicate family dynamics and decision-making around smoking behaviors [11,20,26].

Public health campaigns and smoking cessation programs have played a pivotal role in shaping family behaviors. As smoking rates have declined in many countries, households have increasingly become environments where non-smokers and former smokers can interact more comfortably. These interventions reduce familial conflict related to smoking and foster healthier living conditions for children and non-smokers. Campaigns that emphasize the collective health benefits of quitting, including the positive impacts on family relationships, have proven especially effective in encouraging smoking cessation within households [12].

1.5. Long-Term Effects on Family Cohesion

Smoking behaviors within families often have long-term, intergenerational effects, perpetuating cycles of tobacco use. Children raised in households where smoking is prevalent are more likely to view it as a normative behavior, increasing their likelihood of becoming smokers themselves. Data from the UK government reveal that teenagers whose parents or caregivers smoke are four times as likely to start smoking [27]. This intergenerational transmission underscores the profound impact of parental smoking on youth behavior. Additionally, research by Alves et al. indicates that parental smoking increases the likelihood of adolescent daily smoking, with maternal smoking having a stronger association for girls and paternal smoking for boys [28]. This cycle can also influence how future generations approach health, communication, and conflict resolution within families. Breaking this pattern requires interventions that address not only individual behaviors but also the familial and cultural contexts in which these behaviors are embedded [12,22].

By examining the dynamics within families affected by traditional tobacco use and e-cigarette consumption, researchers aim to illuminate the nuanced ways smoking behaviors influence communication patterns, conflict resolution, and emotional bonding [12]. As smoking rates continue to decline in many populations, the distinctions between smokers and non-smokers within families grow more pronounced, raising critical questions about their impact on family cohesion [12].

This research underscores the importance of considering both individual smoking behaviors and their collective implications within familial contexts to inform smoking prevention and support initiatives.

2. Materials and Methods

This study used a cross-sectional survey design to investigate the relationship between smoking behaviors, including traditional tobacco use and electronic cigarettes, and family dynamics. This research aimed to capture a comprehensive snapshot of participant smoking habits and familial interactions through structured data collection and advanced analytical methods. The stages of the research are shown in Figure 1.



Figure 1. The stages of the research.

2.1. Survey Instruments

The questionnaire for this study was designed to explore the relationship between smoking behaviors and family dynamics. It included three main sections: Demographic Information, Smoking Habits, and Family Dynamics, alongside validated tools like the Penn State Electronic Cigarette Dependence Index (PSECDI) and the Family Relationship Assessment Scale (FRAS). A literature review guided the inclusion of key variables, and Likert-scale items were extensively used for quantifying subjective experiences [29].

The Demographic Information section collected data on participants' age, gender, education level, and living environment (rural, suburban, or urban) to analyze sociocultural and geographic influences. The Smoking Habits section assessed smoking type (traditional or electronic), frequency, age of initiation, and duration, enabling comparisons between the impact of tobacco and e-cigarettes on family relationships. The Family Dynamics section used Likert-scale items adapted from FRAS to evaluate communication, conflict resolution, shared activities, and emotional cohesion [30].

The PSECDI, a 10-item measure developed by Foulds et al. [26], was used to assess addiction levels for both traditional and electronic cigarettes, since the test items can also be modified to evaluate dependence on traditional cigarettes, using the Penn State Cigarette Dependence Index (PSCDI). It was administered as one of three components of the questionnaire: (1) author-designed items, (2) the PSECDI scale, and (3) the FRAS family relationship indicators. The PSECDI provides cumulative scores ranging from 0 to 20, categorized as no, low, moderate, or high dependence. The original scale has demonstrated convergent validity (correlation: 0.71 with the E-cigarette Dependence Scale) and construct validity, supported by the observed correlation between test scores and the nicotine concentration of the e-liquids consumed [31]. The PSECDI and FRAS questionnaires were translated using the back-translation method, as no validated Polish versions of these instruments were available. This approach was employed to ensure linguistic and conceptual equivalence between the original and translated versions.

The FRAS assessed family dynamics across three subscales: Family Support, Family Conflicts, and Family Togetherness. Items rated on a 5-point Likert scale provided a comprehensive view of family relationships, with a Cronbach's alpha of 0.89 for the overall scale and 0.77–0.87 for the subscales [30].

E-cigarette and traditional cigarette use were recorded as binary variables (yes/no) to assess general usage prevalence. Additional items assessed usage frequency and de-

pendence levels using Likert scales and the PSECDI score. Correlation analyses involving binary smoking use variables were interpreted cautiously due to scale limitations.

Additional self-administered questions captured perceptions of smoking-related family issues, including conflicts, relationship impacts, and quitting attempts, offering further insights into the interplay between smoking behaviors and family dynamics.

2.2. Participant Recruitment

Participants for this study were recruited using a convenience sampling strategy through online platforms, community forums, email invitations, and local networks to ensure accessibility and diversity. Eligibility criteria included being 18 years or older, providing informed consent, and proficiency in Polish to complete the survey. Exclusion criteria encompassed individuals under 18, those who declined consent, or were unable to complete the questionnaire. The final sample of 100 participants represented a range of age groups, gender identities, educational backgrounds, and living environments (urban, suburban, rural).

Ethical standards were rigorously upheld throughout the study. Participants were provided with detailed information about the study's purpose and assured of anonymity. Electronic informed consent was obtained, and participants were reminded of their right to withdraw at any point. The survey collected no personally identifiable information, ensuring privacy and compliance with ethical guidelines. This study was conducted with the approval of the Bioethical Committee of Medical University of Silesia in Katowice, Poland, dated 16 October 2018, approval number KNW/0022/KB1/79/18.

2.3. Data Collection

Data collection was conducted using Google Forms, selected for its accessibility, compatibility across devices, and ease of use. The survey link was distributed via social media, community groups, and email lists to ensure broad outreach and inclusivity. This digital format minimized human error and allowed participants to complete the survey conveniently on various devices [26].

The collected data were examined through a combination of statistical tests and machine learning techniques to identify significant associations and patterns. Descriptive statistics provided a foundational understanding of the sample's characteristics, while statistical tests were employed to examine potential relationships between variables. Machine learning algorithms were then used to predict smoking behaviors based on the identified factors.

2.4. Statistical Analysis

The statistical analysis was conducted to investigate the relationships between socio-demographic, familial, and behavioral factors influencing smoking behaviors, cessation attempts, and related variables. The dataset included categorical, ordinal, and continuous variables, which were preprocessed and categorized as needed. For example, for variables such as age, participants were grouped into three age categories—18–22, 23–27, and 28–39 years—for ANOVA analysis, based on tertile distribution. Chi-square tests were employed to evaluate associations between categorical variables (e.g., gender and type of smoking product). Spearman's rank correlation was used to assess relationships involving ordinal or non-normally distributed variables (e.g., Likert-scale ratings and initiation age). One-way ANOVA was applied to compare group means for continuous variables that met the assumptions of normality and homogeneity of variance (e.g., PSECDI scores). Assumptions for ANOVA were verified using the Shapiro-Wilk test for normality and Levene's test for equality of variances. Statistical significance was set at a p -value of 0.05.

All analyses were conducted in Matlab R2019b for academic use (MathWorks Inc., Natick, MA, USA).

2.5. Machine Learning Methods

Machine learning techniques were employed to classify and predict smoking behaviors based on socio-demographic, familial, and behavioral factors. The choice of algorithms was guided by their compatibility with the dataset's size and feature characteristics. The decision tree was selected as a baseline model due to its interpretability and ability to handle nonlinear relationships effectively. The ensemble method was employed to enhance robustness and mitigate overfitting by aggregating multiple weak learners, a strategy well suited for managing the variability inherent in the dataset. Support vector machines (SVMs) were chosen for their theoretical advantage in separating classes by maximizing decision margins, although their practical performance was constrained by the limited dataset size. Finally, the k-NN algorithm was implemented for its simplicity and strength in capturing localized relationships, making it an effective tool for identifying proximity-based patterns within the data.

To better understand the structure of the data and assess the complexity of the classification task, a Principal Component Analysis (PCA) was conducted. The initial PCA was performed using all available features from the demographic, FRAC, and PSECDI sections of the questionnaire. In addition, a refined PCA was carried out on the six most statistically discriminative variables, identified via ANOVA F-test, to enhance interpretability. These projections aimed to explore class separability and identify meaningful clustering patterns within the dataset.

The preprocessing and analysis of the dataset were designed to facilitate robust machine learning modeling while addressing data quality issues and extracting meaningful insights. Initially, the data were subjected to preprocessing steps, including the removal of rows with missing values to maintain the integrity of the dataset. Continuous variables, such as smoking frequency and family support ratings, were normalized using z-score normalization to ensure compatibility with machine learning algorithms and to avoid biases due to differing scales. In addition, categorical variables, including family smoking history, conflict levels, and type of smoking, were encoded in numerical formats. Feature engineering was applied to construct composite variables that represent the impact of smoking on family relationships and behaviors based on responses to the Likert scale. The class imbalance was addressed by oversampling the minority class, particularly for variables with significant disparity in the response distribution. The data were then partitioned into training (70%) and testing subsets (30%).

Several algorithms were implemented, including a decision tree classifier, ensemble learning methods (using a bagging approach), k-nearest neighbors (k-NNs), and support vector machines (SVMs). Each model was trained and validated using stratified k-fold cross-validation to minimize overfitting and assess generalizability. Metrics such as accuracy and loss were used to evaluate model performance, and confusion matrices were generated to analyze classification consistency. All machine learning analyses were performed using Matlab R2019b for academic use (Mathworks Inc., Natick, MA, USA) and machine learning tools, ensuring a reproducible and systematic approach to analysis.

The classification task was aimed to predict how participants perceived the impact of their smoking behavior on family relationships. The target variable was derived from a survey item with four ordinal response categories, 0.00, 0.33, 0.66, and 1.00, reflecting increasing levels of perceived negative impact on family dynamics. These values served as discrete class labels for supervised learning. Out of the total sample of 100 participants, the distribution of classes was imbalanced, with the majority of responses concentrated in the

0.33 and 0.66 categories. To address this imbalance and ensure fair model training, random oversampling of the minority classes was applied during preprocessing. The models were trained on a set of 9 to 12 features, selected from all three sections of the questionnaire: (1) original demographic and behavioral items, (2) FRAC subscales (Support, Conflict, Togetherness), and (3) PSECDI-derived items related to smoking habits and dependence. The selected features included variables such as age, gender, type, and frequency of smoking, presence of smokers in the family, conflict levels, perceived family acceptance, and time to first cigarette. Given the relatively small sample size ($N = 100$) compared to the number of input features, care was taken to mitigate potential overfitting and dimensionality issues. This was achieved through feature selection, model regularization, and cross-validation techniques during training and evaluation.

3. Results

3.1. Statistical Analysis

Understanding the demographic and behavioral characteristics of survey respondents is crucial for interpreting patterns in their responses. This section explores key variables through statistical distributions, aiming to contextualize the broader study. These variables include gender, age, living environment, educational attainment, and cigarette use preferences (Table 1).

The dataset analyzed in this chapter was derived from a structured survey. Key columns were selected for relevance, including gender, age, living environment, educational level, and type of cigarettes used. Gender was classified as male, female, or other, while age was reported in years. Living environments were grouped into cities over 500,000 residents, cities 150,000–500,000 residents, cities 50,000–150,000 residents, cities up to 50,000 residents, and rural areas. Educational levels were categorized as university, secondary, vocational, lower secondary or primary. Cigarette use was divided into three categories: electronic, traditional, or both.

Table 1. Participant demographics and smoking preferences ($N = 100$).

Variable	Categories	Frequency (%)
Gender	Male/Female/Other	44/54/2
Age	Mean (SD): 23.4 (4.6); Range: 18–39	—
Living Environment	Rural/<50 k/50–150 k/150–500 k/>500 k	12/9/15/30/34
Educational Attainment	Primary/Lower Secondary/Vocational/Secondary/University	2/6/12/42/38
Smoking Behavior	Electronic/Traditional/Both	43/21/36

After collecting 100 completed surveys, the following results were obtained. The age distribution of respondents was primarily concentrated in the early twenties, with the majority being under 30 years of age, forming a unimodal pattern. Regarding the living environment, a significant proportion of participants reported residing in large urban areas, followed by those living in medium-sized cities. Educational attainment skewed toward higher levels, with most respondents reporting secondary or university education, while vocational and primary education were less represented. As for smoking preferences, electronic cigarettes emerged as the most commonly used product, followed by a substantial number of individuals who used both electronic and traditional cigarettes. Exclusive use of traditional cigarettes was the least common among the sample.

The Family Relationship Assessment Scale (FRAC) (Table 2) provides valuable insights into familial dynamics by evaluating family support, family conflicts, and family togetherness. Each FRAC subscale (Family Support, Family Conflict, Family Togetherness) is based on a 5-point Likert scale, where 1 indicates the lowest and 5 the highest level of the

measured dimension). In this study, all scores are reported as group means within the valid range of 1–5. This analysis investigates these dimensions among individuals with different smoking behaviors: electronic cigarette (e-cigarette) users, traditional cigarette smokers, and both types of cigarettes smokers.

Table 2. Comparison of family relationship indicators (FRAC) and nicotine dependence (PSECDI) across smoking groups.

Category	Indicator	E-Cigarette Smokers	Traditional Smokers	Dual Users
FRAC	Family Support (mean)	4.22	3.50	3.67
	Family Conflict (mean)	1.81	2.00	1.89
	Family Togetherness (mean)	3.26	3.12	2.83
PSECDI	No Dependence (%)	0.00	4.76	0.00
	Low Dependence (%)	21.05	33.33	16.67
	Moderate Dependence (%)	31.58	19.05	33.33
	High Dependence (%)	47.37	42.86	50.00
	PSECDI Score (mean)	13.11	12.05	13.50

E-cigarette users reported the highest levels of family support, with an average score of 4.22. This suggests that they perceive strong support within their family environment. Conversely, traditional cigarette smokers reported the lowest level of support, averaging 3.50, indicating weaker familial bonds or a sense of reduced support. Dual users, who consume both e-cigarettes and traditional cigarettes, fell in between with a support score of 3.67, reflecting moderate family support but potentially influenced by the complexity of their smoking behaviors.

In terms of family conflicts, the interpretation of scores is inverted—lower scores indicate fewer conflicts. E-cigarette users had the lowest conflict score, averaging 1.81, which reflects minimal tensions within their family dynamics. Dual users also reported relatively low conflict levels, with a score of 1.89, while traditional cigarette smokers had the highest level of conflict among the groups, scoring 2.00. These results suggest that families are more accepting of e-cigarette use, potentially due to its perceived reduced risks compared to traditional smoking. Meanwhile, the higher conflict scores among traditional cigarette smokers may stem from the stronger stigma and health concerns associated with conventional smoking.

The dimension of family togetherness revealed additional differences. E-cigarette users reported the highest levels of togetherness, averaging 3.26, which underscores a greater engagement with family activities. Traditional cigarette smokers scored slightly lower at 3.12, while dual users reported the least amount of shared time, with an average score of 2.83.

The results indicate that social actions need improvement through educational interventions, which tackle how families understand e-cigarettes differently from traditional cigarettes. The perceived lower risk of e-cigarettes explains why families show more acceptance toward their use so educational campaigns should deliver accurate scientific information about both products' actual dangers. The programs should create opportunities for families to discuss nicotine use without confrontation to minimize conflict and reduce stigma. When families focus on mutual health protection goals, they might transform accusatory dialogues into supportive exchanges that lead to better cessation and prevention practices.

The Penn State Electronic Cigarette Dependence Index (PSECDI) (Table 2) is a validated tool designed to assess the degree of dependence among users of electronic cigarettes, which ranges from 0 to 20, and was used to evaluate nicotine dependence among e-cigarette users.

Dependence levels were categorized as follows: no (0), low (1–4), moderate (5–8) and high (≥ 9) dependence. Its adaptation for the current study allows for comparative analysis of dependence levels across three groups: e-cigarette smokers, traditional cigarette smokers, and both types of cigarettes smokers.

PSECDI results are presented both as percentages of respondents falling into each dependence category and as a mean score for each group, reflecting the average level of nicotine dependence. This dual presentation enables both categorical comparison and identification of trends in severity within each smoking group.

The levels of dependence, categorized as no dependence, low dependence, moderate dependence, and high dependence, varied significantly between the groups. Among e-cigarette users, 47.37% fell into the high-dependence category, while 31.58% exhibited moderate dependence, and 21.05% reported low dependence. Notably, no respondents in this group reported an absence of dependence. For traditional cigarette smokers, the distribution was more diverse. While 42.86% demonstrated high dependence, 33.33% exhibited low dependence, and 19.05% fell into the moderate dependence category. A small proportion of this group (4.76%) reported no dependence, reflecting some variability in addiction levels within this cohort. Individuals who smoke both e-cigarettes and traditional cigarettes showed the highest prevalence of dependence, with 50.00% classified as highly dependent and 33.33% moderately dependent. Like e-cigarette users, no respondents in this group reported an absence of dependence, while 16.67% demonstrated low dependence. The average PSECDI scores further illustrate the differences in dependence levels among the groups. Dual users had the highest mean score of 13.50, indicating the most severe dependence on nicotine products. E-cigarette users followed closely with an average score of 13.11, suggesting a significant level of addiction within this group. Traditional cigarette smokers exhibited the lowest mean PSECDI score at 12.05, although this still reflects a considerable degree of dependence.

Results showed significant differences in family support ($p = 0.021$) and family togetherness ($p = 0.043$) among smoking groups. Post hoc comparisons indicated that e-cigarette users reported significantly higher family support than traditional smokers, and significantly greater family togetherness than dual users. No significant differences were observed between dual users and traditional smokers in either dimension.

PSECDI scores were highest among dual users (mean = 13.50), followed closely by e-cigarette users (13.11). Traditional smokers had the lowest average dependence (12.05). A one-way ANOVA test confirmed a statistically significant difference in dependence scores between e-cigarette users and traditional cigarette smokers ($p = 0.037$). No significant differences were observed between dual users and the other two groups.

This study examined the influence of socio-demographic, familial, and behavioral factors on smoking behaviors and cessation attempts, yielding critical insights into underlying patterns and associations (Table 3).

Age was found to have a statistically significant relationship with the type of smoking product used ($F = 8.787, p = 0.0003$). Additionally, age correlated positively with the age of smoking initiation ($\rho = 0.22546, p = 0.0241$), indicating that older participants tended to start smoking later in life. Gender was also significantly associated with the type of smoking product ($\chi^2 = 10.63, p = 0.031$). In contrast, education level ($\chi^2 = 6.41, p = 0.60111$), place of residence ($\chi^2 = 7.02, p = 0.53404$), and a family history of smoking ($\chi^2 = 2, p = 0.36788$) showed no significant associations with the type of smoking product used.

Behavioral patterns demonstrated critical findings. Nocturnal smoking behavior was significantly correlated with higher smoking frequency ($\chi^2 = 14.2456, p = 0.014122$). A strong positive Spearman correlation was observed between e-cigarette use and prior conventional smoking ($\rho = 0.67921, p = 8.0027 \times 10^{-15}$), emphasizing a behavioral linkage

between these habits. The time to the first cigarette after waking was negatively correlated with willingness to quit smoking ($\rho = -0.30509$, $p = 0.002$), indicating that individuals who smoked earlier in the day were less likely to exhibit cessation intent. However, smoking frequency itself showed no significant correlation with the willingness to quit ($\rho = -0.07068$, $p = 0.4847$).

Familial dynamics were found to play a significant role in smoking behaviors. Family tension correlated positively with the number of cigarettes smoked ($\rho = 0.22$ to 0.34 , p -values ranging from 0.029 to 0.001). However, the impact of smoking on relationships ($\rho = -0.15043$, $p = 0.1352$), family conflicts ($\chi^2 = 5.15$, $p = 0.27194$), family support (coefficients: 1.37 , -0.18 , $p = 0.0583$, $p = 0.3000$), and family acceptance ($\rho = -0.088$ to -0.076 , p -values ranging from 0.334 to 0.467) did not show statistically significant relationships with smoking behaviors. In Table 3, we present the influence factors on smoking behavior analysis.

Table 3. Analysis of factors influencing smoking behaviors and family dynamics.

Variables	Test	Results	p-Value	Interpretation
Participant age and type of smoking product	ANOVA	$F = 8.79$	$p < 0.001$	Significant differences in smoking products among age groups
Education level and type of smoking product	Chi-Square	$\chi^2 = 6.41$	0.601	No significant association
Gender and type of smoking product	Chi-Square	$\chi^2 = 10.63$	0.031	Significant differences between genders in smoking products used
Participant age and age of smoking initiation	Spearman Correlation	$\rho = 0.23$	0.024	Older participants started smoking at later ages
Place of residence and type of smoking product	Chi-Square	$\chi^2 = 7.02$	0.534	No significant association
Family history of smoking and type of smoking product	Chi-Square	$\chi^2 = 2.00$	0.566	No significant association
Perceived impact of smoking on relationships and number of cigarettes smoked	Spearman Correlation	$\rho = -0.15$	0.135	Weak negative correlation, not statistically significant
Smoking frequency and willingness to quit	Spearman Correlation	$\rho = -0.07$	0.405	Very weak negative correlation, not significant
Time to first cigarette after waking and willingness to quit	Spearman Correlation	$\rho = -0.31$	0.002	Moderate negative correlation, statistically significant
Family conflict score and willingness to quit	Chi-Square	$\chi^2 = 5.15$	0.272	No significant association
Family support score and willingness to quit	Logistic Regression	Coefficients: 1.37 , -0.18	$p = 0.058$, $p = 0.300$	Trend toward significance, but not significant
Family tension score and number of cigarettes smoked per day	Spearman Correlation	$\rho = 0.22$ – 0.34	0.029 – 0.001	Significant positive correlation
Family acceptance score and smoking frequency	Spearman Correlation	$\rho = -0.09$ to -0.08	0.334 – 0.467	No significant correlation
Quit attempts and urge to smoke	Chi-Square	$\chi^2 = 5.15$	0.272	No significant correlation
Nocturnal smoking behavior and smoking frequency	Chi-Square	$\chi^2 = 14.25$	0.014	Significant association
Current e-cigarette use and prior traditional cigarette use	Chi-Square	$\chi^2 = 8.30$	$p = 0.0096$	Statistically significant association between variables

The results in Table 3 demonstrate the diverse influences of socio-demographic, behavioral, and familial factors on smoking behaviors. For example, the analysis of variance

(ANOVA) revealed significant differences in smoking product preferences across different age groups ($F = 8.787, p = 0.0003$), suggesting that age influences the type of smoking products individuals use. This may reflect generational trends, with younger participants possibly favoring e-cigarettes due to cultural perceptions or accessibility. Conversely, older individuals may be more inclined to use traditional tobacco products. In contrast, education level was not significantly associated with the type of smoking product used ($\chi^2 = 6.41, p = 0.6011$), indicating that smoking habits in this sample appear to transcend educational boundaries.

A chi-square test revealed a statistically significant association between current e-cigarette use and prior use of traditional cigarettes ($\chi^2 = 8.30, p = 0.00396$), suggesting that many individuals transitioned from conventional smoking to electronic nicotine delivery systems. This relationship, captured by the variable “prior use of traditional cigarettes”, highlights a behavioral continuum between the two forms of smoking. Additionally, a moderate negative correlation was found between the time to the first cigarette after waking and willingness to quit smoking ($r = -0.30509, p = 0.002$), implying that individuals who smoke shortly after waking may be more addicted and less likely to consider cessation.

Interestingly, family acceptance showed no significant correlation with smoking frequency ($r = -0.088$ to $-0.076, p > 0.05$), suggesting that perceived family approval or disapproval may not directly influence how often participants smoke. These findings reinforce the importance of designing interventions that reflect the specific behavioral patterns and psychosocial predictors identified through analysis.

3.2. Machine Learning Analysis

This study utilized machine learning methodologies to explore the associations between smoking behaviors and familial dynamics, leveraging a dataset with numerically encoded responses. Key variables included smoking frequency, family smoking history, conflicts arising from smoking, perceived relational impacts, and levels of familial acceptance. The comparative performance of different models provided insights into the predictive value of these variables and the efficacy of advanced analytical approaches.

To assess class separability and identify structure in the feature space, a Principal Component Analysis was conducted. In the initial projection using all available variables (demographic, FRAC, and PSECDI), class overlap was substantial, suggesting high complexity and limited separability. To improve interpretability, a second PCA was performed using the six most discriminative features, selected via ANOVA F-test. As shown in Figure 2, this reduced-dimensional projection revealed improved clustering of participants based on their perceived impact of smoking on family relationships. Some degree of class separation, especially for extreme values, supports the existence of meaningful patterns and justifies the use of supervised learning methods.

In the data preprocessing phase for machine learning (ML) applications, it is crucial to visualize and inspect the data to ensure its integrity and suitability for modeling. The written code implemented two sample visualizations to assess the quality and interpretability of the dataset before using it in ML algorithms. Initially, categorical responses regarding the perceived impact of smoking on interpersonal relationships were converted to numeric values using ‘containers.Map’ in MATLAB, where predefined text responses were mapped to corresponding numeric values. The question that elicited these responses was “What is your perception of the impact of your smoking on family relationships?”. We mapped the responses as follows: “I believe it clearly harms our relationships” was mapped to 1, indicating a strong negative impact; “I think it has a positive effect” was mapped to 0, indicating a positive effect; “It has a certain negative impact, but not large” was mapped to 0.66, representing a mild negative impact; and “I don’t notice any impact” was mapped

to 0.33, indicating a minimal or no impact. A scatter plot (Figure 3) was then generated to examine the relationship between the age at respective person started smoking and his/her perceived impact on relationships. This visualization simplified the identification of trends or potential correlations between variables of interest. The second visualization uses a histogram (Figure 4) to illustrate the distribution of smoking frequency among participants. This allowed for a detailed examination of the shape of the distribution, central tendency, and spread, which could inform decisions about scaling or transforming the function. Taken together, these graphs serve as an exploratory tool for detecting issues such as outliers, data skewness or inconsistencies, thus ensuring that the data are properly prepared before entering it into learning models.

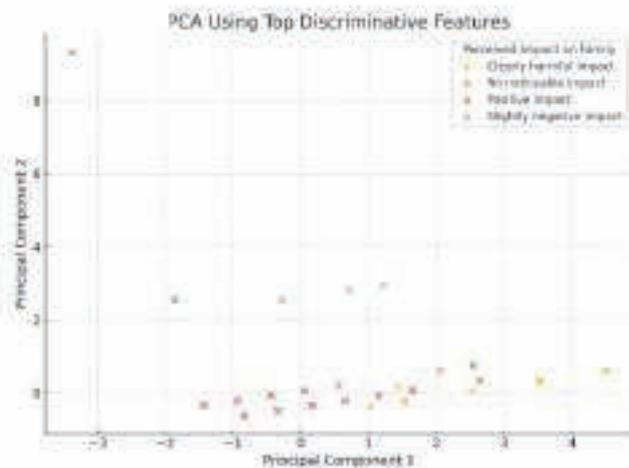


Figure 2. PCA projection using the top six most discriminative features. The plot shows class clustering based on participants' responses regarding the perceived impact of smoking on family relationships. Although class separation is not complete, the projection highlights informative structure in the data.

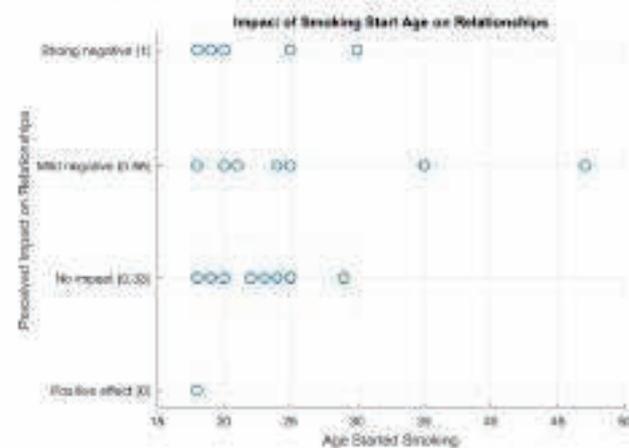


Figure 3. Self-reported effects of smoking by age at smoking onset.

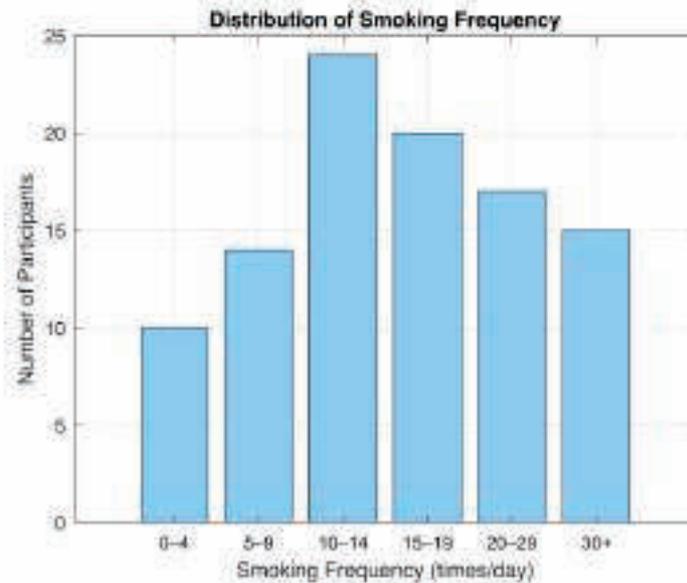


Figure 4. Self-reported smoking frequency among participants.

Hyperparameter adjustment was critical in improving the performance of the machine learning models deployed. The ensemble model's parameters, such as the number of trees in the forest and the maximum depth of each tree, were carefully improved using a grid search method. This approach entailed analyzing various parameter combinations using cross-validation, allowing for the selection of those that minimized error while increasing model generalizability. Similarly, the k-NN model was tuned by changing the number of neighbors (k) and using cross-validation to find the best balance of underfitting and overfitting. The best performance was obtained when k was adjusted to 5, which adequately captured the underlying data patterns without becoming too complicated. In this context, several key features were used in the models:

- *NumericImpactResponses*—questions assessing the impact on family relationships;
- *NumericConflictResponses*—questions about family conflicts;
- *NumericAcceptanceResponses*—questions about family acceptance of smoking;
- *NumericFamilySmoking*—question whether anyone in the family smokes;
- *ClaimedSmokingFrequency*—represents the individual's smoking frequency.

In this study, a decision tree model was developed to classify data based on two primary features: *NumericImpactResponses* and *NumericConflictResponses*. Although the algorithm initially had access to nine features, it automatically selected these two as the most relevant for predicting outcomes. The structure of the decision tree is hierarchical (Figure 5), with the root node splitting the dataset based on the value of *NumericImpactResponses*, applying a threshold of 0.495. Instances with *NumericImpactResponses* values below this threshold are directed to the left child node, while those with values equal to or exceeding 0.495 are directed to the right child node. This primary division reflects the perceived impact of smoking on relationships, as measured by *NumericImpactResponses*, and serves as the foundation for subsequent classifications.

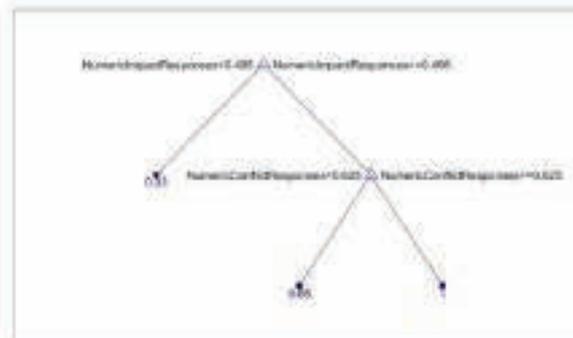


Figure 5. Decision tree for predicting outcomes based on *NumericImpactResponses* and *NumericConflictResponses*.

At the second level of the tree, the child nodes resulting from the initial split are further divided based on the value of *NumericConflictResponses*, with a threshold of 0.625. The terminal nodes correspond to a unique combination of values for *NumericImpactResponses* and *NumericConflictResponses*:

- When *NumericImpactResponses* is less than 0.495, the model predicts an outcome of 0.33.
- When *NumericImpactResponses* is greater than or equal to 0.495 and *NumericConflictResponses* is equal to or above 0.625, the predicted outcome is 1.
- When *NumericImpactResponses* is greater than or equal to 0.495 and *NumericConflictResponses* is below 0.625, the predicted outcome is 0.66.

Beyond the structural insights, the importance of the selected features was analyzed to understand their relative contribution to the model's performance. The results demonstrate that for the decision tree (Figure 6), *NumericImpactResponses* is far more influential, with an importance score of 0.1875, compared to *NumericConflictResponses*, which has a score of 0.03807. This finding suggests that the perceived impact of smoking on relationships (*NumericImpactResponses*) is the dominant driver of decision-making within the model, while conflict-related considerations (*NumericConflictResponses*) play a secondary role.

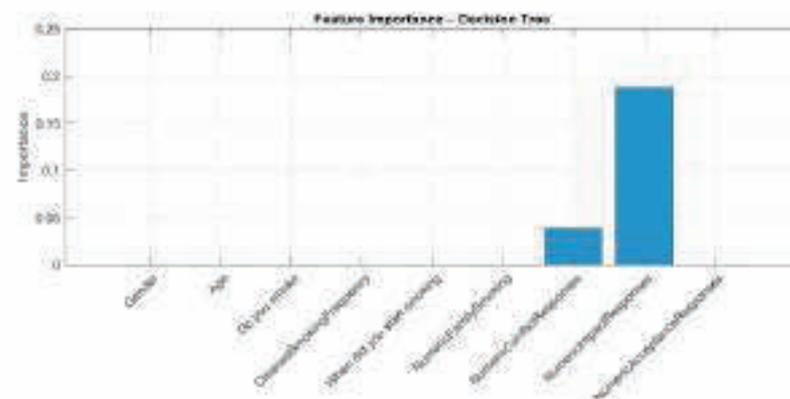


Figure 6. The feature importance analysis by decision tree.

The feature importance analysis is particularly significant because it underscores the model's capacity to discern and prioritize the most predictive features from a broader set of

variables. The substantial difference in importance scores indicates that *NumericImpactResponses* is central to understanding the relationships in the data, aligning with its role as the root node's splitting criterion.

The ensemble method aggregates feature importance (Figure 7) across multiple base learners (e.g., decision trees) to provide a robust measure of feature contribution. In this case, the most influential feature is *NumericImpactResponses*, with a score of 0.1499, far exceeding the contributions of other features. Other features, such as *Gender* (0.0085), *CleanedSmokingFrequency* (0.0023), and *When did you start smoking* (0.0031), contribute marginally, while several features exhibit no measurable importance.

This sparse distribution of importance scores is characteristic of ensemble methods when dealing with datasets where only a subset of features holds predictive power. The dominance of *NumericImpactResponses* underscores its centrality to the predictive mechanism of the ensemble model, likely reflecting a strong and consistent relationship with the target variable.

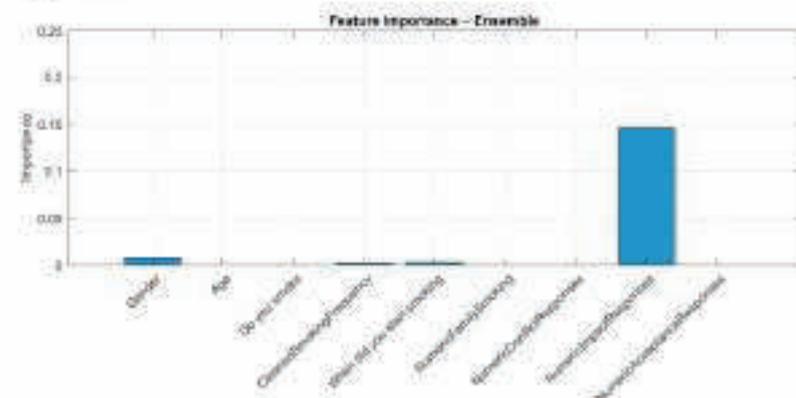


Figure 7. The feature importance analysis by ensemble method.

The feature importance for the SVM model (Figure 8) was determined using the permutation method, which assesses the impact of randomly shuffling a feature on model performance. Here, *NumericImpactResponses* emerges as the dominant feature, with an importance score of 0.1867, followed by *NumericFamilySmoking* (0.0133), *Age* (0.0167), and *When did you start smoking* (0.0067). The remaining features have negligible or zero importance.

This result suggests that the SVM model, which relies on maximizing the margin between classes, identifies *NumericImpactResponses* as critical to defining the decision boundary. The relative importance of *NumericFamilySmoking*, *Age*, and *When did you start smoking* highlights secondary relationships that contribute to the model's performance, albeit at a smaller scale.

Feature importance for the k-NN model (Figure 9), also derived using the permutation method, reveals *NumericImpactResponses* as the most significant contributor, with an importance score of 0.2433. This far exceeds the contribution of *NumericConflictResponses* (0.008) and other features, which have zero measurable importance.

The dominance of *NumericImpactResponses* indicates that it plays a critical role in determining proximity-based classifications within the k-NN framework. Unlike tree-based models, k-NN relies on feature similarity, and the high importance score of *NumericImpactResponses* suggests that it provides the most discriminative power in defining neighborhood relationships.

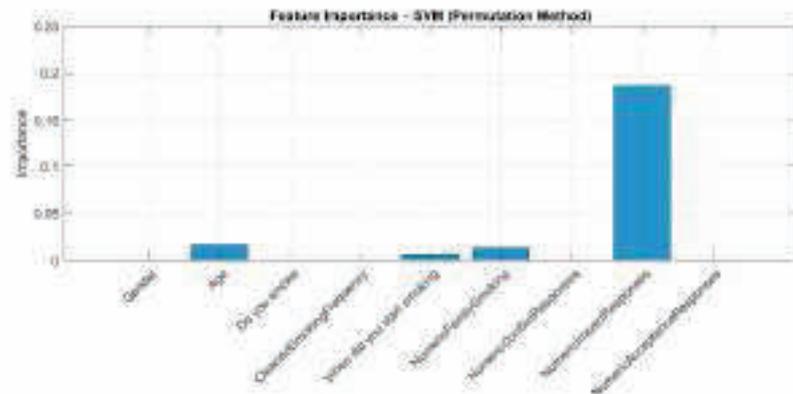


Figure 8. Feature importance analysis by SVM.

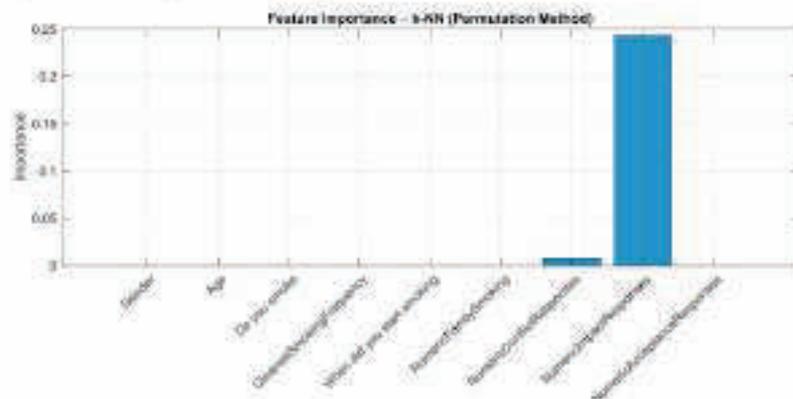


Figure 9. The feature importance analysis by k-NN.

The high importance of *NumericSatisfactionResponses* across all models highlights its pivotal role in determining outcomes. This feature, which quantifies participants' perceptions of smoking's impact on relationships, likely reflects their personal and familial experiences. Its dominance in feature importance suggests that individuals are acutely aware of how smoking behaviors affect interpersonal dynamics, making this variable a strong predictor of relational patterns.

The secondary role of features such as *NumericConflictResponses* and *NumericAcceptanceResponses* across models suggests that while these factors contribute to relational dynamics, they are not as consistently or strongly predictive. Their lower importance indicates that conflict or acceptance dynamics may only manifest in specific familial contexts, making them less universally applicable predictors.

Among the models tested (Table 4), the ensemble model achieved the highest cross-validation accuracy of 93.33% and a minimal loss of 1.43%, effectively classifying complex relationships within the dataset. The decision tree classifier demonstrated moderate performance with an accuracy of 83.33% and a loss of 18.57%, identifying key decision points but struggling with intricate patterns. Similarly, the k-nearest neighbor (k-NN) model achieved an accuracy of 90% and a loss of 14.29%, demonstrating high sensitivity to localized data structures. The support vector machine (SVM) model underperformed, with a

cross-validation accuracy of 80% and a loss of 44.29%, reflecting challenges in handling nonlinear and high-dimensional data.

Table 4. Performance evaluation of the models.

Model	Accuracy (%)	Precision	Recall	F1 Score
Decision Tree*	83.33	0.79	0.70	0.74
Ensemble Method*	93.33	0.91	0.91	0.91
SVM*	80.00	0.60	0.75	0.67
k-NN*	90.00	0.90	0.82	0.86

* Top feature: *NumericImpactResponses* for all models.

To improve comparability between models, feature importance results were summarized across all four approaches—decision tree, SVM, ensemble, and k-NN—using both built-in importance metrics and permutation-based methods. As shown in Figures 6–9, one feature—*NumericImpactResponses*—consistently dominated all models in predictive strength, followed by *NumericConflictResponses* and, in some models, *FamilySmoking* and *Age*. To synthesize these findings, Table 5 presents a side-by-side ranking of the top features by normalized importance score across models. Although the absolute values differ slightly depending on the method, the relative influence of the variables remains largely consistent.

Table 5. Comparative feature importance across machine learning models (normalized scores).

Feature	Decision Tree	Ensemble	SVM	k-NN
Gender	0.0000	0.0085	0.0000	0.0000
Age	0.0000	0.0000	0.0167	0.0000
Do you smoke	0.0000	0.0000	0.0000	0.0000
ClearedSmokingFrequency	0.0000	0.0023	0.0000	0.0000
When did you start smoking	0.0000	0.0051	0.0067	0.0000
NumericFamilySmoking	0.0000	0.0000	0.0133	0.0000
NumericConflictResponses	0.0381	0.0000	0.0000	0.0080
NumericImpactResponses	0.1875	0.1459	0.1867	0.2433
NumericAcceptanceResponses	0.0000	0.0000	0.0000	0.0000

The comparative feature importance table highlights both convergence and variability across models. All four algorithms consistently identified *NumericImpactResponses* as the most predictive feature, capturing participants' perceived impact of smoking on family relationships. Additional variables such as *NumericConflictResponses* and *FamilySmoking* showed moderate influence in specific models (notably SVM and k-NN), while demographic factors such as age and gender had minimal impact. These results suggest that psychosocial and relational variables play a more central role in model predictions than basic demographic characteristics, reinforcing the importance of family dynamics in smoking behavior analysis.

The features that were most influential in supervised models also contributed significantly to separation in the PCA projection. *NumericImpactResponses* and *ConflictResponses*, which ranked highest across multiple algorithms, were also key drivers of visible clustering in the reduced two-dimensional feature space. This consistency between supervised and unsupervised analyses supports the robustness and interpretability of the selected predictors.

Confusion matrices (Figure 10) highlighted the strengths and weaknesses of these models. The ensemble model consistently minimized misclassification across all response categories, while the decision tree and k-NN models exhibited moderate misclassification rates, capturing general trends but struggling with ambiguous cases. The SVM model demonstrated significant classification errors, underscoring its limitations in capturing nuanced distinctions among complex response variables.

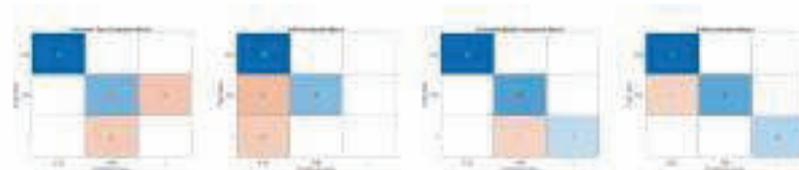


Figure 10. Confusion matrix of ML models in sequence: decision tree confusion matrix, SVM confusion matrix, ensemble model confusion matrix, and k-NN confusion matrix. Color intensity of each cell represents the relative frequency of predictions. Darker shades of blue indicate a higher number of correctly classified instances, typically seen along the diagonal. Conversely, light blue to white indicates fewer correct predictions, while light red has highlight misclassifications, positioned off the diagonal.

4. Discussion

Smoking significantly increases the risk of developing respiratory diseases, cardiovascular problems, and various forms of cancer, severely impacting overall health and longevity [32].

The findings of this study provide valuable insights into the socio-demographic, familial, and behavioral factors influencing smoking behaviors and cessation attempts. The lack of significant association between strong urges to smoke and cessation attempts ($\chi^2 = 3.1532$, $p = 0.27194$) challenges prior studies, such as Fidler et al. (2011) [33], which emphasized craving intensity as a predictor of cessation efforts. This suggests that a more comprehensive understanding of cessation predictors is necessary.

Nocturnal smoking behavior was significantly correlated with higher cigarette consumption ($\chi^2 = 14.2456$, $p = 0.014122$), reinforcing findings by Foulds et al. (2015) that such behavior reflects deeper addiction patterns [26]. The strong correlation between e-cigarette use and traditional smoking ($\rho = 0.67921$, $p = 8.0027 \times 10^{-15}$) highlights the behavioral overlap and concurrent use of these products, as supported by Glantz and Borcham (2024) [32]. Age also played a critical role, with older participants initiating smoking at later ages ($\rho = 0.22546$, $p = 0.0241$), underscoring age-related differences in smoking initiation and patterns. Gender differences in smoking type ($\chi^2 = 10.63$, $p = 0.001$) further emphasize the need to consider gender-specific interventions.

The negative correlation between the time to the first cigarette after waking and willingness to quit ($\rho = -0.30509$, $p = 0.002$) suggests that earlier smoking upon waking may signify more entrenched addiction and lower cessation intent. Additionally, family dynamics significantly influenced smoking behaviors, with familial tension positively correlated with cigarette consumption ($\rho = 0.22$ to 0.34). This finding aligns with Sharma et al. (2020), who highlighted the impact of family conflict on smoking [34].

Machine learning models provided additional insights. The ensemble model's superior performance, with a cross-validation accuracy of 93.33%, demonstrates its robustness in identifying complex relationships within the dataset. This aligns with Dietterich (2000), who emphasized the effectiveness of ensemble methods in handling intricate data structures [35]. The decision tree classifier demonstrated moderate predictive power, with a cross-validation accuracy of 83.33% and a loss of 18.57%, reflecting its ability to identify key decision nodes but with limitations in handling intricate patterns. The k-nearest neighbor (k-NN) model achieved a cross-validation accuracy of 90.00% and a loss of 14.29%, suggesting high sensitivity to localized data structures. Similar studies in behavioral prediction have also noted such trade-offs (Chang, 2024) [36]. The SVM model's lower performance (80.00% accuracy) reflects its challenges with mixed-variable datasets, consistent with findings by Guido et al. (2024) [37].

The feature importance analysis across all four models (ensemble, SVM, decision tree, and k-NN) revealed a consistent pattern, highlighting the dominant role of the variable *NumericImpactResponses*. This feature was the most influential in predicting perceived impact regardless of the algorithm used, suggesting a strong and stable relationship between participants' responses regarding personal impact and the classification outcomes. In contrast, demographic variables such as gender, age, and smoking status contributed minimally across models, indicating that these factors were not key discriminators in this context. The ensemble and k-NN models concentrated importance almost exclusively on the *NumericImpactResponses*, while the SVM and decision tree models distributed minor importance to features such as *NumericFamilySmoking* and *NumericConflictResponses*, pointing to potential secondary influences. These findings emphasize the value of subjective self-assessment measures in predictive modeling over more traditional demographic or behavioral variables and support the robustness of *NumericImpactResponses* as a primary indicator across various algorithmic approaches.

Machine learning (ML) models have demonstrated substantial utility in predictive analysis based on smoking behavioral patterns, notably in the area of smoking cessation. The integration of ML models in public health strategies provides a sophisticated approach to understanding and intervening in smoking behaviors effectively.

Particularly in the field of smoking cessation, machine learning (ML) models have shown significant value in predicting analysis based on smoking behavioral patterns. A sophisticated method for comprehending and successfully addressing smoking behaviors is offered by the incorporation of machine learning algorithms into public health initiatives.

Recent studies have successfully used machine learning (ML) models to predict smokers' cessation results and identified important factors that influence quitting. To predict smoking cessation among US citizens, for example, a study that used data from the Population Assessment of Tobacco and Health (PATH) used a variety of binary classifiers. This study demonstrated the ability of ML models to detect intricate associations within longitudinal data by identifying both known and new factors impacting the shift from current to former cigarette consumption [38].

Furthermore, applications that doctors and patients might use directly have been incorporated into the construction of prediction models for quitting smoking. These models provide tailored predictions that may dynamically respond to new data, modifying the expected success rates for quitting smoking in response to shifting input values [39]. This flexibility is essential in therapeutic settings because the unique qualities of each patient can have a big impact on how well they respond to treatment.

In this area, machine learning is being used to solve problems like class imbalance in datasets, where the proportion of people quitting smoking is much lower than that of those who do not. To improve the predicted accuracy and dependability of ML models, sophisticated strategies such as ensemble methods and random oversampling and undersampling have been used [38]. By balancing the dataset, these techniques make sure that the majority class is not favored by the predictive models.

Additionally, researchers can identify the elements that are most predictive of quitting smoking thanks to the variable importance and selection process in machine learning models. In order to guarantee that the models are trained on relevant, high-quality data, this procedure entails a great deal of data preparation and cleaning. The development of focused smoking cessation programs requires the identification of important predictors, such as nicotine dependency and the use of additional tobacco products [38,39]. In our work, we propose predictive models that can be relatively simply implemented into social smoking cessation programs based on patient interviews, which take into account factors studied by questionnaire, as in our case.

The findings of Hammed et al. (2017) [40] demonstrated that subjective measures of intention can be robust predictors of cessation behavior. Gallus et al. (2023) [41] studied the role of self-efficacy, a subjective self-assessment measure, in predicting smoking cessation among smokers attending a cessation program. The results confirmed that higher levels of self-efficacy were significant predictors of successful cessation, highlighting the importance of subjective confidence in one's ability to quit over other demographic factors.

The performed PCA shows that self-reported perceptions can be meaningfully distinguished in reduced-dimensional space. This supports the interpretive value of subjective assessments in modeling family-related outcomes, even when working with a relatively small sample. The satisfactory result of this reduction further validates the relevance of the selected features and justifies their use in subsequent classification analyses. These findings align with previous research emphasizing the significance of self-reported perceptions in understanding smoking behaviors and their impacts on family dynamics. Previous studies have demonstrated that adolescents' perceptions of smoking-related risks and benefits are closely associated with their smoking behaviors, which underscores the importance of subjective assessments in predicting smoking initiation and cessation [42]. Additionally, research has demonstrated that self-reported measures of nicotine dependence are effective predictors of smoking cessation outcomes, underscoring the value of subjective assessments in modeling smoking behaviors [43].

Overall, the results emphasize the need for targeted interventions addressing specific behavioral patterns, such as nocturnal smoking and early-morning cigarette use, as well as familial dynamics. The study's results provide actionable insights that can guide social interventions. For instance, the positive correlation between family tension and cigarette consumption highlights the need to integrate family counseling or stress-reduction strategies into smoking cessation programs. Social campaigns should not only target individual behavior but also promote healthy communication and shared activities within households, especially those with dual users. Additionally, machine learning models developed in this study could be further adapted to identify individuals at high risk of dependence and tailor prevention strategies accordingly. The strong predictive performance of the ensemble model suggests its potential application in future behavioral studies. Further research is needed to refine machine learning approaches for health behavior prediction and to explore the nuanced roles of socio-demographic factors in smoking cessation.

ML models are a potent tool for studying the behavioral patterns linked to smoking and forecasting the results of quitting. These models can reveal complex patterns and correlations that conventional analytical techniques would overlook by using huge, varied datasets and advanced algorithms. The advancement of public health initiatives targeted at lowering smoking rates and enhancing the results for those trying to stop smoking depends on the ongoing development and use of machine learning techniques in this field [39].

This paper is not free of limitations. Although the findings are informative, the relatively small sample size of 100 participants presents a notable limitation. Small sample studies can yield useful insights, especially in exploratory research, but they limit the statistical power and generalizability of the results. In particular, subgroup-specific analyses—such as those based on gender or living environment—should be interpreted with caution. Future research should aim to recruit a larger and more diverse cohort to ensure greater external validity and robustness of the observed patterns.

This relatively small sample size, though sufficient for preliminary insights, imposes limitations on the generalizability of the findings. A small sample reduces the statistical power of the analysis and increases the likelihood of sampling bias, where the observed results may not accurately represent the broader population. This constraint is particularly relevant when using machine learning models, which typically perform better with larger

datasets to capture complex patterns and interactions effectively. For instance, the ensemble learning model, which achieved a solid accuracy in this study, may demonstrate reduced robustness when applied to more diverse or significantly larger populations. It also affects the using of Principal Component Analysis (PCA). While PCA is a widely used method for exploratory data analysis and dimensionality reduction, its effectiveness can be limited in smaller datasets, where the stability and generalizability of the extracted components may be reduced. The PCA assumes linear relationships among variables and may not fully capture complex or nonlinear interactions relevant to the constructs studied. To address these limitations, future studies could consider using nonlinear dimensionality reduction techniques such as t-distributed Stochastic Neighbor Embedding (t-SNE) or Uniform Manifold Approximation and Projection (UMAP), which are often better suited to reveal subtle patterns and groupings in high-dimensional data, particularly in small to medium-sized samples.

Another limitation of this study is the use of Google Forms as the data collection tool, which, while accessible and efficient, may be subject to self-selection bias and limited control over respondent authenticity, potentially affecting the generalizability of the findings. Future research could strengthen reliability by incorporating follow-up interviews or triangulating responses with other data sources.

5. Conclusions

This study provides critical insights into the complex interplay between smoking behaviors, familial dynamics, and addiction patterns, emphasizing the importance of addressing these factors in public health interventions. Key findings reveal that gender differences, family tension, and the timing of smoking after waking are pivotal factors influencing smoking habits and cessation efforts. Gender-specific smoking product choices and the association between higher family tension and increased smoking frequency highlight the need for personalized strategies to support individuals in high-stress familial environments. The correlation between smoking soon after waking and reduced willingness to quit underscores the importance of early behavioral patterns in shaping cessation outcomes.

The analysis of familial dynamics revealed distinct differences among smoking groups. E-cigarette users reported stronger family support, higher levels of shared family time, and fewer conflicts compared to traditional cigarette smokers and dual users. However, they exhibited high nicotine dependence, with no participants in the e-cigarette or dual-use groups reporting an absence of dependence. Traditional cigarette smokers faced weaker familial bonds, marked by higher conflict levels and lower support. Dual users experienced the most challenging family dynamics, including the least shared time with family, coupled with the highest levels of nicotine dependence. These findings highlight the need for tailored interventions that simultaneously address familial challenges and addiction levels, particularly for dual users, who face compounded behavioral and relational difficulties.

Machine learning techniques, particularly ensemble models, demonstrated significant potential in analyzing the relationships between smoking behaviors and associated factors. The ensemble model outperformed traditional methods, such as decision trees and support vector machines (SVMs), achieving superior accuracy and effectively identifying complex patterns within the dataset [37]. However, the study's relatively small sample size of 100 participants limits the generalizability of these findings. Small datasets reduce statistical power, increase sampling bias, and constrain the ability to identify subgroup-specific trends, such as those based on age, gender, or familial characteristics.

Future research should address these limitations by increasing the sample size to enhance statistical robustness and generalizability. Expanding the diversity of the sample population and incorporating additional variables, such as socioeconomic status, stress,

coping mechanisms, and mental health factors, would provide a more comprehensive understanding of smoking behaviors. Furthermore, testing machine learning models on external datasets from diverse populations will validate their reliability in broader contexts. Advanced feature engineering and improvements in ensemble techniques could further refine model performance and uncover additional nuanced relationships.

In conclusion, this study highlights the profound influence of familial dynamics, addiction patterns, and demographic factors on smoking behaviors. It underscores the value of machine learning as a tool for behavioral research, offering a powerful means of analyzing complex datasets and informing targeted interventions. Public health strategies should consider the unique needs of different smoking groups. For example, interventions aimed at reducing family conflicts and promoting shared activities may benefit dual users, while cessation programs targeting e-cigarette and dual users should focus on mitigating high nicotine dependence. By addressing these multifaceted challenges, future efforts can more effectively reduce smoking prevalence and improve outcomes for individuals and their families.

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Article

Body Composition and Metabolic Profiles in Young Adults: A Cross-Sectional Comparison of People Who Use E-Cigarettes, People Who Smoke Cigarettes, and People Who Have Never Used Nicotine Products

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Abstract

Background: Recent research highlights uncertainties surrounding the metabolic effects of nicotine in young adults, particularly among people who use e-cigarettes. While traditional smoking is known to alter body composition, the metabolic impact of using e-cigarettes remains less understood. **Methods:** In this cross-sectional study, body composition (via bioelectrical impedance analysis) and lifestyle data were collected from 60 university students (mean age: 21.7 ± 1.9 years), who were classified as people who use e-cigarettes exclusively, people who smoke cigarettes exclusively, or people who have never used nicotine products. To address confounding by sex and age, inverse probability of treatment weighting (IPTW) was applied. **Results:** After adjustment, people who use e-cigarettes had significantly higher body fat percentage compared to people who have never used nicotine ($\beta = 5.45$, $p = 0.001$), while no significant differences were found between people who smoke cigarettes and other groups. Energy drink consumption was also positively associated with body fat percentage and metabolic age. Machine learning models, particularly k-nearest neighbors, achieved moderate classification accuracy (up to 72%) in distinguishing people who use nicotine from people who have never used nicotine based on physiological and lifestyle features. **Conclusions:** It is important to note that the majority of participants were metabolically healthy, and the observed differences occurred within a clinically normal range. While these findings suggest associations between e-cigarette use and higher adiposity in young adults, no causal inferences can be made due to the observational design. Further longitudinal studies are needed to explore the potential metabolic implications of nicotine use.

Keywords: e-cigarettes; metabolic health; body composition; nicotine; bioelectrical impedance analysis; young adults; smoking; adiposity



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1. Introduction

Tobacco smoking stands as a major preventable cause of chronic diseases and premature deaths throughout the world [1]. Cigarette smoking produces significant metabolic effects in addition to its established cardiovascular and respiratory dangers. Research evidence shows that smoking leads to higher rates of metabolic syndrome and type 2 diabetes development [2]. The appetite-suppressant and thermogenic properties of nicotine result in lower body weight and BMI among people who smoke cigarettes when compared to people who have never used nicotine products [3]. The nicotine found in cigarettes activates neurotransmitters that decrease hunger while increasing resting energy expenditure, leading to weight reduction [1,4,5]. The fact that people who smoke cigarettes weigh less does not mean they have better metabolic health. People who smoke tend to develop more abdominal (visceral) fat even though they maintain a lower weight. The growth of central adiposity presents a major risk factor because it leads to insulin resistance, dyslipidemia, and elevated cardiometabolic risk. People who smoke cigarettes develop an unhealthy lean body composition profile, which includes reduced lean mass and abnormal fat distribution patterns that increase their risk for adverse metabolic outcomes even among young adults [6,7].

Electronic cigarettes (e-cigarettes) have become popular tobacco alternatives since their emergence two decades ago, especially among younger individuals [1,8]. The battery-powered devices produce inhalable vapor that contains nicotine without burning tobacco. E-cigarettes serve as a less harmful alternative to traditional cigarettes, thus attracting people who smoke and want to decrease their tobacco consumption [9]. Although e-cigarettes do not contain tobacco leaves or undergo combustion, they deliver nicotine in vaporized form. This distinction is important when comparing their physiological impact to that of traditional cigarettes. The metabolic consequences of using e-cigarettes on a long-term basis continue to be unknown. The majority of e-cigarettes deliver significant nicotine amounts, which could lead people who use them to experience weight-modulating effects similar to those of traditional cigarettes. Research indicates that people who use e-cigarettes share similar lower average BMI levels with people who smoke cigarettes [1,8]. The observed lower BMI in people who use e-cigarettes might stem from nicotine-induced appetite reduction and elevated metabolic rate, which resemble people who smoke cigarettes characteristics. The use of e-cigarettes has been linked to possible metabolic complications. Studies have found that using e-cigarettes leads to specific metabolic syndrome features, including central obesity and elevated blood pressure [2]. The ongoing research into e-cigarette health effects requires clarification about whether using e-cigarettes replaces cigarette use to reduce metabolic problems or simply changes their nature.

Body composition functions as a vital element of metabolic health, which shows different responses based on smoking habits. The distribution between fat and lean mass within normal body weight determines metabolic risk to a significant extent. The combination of body fat accumulation with decreased muscle mass, which some people who smoke cigarettes develop, leads to insulin resistance and dyslipidemia [6,7]. The assessment of body composition together with metabolic indicators in people who smoke cigarettes, people who use e-cigarettes, and people who have never used nicotine products enables researchers to detect the initial health impacts of these behaviors. Bioelectrical impedance analysis (BIA) serves as a useful noninvasive tool to measure body composition during population research. The harmless electrical current measurement through BIA enables fast calculations of fat mass, lean body mass, and total body water by determining the body's electrical resistance [10]. BIA technology enables researchers to identify minimal variations in body fat distribution, muscle size, and basic metabolic rates between people with varying lifestyle patterns. The combination of BIA data with lifestyle questionnaire results

enables researchers to evaluate the impact of smoking behaviors on body composition and metabolic state among healthy young adults.

Building upon our previous research, which employed machine learning techniques to identify demographic, familial, and social predictors of smoking and e-cigarette use among young adults [11], this study shifts focus toward physiological outcomes—specifically the metabolic profile associated with e-cigarette use.

The increasing popularity of e-cigarettes alongside ongoing smoking health issues requires researchers to analyze their effects on metabolic health indicators. Research about body composition variations between people who smoke traditional cigarettes, people who use e-cigarettes, and people who have never used nicotine products remains scarce, especially when studying university students. This research aimed to analyze body composition and metabolic indicators between conventional people who smoke cigarettes, people who use e-cigarettes, and people who have never used nicotine products among Silesian University of Technology students. The research combines BIA measurements with lifestyle questionnaires to explore whether using e-cigarettes is associated with differences in body fat distribution and metabolic profiles when compared to smoking, and to establish fundamental evidence about the metabolic effects of cigarette and e-cigarette use in young adults. The research results will provide essential knowledge about how tobacco and nicotine products affect early indicators of metabolic health.

2. Materials and Methods

The study protocol was designed to examine the association between nicotine/tobacco use status and selected anthropometric and metabolic parameters in a university student population. To achieve this objective, comprehensive data were collected through standardized body composition measurements and structured lifestyle questionnaires. The following subsections provide detailed descriptions of the participants, procedures, and statistical methods used in the analysis.

2.1. Participants and Data Collection

Young adult volunteers from the Faculty of Biomedical Engineering at the Silesian University of Technology in Gliwice, Poland, recruited through student mailing lists, on-campus advertisements, and classroom announcements, made up the study population. The research participants joined the study through convenience sampling during the academic year 2024/2025. The study included participants who were older than 18 years old and obtained necessary consent before joining the research. The Ethics Committee for Research Involving Human Participants at the Silesian University of Technology in Gliwice, Poland approved this study through resolution No. 3/2025 on 11 March 2025. The participants received group assignments according to their self-reported tobacco consumption habits between traditional cigarettes (T), electronic cigarettes (E), and none (N). The study did not use biochemical validation methods such as cotinine testing.

Anthropometric and body composition data were collected using a commercially available bioelectrical impedance analysis (BIA) device, the Tanita MC 780 (Tanita Corp., Meguro-ku, Japan). Measurements included body weight (kg), height (cm), body mass index (BMI), total body water (TBW), visceral fat level, muscle mass, fat mass, and metabolic age, among others. All measurements were taken under standardized conditions. Measurements were conducted barefoot and in light clothing. For each participant, the measurement protocol was conducted by a trained examiner following the manufacturer's guidelines.

The participants filled out a validated lifestyle questionnaire to measure their dietary behavior, beverage consumption, physical activity, and sedentary time. In addition, they were asked to report their average number of daily smoking or e-cigarette use sessions. For

the purpose of standardization, one e-cigarette session was defined as approximately 15 inhalations or 10 min of use. Only participants who reported regular use (more than 1 year) and more than 10 sessions per day were included in the analysis. For people who smoke cigarettes, one session was considered equivalent to smoking one full cigarette. Participants in this group also reported more than 10 cigarettes per day and had a smoking history of over one year. Based on self-reported nicotine use, respondents were classified into three groups. People who have never used nicotine products were defined as those who reported no current or past use of any nicotine or tobacco products, including even occasional use. People who smoke cigarettes were defined as those who exclusively smoked combustible cigarettes for at least one year, with no history of e-cigarette use. People who use e-cigarettes were defined analogously, as individuals who exclusively used e-cigarettes for at least one year without any use of traditional cigarettes. Those reporting dual use, or use of either product for less than one year, were excluded to reduce heterogeneity and isolate the effects of sustained, single-product use.

The questionnaire data were recorded through structured fields and manually checked for completeness. The final dataset was compiled in a spreadsheet format (Excel ".xlsx", Microsoft Excel, Office 365, version 16.98 (25060824) for Mac), comprising both continuous and categorical variables. All identifying information was pseudonymized before analysis to ensure confidentiality.

2.2. Variable Selection

The dataset consisted of both numerical (continuous) and categorical variables. A total of 21 numerical variables were initially considered for analysis, including anthropometric measurements (e.g., body weight, height, BMI), body composition parameters (e.g., fat mass, visceral fat level, skeletal muscle mass, phase angle, total body water, extracellular water, intracellular water), metabolic indicators (e.g., metabolic age, basal metabolic rate), and selected lifestyle factors (e.g., daily sitting time, number of meals consumed per day, daily water intake, number of cups of coffee consumed per day, and frequency of energy drink consumption).

Eight categorical variables were included, covering demographic and lifestyle information such as sex, place of residence (urban vs. rural), occupational status, level of physical activity, declared dietary habits (e.g., regularity of meals, type of diet), transportation habits (e.g., commuting mode), and methods of food preparation (e.g., cooking vs. processed food).

Prior to analysis, numerical variables were converted to a double-precision floating-point format to enable statistical calculations. Categorical variables were encoded using embedded in Matlab software (Matlab 2024b, The Mathworks Inc., Natick, MA, USA) 'categorical' data type to facilitate proper handling in statistical tests and classification models. Missing data were assessed, and observations containing missing or non-convertible entries for critical variables were excluded listwise from multivariate analyses (e.g., principal component analysis, classification).

Variable selection for classification models was based on initial feature importance derived from a decision tree classifier, with the top-ranked variables subsequently used for model building and validation. In particular, eight features with the highest predictive value were selected for the final classification analysis.

2.3. Group Coding and Preprocessing

Participants were assigned to groups based on their self-assessment of smoking/using e-cigarette habits: people who smoke conventional cigarettes (T), people who use electronic cigarettes (E), and people who have never used nicotine products (N). The participant

identity codes identified group membership using their suffixes ('_T' for people who smoke conventional cigarettes, '_E' for people who use e-cigarettes, and no suffix for people who have never used nicotine products), which were validated by structured questionnaire replies. The classification model combined participants from groups T and E into a single "smoking" group labeled '1', while people who have never used nicotine products (group N) received the label '0'. The re-coding allowed researchers to evaluate variables that distinguish people who use nicotine from people who have never used nicotine products using future classification models.

Prior to analysis, all numerical variables imported from the spreadsheet were converted to a double-precision floating-point format to enable proper statistical processing. Categorical variables were encoded using Matlab's categorical data type to ensure compatibility with statistical tests and machine learning algorithms. Records containing missing or non-convertible entries for critical variables were excluded from analyses using a listwise deletion approach. Numerical variables were standardized where required, particularly in multivariate analyses such as principal component analysis. Finally, group labels were encoded as categorical variables to support consistent handling across classification tasks. All preprocessing steps were conducted to guarantee data integrity, minimize bias due to missing information, and optimize the performance of the statistical and machine learning models employed in the study.

2.4. Statistical Analysis

All statistical analyses were performed using Matlab R2024b. Prior to comparative testing, the distribution of continuous variables was assessed using the Lilliefors test for normality. The majority of variables showed significant deviations from normality ($p < 0.05$) so non-parametric statistical methods were used for analysis.

The Kruskal-Wallis H test served as a non-parametric replacement for one-way ANOVA to evaluate continuous variable differences between T, E, and N groups. The Mann-Whitney U test was used to conduct post-hoc comparisons between specific groups after detecting a statistically significant overall effect ($p < 0.05$). The p -values needed adjustment through Bonferroni correction because of multiple comparisons risk ($n = 3$) to prevent Type I errors. The Chi-square test of independence served to analyze differences between groups for categorical variables. The analysis used a two-tailed p -value threshold of less than 0.05 for statistical significance, while applying Bonferroni correction when necessary.

The analysis presented descriptive statistics through median values and interquartile ranges (IQRs) for continuous variables together with categorical variable data presented as counts and percentages. The analysis excluded cases with missing data by using listwise deletion to only include complete cases. The distribution of continuous variables across groups was displayed through boxplots, while contingency tables were used to present categorical variables.

The study presented descriptive statistics through median values and interquartile ranges (IQRs) for continuous data and counts with percentages for categorical data. The analysis excluded cases with missing data through listwise deletion, so only complete cases were used for comparative evaluations. The distribution of continuous variables across groups was displayed through boxplots and contingency tables were used to present categorical variables.

Due to differences in covariates across groups, particularly sex distribution, a propensity score weighted analysis was used to examine adjusted differences in body fat percentage. The analysis focused on three pairwise comparisons: (1) people who use e-cigarettes vs. people who have never used nicotine products, (2) people who use e-cigarettes vs. people who smoke conventional cigarettes, and (3) people who smoke cigarettes vs. people

who have never used nicotine products. For each comparison, propensity scores were estimated using logistic regression based on sex and age. Inverse probability of treatment weighting (IPTW) was then applied to create a pseudo-population with balanced covariate distributions. Weighted linear regression models were used to estimate differences in body fat percentage between groups.

To evaluate the effectiveness of inverse probability of treatment weighting (IPTW), covariate balance was assessed using standardized mean differences (SMD) for sex and age. A threshold of SMD < 0.1 was considered acceptable. Separate diagnostics were conducted for each pairwise comparison (people who use e-cigarettes vs. people who have never used nicotine products, people who use e-cigarettes vs. people who smoke cigarettes, and people who smoke cigarettes vs. people who have never used nicotine products).

2.5. Correlation Analysis

The analysis of correlation between continuous variables used correlation analysis methods. The study calculated two types of correlation coefficients, which included the Pearson product-moment correlation coefficient for linear relationships between normally distributed variables and the Spearman rank correlation coefficient for non-parametric analysis of ordinal or non-normal variables. The Lilliefors test revealed most variables deviated from normality, so researchers focused their interpretation on Spearman correlations. The research produced correlation matrices for both Pearson and Spearman coefficients to evaluate statistical significance between each pair of variables. The study used a *p*-value threshold of 0.05 to establish statistical significance. The correlation structure was visualized through heatmaps that displayed correlation coefficients by their magnitude and direction through color coding.

In addition to the general correlation matrices, targeted correlation analyses were performed between selected lifestyle variables (e.g., sedentary time, coffee intake, energy drink consumption) and physiological parameters such as body mass index (BMI), basal metabolic rate (BMR), and metabolic age. The strength and direction of these associations were evaluated, and where appropriate, scatter plots were generated to illustrate significant findings. All correlation analyses were conducted using built-in functions from the Matlab Statistics and Machine Learning Toolbox.

2.6. Classification and Feature Importance

To evaluate the ability of physiological and lifestyle variables to discriminate between people who use nicotine and people who have never used nicotine products, several supervised classification models were developed. The rationale for including this approach was to complement group-based comparisons with data-driven pattern recognition across multiple variables, such as body composition metrics, physical activity, and dietary habits. Unlike traditional hypothesis testing, ML enables the detection of complex, potentially non-linear associations between input features and classification outcomes.

An initial attempt was made to classify participants into three groups: people who have never used nicotine products, people who smoke cigarettes exclusively, and people who use e-cigarettes exclusively. However, model performance was suboptimal, with high misclassification rates between the two groups of people who use nicotine. This outcome was attributed to overlapping physiological characteristics and unequal sample sizes. To address this limitation, a binary classification approach was adopted, where participants using either traditional cigarettes or electronic cigarettes were combined into a single people who use nicotine group (label = 1), and people who have never used nicotine products were labeled as 0. Initially, a decision tree classifier (CART algorithm) was trained using the entire set of continuous variables. Feature importance scores were

extracted based on the reduction of the Gini impurity criterion at each split node. The eight most important features were subsequently selected for further model development to reduce dimensionality and minimize the risk of overfitting. Classification models were trained using the selected top eight variables and included a Decision Tree classifier, a Random Forest classifier consisting of 100 trees, and a k-Nearest Neighbors (kNN) classifier with $k = 5$.

Model performance was evaluated using 5-fold cross-validation to assess generalization ability. Accuracy was calculated as the proportion of correctly classified instances. Confusion matrices were generated to provide detailed insights into classification performance, including sensitivity and specificity. All classification analyses were performed using Matlab's Statistics and Machine Learning Toolbox. Hyperparameters were selected based on standard defaults without extensive tuning, reflecting an exploratory approach rather than model optimization.

3. Results

The sixty participants in the final analysis were split into three groups: twenty were people who smoke cigarettes (Group T), twenty were people who use e-cigarettes (Group E), and twenty were people who have never used nicotine products (Group N). All participants had an average body mass index (BMI) of 22.3 kg/m², with a median age of 22 years. Height, weight, body fat percentage, visceral fat level, skeletal muscle mass, total body water, and metabolic age are among the participants' physiological and demographic details shown in Table 1. There were no differences between the groups in terms of home location or sex distribution. For continuous variables, the study used medians and interquartile ranges (IQRs); for categorical variables, it used counts and percentages to provide descriptive statistics.

Table 1. Baseline characteristics of participants by group. Data are presented as median [interquartile range] for continuous variables and as number (percentage) for categorical variables.

Variable	All Participants (n = 60)	People Who Smoke Cigarettes (n = 20)	People Who Use E-Cigarettes (n = 20)	People Who Have Never Used Nicotine Products (n = 20)
Age (years)	22.0 [2.25]	22.0 [2.25]	20.5 [3.0]	22.0 [1.75]
Height (cm)	173.5 [16.25]	176.5 [8.0]	170.0 [12.25]	171.5 [20.75]
Weight (kg)	65.35 [13.35]	68.75 [20.15]	65.35 [4.8]	62.1 [21.08]
BMI (kg/m ²)	22.3 [3.55]	22.05 [4.62]	23.4 [1.33]	21.05 [3.2]
Body fat (%)	15.35 [5.87]	12.95 [7.17]	16.35 [4.32]	11.2 [5.15]
Visceral fat level	2.0 [2.0]	2.0 [2.25]	2.0 [2.0]	1.0 [1.0]
Muscle mass (kg)	47.35 [17.7]	52.25 [15.88]	46.6 [10.2]	45.75 [20.67]
Total body water (TBW) (%)	32.1 [13.12]	39.7 [14.9]	31.05 [6.1]	30.85 [14.55]
Metabolic age (years)	18.0 [13.25]	23.5 [17.0]	23.5 [13.0]	15.5 [5.5]
Sex—Male (%)	15 (41.7%)	7 (58.3%)	2 (16.7%)	5 (41.7%)
Sex—Female (%)	21 (58.3%)	5 (41.7%)	10 (83.3%)	7 (58.3%)

The analysis showed that groups differed significantly regarding metabolic age ($p = 0.0429$) (Figure 1), body fat percentage ($p = 0.0203$) (Figure 2), BMI ($p = 0.0295$) (Figure 3), and the number of energy drink consumed ($p = 0.0007$) (Figure 4). The results of the Mann–Whitney U test with Bonferroni correction showed that people who use e-cigarettes had higher BMI ($p = 0.0199$), higher body fat percentage ($p = 0.0127$), and higher metabolic age ($p = 0.0248$) than people who have never used nicotine products.

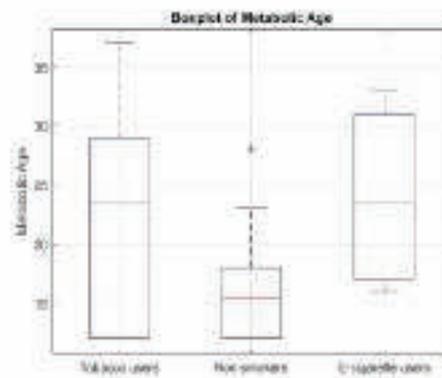


Figure 1. Boxplot of metabolic age across smoking/using e-cigarettes status groups. The red line represents the median. The red "+" symbol indicates an outlier.

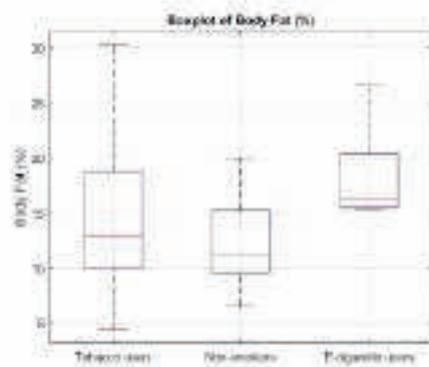


Figure 2. Boxplot of body fat percentage across smoking/using e-cigarettes status groups. The red line represents the median.

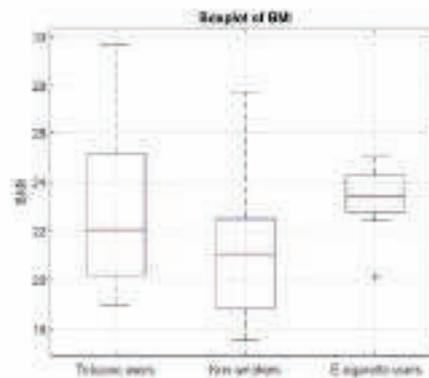


Figure 3. Boxplot of BMI across smoking/using e-cigarettes status groups. The red line represents the median. The red "+" symbol indicates an outlier.

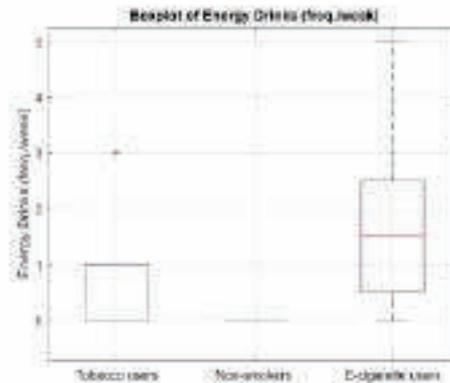


Figure 4. Boxplot of energy drink consumption frequency across smoking/using e-cigarettes status groups. The red line represents the median. The red “+” symbol indicates an outlier.

According to the data, energy drink consumption was higher among people who use e-cigarettes than among people who smoke cigarettes and people who have never used nicotine products ($p = 0.0480$ and $p = 0.0011$, respectively). There were no differences in these characteristics between the people who smoke cigarettes and the other groups after controlling for multiple comparisons.

After controlling for multiple comparisons, there were no discernible differences in these variables between the people who smoke cigarettes and the other groups. Table 2 offers a thorough summary of the comparisons, complete with p -values from post-hoc analyses and Kruskal–Wallis tests.

Table 2. Group comparisons for continuous variables between smoking/using e-cigarettes status groups. Data are presented as p -values from Kruskal–Wallis tests. Significant pairwise comparisons were assessed using Mann–Whitney U tests with Bonferroni correction.

Variable	Kruskal–Wallis p -Value	Significant Comparisons (Bonferroni-Corrected p)
Metabolic Age	0.0428	People who use e-cigarettes vs people who have never used nicotine products ($p = 0.0248$)
Body Fat	0.0203	People who use e-cigarettes vs people who have never used nicotine products ($p = 0.0127$)
BMI	0.0295	People who use e-cigarettes vs people who have never used nicotine products ($p = 0.0199$)
Chronological Age	0.0721	People who use e-cigarettes vs people who have never used nicotine products (trend, $p = 0.0938$)
Energy Drink Consumption	0.0007	People who use e-cigarettes vs people who have never used nicotine products ($p = 0.0011$)
		People who use e-cigarettes vs people who smoke cigarettes ($p = 0.0480$)

The boxplot presents the distribution of metabolic age in people who smoke cigarettes, people who use e-cigarettes, and people who have never used nicotine products. The median, interquartile range (IQR), and outliers are shown. A significant difference was observed between people who use e-cigarettes and people who have never used nicotine products ($p = 0.0248$, Bonferroni corrected).

The boxplot illustrates the differences in body fat percentage among people who smoke cigarettes, people who use e-cigarettes, and people who have never used nicotine products. People who use e-cigarettes exhibited significantly higher body fat percentage compared to people who have never used nicotine products ($p = 0.0127$, Bonferroni corrected).

The boxplot shows the distribution of BMI values among people who smoke cigarettes, people who use e-cigarettes, and people who have never used nicotine products. A significant increase in BMI was found in people who use e-cigarettes compared to people who have never used nicotine products ($p = 0.0199$, Bonferroni corrected).

The figure presents the frequency of energy drink consumption per week among the three groups. People who use e-cigarettes reported significantly higher consumption compared to both people who have never used nicotine products ($p = 0.0011$) and people who smoke cigarettes ($p = 0.0480$).

Correlation analyses were conducted using both Pearson's and Spearman's methods to examine the relationships between continuous variables. The majority of variables demonstrated consistent patterns across both methods. The Pearson's correlation analysis revealed that body weight demonstrated strong positive relationships with muscle mass ($r = 0.83$), total body water ($r = 0.81$), and body fat percentage ($r = 0.54$). BMI showed positive relationships with body fat percentage ($r = 0.81$) and visceral fat level ($r = 0.78$). Body fat percentage and visceral fat levels showed strong correlations with metabolic age ($r = 0.84$ and $r = 0.74$, respectively). The number of energy drinks consumed per week demonstrated moderate positive associations with metabolic age ($r = 0.61$, $p < 0.001$) and body fat percentage ($r = 0.65$, $p < 0.001$). The results from Spearman's rank correlation coefficients validated the observed patterns. Body weight maintained a strong positive relationship with muscle mass, total body water, and body fat percentage measurements. The results from Spearman's rank correlation coefficients confirmed the previously identified relationships between energy drink consumption frequency and metabolic age ($p = 0.61$) and body fat percentage ($p = 0.65$). The heatmaps in Figures 5 and 6 present a visual representation of the correlation strengths and directions between variables. The diagrams use $p < 0.05$ as the threshold to mark significant associations. The heatmaps display yellow for positive correlations and blue for negative correlations, where darker shades represent stronger negative relationships and lighter shades represent stronger positive relationships.

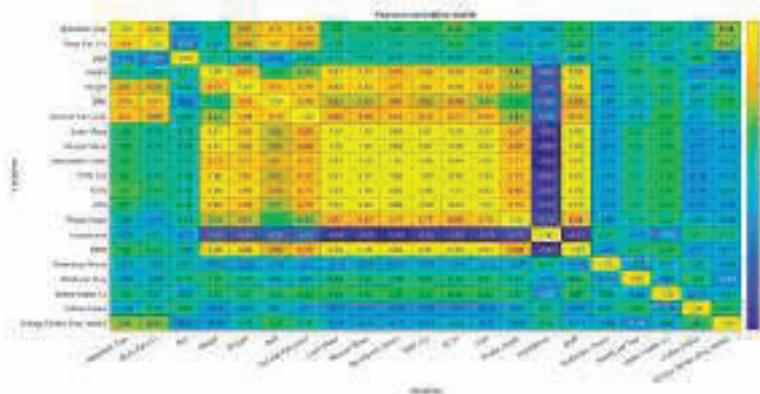


Figure 5. Pearson's correlation matrix between continuous variables, ($p < 0.05$).

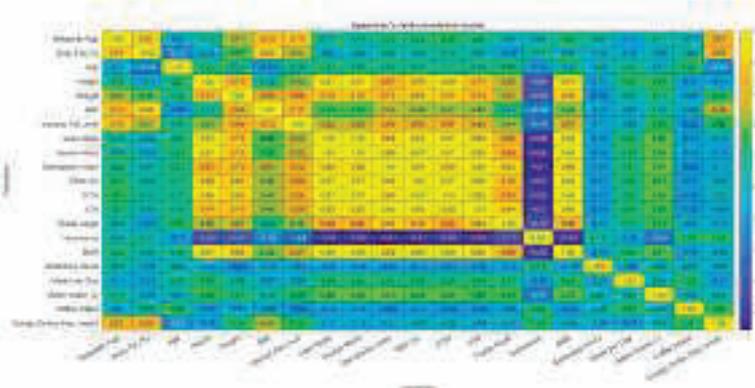


Figure 6. Spearman's rank correlation matrix between continuous variables, ($p < 0.05$).

The research included both correlation matrices and specific pairwise correlation tests to study the connections between certain lifestyle elements and body composition and metabolic results. The analysis revealed no meaningful relationships between daily sedentary time and BMI ($r = -0.10$, $p = 0.5615$), basal metabolic rate (BMR) ($r = -0.15$, $p = 0.3819$), metabolic age ($r = 0.09$, $p = 0.6025$), or body fat percentage ($r = -0.04$, $p = 0.8170$). The analysis showed that coffee consumption did not correlate with BMI ($r = -0.06$, $p = 0.7151$), BMR ($r = -0.16$, $p = 0.3499$), metabolic age ($r = -0.01$, $p = 0.9357$), or body fat percentage ($r = 0.09$, $p = 0.5850$). The analysis revealed that energy drink consumption had statistically significant positive relationships with BMI ($r = 0.49$, $p = 0.0025$), metabolic age ($r = 0.61$, $p = 0.0001$), and body fat percentage ($r = 0.65$, $p < 0.0001$), which indicates that regular energy drink consumption might be associated with negative metabolic effects.

To address baseline differences in covariates, particularly sex and age, a series of propensity score weighted (PSW) linear regression models were used to estimate adjusted differences in body fat percentage between groups. In the comparison between people who use e-cigarettes and people who have never used nicotine products, the model showed a statistically significant difference in body fat percentage, with people who use e-cigarettes having higher levels than people who have never used nicotine products ($\beta = 5.45$, $p = 0.001$, $R^2 = 0.38$). This result remained consistent after weighting for sex and age using inverse probability of treatment weighting (IPTW). In contrast, no statistically significant differences were observed between people who use e-cigarettes and people who smoke cigarettes ($\beta = 1.91$, $p = 0.39$, $R^2 = 0.03$), nor between people who smoke cigarettes and people who have never used nicotine products ($\beta = 2.06$, $p = 0.39$, $R^2 = 0.03$). These results (Table 3) suggest that the elevated body fat observed in people who use e-cigarettes is not meaningfully different from that of people who smoke cigarettes when controlling for sex and age and may reflect general associations with nicotine exposure.

Table 3. Results of propensity score weighted linear regression models comparing body fat percentage between groups.

Comparison	β (Body Fat %)	95% CI	p-Value	R ²	n
People who use e-cigarettes vs. people who have never used nicotine products	5.45	[2.38, 8.52]	0.001	0.38	24
People who use e-cigarettes vs. people who smoke cigarettes	1.91	[-2.6, 6.4]	0.391	0.03	24
People who smoke cigarettes vs. people who have never used nicotine products	2.06	[-2.8, 6.9]	0.390	0.03	24

The IPTW procedure improved covariate balance across all comparisons. In particular, the standardized mean difference (SMD) for sex was reduced to near-zero levels in all pairwise contrasts, while age balance improved and met the conventional threshold (SMD < 0.1) in both comparisons between people who use e-cigarettes and people who have never used nicotine products, and between people who use e-cigarettes and people who smoke cigarettes. These results support the adequacy of the weighting procedure (Figures 7–9), though some degree of residual confounding cannot be entirely excluded. There is also the possibility of residual confounding, as the propensity score weighting model included only age and sex. Notably, the small number of male participants in the e-cigarette group may limit the ability to fully control for sex differences in the analysis, particularly given the strong confounding effect of sex observed in unadjusted comparisons. Other potentially relevant confounders such as socioeconomic status, dietary habits, physical activity, or psychological stress were not available for inclusion and may have influenced the results.

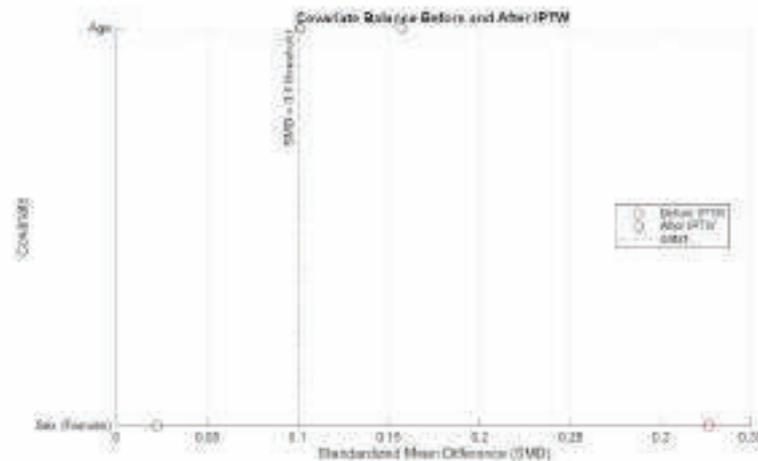


Figure 7. Covariate balance: people who smoke cigarettes vs. people who have never used nicotine products.

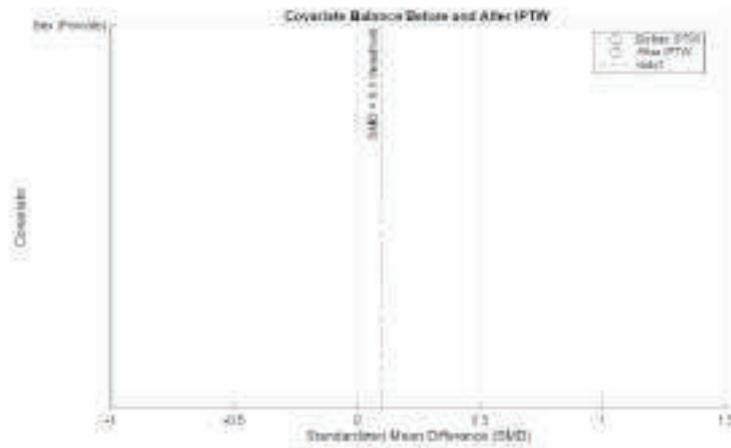


Figure 8. Covariate balance: people who use e-cigarettes vs. people who have never used nicotine products.

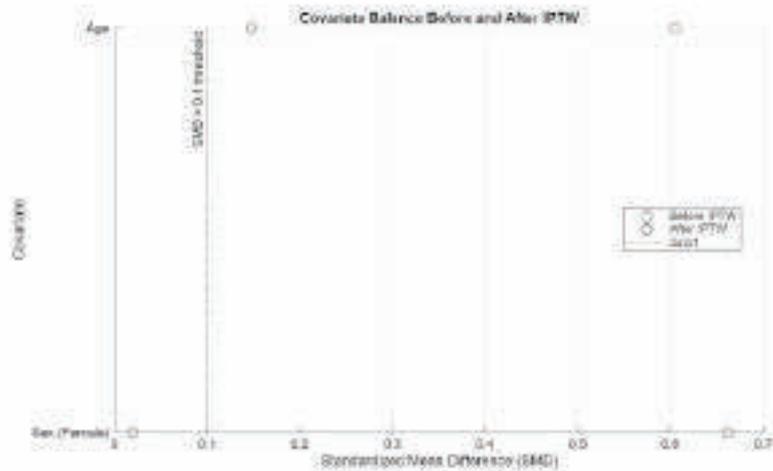


Figure 9. Covariate balance: people who use e-cigarettes vs. people who smoke cigarettes.

Supervised machine learning models were developed to classify participants based on their smoking/using e-cigarette status, in order to distinguish between people who use nicotine (those who smoke cigarettes and those who use e-cigarettes) and people who have never used nicotine products. Initially, a decision tree classifier (Figure 10) was built using all available continuous variables. The model was evaluated with 5-fold cross-validation to prevent overfitting. The initial decision tree yielded an accuracy of 50.0%, indicating a modest predictive capability. Feature importance analysis (Figure 11) revealed that metabolic age, body fat percentage, and BMI were the most influential variables.

Table 4. Performance of machine learning classifiers in distinguishing people who use nicotine from people who have never used nicotine products.

Classifier	Features Used	Cross-Validated Accuracy (%)
Decision Tree	All features	50.0%
Decision Tree	Top 8 features	66.67%
Random Forest (100 trees)	Top 8 features	61.1%
k-Nearest Neighbors (k = 5)	Top 8 features	72.22%

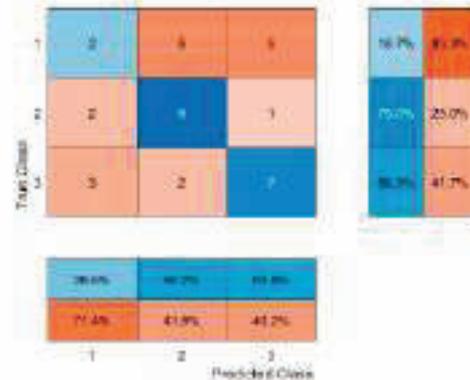


Figure 12. Confusion matrix for Decision Tree classifier for all features and 3 classes: 1—people who have never used nicotine products, 2—people who use e-cigarettes, 3—traditional cigarette people who smoke cigarettes. The central matrix shows the number of correctly and incorrectly classified instances (absolute counts). The right panel displays class-wise recall (sensitivity), and the bottom panel shows class-wise precision. Cell background colors represent the magnitude of values, from low (light blue) to high (dark red).

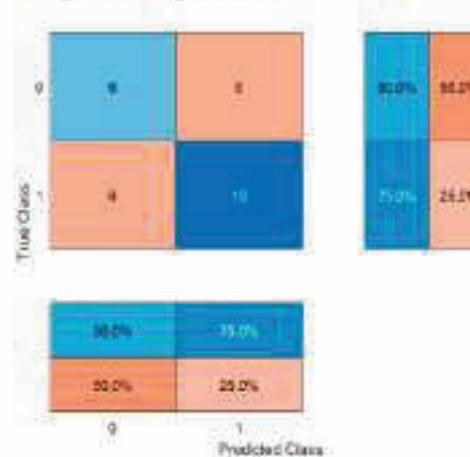


Figure 13. Confusion matrix for Decision Tree classifier for 8 features. 0—people who have never used nicotine products, 1—people who use nicotine altogether. The central matrix shows the number of correctly and incorrectly classified instances (absolute counts). The right panel displays class-wise recall (sensitivity), and the bottom panel shows class-wise precision. Cell background colors represent the magnitude of values, from low (light blue) to high (dark red).

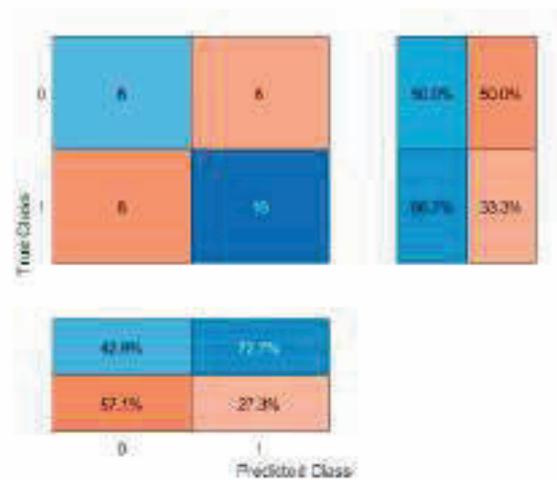


Figure 14. Confusion matrix for Random Forest classifier. 0—people who have never used nicotine products, 1—people who use nicotine altogether. The central matrix shows the number of correctly and incorrectly classified instances (absolute counts). The right panel displays class-wise recall (sensitivity), and the bottom panel shows class-wise precision. Cell background colors represent the magnitude of values, from low (light blue) to high (dark red).

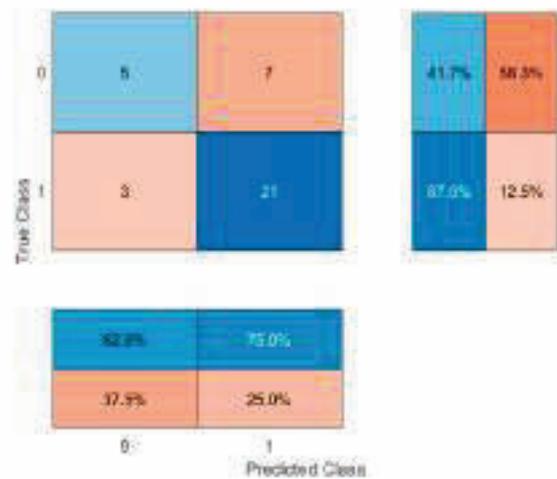


Figure 15. Confusion matrix for k-Nearest Neighbors (k = 5) classifier. 0—people who have never used nicotine products, 1—people who use nicotine altogether. The central matrix shows the number of correctly and incorrectly classified instances (absolute counts). The right panel displays class-wise recall (sensitivity), and the bottom panel shows class-wise precision. Cell background colors represent the magnitude of values, from low (light blue) to high (dark red).

4. Discussion

The current research revealed that people who use e-cigarettes maintained greater body fat percentage, BMI, and metabolic age than people who have never used nicotine products, while people who smoke cigarettes showed no differences with people who have never used nicotine products in these measurements. The findings indicate that e-cigarette use was associated with less favorable body composition indicators in young

adults. Although nicotine has been widely regarded as an appetite suppressant and is sometimes used for weight control, the present findings suggest that habitual e-cigarette use in young adults was associated with increased body fat percentage. However, it is important to note that the relationship between nicotine and metabolic outcomes is likely multifactorial and may be modulated by behavioral patterns, sex differences, and lifestyle characteristics. Therefore, our results do not negate the appetite-suppressing potential of nicotine in some contexts but rather emphasize that long-term use does not necessarily lead to lower adiposity. The observation that both people who smoke cigarettes and people who use e-cigarettes exhibited similar levels of metabolic disturbance suggests that nicotine exposure—regardless of delivery method—may be associated with comparable differences in metabolic indicators, assuming similar usage intensity. While nicotine intake was habitual in both groups, the patterns of consumption differed between people who smoke cigarettes and people who use e-cigarettes. Traditional cigarette smoking typically occurs in defined units (e.g., one cigarette), whereas e-cigarette use is often more fragmented, involving multiple short inhalation sessions throughout the day. These behavioral differences make the direct comparison of “amount of tobacco” unfeasible. Therefore, this study focused on frequency and regularity of use as the most practical and behaviorally relevant measure of nicotine exposure across both groups. It should be noted that all three groups demonstrated average BMI values within the clinically healthy range (22–23 kg/m²), and metabolic age estimates were close to participants’ chronological age. Thus, although statistically significant differences were observed, the overall metabolic health of the sample was within normative values.

While our inclusion criteria ensured that participants had used only one type of nicotine product for at least one year, we acknowledge that relying on self-reported data may not fully capture occasional or unreported prior use. Therefore, although people who have never used nicotine products were defined as having never used any nicotine products, and people who use nicotine were categorized based on exclusive and sustained use, the possibility of recall bias or misclassification cannot be entirely excluded. Given the cross-sectional design and self-selected exposure groups, the observed associations do not establish temporal or causal relationships. It remains unclear whether these metabolic differences preceded or followed the initiation of nicotine use.

Multiple recent studies involving comparable age groups validate our research findings. A cross-sectional study of Slovak young adults (mean age ~22 years) demonstrated that people who smoke cigarettes regularly possessed larger waist circumference measurements and higher BMI and fat mass values, including percent body fat and visceral fat area, compared to people who have never used nicotine products [8]. The research shows that people who smoke cigarettes in early adulthood tend to have greater total body fat and central fat distribution. The study by Radmilović et al. demonstrated that middle-aged people who smoke cigarettes displayed higher body fat percentages and their biological age exceeded their actual age, while people who have never used nicotine products maintained equivalent values [12]. The observed increase in “metabolic age” among people who use nicotine matches our findings and suggests that tobacco use over time speeds up metabolic aging. The research supports that people who smoke cigarettes typically experience poor weight and fat distribution patterns even though their weight changes are not always obvious.

The current research supports previous studies that establish links between using e-cigarettes and metabolic risks even though data about e-cigarette use and body composition remains limited. A Korean population-based study discovered that people who used e-cigarettes who were active at the time of the study had larger waist measurements and the highest risk of developing abdominal obesity and hypertriglyceridemia when compared

to people who have never used nicotine products. The research showed that people who use e-cigarettes developed metabolic syndrome at higher rates than both people who smoke cigarettes exclusively and people who have never used nicotine products, with the people who use e-cigarettes currently showing the highest risk [13]. The epidemiological evidence supports our findings of increased metabolic age in people who use e-cigarettes because using e-cigarettes does not provide any health benefits and may actually cause harm to metabolic health and body composition. Research indicates that youth who use conventional cigarettes have the same BMI increases as those who use electronic cigarettes. Longitudinal research showed that overweight adolescents used tobacco products more often and electronic tobacco products and conventional tobacco products showed equal positive effects on BMI when used separately [14]. The traditional understanding of people who smoke cigarettes being lean based on older adult data does not apply because weight and nicotine use relationships differ across various population ages and factors.

The relationship between nicotine use and weight outcomes shows complexity because of behavioral elements at play. Young people who use e-cigarettes may experience higher adiposity because they tend to engage in multiple health-risk behaviors simultaneously. The e-cigarette group consumed significantly more energy drinks according to our research and similar patterns have been observed in other studies. The research by Falbová et al. (2018) showed that young adults who smoked had higher consumption of energy drinks, alcohol, and coffee while engaging in less physical activity [5]. The combination of behaviors that include consuming high-calorie sugary drinks and being sedentary may result in weight gain and increased body fat, which opposes the immediate appetite-suppressing effects of nicotine. Young people commonly believe that nicotine serves as a weight management tool. Research shows that overweight individuals tend to use e-cigarettes due to the belief that these devices will help them maintain their weight [13]. Young people who use e-cigarettes and people who smoke cigarettes demonstrate paradoxically higher BMI and body fat, according to multiple studies—including ours—despite their weight-control intentions. The short-term appetite suppression from nicotine appears to be outmatched by metabolic changes and compensatory behaviors such as increased snacking or sugary drink consumption. The observed weight gain following smoking cessation in clinical settings also occurs when people use e-cigarettes as cessation aids because nicotine replacement through using e-cigarettes does not fully duplicate all metabolic effects of smoking [15].

Chronic nicotine exposure creates conditions that lead to undesirable fat distribution patterns and metabolic problems even though it suppresses appetite. The combination of insulin resistance and elevated circulating cortisol levels caused by nicotine leads to increased visceral fat accumulation and dyslipidemia [16]. Research shows that young people who smoke cigarettes possess more visceral adipose tissue than people who have never used nicotine products who have the same BMI [8], and males who use e-cigarettes in this study had elevated triglyceride levels compared to people who have never used nicotine products [13]. The observed changes lead to an increased “metabolic age”, which indicates that the body functions older than its actual age when measuring basal metabolic rate and fat storage. The elevated metabolic age in people who use e-cigarettes indicates early signs of metabolic changes, including metabolic slowdown and reduced lean body mass compared to fat mass. These changes will eventually raise the probability of developing metabolic syndrome and cardiovascular disease. The study needs to consider the social environment through which youth consume e-cigarettes. The widespread use of e-cigarettes among university students stems from their belief that these devices are safer than traditional cigarettes, as well as their social approval and digital marketing strategies [17–19]. The mentioned factors tend to support patterns of use that combine with additional risky behaviors, including excessive energy drink consumption and inactive

lifestyles [20–23]. Future research needs to use objective biomarkers such as cortisol and lipid profiles, inflammatory markers, and insulin resistance indices to fully understand metabolic dysregulation in people who use nicotine. Wearable devices that track physical activity and sleep patterns should be integrated to improve the precision of lifestyle data analysis for body composition results.

Our research expands existing studies that demonstrate that both smoking and using e-cigarettes create negative impacts on body composition and metabolic indicators among young individuals. The weight-suppressive effects of smoking observed in older adults do not apply to college-aged and adolescent populations according to this study and other research in these age groups. The study shows that people who use nicotine among young people tend to have increased body fat while maintaining their BMI levels and developing preliminary signs of metabolic problems. The e-cigarette group demonstrated higher adiposity and metabolic age, which suggests that using e-cigarettes may not be metabolically neutral, although causality cannot be inferred from the data. The risks using e-cigarettes pose to obesity-related conditions match or surpass those associated with traditional tobacco use. These findings demonstrate the necessity for additional research into how new nicotine delivery systems affect students' physical health and support public health warnings that both smoking and using e-cigarettes are ineffective for weight control and body composition maintenance. The study provides vital information to campus health programs by showing that using e-cigarette intervention programs must address dietary and lifestyle factors that lead to excessive body fat among students. A detailed understanding of weight and metabolic health effects between people who use nicotine and people who have never used nicotine products among young adults is essential for creating effective prevention measures and disproving the misconception that using e-cigarettes has no negative impact on weight or metabolic health.

The research contains several limitations that need to be recognized. The cross-sectional study design makes it impossible to determine how smoking behaviors affect metabolic results. The study found associations between using e-cigarettes and increased body fat and metabolic age, but it does not show whether using e-cigarettes caused these changes or if people with poor body composition were more likely to use them. Additional longitudinal research is needed to determine the exact cause-and-effect relationship between these observed effects. The study's findings have limited general applicability because it included a small group of biomedical engineering students from one technical university. The study results might not represent the entire population because they do not capture diverse socioeconomic groups and do not show how gender influences nicotine and lifestyle responses. Although biochemical markers of nicotine exposure were not collected, we attempted to control for exposure consistency by excluding people who use nicotine occasionally and quantifying daily session frequency through a standardized questionnaire. BIA provides a non-invasive body composition assessment, but its accuracy falls short of DEXA or MRI imaging techniques, especially when measuring visceral adipose tissue. BIA-derived metabolic age serves as a useful measure of physiological condition yet it represents a calculated value that does not measure actual metabolic function. The self-reported data from questionnaires about lifestyle habits contains potential biases from recall errors and social desirability biases. The accuracy of specific variables might be affected by these limitations especially when people fail to report their unhealthy behaviors. Another important limitation is the relatively small sample size ($N = 60$), which may limit the generalizability and statistical power of the findings. The modest number of participants may reduce the ability to detect subtle effects or interactions and limit the extent to which results can be extrapolated to broader populations. The machine learning models used for classification faced restrictions because of the dataset's limited size and structure.

The identified predictive patterns were limited by both the number of input variables and the class distribution, which resulted in modest model performance. Future research needs to analyze bigger datasets with diverse populations to enhance both predictive accuracy and model robustness.

5. Conclusions

This study provides new evidence regarding the differences in body composition and metabolic profiles among young adults who use e-cigarettes compared to those who do not use nicotine products. Participants who used e-cigarettes demonstrated higher body fat percentage, BMI, and metabolic age relative to individuals who reported no history of nicotine use. These differences were not observed among people who smoke cigarettes compared to people who have never used nicotine products. Additionally, people who use e-cigarettes reported higher energy drink consumption, which was positively associated with indicators of increased adiposity and metabolic age. These findings highlight potential patterns of co-occurring lifestyle behaviors that may be important in understanding overall metabolic risk.

The best performing machine learning model that used *k*-nearest neighbors achieved 72.2% accuracy in differentiating between people who use nicotine and people who have never used nicotine products using physiological and lifestyle characteristics, although the models demonstrated moderate accuracy. The metabolic differences detected between people who use nicotine and people who have never used nicotine products were not fully explained by the model, which raises the possibility of behavioral hormonal or genetic factors as contributors to these differences.

Our findings highlight the need to further explore the potential relationships between e-cigarette use and indicators of metabolic health in young adults. The results suggest that e-cigarette use may be associated with differences in body composition and metabolic profiles that resemble or exceed those observed in people who smoke cigarettes. However, given the cross-sectional and observational nature of the study, no conclusions can be drawn regarding the direction or causality of these associations. Public health discussions around nicotine use should consider the broader set of lifestyle factors that tend to co-occur with e-cigarette use, rather than framing these products as metabolically safer alternatives. These findings contribute to the growing body of literature examining the health correlates of nicotine use in young populations and underscore the importance of further research and preventive efforts targeting overall health behaviors.

Given the study's cross-sectional design, it is not possible to determine the temporal order of nicotine use and metabolic differences, and the observed associations may be influenced by unmeasured or insufficiently adjusted confounding factors, particularly the strong imbalance in sex distribution between groups, as well as other variables such as socioeconomic status, dietary patterns, or stress. Therefore, we do not interpret these findings as evidence for the causal effects of e-cigarette use on metabolic health. Instead, they should be viewed as a basis for generating hypotheses to be tested in future longitudinal and experimental studies that can better clarify the directionality and mechanisms underlying these associations.

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POSTURAL CONTROL AND GAIT ALTERATIONS IN YOUNG ADULT TOBACCO AND E-CIGARETTE USERS: A COMPARATIVE STABILOMETRIC AND TREADMILL-BASED ANALYSIS

The research investigates how tobacco and electronic cigarette (e-cigarette) consumption affects postural control and walking patterns in young adult populations. The study included 60 participants who were divided into three groups of 20 each: non-smokers and traditional smokers and e-cigarette users. The participants completed stabilometric tests under static conditions with eyes open and closed while undergoing treadmill-based dynamic gait analysis. The researchers used parametric or non-parametric statistical tests together with Spearman's correlation and principal component analysis (PCA) and supervised machine learning classifiers to analyze biomechanical features. The study revealed substantial differences between non-smokers and e-cigarette users regarding body mass index (BMI) and foot force distribution and walking speed and step length measurements. Correlation analysis revealed strong associations between center of pressure dynamics and plantar pressure distribution, with group-specific interaction patterns. PCA demonstrated partial group separation, especially for non-smokers versus e-cigarette users. Machine learning models, especially logistic regression, achieved the highest classification accuracy (up to 82.8%) in distinguishing non-smokers from e-cigarette users. These findings suggest that habitual use of tobacco or e-cigarettes may influence balance and locomotor control in subtle but measurable ways, with potential implications for neuromuscular health monitoring in young populations.

Keywords: postural stability, e-cigarettes, tobacco use, gait analysis, stabilometry, young adults, machine learning, PCA.

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КОНТРОЛЬ ПОЗИ ТА ЗМІНИ ХОДИ У МОЛОДИХ ДОРΟΣЛИХ КОРИСТУВАЧІВ ТЮТЮНУ ТА ЕЛЕКТРОННИХ СИГАРЕТ: ПОРІВНЯЛЬНИЙ АНАЛІЗ СТАБІЛОМЕТРИЇ ТА ХОДИ НА БІГОВІЙ ДОРОЖЦІ

Дослідження вивчає вплив вживання тютюну та електронних сигарет (e-сигарет) на контроль пози та особливості ходи у молодих дорослих. У дослідженні взяли участь 60 осіб, яких розподілили на три групи по 20: некурючі, курючі традиційні сигарети та користувачі електронних сигарет.

Учасники виконували стабілометричні тести у статичних умовах із закритими та відкритими очима, а також проходили динамічний аналіз ходи на біговій дорожці. Для аналізу біомеханічних показників дослідники застосували параметричні та непараметричні статистичні тести, кореляцію Спирмена, метод головних компонентів (PCA) та контрольовані класифікатори величезного виміру. Дослідження виявило значні відмінності між некурючими та користувачами електронних сигарет за індексом маси тіла (ІМТ), розподілом сили стопи, швидкістю ходи та довжиною кроку. Кореляційний аналіз

показав піки змін швидкості центру тяжкості та розподілом плантарного тиску, з характерними для кожної групи податками кожен раз. PCA продемонстрував чіткіше розділення груп, особливо між нерегульними та регулярними в-сигарет.

Модель максимального навантаження, зокрема постійного розподілу, досягла найвищої точності класифікації (до 82,8%) у розмежуванні нерегулярної та регулярної вимірювання сигарет. Ці результати свідчать, що регулярне вживання тютюну або в-сигарет може впливати на баланс та контроль рухів у тандемі, але невизначеною є можливість, що це має потенціальне значення для моніторингу нейронного здоров'я мозку.

Ключові слова: поструральна стабільність, в-сигарети, вживання тютюну, аналіз коду, стабілометрия, метод даних машинного навчання, PCA.

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1. INTRODUCTION

Postural control and human gait are governed by complex neurophysiological mechanisms that integrate sensory inputs and coordinate motor outputs. The ability to maintain body center of mass over base of support depends on multiple systems working together [1,2]. The brain receives body position and movement information through three main sensory modalities which include vision from the visual system and balance information from the vestibular system and proprioceptive feedback from the somatosensory system. The central nervous system tracks these inputs to identify postural instability which leads to corrective responses. Key neural structures are involved in processing this sensory information and maintaining balance: for example, vestibular signals travel to the brainstem and cerebellum to help orient the body upright, while proprioceptive and visual cues are integrated in the cerebellum and cortex to fine-tune posture [3]. Maintaining an upright stance thus depends on dynamic sensory reweighting, where the relative contribution of vision, vestibular, and proprioception can shift depending on conditions (e.g. standing in the dark increases reliance on vestibular/proprioception) [3,4]. Ultimately, motor commands to postural muscles (especially in the legs and trunk) are adjusted via spinal and brainstem pathways to keep the center of pressure within the base of support [5].

Walking (locomotion) builds upon this postural control foundation, adding rhythmic leg movement and forward propulsion. Human gait is generated by neural circuits known as central pattern generators (CPGs) in the spinal cord, which can produce the basic alternating flexion-extension pattern of the legs even without conscious thought. These spinal locomotor networks provide an automatic, rhythmic stepping ability – essentially the “stepping reflex” that underlies walking. In intact humans, however, gait is normally modulated by supraspinal centers. Descending pathways from the brainstem – particularly reticulospinal tracts arising from the mesopontine tegmentum (in the region of the midbrain locomotor centers) – activate and coordinate the spinal CPGs and associated postural reflexes. This automatic gait control through brainstem and spinal circuits ensures basic stepping motion, appropriate muscle tone, and reflexive adjustments (like keeping the head and eyes stable via vestibulo-ocular reflexes) during steady-state walking [3,6]. On the other hand, higher-level control from the cerebral cortex is engaged when navigating novel or complex environments. Walking in an unfamiliar situation or performing precise movements requires cognitive postural control: the brain must incorporate a “body schema” (awareness of body position in space) and plan movements accordingly [7]. Cortical motor areas generate anticipatory postural adjustments – subtle shifts in weight or posture that prepare the body for an intended movement (for example, shifting weight before lifting a foot) [8]. The cerebellum and basal ganglia play critical modulatory roles in these processes by linking with both brainstem and cortical centers. The cerebellum helps calibrate and coordinate movements, ensuring smooth gait and balance, while the basal ganglia contribute to the initiation and automaticity of gait patterns [5,7]. In summary, normal gait and posture emerge from an interplay between automatic neural processes (spinal and brainstem circuits handling rhythm and basic balance) and cognitive processes (cortical supervision for adaptation and goal-directed movement). This multilayered control system allows healthy young adults to maintain stability and walk efficiently under most conditions, with a reserve capacity to adjust when terrain or task demands change. Any disruption to these neural mechanisms – whether by neurological disease or potentially by exogenous substances – can impair balance and gait.

The complex neurophysiological processes of the body create a situation where minor nervous system disruptions result in noticeable problems with balance and gait. Tobacco smoking represents a disturbance that could produce neuromotor effects. The body absorbs nicotine and multiple other substances from cigarette smoke which eventually modifies neural system operations [9,10]. Nicotine binds to nicotinic acetylcholine receptors that exist throughout the brain and peripheral nervous system including those regions that control motor coordination. Research shows that nicotine causes balance problems because it affects cholinergic neurons which run through vestibular and motor pathways [9,11,12]. Acute nicotine exposure to people who do not regularly use the substance leads to temporary vestibular problems (nystagmus, dizziness, unsteadiness) which demonstrate how the drug affects inner ear and brainstem balance centers [9,10]. The use of cigarettes over time has been proven to cause permanent damage to postural stability. A research study using posturography methods demonstrated that smokers displayed larger body movements when their eyes were closed compared to non-smokers thus showing reduced balance stability. The study showed that smoking intensity directly affected the results and the effect remained consistent after researchers eliminated age- and other confounding variables. The authors established that smoking causes permanent damage to

the postural control system [13]. Research shows that prolonged smoking damages both vestibular function and proprioception which raises the chances of experiencing balance problems and falling incidents [14]. The gait of smokers shows subtle impairments when compared to non-smokers because they walk more slowly and take shorter steps [15].

The alternative nicotine delivery system known as electronic cigarettes (e-cigarettes) has appeared during the last decade to generate concerns about their nervous system effects compared to traditional tobacco products. The aerosolized delivery of nicotine through e-cigarettes eliminates combustion-based toxins like carbon monoxide and tar yet users still encounter nicotine along with propylene glycol, glycerol, flavor chemicals and trace metals from the device. Nicotine itself remains a concern for neurophysiological health. Similar to smoking, e-cigarette use (or “vaping”) can acutely cause sympathetic stimulation and vasoconstriction, potentially affecting cerebral and muscular blood flow [16,17]. Nicotine’s known effects on the adolescent and young adult brain include altered synaptic development, which can impair cognitive functions, and it stands to reason that motor circuits could likewise be affected [18]. Indeed, recent reviews caution that nicotine from e-cigarettes can disrupt brain maturation in adolescents and young adults [19]. While direct research on posture and gait in e-cigarette users is still limited, any nicotine-containing product may influence the fine balance of neuromotor control. For instance, case observations suggest that vaping has similar acute cardiovascular effects as smoking (e.g. transiently elevated heart rate and blood pressure), which over time could translate into vascular changes affecting muscle function and balance [20]. Moreover, some preliminary data indicate that the toxins in e-cigarette vapor (including nicotine and certain flavoring chemicals) might have neurotoxic effects analogous to those of cigarette smoke [21]. However, because e-cigarettes lack many of the combustion byproducts of tobacco, it is hypothesized that their impact on postural control may be less pronounced than that of traditional cigarettes – a hypothesis that needs empirical validation.

The research on smoking and vaping effects on postural control and gait in young adults holds significant importance for multiple reasons. Young adults experience their best sensorimotor performance and resilience during this life stage. Any deficits detected in balance or gait among young smokers or vapers would indicate an early departure from optimal neurological function, raising concerns about longer-term consequences. The second important factor is that nicotine use is very common in this age group. The epidemiological data show that the consumption of nicotine products (either cigarettes or e-cigarettes) is widespread among young people. For instance, in Poland, about 45% of university students have tried e-cigarettes and about 13% are current smokers [22]. The prevalence of vaping in the United States in 2021 was more than ten times higher in young adults than in older adults [23]. The growing popularity of e-cigarettes among youth and young adults has created a population that faces high levels of nicotine exposure through this innovative delivery method. The established health risks of smoking for cardiovascular and nervous system health exist but the permanent effects of e-cigarettes remain uncertain. The current young adult population represents the first generation to experience vaping from adolescence through early adulthood so researchers need to determine any motor control impairments affecting this group. Such knowledge can be used to inform public health interventions, especially since balance and gait issues in young people could translate into safety risks (sports injuries, accidents) and may foreshadow more serious neurological problems later in life. Given these factors, the present study was conducted to compare postural stability and gait in young adult traditional smokers and e-cigarette users, with the aim of determining whether nicotine use is associated with measurable motor control alterations in this high-use age demographic.

2. MATERIALS AND METHODS

To comprehensively assess the impact of tobacco and e-cigarette use on postural and locomotor function, a multimodal biomechanical evaluation was employed. The study combined static measurements under static conditions and treadmill-based gait assessments to capture both balance and dynamic walking characteristics. All procedures were carried out in accordance with ethical standards, and detailed methodological steps are outlined below.

2.1. Study Design and Data Collection

The present study was conducted to investigate potential biomechanical differences in postural stability and gait parameters among individuals with different smoking habits. The research aimed to evaluate non-smokers and users of electronic cigarettes and traditional tobacco smokers through both stationary and active movement assessments. The study participants come from the Faculty of Biomedical Engineering at the Silesian University of Technology in Gliwice, Poland during the 2024/2025 academic year. The researchers selected participants through convenience sampling methods. The study required participants to be at least 18 years old and to sign an informed consent form before starting the research. The Ethics Committee for Research Involving Human Participants at the Silesian University of Technology approved the study protocol through Resolution No. 3/2025 on March 11, 2025.

Smoking status was self-reported, and based on these declarations, individuals were classified into one of three experimental groups: N – non-smokers, E – electronic cigarette users, T – traditional cigarette smokers. No biochemical verification (e.g., cotinine or CO measurement) was performed. All measurements were carried out under controlled laboratory conditions using a Zebris Medical GmbH pressure-sensing platform and treadmill-based gait analysis system (Isny, Germany). Participants completed three standardized test conditions:

- Static balance with open eyes – upright stance on the platform with visual input maintained by fixating on a point at eye level.
- Static balance with closed eyes – the same stance was repeated with eyes closed to eliminate visual input.
- Treadmill gait – barefoot walking at a comfortable, self-selected pace over a Zebris treadmill for 6 minutes, at least 10 consecutive gait cycles.

Measurements were acquired using Zebris WinFDM and FDM-T software and exported to Excel format. Data from each testing condition were stored in separate worksheets within a single file. Group classification was automated by parsing participant IDs in a column for substrings `_E_`, `_T_`, or neither. Testing was performed in a standardized environment with controlled temperature and lighting. All sessions were supervised by trained personnel using consistent procedural instructions to ensure uniformity.

2.2. Preprocessing and Grouping

Initial data preprocessing was performed in MATLAB R2024a (The MathWorks Inc, Natick, MA, USA). Raw datasets were imported from the three worksheets (“Eyes open”, “Eyes closed”, and “Treadmill”) contained in the source Excel file. Each worksheet represented one of the experimental conditions, and each row corresponded to a single participant’s trial.

Participants were identified using alphanumeric IDs contained in the “`name`” column. Group assignment was automated based on predefined string patterns:

- IDs containing `_T_` were classified as traditional cigarette smokers.
- IDs with `_E_` indicated electronic cigarette users.
- all remaining IDs were classified as non-smokers (group “N”).

For each worksheet, numeric variables were extracted using MATLAB’s `varfun(@isnumeric)` function, ensuring the selection of only continuous biomechanical features. Variables included pressure distribution metrics, postural sway characteristics (in the static trials), and spatiotemporal gait parameters (in the treadmill condition). Missing values (NaNs) were identified and excluded on a per-variable basis to preserve statistical power while minimizing data loss. Data were normalized using z-score transformation (`normalize` function in MATLAB) before further statistical analysis and machine learning. All preprocessing steps were standardized and scripted to ensure reproducibility across the three experimental conditions.

2.3. Statistical Analysis

To assess data suitability for parametric statistical testing, statistical comparisons between the three study groups (N, E, T) were performed separately for each experimental condition. Normality of data distribution within each group was assessed using the Jarque-Bera test (significance level $\alpha = 0.05$). Depending on the test outcome, either a one-way ANOVA (for normally distributed data) or a Kruskal-Wallis H-test (for non-normal data) was used to assess overall group differences. When the main test indicated statistically significant differences ($p < 0.05$), pairwise post-hoc comparisons were conducted using Bonferroni correction to control for multiple testing. The type of test applied (parametric vs. non-parametric) was recorded for each variable.

All analyses were performed independently for each of the three data sheets (open eyes, closed eyes, treadmill), allowing for condition-specific interpretation of group differences. Test results were recorded programmatically and visualized using boxplots for each significant variable.

2.4. Correlation Analysis

To explore interrelationships among biomechanical variables, pairwise Spearman’s rank correlation coefficients were computed for all numeric features. Correlations were calculated in two contexts: (1) across the entire dataset for each condition, and (2) separately within each experimental group (N, E, T). This allowed for both global and group-specific patterns of association to be identified. For each variable pair, the correlation coefficient (ρ) and its corresponding p-value were recorded. Correlations were considered statistically significant at $p < 0.05$. Strong correlations were defined as those with $|\rho| > 0.5$. The resulting correlation matrices were visualized using color-coded heatmaps.

2.5. Dimensionality Reduction

Principal Component Analysis (PCA) was used to reduce the dimensionality of the dataset and to visualize the distribution of participants across groups based on multivariate biomechanical features. PCA was applied separately to each condition (open eyes, closed eyes, treadmill), using all standardized numeric variables. Prior to PCA, each variable was normalized using z-score transformation. The first two principal components (PC1 and PC2) were retained and used for two-dimensional scatter plots, with participants color-coded according to group assignment (N, E, T). These plots provided an unsupervised view of potential clustering or overlap between groups.

2.6. Feature Selection and Classification

To identify variables most relevant for distinguishing between participant groups, the RELIEFF algorithm was applied to the N vs. E binary subset. RELIEFF estimates the importance of each feature based on its ability to separate instances from different classes within local neighborhoods. Features were ranked by their assigned weights, and the top 5 were retained for further analysis. Classification models were trained using four commonly applied

supervised learning algorithms: decision tree, linear support vector machine (SVM), k-nearest neighbors ($k = 5$), and logistic regression.

Models were implemented in MATLAB using the Classification Learner framework and trained with 5-fold cross-validation. Performance was evaluated based on classification accuracy. Two types of classification were conducted:

1. Multiclass classification – differentiating between all three groups (N, E, T).
2. Binary classification – comparing each pair of groups separately: N vs E, N vs T, and E vs T.

Feature selection and classification procedures were performed independently for each of the three experimental conditions.

2.7. Confusion Matrix Visualization

To illustrate the performance of the classification models in the binary comparisons, confusion matrices were generated for each group pair (N vs E, N vs T, and E vs T). For each comparison, the classifier achieving the highest cross-validated accuracy was selected. Confusion matrices provided a visual summary of true positives, true negatives, false positives, and false negatives for the selected model, allowing for an intuitive assessment of classification reliability. The matrices were displayed using color-coded charts, with actual class labels on the vertical axis and predicted labels on the horizontal axis. This visualization step supported interpretation of classification outcomes, particularly in cases where accuracy alone may not reflect class-specific performance (e.g., in the presence of class imbalance).

3. RESULTS

A total of 60 participants (20 per group) were included in the final analysis, based on the ID parsing and self-declared tobacco use status. Median age was comparable across groups, with a total sample median of 22.0 years (interquartile range [IQR]: 2.25). Traditional smokers tended to be taller (median 176.5 cm) than e-cigarette users (170.0 cm) and non-smokers (171.5 cm). Body weight was slightly higher in tobacco users, while BMI values varied more distinctly between groups. The highest median BMI was observed among e-cigarette users (23.4 kg/m²), whereas non-smokers had the lowest (21.05 kg/m²). The distribution of sex differed across groups: overall, 41.7% of participants were male and 58.3% female. Traditional smokers had the highest proportion of males (58.3%), while e-cigarette users had the lowest (16.7%). In contrast, 83.3% of e-cigarette users were female, compared to 41.7% in the smoker and non-smoker groups. These intergroup differences in anthropometric parameters were subsequently evaluated using nonparametric statistical tests. All participants completed the three test conditions: open eyes (static balance), closed eyes (static balance), and treadmill gait. No participants were excluded due to missing or corrupted data. Each test condition yielded a distinct set of numerical features. Static balance trials (open and closed eyes) included parameters related to center of pressure (COP) displacement, sway path, and foot loading distribution. The treadmill condition included additional dynamic gait parameters such as stride length, cadence, gait speed, and peak plantar pressures.

Statistical comparisons between the three groups (N, E, T) were conducted separately for each numeric variable recorded during the treadmill walking task. Depending on the distribution characteristics (as assessed via the Jarque-Bera test), either one-way ANOVA or the Kruskal-Wallis test was applied. Out of the full set of gait parameters, 5 variables showed statistically significant differences between groups ($p < 0.05$) (Table 1). Pairwise post-hoc comparisons with Bonferroni correction revealed that the most prominent differences were observed between the non-smoker group (N) and electronic cigarette users (E), particularly in walking speed and step length parameters.

In the closed-eyes static balance trial (Table 1), group differences were analyzed using Kruskal-Wallis or ANOVA depending on the distribution of each variable. Among the evaluated parameters, Body Mass Index (BMI) and medio-lateral postural sway (Y-axis deviation) showed notable between-group differences. Pairwise post-hoc comparisons revealed a statistically significant difference in BMI between non-smokers and electronic cigarette users. Differences in sway (Deviation Y) were not statistically significant after correction, although a trend toward higher instability in e-cigarette users was observed.

In the open eyes static balance trial (Table 1), several parameters were analyzed for group differences using Kruskal-Wallis or ANOVA tests. Significant differences were found in the force distribution under the left forefoot and left backfoot. Post-hoc pairwise comparisons revealed that traditional cigarette users (T) exhibited higher force under both the left forefoot and left backfoot compared to non-smokers (N). However, no significant differences were observed between e-cigarette users (E) and non-smokers in these variables.

Boxplots were generated for key variables showing significant differences between the groups. These plots visually depict the distribution of the variables for non-smokers (N), electronic cigarette users (E), and traditional cigarette smokers (T). The whiskers represent the data range, while the horizontal lines inside the boxes represent the median values. Group comparisons reveal how the distribution of values differs across conditions.

Table 1.
Post-hoc pairwise comparisons for all conditions. Dashes (—) indicate that the pairwise comparison was not among the lowest p-values

Variable	Test Used	N vs. E	N vs. T	E vs. T
Body Mass Index (BMI)	Kruskal-Wallis	0.001	0.323	0.218
Force under Left Forefoot (N)	ANOVA	0.474	0.037	0.001
Force under Left Backfoot (N)	ANOVA	0.389	0.033	0.066
Gait Cycle Duration (s)	Kruskal-Wallis	0.012	—	0.282
Max Force – Forefoot Left (N)	Kruskal-Wallis	0.067	—	0.116
Max Force – Forefoot Right (N)	Kruskal-Wallis	0.055	—	0.148
Max Load – Hindfoot Left (N)	Kruskal-Wallis	—	0.042	0.081
Max Load – Backfoot Right (N)	Kruskal-Wallis	0.023	0.071	—
Step Length – Min (cm)	ANOVA	0.005	0.155	0.071
Average Max. Load – Forefoot Left (N)	Kruskal-Wallis	0.047	—	0.118
Step Length (Right, cm)	ANOVA	0.003	0.125	0.236

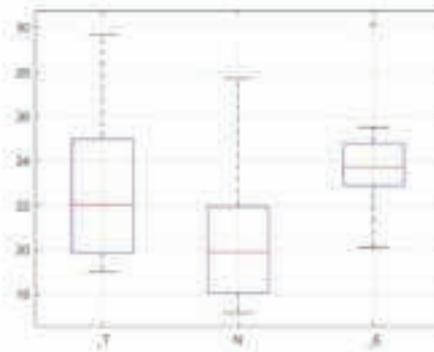


Fig. 1. Boxplot for Body Mass Index (BMI)

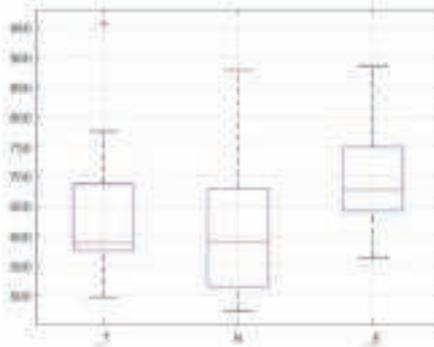


Fig. 2. Boxplot for Force under Left Forefoot

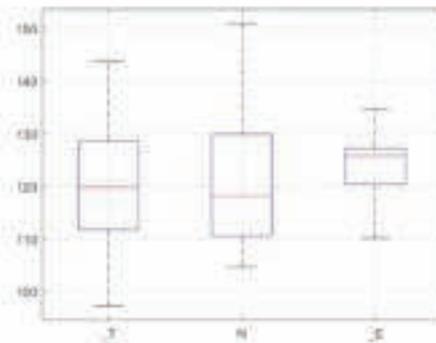


Fig. 3. Boxplot for Step Length

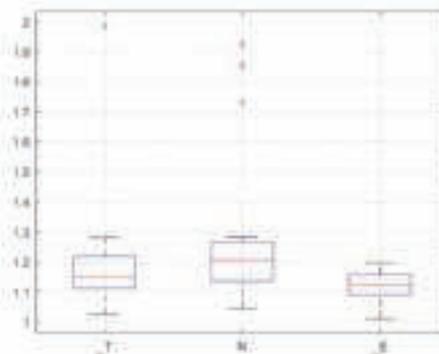


Fig. 4. Boxplot for Gait Cycle Duration

To investigate interrelationships among stabilometric and anthropometric variables, Spearman's rank correlation analysis was performed for the open eyes condition. The global analysis across all participants revealed a number of strong and statistically significant associations. Extremely high inverse correlations ($r = -1.00$, $p < 0.0001$) were observed between left and right foot regions (e.g., ForceLeftForefoot vs ForceLeftBackfoot, ForceRightForefoot vs ForceRightBackfoot), as well as between total force under the left and right feet. A nearly perfect positive correlation was also present between the center of pressure (COP) path length and its average velocity ($r = 0.99$, $p < 0.0001$), highlighting the biomechanical coherence of these measures. Measures of postural sway geometry, such as the 95% confidence ellipse area, showed strong correlations with both the length of the major and minor axes ($r > 0.80$, $p < 0.0001$), indicating a close relationship between overall sway amplitude and its directional components. Similarly, medial-lateral deviation of the center of pressure (DeviationY) correlated strongly with right foot force distribution (e.g., $r = 0.77$ for ForceRightForefoot and $r = -0.77$ for ForceRightBackfoot, $p < 0.0001$).

When analyzed separately by group, distinctive patterns emerged. In non-smokers, BMI negatively correlated with postural sway measures, including COP path length ($r = -0.78$, $p = 0.0009$) and COP average velocity ($r = -0.76$, $p = 0.0010$). The area of the 95% confidence ellipse also correlated positively with its major axis and minor axis ($r = 0.87$, $p < 0.0001$). In the e-cigarette group, BMI was significantly associated with force asymmetry, particularly lower pressure under the right forefoot and increased load on the backfoot. Deviation metrics were also tightly coupled with foot pressure values ($r = \pm 0.69$). In traditional smokers, body weight showed strong negative correlations with sway area and major axis length ($r = -0.86$ and -0.77 , respectively), while positive associations were found between height and foot force parameters. COP-related variables, such as path length and velocity, remained strongly correlated ($r = 0.97$), consistent with global findings. These results underscore the biomechanical interdependence of sway geometry and plantar pressure distribution, as well as group-specific patterns in how anthropometric factors modulate postural control. The top 10 correlations globally are summarized in Table 2.

Table 2.

Top 10 global Spearman correlations (Open Eyes Condition)			
Variable 1	Variable 2	r	p-value
Force – Left Forefoot [N]	Force – Left Backfoot [N]	-1.00	< 0.0001
Force – Right Forefoot [N]	Force – Right Backfoot [N]	-1.00	< 0.0001
Total Force – Left [N]	Total Force – Right [N]	-0.999	< 1e-50
COP Path Length [mm]	COP Average Velocity [mm/s]	0.983	< 1e-50
95% Confidence Ellipse Area [mm ²]	Length of Minor Axis [mm]	0.833	< 1e-10
95% Confidence Ellipse Area [mm ²]	Length of Major Axis [mm]	0.805	< 1e-10
COP Deviation Y [mm]	Force – Right Forefoot [N]	0.771	1.2e-09
COP Deviation Y [mm]	Force – Right Backfoot [N]	-0.771	1.2e-09
Force – Left Forefoot [N]	Force – Right Forefoot [N]	0.717	9.4e-08
Force – Left Forefoot [N]	Force – Right Backfoot [N]	-0.717	9.4e-08

To illustrate the structure of intervariable relationships in the open eyes condition, two complementary visualization methods were applied: a heatmap of Spearman's correlation matrix for each group and a correlation network graph. These tools enable the detection of clusters of co-varying features and provide a global view of the biomechanical interplay between sway parameters and plantar force distribution. Strong positive (blue) and negative (yellow) correlations are observed in symmetry-related force variables and center of pressure metrics on a heatmap (Figure 5-7). The matrix highlights patterns such as the inverse coupling of left/right plantar regions and the proportionality between sway amplitude and ellipse dimensions. Nodes on a correlation network graph (Figure 8) represent individual biomechanical variables, while edges indicate statistically significant high correlations (edge thickness reflects r strength). The graph illustrates modular groupings of variables linked to postural geometry, force symmetry, and sway velocity.

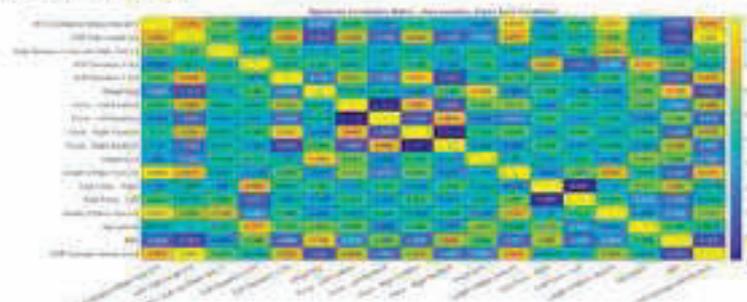


Fig. 5. Heatmap of Spearman's correlation coefficients for 20 most important numerical variables in the Open Eyes Condition (Non-studies)

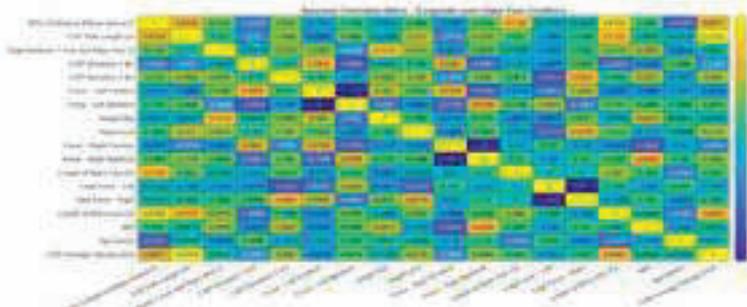


Fig. 6. Heatmap of Spearman's correlation coefficients for 20 most important numerical variables in the Open Eyes Condition (E-ergotic users)

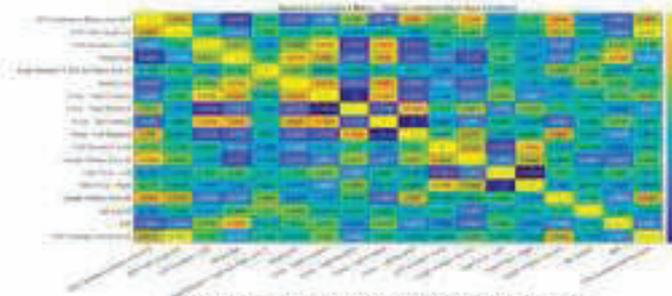


Fig. 7. Heatmap of Spearman's correlation coefficients for 20 most important numerical variables in the Open Eyes Condition (Tobacco smokers)

To explore the interrelationships between stabilometric and anthropometric variables under the closed eyes condition, Spearman's rank correlation analysis was conducted across the entire study population ($N = 60$). The global correlation matrix revealed a number of statistically significant and biomechanically relevant associations. The most pronounced relationships ($|r| \geq 0.80$, $p < 0.0001$) were observed between force distribution parameters and postural sway metrics. Perfect inverse correlations ($r = -1.00$) occurred between opposing plantar regions (e.g., Force - Left Forefoot [N] vs Force - Left Backfoot [N], Force - Right Forefoot [N] vs Force - Right Backfoot [N]), as well as between total force under the left and right limbs (Total Force - Left [N] vs Total Force - Right [N]). A nearly perfect direct association ($r = 0.98$, $p < 0.0001$) was again noted between COP path length and average velocity, consistent with results observed in the open eyes condition.

Other notable findings included very strong correlations between the 95% confidence ellipse area and both the length of the minor ($r = 0.94$) and major ($r = 0.86$) axes, indicating that the sway amplitude scales proportionally in both directions. Deviation metrics in the mediolateral plane (COP Deviation Y [mm]) were significantly related to plantar force values, particularly under the right forefoot and backfoot. The top 10 most significant correlations identified globally in this condition are summarized in Table 3.

To further investigate group-specific stabilometric patterns, separate correlation heatmaps were generated for non-smokers (N), e-cigarette users (E), and traditional smokers (T). These visualizations, presented in Figure 8-10, revealed distinct inter-variable dependencies in each group, particularly regarding how body mass index (BMI) and deviation metrics modulated foot pressure and sway geometry.

Table 3.

Top 10 global Spearman correlations (Closed Eyes Condition)			
Variable 1	Variable 2	r	p-value
Force - Left Forefoot [N]	Force - Left Backfoot [N]	-1.00	< 0.0001
Force - Right Forefoot [N]	Force - Right Backfoot [N]	-1.00	< 0.0001
Total Force - Left [N]	Total Force - Right [N]	-0.999	< 1e-50
COP Path Length [mm]	COP Average Velocity [mm/s]	0.985	< 1e-50
95% Confidence Ellipse Area [mm²]	Length of Minor Axis [mm]	0.813	< 1e-10
95% Confidence Ellipse Area [mm²]	Length of Major Axis [mm]	0.805	< 1e-10
COP Deviation Y [mm]	Force - Right Forefoot [N]	0.771	2.2e-09
COP Deviation Y [mm]	Force - Right Backfoot [N]	-0.771	2.2e-09
Force - Left Forefoot [N]	Force - Right Backfoot [N]	0.717	9.4e-08
Force - Left Backfoot [N]	Force - Right Forefoot [N]	-0.717	9.4e-08

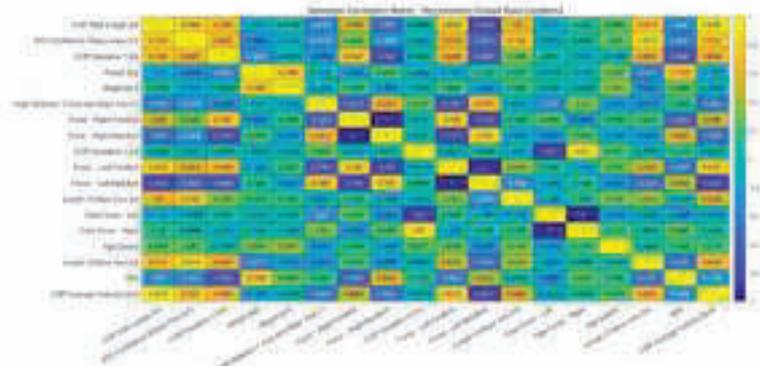


Fig. 8. Heatmap of Spearman's correlation coefficients for 20 most important numerical variables in the Closed Eyes Condition (Non-smokers)



Fig. 9. Heatmap of Spearman's correlation coefficients for 20 most important numerical variables in the Closed Eyes Condition (Cigarette users)

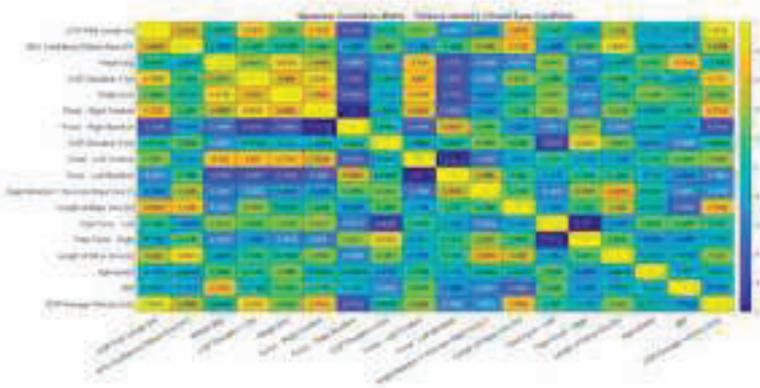


Fig. 10. Heatmap of Spearman's correlation coefficients for 20 most important numerical variables in the Closed Eyes Condition (Tobacco smokers)

To investigate interrelationships among gait and pressure distribution parameters, Spearman's rank correlation analysis was conducted for the treadmill condition using the full sample ($N = 60$). The global analysis

(Table 4) revealed a number of strong, statistically significant associations ($|r| > 0.70$, $p < 0.001$). Perfect or near-perfect correlations were observed between biomechanically related variables such as forefoot and backfoot forces on the same foot (e.g. ForceLeftForefoot vs ForceLeftBackfoot, $r = -1.00$), as well as total forces between the left and right foot ($r = -0.999$). Gait cycle time was positively correlated with step length ($r = 0.81$) and negatively with walking speed ($r = -0.86$), reflecting expected temporal-spatial dependencies. Measures of maximum pressure and maximum force in corresponding foot zones also demonstrated high internal consistency ($r > 0.8$).

Separate analyses by group revealed partially distinct correlation profiles. In non-smokers, stride-related variables such as walking speed and step length were tightly correlated with body composition indices (e.g. BMI vs speed; $r = -0.66$). E-cigarette users showed a pattern of reduced gait symmetry, with notable asymmetries between left and right force distributions. In contrast, traditional smokers demonstrated more homogeneous force correlations but weaker associations with anthropometric variables. These differences suggest group-specific adaptations in gait biomechanics, possibly modulated by lifestyle-related physiological factors. Heatmaps of Spearman correlations are provided for each group (N, E, T) in Figures 11–13. These highlight group-specific interaction structures among gait parameters.

Table 4.

Top 10 global Spearman correlations (Treadmill Condition)				
Variable 1	Variable 2	r		p-value
Force – Left Forefoot [N]	Force – Left Backfoot [N]	-1.000		< 0.0001
Force – Right Forefoot [N]	Force – Right Backfoot [N]	-1.000		< 0.0001
Total Force – Left [N]	Total Force – Right [N]	-0.999		< 1e-30
Max Force – Heel (Left) 1-Zones [N]	Max Pressure – Heel (Left) [N/cm²]	0.985		< 1e-30
Gait Cycle Duration [s]	Step Length [cm]	0.813		< 1e-10
Gait Cycle Duration [s]	Walking Speed [km/h]	-0.805		< 1e-10
Walking Speed [km/h]	Step Length [cm]	0.771		2.2e-09
Walking Speed [km/h]	Step Length Right [cm]	0.717		0.4e-08
BMI	Walking Speed [km/h]	-0.653		4.5e-07
Max Pressure – Midfoot (Right) [N/cm²]	Max Force – Midfoot (Right) [N]	0.605		0.2e-06

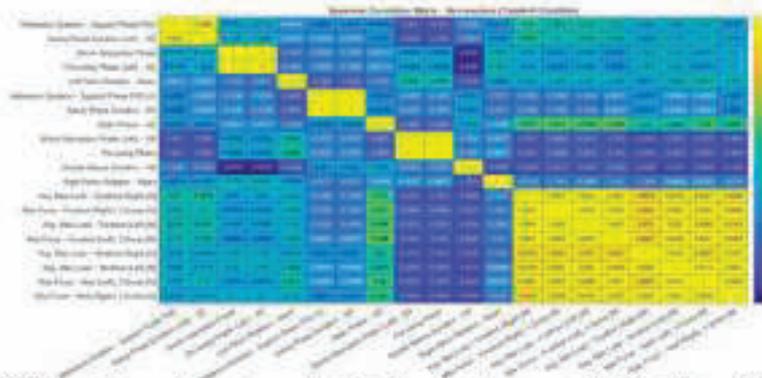


Fig. 11. Heatmap of Spearman's correlation coefficients for 20 most important numerical variables in the treadmill condition (non-smokers)

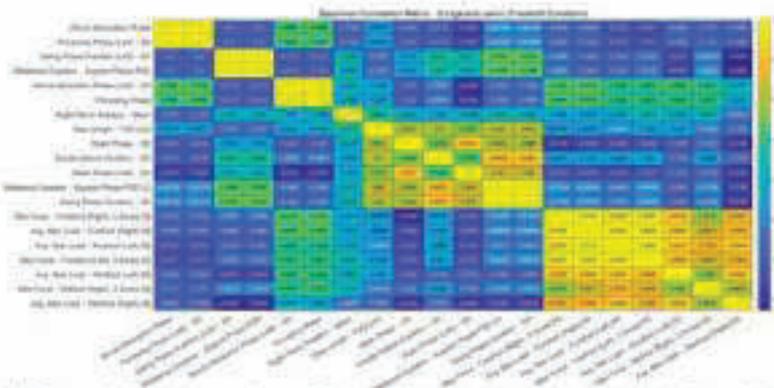


Fig. 12. Heatmap of Spearman's correlation coefficients for 20 most important numerical variables in the treadmill condition (E-cigarette users)

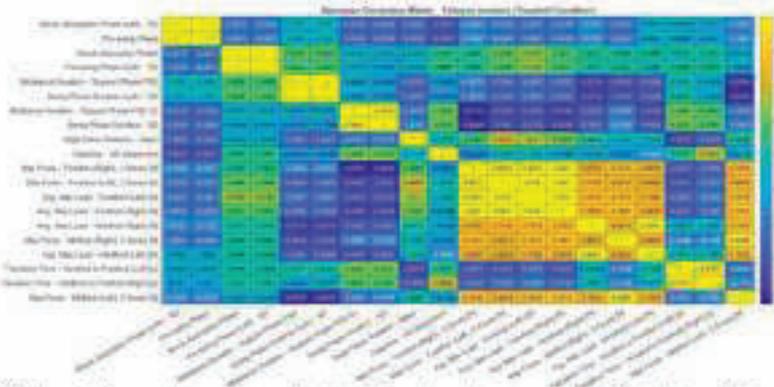


Fig. 13. Heatmap of Spearman's correlation coefficients for 20 most important numerical variables in the treadmill condition (Tobacco smokers)

An initial PCA was conducted using the full set of stabilometric and gait-related variables across all participants to explore the global structure of the dataset. However, the resulting projection did not reveal clear clustering patterns or meaningful separation between the three groups (traditional smokers, e-cigarette users, and non-smokers), suggesting that group-related differences might be obscured by high-dimensional noise or irrelevant features. To address this limitation, a feature selection step using the Relief algorithm was applied prior to subsequent PCA. This approach allowed us to focus on the most discriminative variables for each pairwise group comparison, resulting in improved visual separation and interpretability of the principal component space. The following sections present the PCA projections for N vs. E, T vs. E, and T vs. N, based on their respective top five features.

To explore the variance structure and assess the potential for group discrimination based on the most informative features, a Principal Component Analysis (PCA) was conducted using the top 5 variables selected via the Relief algorithm for the comparison between non-smokers (N) and electronic cigarette users (E). These variables included walking speed, BMI, step length, and two plantar pressure indicators, which were previously shown to be most relevant for group separation in classification models. The PCA projection onto the first two principal components is presented in Figure 9. The first component (PC1) accounted for 64.5% of the total variance, while the second (PC2) explained an additional 24.2%, resulting in a cumulative variance of nearly 89%. This indicates that the low-dimensional projection effectively captures the majority of data variability related to the selected features. The resulting scatterplot (Figure 14) revealed a visible tendency toward group separation along PC1. Specifically, non-smokers (N) were distributed predominantly on the negative side of PC1, while e-cigarette users (E) clustered on the positive side. This pattern is consistent with the classification outcomes and suggests that the identified features

differentiate the groups not only through supervised learning models but also in an unsupervised dimensionality reduction context.

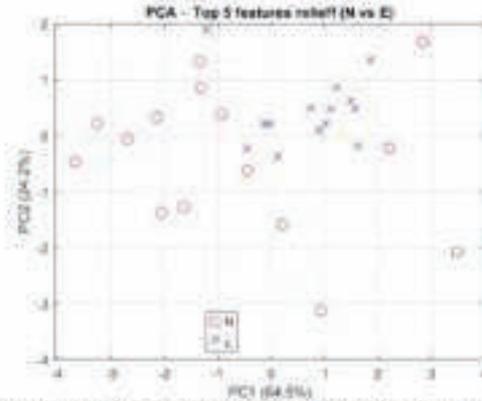


Fig. 14. PCA projection onto the first two components based on top 5 ReliefF-ranked features for N vs. E comparison. Red circles: non-smokers (N); blue crosses: e-cigarette users (E). Axis indicate the proportion of variance explained.

A second Principal Component Analysis (PCA) was conducted to investigate the differentiation between traditional cigarette users (T) and electronic cigarette users (E), based on the top five features identified by the ReliefF ranking for this specific comparison (Figure 15). The two principal components extracted accounted for 57.6% (PC1) and 18.3% (PC2) of the total variance, respectively (Figure 10), yielding a cumulative explanation of approximately 76%. While this is slightly lower than the variance captured in the N vs. E model, it still reflects a substantial proportion of the total variability in the selected feature space. In the PCA projection, some degree of overlap between the T and E groups was observed, with more dispersion present in the E group along PC1. This suggests a less distinct separation compared to the N vs. E configuration, potentially reflecting more similar gait or pressure profiles between traditional and electronic cigarette users. Nevertheless, the directionality of PC1 still captures a subtle gradient between the two groups, implying partial discriminative capability.

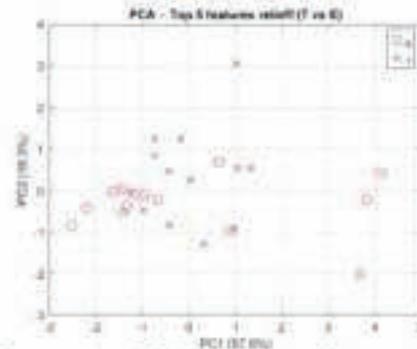


Fig. 15. PCA projection for T vs. E groups using top 5 ReliefF-ranked features. Blue crosses: traditional smokers (T); red circles: e-cigarette users (E). PC1 and PC2 denote the first and second principal components, with the explained variance indicated on the axes.

The third PCA was performed to explore the separation between traditional smokers (T) and non-smokers (N) using the top five discriminative features identified via the ReliefF algorithm (Figure 16). The first two principal components explained 40.1% and 24.6% of the total variance, respectively, summing to 64.7% of the data variability (Figure 11). In contrast to the N vs. E comparison, the T vs. N projection revealed greater overlap between the groups in the principal component space, indicating limited discriminatory power of the selected features for this pair. While there is a slight directional tendency along PC1, suggesting some group-level differentiation, individuals from both groups remain broadly intermixed. The moderate proportion of explained variance and lack of clear clustering suggest that either the features selected via ReliefF are less informative for distinguishing traditional smokers from non-smokers, or that gait and pressure-related differences between these two groups are subtle.

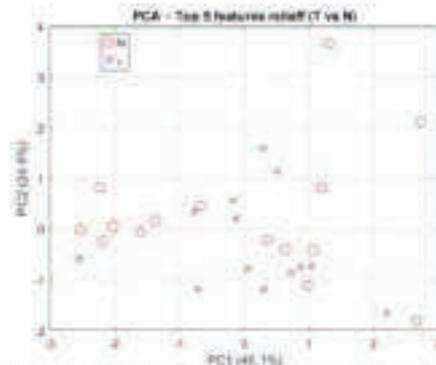


Fig. 16. PCA projection for T vs. N using the five most relevant ReliefF features. Blue crosses represent traditional smokers (T), and red circles denote non-smokers (N). PC1 and PC2 account for 46.1% and 24.6% of the total variance, respectively

To explore the discriminative potential of gait and anthropometric parameters across the three study groups (non-smokers, electronic cigarette users, and traditional smokers), several supervised machine learning models were evaluated using five-fold cross-validation. The tested classifiers included decision trees, linear support vector machines (SVM), k-nearest neighbors (k-NN, k=5), and logistic regression. The dataset comprised normalized numerical variables from the treadmill measurements. As shown in Table 5, overall classification accuracy varied considerably between models. The logistic regression model consistently yielded the highest accuracy across folds (mean = 57%), while decision trees and k-NN performed close to random chance levels (~31%). Notably, AUC values could not be computed reliably due to the multiclass nature of the problem and the encoding method used. These results suggest that, although some class separation exists, the three-group classification task remains challenging when using the full feature space without dimensionality reduction or feature selection.

Table 5.

Classification accuracy across folds for each machine learning model (multiclass classification across all three groups)

Model	Best Accuracy
Decision Tree	0.31
SVM (linear)	0.50
k-NN (k = 5)	0.30
Logistic Regression	0.57

Table 6.

Classification accuracy for each group pair and model (5-fold cross-validation)

Group 1	Group 2	Model	Accuracy
Non-smokers	Tobacco smokers	Decision Tree	0.399
		SVM (linear)	0.571
		k-NN (k = 5)	0.536
		Logistic Regression	0.530
Non-smokers	E-cigarette smokers	Decision Tree	0.621
		SVM (linear)	0.795
		k-NN (k = 5)	0.552
Tobacco smokers	E-cigarette smokers	Logistic Regression	0.828
		Decision Tree	0.370
		SVM (linear)	0.481
		k-NN (k = 5)	0.444
		Logistic Regression	0.519

To further explore the discriminatory potential of gait variables, we performed binary classification separately for each pair of study groups: non-smokers (N) vs. traditional smokers (T), non-smokers (N) vs. e-cigarette users (E), and traditional smokers (T) vs. e-cigarette users (E). Four supervised machine learning models were

evaluated using 5-fold cross-validation: decision tree, linear support vector machine (SVM), k-nearest neighbors ($k = 5$), and logistic regression. The highest classification accuracies obtained for each pair are presented in Table 6. The most promising separation was achieved between non-smokers and e-cigarette users, with logistic regression reaching an accuracy of 82.76%, followed by linear SVM at 79.31%. The comparison between non-smokers and traditional smokers yielded lower accuracies across models, with k-NN achieving the best performance at 53.57%. The most challenging pair was traditional smokers vs. e-cigarette users, where none of the models exceeded 52% accuracy, indicating overlapping gait characteristics in these groups. The confusion matrices presented in Figures 17-19 provide additional insight into the performance of the best classifiers for each group comparison.

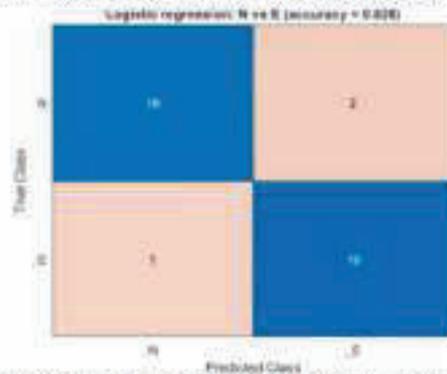


Fig. 17. Confusion matrix for logistic regression model for non-smokers vs e-cigarette users (accuracy = 0.828)

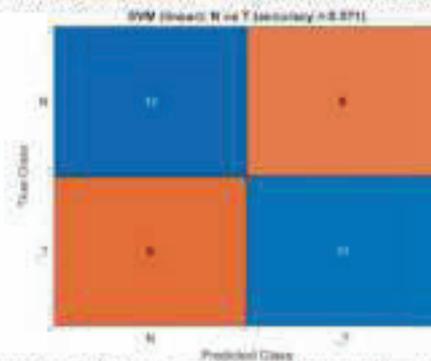


Fig. 18. Confusion matrix for SVM (linear kernel) for non-smokers vs traditional smokers (accuracy = 0.571)

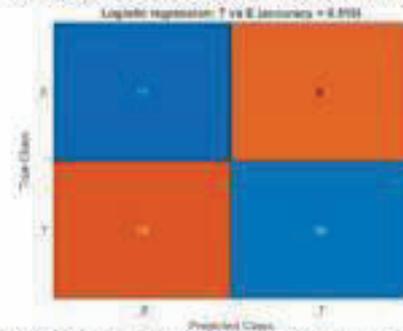


Fig. 19. Confusion matrix for logistic regression for traditional smokers vs e-cigarette users (accuracy = 0.519)

Each matrix displays true labels versus predicted labels across all cross-validation folds. Models were trained using all numerical features normalized to zero mean and unit variance.

4. DISCUSSION

The research delivers fresh knowledge about how tobacco smoking habits and e-cigarette consumption differently impact postural control and gait in young adults. The study reveals that young healthy smokers demonstrate significant changes in balance and walking ability compared to non-smokers and e-cigarette users show less severe effects. Our study participants who smoked traditional cigarettes maintained lower body mass index (BMI) values than both never-smokers and exclusive e-cigarette users. The smokers in our study walked shorter steps while their gait patterns differed from non-smokers during treadmill tests and they displayed greater postural instability during stabilometric assessments. E-cigarette users displayed intermediate results because their BMI values exceeded those of smokers while remaining close to non-smoker levels and their gait and balance test results fell between those of smokers and non-smokers. Multiple measures showed significant differences between smokers and vapers which indicates that the method of nicotine delivery through combustion or electronic devices affects the extent of motor control impairment. The research findings need evaluation through existing scientific literature and established physiological principles.

The observed lower BMI in smokers is consistent with well-established trends. Numerous studies have documented that current smokers tend to weigh less and have lower BMI than non-smokers of similar age [24,25]. Nicotine is known in suppressing appetite and increasing resting metabolic rate, which likely explains why smokers in our study, as in others, were leaner on average [26]. By contrast, the e-cigarette users did not show this weight-suppressing effect as strongly. One possible reason is that some e-cigarette users are former smokers who may have gained weight after switching from combustible cigarettes (a common occurrence when smoking cessation or reduction alleviates nicotine's anorectic effects). E-cigarette users may adjust their nicotine intake through different methods (such as frequent puffing versus intermittent smoking) which results in reduced appetite suppression. The higher BMI observed in vapers compared to smokers could stem from factors unrelated to nicotine such as lifestyle or dietary choices. The BMI difference between vapers and smokers affects motor function because small variations in healthy BMI do not directly lead to gait changes but body composition might impact balance. For instance, smokers' lower body weight might give them a slight mechanical advantage in certain balance tasks (less mass to stabilize), but on the other hand, being underweight or having lower muscle mass (if that accompanies lower BMI) can impair physical performance. In our data, despite smokers being lighter, their balance was worse – indicating that factors beyond body weight (neurological factors) are the dominant cause of their postural instability, as discussed below.

The gait alterations found in smokers – particularly a reduced step/stride length – align with prior research showing that smoking can detrimentally affect walking patterns. In a recent study examining gait in young adults, male smokers had a significantly shorter stride length and lower cadence compared to non-smokers of the same age [27]. Our smokers showed a similar trend of shorter steps. Biomechanically, a shorter stride length at a given cadence usually corresponds to a slower walking speed and a more cautious gait. Indeed, smokers in other studies often exhibit reduced gait velocity and a prolonged double-support phase (keeping both feet on the ground longer) – patterns typically indicative of reduced confidence in balance or lower endurance. Several mechanisms might explain why young smokers walk differently. One factor is cardiorespiratory fitness. Smoking, even in young adults, impairs cardiovascular and pulmonary function; chronic smokers can have lower exercise tolerance, early signs of pulmonary obstruction, or peripheral arterial changes. Diminished aerobic capacity could cause smokers to adopt a slower, conservative gait to avoid overexertion [28,29]. The analogy to patients with mild chronic lung disease is pertinent – for example, individuals with early-stage COPD (often caused by smoking) tend to walk more slowly with shorter strides and longer support times than healthy controls [28]. In our study, although participants were young and presumably free of overt disease, even subtle reductions in aerobic fitness or muscle endurance in the smokers might have manifested as a less vigorous gait. The neuromuscular control system also plays a role in this process. The neuromuscular system responds to nicotine in multiple ways through its effects on neurotransmitter release and muscle contraction but chronic exposure leads to receptor desensitization and changes in motor neuron excitability. The long-term effects of nicotine exposure together with systemic inflammation may cause slight muscle weakness in the lower extremities and delayed motor unit recruitment in smokers. Smoking over time causes peripheral vascular damage and possible subclinical neuropathy (damage to peripheral nerves) because of reduced blood flow and tobacco toxins. Even a mild sensory neuropathy in the feet or impaired proprioception could cause smokers to take shorter, more guarded steps to maintain stability. While our study did not directly assess nerve function, this hypothesis is supported by evidence that smoking can contribute to peripheral nerve damage over time [7,30,31]. The net effect of these factors is that smokers may unconsciously adjust their gait to compensate for diminished physical capacity or sensory feedback, resulting in the differences observed.

E-cigarette users, on the other hand, showed gait metrics closer to non-smokers, which suggests that many of the smoking-related gait deficits might be attributable to the additional harms of combustion products rather than nicotine alone. If, for instance, reduced stride length in smokers were largely due to chronic hypoxia from carbon

monoxide or extensive oxidative damage from tar and other chemicals, it stands to reason that e-cigarette users (who avoid those particular insults) would be relatively spared. The vapers in our cohort did not significantly differ from controls in stride length (based on our findings), and their cadence and walking speed were in a normal range. This could indicate that nicotine by itself (at the doses obtained via vaping) is not enough to cause marked gait impairment in the short term. However, we should interpret this cautiously. E-cigarette users are a heterogeneous group – some are ex-smokers carrying over effects of past smoking, whereas others might be “new” nicotine initiates. Additionally, many vapers maintain nicotine dependence that is comparable to smokers in intensity, meaning they could eventually experience similar physiological consequences (nicotine-driven increases in heart rate and blood pressure, leading to vascular stiffness or mild endothelial dysfunction [32]). The relatively preserved gait in e-cig users might simply reflect the shorter history of their nicotine use (e.g. vaping has been popular for fewer years), and problems could arise with longer exposure. It is also possible that e-cig users engage in more physical activity or health-conscious behavior overall (some may have switched to vaping as a “harm reduction” step to improve fitness), which could confound direct comparisons with smokers. Nonetheless, our data tentatively suggest that combustion-related factors in cigarettes contribute more strongly to gait deterioration than nicotine alone – a point that aligns with the general understanding that smoking’s impact on exercise capacity (and by extension gait) is partly due to lung damage and systemic toxin effects.

Perhaps the most striking differences we found were in postural stability (stabilometric measures). Young adult smokers showed greater postural sway and poorer balance control than non-smokers, especially in challenging conditions (e.g. narrow stance or eyes closed). This finding is in line with earlier studies that have reported long-term smokers have impaired balance. Iki et al. (1994) observed that middle-aged smokers had significantly higher sway velocities on force platform tests than non-smokers, indicating more difficulty maintaining steady stance [13]. They even noted a dose-response relationship: heavy smokers swayed more than light smokers. Our study extends this observation to a younger demographic, suggesting that such balance impairments can manifest even by the third decade of life if the individual has been smoking since adolescence. The physiological underpinnings of reduced postural stability in smokers likely involve multiple systems. The vestibular system is one of the chief contributors to balance, and there is evidence that smoking can damage the inner ear’s balance organs. Nicotine and other chemicals can compromise the microcirculation of the inner ear; over time this may lead to vestibular dysfunction (indeed, smokers have a higher incidence of vertigo and vestibular disorders) [33]. Nicotine also directly interacts with vestibular and cerebellar pathways: research has shown that stimulation of nicotinic receptors can alter vestibulo-ocular reflexes, sometimes causing nystagmus and dizziness [9,34]. Thus, chronic nicotine exposure might desensitize or dysregulate these balance pathways. Additionally, smoking is associated with degeneration in the proprioceptive system – for instance, peripheral neuropathy as mentioned earlier can reduce sensation in the feet, and spinal degeneration (intervertebral disc deterioration accelerated by nicotine) can affect sensory feedback from the spine [35]. If a smoker has even a slight loss of position sense in the ankles or a delayed postural reflex, maintaining equilibrium becomes more difficult, especially with eyes closed when visual compensation is removed. Another factor is central integration: balance requires effective integration of sensory inputs in the cerebellum and brainstem. Chronic smoking has been linked to structural and functional changes in the brain; for example, studies have noted that smokers can have reduced volume in cerebellar regions and other brain areas involved in motor control [36]. It is plausible that long-term smoking leads to microdamage or inflammation in neural networks crucial for balance (perhaps via oxidative stress and small-vessel ischemic effects), thereby degrading the precision of postural adjustments. Our finding that smokers had worse stability even as young adults might be an early sign of such neurodegenerative processes. Importantly, this was a cross-sectional observation – longitudinal studies would be needed to confirm that smoking precedes and contributes to balance decline, but our results align with that interpretation.

Comparatively, the e-cigarette users in our study showed milder balance impairments. In some stabilometric tests, the e-cig group performed between the smokers and the non-smokers, sometimes not significantly different from the latter. The results indicate that combustible smoking produces greater effects on balance than vaping during the short term. The main reason for this difference could be the hypoxia-inducing components such as carbon monoxide present in cigarette smoke. CO reduces tissue oxygen delivery to the brain and peripheral nerves in a chronic manner. Over years, this could cause subtle diffuse damage (akin to aging-related small vessel disease) that impairs the central processing of balance. E-cigarette aerosol does not contain CO, so e-cig users avoid chronic CO exposure. Additionally, cigarettes contain thousands of chemicals, many of which are neurotoxic (e.g. lead, arsenic, and cadmium have been found in tobacco smoke). Heavy metals like cadmium (abundant in cigarette smoke) can accumulate and cause peripheral neuropathy or vestibular toxicity; e-cig vapor can contain metals from the heating coil (nickel, chromium), but typically in lower amounts than cigarette smoke delivers [37]. Therefore, e-cig users may experience less cumulative neurotoxic burden. Nicotine itself, common to both exposures, undoubtedly can acutely disturb balance – for instance, both smokers and vapers sometimes report dizziness after a large dose of nicotine – but if the chronic balance deficits in smokers were due mostly to non-nicotine factors, it makes sense that vapers fare better. Nonetheless, our e-cigarette group did show a slight trend toward worse balance than pure non-users (though not as bad as smokers), which could mean that nicotine alone does have some chronic impact on postural control. Nicotine’s action on the central nervous system might induce subtle changes in reflex timing or muscle tone. There is

some evidence from pharmacological studies that nicotine can affect cerebellar function and delay postural reflexes (interestingly, nicotine agonists are being studied for certain balance disorders, indicating the complexity of its effects). Another possibility is that some e-cig users in our study were dual users (both smoking and vaping) or former smokers, which would carry over the balance deficits from smoking. We tried to select exclusive e-cig users, but undisclosed dual use could confound the results. If any dual users were present, their balance would reflect the worse of the two habits, potentially explaining why the e-cig group wasn't entirely "normal" in stability.

Beyond comparing our results with prior studies, it is important to consider the broader implications and possible interpretations of these findings. One interpretation is that the neuromuscular system of young adults is more vulnerable to substance use than traditionally thought. While young people generally have a high physiological reserve, the fact that we detected clear gait and balance differences suggests that nicotine and tobacco are impacting neural control mechanisms relatively early in the exposure timeline. This raises concern that such changes could accumulate and intensify with longer duration of use, potentially leading to clinical balance or gait impairments in mid-life. It also suggests a dose-response relationship: heavy traditional smoking conferred the greatest changes, lighter or non-combustive nicotine use (vaping) showed smaller changes. This mirrors known health gradients, where complete non-use is safest, vaping is intermediate, and smoking is most harmful. Our findings thus support the concept of tobacco harm reduction in one sense (e-cigarettes might pose less risk to balance and gait than cigarettes), but they also serve as a warning that e-cigarettes are not without risk. The presence of any deviation in postural control among e-cig users, even if mild, means that chronic vaping could still have neurologic consequences – possibly via nicotine's effect on the brain or other toxic constituents in the vapor.

5. LIMITATIONS

The study contains multiple limitations which need to be considered when evaluating the research results. The cross-sectional study design prevents researchers from establishing cause-effect relationships between tobacco or e-cigarette use and the observed postural control and gait impairments. The study reveals significant group differences but it remains uncertain whether these changes stem from nicotine exposure or pre-existing differences or a combination of both factors. Research following participants over time would help determine both the sequence of events and whether neuromotor changes can be reversed after people stop using tobacco products. Second, self-reported smoking and vaping status was used to assign participants to groups. Although widely used in behavioral research, self-report introduces a risk of misclassification or underreporting, particularly among dual users or individuals transitioning between products. No biochemical verification (e.g., cotinine testing or carbon monoxide monitoring) was performed to objectively confirm nicotine exposure levels. Third, while efforts were made to control testing conditions, the timing and recency of nicotine intake prior to testing were not standardized. Acute effects of nicotine (e.g., withdrawal or intoxication) may have influenced performance, especially in tasks requiring fine motor coordination or balance. Future research should establish protocols to monitor or document the duration since nicotine consumption to distinguish between persistent and short-term effects. The study used a small participant number (N = 60) from a university-based convenience sample of young adults. The study results might not apply to diverse populations because the participants were evenly distributed between groups but the results could differ from other populations with varying socioeconomic status and physical activity levels and nicotine consumption patterns. The study population consisted mainly of healthy participants which might reduce the observed level of functional impairment in heavier or older users. The study obtained complete biomechanical data but did not include neurophysiological tests such as vestibular testing and proprioceptive thresholds and neuroimaging assessments. The study cannot determine the exact motor impairment source because it lacks neurophysiological and clinical diagnostic measures. Future research should include neurophysiological and clinical diagnostic measures to enhance understanding of how nicotine and tobacco products impact balance and gait through specific pathways. The study delivers important first evidence about early functional effects of tobacco and e-cigarette use in young adults while demonstrating the need for additional focused research.

6. CONCLUSIONS

The present study provides compelling evidence that regular tobacco smoking is associated with measurable impairments in both postural stability and gait parameters among young adults. Despite the relatively short exposure duration typical for this age group, tobacco smokers in our cohort exhibited increased postural sway, shorter step length, and altered gait dynamics compared to non-smokers, suggesting that the deleterious effects of cigarette use on neuromotor control can manifest early in life, long before clinical symptoms or comorbidities become apparent. These findings align with neurophysiological theories indicating that balance and locomotor control are highly sensitive to chronic disruptions in sensory integration, central processing, and peripheral feedback — all of which can be influenced by the neurovascular and toxicological effects of tobacco smoke.

Our comparative study design enabled us to identify the separate effects of traditional smoking versus exclusive e-cigarette use. E-cigarette users showed deviations from non-smokers in some parameters but these deviations were significantly smaller than those found in the smoking group. The absence of combustion-related toxins in vaping appears to reduce some postural and gait impairments that cigarette smoking typically causes. The

existence of minimal functional changes in vapers shows that nicotine together with other aerosol components produce small but ongoing effects on neuromuscular function and sensory-motor integration.

The observed differences in BMI, stride characteristics, and stabilometric measures between groups could be attributed to a variety of physiological mechanisms, such as vascular and neurotoxic damage, nicotine-induced modulation of reflexes and proprioception, and other lifestyle factors associated with nicotine product use. The presence of such variations in a young, otherwise healthy population emphasizes the importance of early screening and preventative efforts. It also raises the question of whether stabilometric and gait-based evaluations may be used as early indicators of subclinical impairment or as motivators in clinical smoking cessation programs.

The research findings support public health evidence that tobacco use and e-cigarette use can damage neuromotor integrity in young adults. The study results demonstrate the necessity for additional longitudinal research to study how these impairments develop and whether they can be reversed and to evaluate the effectiveness of cessation and harm-reduction strategies that involve switching from smoking to vaping. Future clinical and epidemiological studies should use objective, biomechanical assessments to determine the functional effects of nicotine exposure on younger populations.

In conclusion, this study bridges the gap between neurophysiological research and public health by demonstrating that everyday motor abilities such as balance and walking — often taken for granted in youth — can be subtly but significantly affected by tobacco and nicotine use. These insights should inform not only clinical practice and preventative strategies, but also public discourse surrounding the relative risks of smoking and vaping among young adults.

Future research needs to build upon these results by studying bigger and more diverse groups of people who differ in age, social status and exercise habits. Longitudinal studies are needed to determine the progression and potential reversibility of neuromotor impairments associated with chronic tobacco or e-cigarette use. Objective biochemical verification of nicotine exposure (e.g., cotinine assays, carbon monoxide breath testing) would strengthen group classification and help distinguish between acute and chronic effects of use.

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E-Cigarette Users Exhibit Stronger Cardiovascular Reactivity than Smokers: Evidence from a Multimodal Signal Analysis in Young Adults

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ABSTRACT

Young adults believe electronic cigarettes (e-cigarettes) are safer than traditional smoking products, yet the complete health effects of continuous vaping on cardiovascular and respiratory systems remain uncertain. This study examined 60 participants aged 18 to 25 years, divided into three groups: non-smokers, traditional cigarette smokers, and regular e-cigarette users. We measured heart rate (HR), blood pressure (BP), oxygen saturation (SpO₂), and recovery time across three phases of physical exertion.

Analysis of physiological signals with statistical and machine learning methods used ΔHR and ΔMAP to build response profiles and determine smoking status. E-cigarette users showed greater HR increases during exercise and significantly longer recovery times than both smokers and non-smokers. Although BP and SpO₂ restitution rates were similar between groups, e-cigarette users displayed enhanced HR responses and delayed recovery, suggesting elevated sympathetic activation with reduced vagal tone.

Multivariate regression and Pearson correlation analysis identified ΔHR as the main predictor of recovery time. Classification models achieved 76.7% accuracy with logistic regression and 85% accuracy with decision trees based on physiological features.

Regular e-cigarette use alters autonomic cardiovascular function, resulting in prolonged exercise recovery compared to cigarette smokers. These findings demonstrate that e-cigarettes impose measurable cardiovascular stress on users, highlighting the need for further research to clarify the full range of health consequences.

Keywords: e-cigarettes; cardiovascular recovery; heart rate; autonomic response; exercise testing; young adults

Introduction

The leading preventable cause of death from cigarette smoking results in severe cardiovascular and respiratory diseases. The first e-cigarettes emerged in 2004 as battery-powered nicotine delivery devices which create vapor instead of burning tobacco¹⁻³. The popularity of e-cigarettes has dramatically increased since their introduction especially among young people⁴. The national market introduction of e-cigarettes in Poland has led to continuous growth in their user numbers. The e-cigarette user base in Poland reached 1.5 million in 2023 while disposable device sales volume exceeded 100 million units which demonstrated a 200% increase from 2022^{5,6}. The large number of people who use e-cigarettes does not match the prevalence of traditional cigarette smoking since only 1% of Polish adults regularly use e-cigarettes according to the Public Opinion Research Center (CBOS) 2021 national survey^{5,7}. The majority of e-cigarette consumers also smoke traditional cigarettes which creates worries about how nicotine and other inhaled substances affect their health⁸.

E-cigarette aerosol contains fewer toxic combustion products than conventional cigarette smoke, but remains non-harmful. The vaping process delivers nicotine, which is an addictive sympathomimetic drug, together with chemical flavoring agents and other constituents (e.g., propylene glycol, glycerol) that have independent health risks^{9,10}. The e-cigarette vapor that people inhale contains ultrafine particulate matter together with trace metals from heating coils which have been proven to cause

harm to the cardiovascular system. The manufacturers of e-cigarettes presented these products as smoking cessation devices and harm reduction solutions at their initial launch¹⁰. The available evidence shows that long-term e-cigarette use produces adverse effects on cardiovascular and pulmonary systems although these effects differ from traditional cigarette effects in terms of severity and underlying mechanisms.

The cardiovascular system experiences acute stress from both nicotine exposure and the oxidative stress which results from inhaling aerosols. Research has demonstrated that vaping causes immediate increases in heart rate and blood pressure because nicotine stimulates sympathetic tone. The analysis of 27 trials revealed that brief e-cigarette use resulted in major increases of resting heart rate and blood pressure when compared to initial measurements¹¹. The repeated inhalation of e-cigarette aerosols leads to vascular dysfunction which was demonstrated by elevated arterial stiffness and blood pressure levels similar to those of long-term smokers^{8,12}. The current evidence about long-term cardiovascular outcomes remains scarce but observational studies have discovered that people who use e-cigarettes daily face increased cardiovascular risks. A cross-sectional study discovered that e-cigarette users developed chest pain, arrhythmia, and coronary heart disease at higher rates than non-users^{1,13}. The observed associations between e-cigarette use and cardiovascular disease risk factors demonstrate valid concerns that long-term e-cigarette consumption might lead to cardiovascular disease in a similar manner to traditional smoking^{14,15}.

Scientists actively study the respiratory consequences of e-cigarette use. The established medical evidence shows that cigarette smoke damages lung tissue by creating airway inflammation and reducing pulmonary function and leading to chronic bronchitis and emphysema. The long-term effects of vaping on pulmonary injury remain unclear although initial research results show concerning findings. The immediate effects of e-cigarette aerosol inhalation result in increased airway resistance while triggering short-term lung inflammation although standard spirometric indices like *FEV₁* show no immediate changes¹⁶. Research shows that e-cigarette users commonly experience respiratory symptoms because vaping increases their chances of developing wheezing and chest tightness and exercise-induced cough compared to non-users. Research on a nationally representative group of 18–24 year-olds who had no lung disease history revealed that current e-cigarette users developed wheezing or whistling in the chest symptoms at 30–50% higher rates during one year¹⁷. Research suggests that prolonged e-cigarette use may lead to permanent respiratory diseases. Studies of population data have discovered connections between e-cigarette consumption and the development of asthma and chronic bronchitis which share similar respiratory complications with conventional tobacco smoking^{18,19}. The long-term effects of regular vaping on pulmonary health remain a major concern because e-cigarettes deliver fewer carcinogens than traditional combustible cigarettes despite this advantage.

The increasing popularity of e-cigarettes among young adults and the ongoing uncertainty about their health effects led to the development of this research to evaluate cardiovascular and respiratory outcomes between e-cigarette users and traditional cigarette users and non-smokers. The research focuses on healthy young adults between 18 and 25 years old while using controlled experimental conditions to measure their physiological responses²⁰.

Our aim was to evaluate how e-cigarette users differ from cigarette smokers and non-smokers in key cardiovascular and respiratory parameters, including measurements of physiological signals (e.g. heart rate, blood pressure, breathing metrics) recorded during controlled physical exertion in all three groups. This approach allows us to characterize the acute cardiorespiratory strain associated with e-cigarette use relative to tobacco smoking and to non-use, providing insight into the potential health risks of vaping in this young population.

Materials and Methods

Our aim is to evaluate how e-cigarette users differ from cigarette smokers and non-smokers in key cardiovascular and respiratory parameters, including measurements of physiological signals (e.g. heart rate, blood pressure, breathing metrics) recorded during controlled physical exertion in all three groups. This approach allows us to characterize the acute cardiorespiratory strain associated with e-cigarette use relative to tobacco smoking and to non-use, providing insight into the potential health risks of vaping in this young population.

Study Design and Participants

The study included 60 adult participants between 18 and 25 years old who were divided into three equal groups of twenty participants each: e-cigarette users, traditional cigarette smokers (control group 1), non-smokers (control group 2). The study included participants who met three conditions: being older than 18 years old and able to give consent and belonging to one of the specified groups according to questionnaire verification. Individuals with acute illness, diagnosed cardiovascular or respiratory disorders, or contraindications to physical exertion were excluded.

Prior to participation, all participants provided informed written consent. The study followed the principles outlined in the Declaration of Helsinki and respected all applicable data protection regulations. Participant recruitment was carried out through local announcements and university channels. Data were collected anonymously and used exclusively for scientific purposes, of which the volunteers were informed, and gave their written consent. The area of this study was beforehand approved by the Ethics Committee for Research Involving Human Participants at the Silesian University of Technology, Gliwice, Poland.

resolution No. 3/2025 dated March 11, 2025. The Committee confirmed that the study meets all ethical and scientific integrity requirements for research involving human subjects.

Measurement Protocol

All assessments were conducted in a controlled clinical setting under the supervision of trained personnel. Each participant was connected to the monitoring system from the beginning of the resting phase and remained connected throughout all three phases of the protocol to assess their physiological response to physical effort and the subsequent recovery. Resting phase - participants sat quietly for at least 10 minutes. Baseline physiological parameters were then recorded in resting conditions. These values served as reference points for the recovery analysis. Effort phase - participants walked on a treadmill for 6 minutes at a self-selected pace, defined as the speed they perceived as natural and comfortable during daily walking. This approach ensured consistency in duration while allowing for individual variability in intensity. Recovery phase - immediately following the effort, participants were seated, and physiological parameters were continuously monitored. The primary recovery endpoint was defined as the moment when the participant's heart rate (HR) returned to its baseline value recorded during the resting phase. To confirm full recovery, non-invasive blood pressure (NIBP) values were also reviewed in relation to baseline measurements. The primary outcome was the time required to reach this physiological restitution, measured in seconds. No adverse events were observed, and all participants completed the protocol in full. Data were segmented into the three measurement phases and analyzed accordingly.

Equipment and Data Acquisition

All physiological parameters were recorded using a Vista 120 S (Dägerwerk AG & Co. KGaA, Lübeck, Germany) multiparameter patient monitor. The device enabled the real-time, simultaneous acquisition of data from multiple physiological systems. The participants received monitor connection at the start of resting phase and stayed under continuous monitoring until the end of the entire protocol. The following parameters were acquired: Heart Rate (HR): recorded through a 3-lead electrocardiogram (ECG). Pulse Rate (PR) and Oxygen Saturation (SpO_2): recorded through a photoplethysmographic (PPG) sensor on the finger. Systolic (SYS), Diastolic (DIA), and Mean Arterial Pressure (MAP): recorded through a non-invasive oscillometric blood pressure cuff (NIBP). The assessment was conducted under the supervision of the clinical engineer and qualified nurse.

The blood pressure cuff was inflated three times per protocol—at baseline, immediately after exercise, and after recovery—provided that the participant was motionless. Additional measurements were taken only when physiological values appeared unstable or questionable, always ensuring the participant was at rest to avoid artifacts.

All parameters except NIBP were recorded continuously. Data were exported in structured form and later segmented into the three protocol phases (rest, effort, recovery) for comparative analysis. The primary recovery indicator was heart rate restitution, with blood pressure used as a secondary confirmation when required.

Multimodal Signal Integration

The physiological data used in this study were acquired through a multimodal monitoring approach, integrating signals from different physiological systems: cardiovascular (HR, PR, NIBP) and respiratory (SpO_2). These signals were recorded in real time and aligned temporally using the same monitoring system (Däger Vista 120 S). Although the measured parameters originated from different sensor modalities—electrocardiography (ECG), photoplethysmography (PPG), and oscillometric pressure measurement—they were synchronized within a single monitoring platform. This ensured signal coherence and enabled direct cross-domain comparisons.

The multimodal nature of the dataset allowed for the comprehensive assessment of physiological responses to effort and recovery. For each participant, vectorized data representations were constructed, containing values from the three defined time points (rest, post-exercise, recovery) across all recorded parameters. This structure enabled integrated, multimodal analysis, including the evaluation of interdependencies between systems (e.g. the relationship between HR response and SpO_2 drop, or blood pressure normalization). The synchronized dataset served as the basis for group comparisons and regression-based outcome analysis.

Signal Processing

Raw physiological data were extracted and processed offline. Continuous signals such as heart rate (HR), pulse rate (PR), and oxygen saturation (SpO_2) were visually inspected to identify potential artifacts, including motion disturbances or sensor disconnections. Non-invasive blood pressure (NIBP) values, recorded at discrete time points, were checked for consistency and accuracy relative to protocol phases. Automated export of raw waveform data was not supported by the device, as no suitable interface was available, therefore physiological values were post hoc annotated from high-resolution screen video recordings of the patient monitor. This method enabled precise phase segmentation and ensured accurate identification of the time point at which each parameter stabilized. Particular attention was given to heart rate recovery dynamics, with annotations based on the monitor's real-time HR trend and numerical displays.

Each participant's data were segmented into three predefined phases, and intra-individual changes in physiological parameters were calculated as follows:

$$\Delta HR_{(Effort-Rest)} = HR_{Effort} - HR_{Rest} \quad (1)$$

represents the change in heart rate between the effort and resting phases.

$$\Delta SpO_2_{(Rest-Effort)} = SpO_2_{Rest} - SpO_2_{Effort} \quad (2)$$

represents the difference in oxygen saturation between the resting phase and post-exercise (effort) phase.

$$\Delta HR_{(Effort-Recovery)} = HR_{Effort} - HR_{Recovery} \quad (3)$$

captures the heart rate difference between the effort and recovery phases.

$$\Delta SYS_{(Rest-Effort)} = SYS_{Effort} - SYS_{Rest} \quad (4)$$

represents the change in systolic blood pressure from the resting phase to the effort phase.

$$\Delta SYS_{(Effort-Recovery)} = SYS_{Effort} - SYS_{Recovery} \quad (5)$$

captures the systolic blood pressure difference between the effort and recovery phases.

$$\Delta DIA_{(Rest-Effort)} = DIA_{Effort} - DIA_{Rest} \quad (6)$$

represents the change in diastolic blood pressure from the resting phase to the effort phase.

$$\Delta DIA_{(Effort-Recovery)} = DIA_{Effort} - DIA_{Recovery} \quad (7)$$

captures the diastolic blood pressure difference between the effort and recovery phases.

$$\Delta MAP_{(Effort-Rest)} = MAP_{Effort} - MAP_{Rest} \quad (8)$$

represents the change in mean arterial pressure between the effort and resting phases.

$$\Delta MAP_{(Effort-Recovery)} = MAP_{Effort} - MAP_{Recovery} \quad (9)$$

captures the mean arterial pressure difference between the effort and recovery phases.

The primary recovery metric was the time (in seconds) required for HR to return to its baseline value. This was determined by identifying the point at which HR stabilized within ± 3 bpm of the initial resting value for a sustained duration of at least 30 seconds. All data were compiled into structured participant-level vectors, containing parameter values across the three phases. These structured vectors served as the basis for statistical comparison, intergroup analysis, and correlation with recovery time.

Statistical Analysis

The evaluation of physiological responses and recovery dynamics between non-smokers and traditional cigarette smokers and e-cigarette users used statistical methods. The Shapiro-Wilk test determined the normality of all continuous variables. The statistical analysis used parametric and non-parametric methods based on the data distribution patterns. The Kruskal-Wallis test served for group-level comparisons of variables that failed to meet normality requirements. The analysis of variables with normal distribution used ANOVA followed by Tukey's HSD test to identify specific differences between groups. Welch's t-tests served for comparing pairs of groups especially when variance heterogeneity occurred.

Intra-individual differences in physiological parameters between protocol phases (rest, effort, recovery) were calculated and used as derived variables in comparative analyses. The association between physiological reactivity and recovery efficiency was examined using correlation analysis. Both Spearman's rank and Pearson's correlation coefficients were calculated, depending on the distributional characteristics of the variables involved. A p-value below 0.05 was considered statistically significant. To complement the analysis of statistical significance, effect sizes were determined using Cohen's d for selected comparisons, enabling the evaluation of the practical magnitude of observed differences. All computations were performed using MATLAB R2024b (MathWorks Inc., Natick, MA, USA).

Classification Performance and Evaluation Metrics

To assess the ability of the models to distinguish between e-cigarette users and non-users, binary classification using logistic regression and decision tree algorithms were implemented. The classification was based on selected physiological response parameters: ΔHR (heart rate), ΔSpO_2 (oxygen saturation), ΔSYS (systolic pressure), and ΔMAP (mean arterial pressure).

The evaluation of model performance relied on confusion matrices to assess true positives (TP), false positives (FP), true negatives (TN) and false negatives (FN). The metrics enabled the interpretation of classification accuracy in terms of clinical relevance, especially the sensitivity to detecting e-cigarette users. Additionally, the logarithmic loss (log-loss) function was computed to evaluate the calibration of predicted class probabilities. Log-loss penalizes incorrect predictions with high confidence more strongly than less certain ones, providing a robust measure of probabilistic accuracy. Confusion matrices and log-loss values were visualized and compared between models using heatmaps. A lower log-loss and reduced number of false negatives were interpreted as indicators of superior model reliability for potential diagnostic applications.

Results

The main purpose of this research was to evaluate recovery time after exercise between non-smokers and traditional cigarette smokers and e-cigarette users. The recovery time was measured as the time (in seconds) it took for heart rate (HR) to get back to its baseline after a 6-minute treadmill walk. This parameter was the main indicator of cardiovascular restitution after physical exertion. In addition to recovery time, a comprehensive analysis of physiological reactivity and restitution across cardiovascular and respiratory domains was conducted. This included the evaluation of both absolute values and intra-individual changes between protocol phases, allowing for a multimodal insight into the acute effects of cigarette and e-cigarette use on systemic regulation.

Prior to group comparisons, the distribution of all key outcome variables was assessed using the Shapiro-Wilk test for normality (Table 1). This step ensured appropriate selection of statistical tests in subsequent analyses. The variables $\Delta SpO_2_{(Pre-Ex/Post-Ex)}$, recovery time, $\Delta MAP_{(Ex/Post-Ex)}$, and $\Delta MAP_{(Ex/Post-Recovery)}$ did not follow a normal distribution ($p < 0.05$). In contrast, $\Delta HR_{(Ex/Post-Ex)}$, $\Delta HR_{(Ex/Post-Recovery)}$, $\Delta SYS_{(Ex/Post-Ex)}$, $\Delta SYS_{(Ex/Post-Recovery)}$, $\Delta MA_{(Ex/Post-Ex)}$, and $\Delta MA_{(Ex/Post-Recovery)}$ did not deviate significantly from normality and were therefore analyzed using parametric tests.

Variable	Shapiro-Wilk p -value	Normal Distribution
$\Delta SpO_2_{(Pre-Ex/Post-Ex)}$	0.00100	No
Recovery time	0.00188	No
$\Delta MAP_{(Ex/Post-Ex)}$	0.00199	No
$\Delta MAP_{(Ex/Post-Recovery)}$	0.00180	No
$\Delta HR_{(Ex/Post-Ex)}$	0.07120	Yes
$\Delta HR_{(Ex/Post-Recovery)}$	0.05540	Yes
$\Delta SYS_{(Ex/Post-Ex)}$	0.05580	Yes
$\Delta SYS_{(Ex/Post-Recovery)}$	0.51090	Yes
$\Delta MA_{(Ex/Post-Ex)}$	0.09800	Yes
$\Delta MA_{(Ex/Post-Recovery)}$	0.36030	Yes

Table 1. Assessment of normality for outcome variables using the Shapiro-Wilk test. Variables that violated the assumption of normality ($p < 0.05$) were further analyzed using non-parametric methods.

Descriptive statistics for recovery time in each group are presented in Table 2. The mean recovery time in the e-cigarette group was significantly longer than in both the traditional smokers and the non-smokers. Non-smokers had the shortest recovery times and relatively low inter-individual variability.

Group	Mean [s]	SD [s]	Median [s]	Min [s]	Max [s]
Non-smokers	65.57	10.88	64.27	45.53	88.37
E-cigarette users	123.94	17.33	123.32	103.09	166.37
Traditional smokers	72.22	14.99	78.06	43.54	95.02

Table 2. Descriptive statistics for recovery time [s] across study groups.

The Kruskal-Wallis test was applied because the data failed to follow a normal distribution ($p = 0.0072$) to show that recovery time between the three groups differed significantly ($p < 0.001$). Post hoc comparisons showed that recovery time

was longer in e-cigarette users than in non-smokers ($p < 0.001$) and traditional smokers ($p < 0.001$). There was no significant difference between non-smokers and traditional smokers ($p = 0.33$). A boxplot comparison of recovery time between the three groups is shown in Figure 1, which shows that the median and interquartile range are increased in the e-cigarette group.

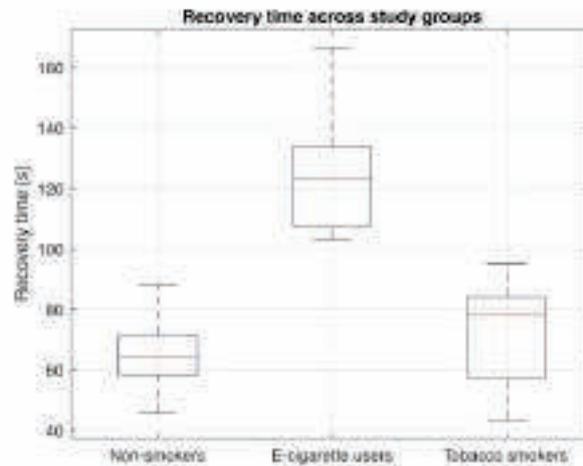


Figure 1. Boxplot of recovery time (in seconds) across study groups. E-cigarette users showed significantly longer recovery times compared to both traditional smokers and non-smokers ($p < 0.001$, Kruskal–Wallis test).

The acute change in heart rate (ΔHR) between resting conditions and immediately post-exercise was analyzed to assess the cardiovascular response to physical exertion. The descriptive statistics for each group are presented in Table 3. The e-cigarette group had the highest mean ΔHR (27.4 bpm) compared to traditional smokers (22.2 bpm) and non-smokers (22.1 bpm).

Group	Mean [s]	SD [s]	Median [s]	Min [s]	Max [s]
Non-smokers	22.10	7.11	25.00	7	51
E-cigarette users	27.35	5.88	26.50	19	43
Traditional smokers	22.15	5.72	23.00	11	30

Table 3. Descriptive statistics for $\Delta HR_{(t_{post-ex} - t_{rest})}$ in each study group. E-cigarette users exhibited the highest mean HR response to effort, although group differences were not statistically significant.

The one-way ANOVA test showed that ΔHR measurements between groups differed significantly ($p = 0.01366$). The results of the Tukey HSD test were used to perform post-hoc pairwise comparisons because of the significant difference. The Tukey HSD Post-Hoc Analysis results showed that ΔHR between non-smokers and e-cigarette users differed by -5.25 bpm with a confidence interval ranging from -10.02 to -0.48 and a p -value of 0.02772. The comparison between non-smokers and traditional smokers did not produce significant results because their ΔHR difference was -0.05 bpm with a confidence interval from -4.82 to 4.72 and a p -value of 0.9996. The analysis between e-cigarette users and traditional smokers revealed a 5.20 bpm difference with a confidence interval spanning from 0.43 to 9.97 and a p -value of 0.02953. The boxplot comparison of ΔHR across groups is shown in Figure 2.

To examine the speed of heart rate normalization following physical effort, we analyzed the difference in HR between post-exercise and recovery phases. Descriptive statistics for each group are shown in Table 4. Although the mean HR recovery appeared greatest in the e-cigarette and tobacco groups, the variability was high across all groups.

The one-way ANOVA test revealed no significant differences between the groups ($p = 0.0675$). As a result, post-hoc pairwise comparisons were performed using the Tukey HSD test. The study observed a -5.05 bpm difference in $\Delta HR_{(t_{post-ex} - t_{recovery})}$ between e-cigarette users and non-smokers, with a 95% confidence interval (CI) of [-10.84, 0.73] and a p -value of 0.105. The difference between non-smokers and conventional smokers was -3.10 beats per minute (CI: [-8.80, 2.69], $p = 0.467$). E-cigarette

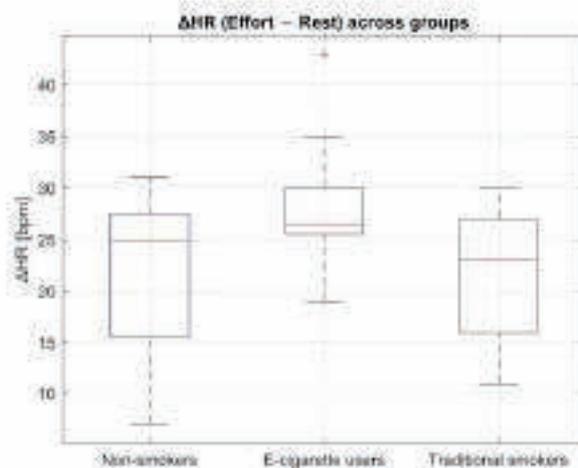


Figure 2. Boxplot of ΔHR across study groups. Although e-cigarette users showed the highest median increase in heart rate, the difference was not statistically significant ($p = 0.01366$, ANOVA test).

Group	Mean [s]	SD [s]	Median [s]	Min [s]	Max [s]
Non-smokers	21.00	6.70	22.50	7	32
E-cigarette users	26.05	6.18	26.00	17	43
Traditional smokers	24.10	8.36	21.50	13	40

Table 4. Descriptive statistics for $\Delta HR_{(Effort-Recovery)}$ in each study group. No significant differences were found in HR recovery between groups.

users and traditional smokers exhibited a 1.95 bpm difference (CI: [-3.84, 7.74], $p = 0.686$). No comparisons were statistically significant. These data indicate that, whereas mean HR recovery was numerically higher among e-cigarette and tobacco users, the observed differences were not statistically significant and are most likely due to individual variation in cardiovascular recovery. No clear group-level pattern emerged, the boxplot comparison of $\Delta HR_{(Effort-Recovery)}$ across groups is shown in Figure 3.

The drop in blood oxygen saturation (SpO_2) during effort was analyzed by calculating the difference between resting and post-exercise values ($\Delta SpO_2_{(Rest-Effort)}$). The descriptive statistics appear in Table 5. The SpO_2 levels decreased slightly for all groups during effort but e-cigarette users experienced the biggest mean decrease at 1.45% followed by traditional smokers at 1.20% and non-smokers at 1.05%.

Group	Mean [s]	SD [s]	Median [s]	Min [s]	Max [s]
Non-smokers	1.05	1.28	1.0	0	4
E-cigarette users	1.45	1.23	1.0	0	5
Traditional smokers	1.20	0.89	1.0	0	5

Table 5. Descriptive statistics for $\Delta SpO_2_{(Rest-Effort)}$.

A Kruskal-Wallis test revealed no statistically significant differences between groups ($p = 0.3712$). The extent of oxygen desaturation was similar across all participants, regardless of smoking status. Figure 4 displays the distribution of ΔSpO_2 across the three groups.

The post-exercise recovery in blood oxygen saturation (SpO_2) was assessed by comparing values obtained during the recovery phase to those recorded immediately after effort. Descriptive statistics are shown in Table 6. E-cigarette users exhibited

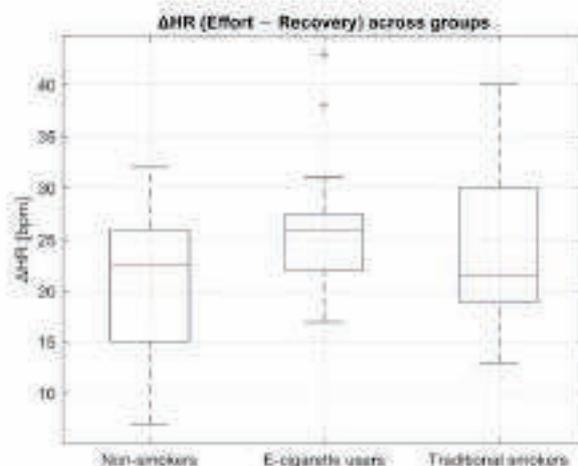


Figure 3. Boxplot of $\Delta HR_{(Effort-Recovery)}$ across study groups. Although e-cigarette users showed a slightly greater average HR decrease during recovery, group differences were not statistically significant ($p = 0.0875$, ANOVA test).

the highest mean improvement in SpO_2 (1.15%), followed by traditional smokers (0.70%) and non-smokers (0.50%).

Group	Mean [s]	SD [s]	Median [s]	Min [s]	Max [s]
Non-smokers	0.50	1.00	0.0	0	4
E-cigarette users	1.15	1.18	1.0	0	4
Traditional smokers	0.70	0.80	1.0	0	3

Table 6. Descriptive statistics for $\Delta SpO_{2(Baseline-Effort)}$.

Although a Kruskal-Wallis test did not reveal statistically significant differences between the groups ($p = 0.0700$), the result suggests a trend toward group-specific variations in oxygen recovery dynamics. Figure 5 visualizes the distribution of ΔSpO_2 across the study groups.

Systolic blood pressure (SYS) changes in response to exercise were calculated by subtracting resting values from post-effort readings. Descriptive statistics are presented in Table 7.

Group	Mean [s]	SD [s]	Median [s]	Min [s]	Max [s]
Non-smokers	6.65	8.96	5.00	-11	23
E-cigarette users	12.40	8.46	11.50	-3	30
Traditional smokers	9.70	10.57	8.00	-9	29

Table 7. Descriptive statistics for $\Delta SP S_{(Effort-Recovery)}$.

Although e-cigarette users exhibited a higher mean SYS increase (12.4 mmHg) compared to traditional smokers (9.7 mmHg) and non-smokers (6.65 mmHg), the differences were not statistically significant ($p = 0.1421$). Figure 6 shows the group distribution for the acute blood pressure response.

To evaluate the recovery of systolic blood pressure following exercise, the difference between post-effort and recovery values was calculated ($\Delta SYS = Effort - Recovery$). Mean recovery was greatest in the e-cigarette group (14.05 mmHg), followed by traditional smokers (10.25 mmHg) and non-smokers (8.60 mmHg). Full details are shown in Table 8.

While no statistically significant differences were found ($p = 0.294$), the trend indicates potentially delayed normalization in e-cigarette users. Figure 7 presents the distribution of ΔSYS recovery values.

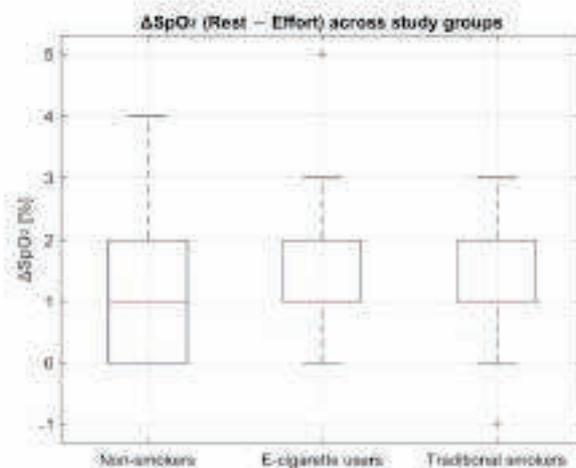


Figure 4. Boxplot of ΔSpO_2 (Rest – Effort) across study groups. E-cigarette users showed the highest mean oxygen desaturation, but group differences were not statistically significant ($p = 0.5712$, Kruskal–Wallis test).

Group	Mean [s]	SD [s]	Median [s]	Min [s]	Max [s]
Non-smokers	8.60	9.78	8.00	-6	24
E-cigarette users	14.05	10.88	17.00	-7	36
Traditional smokers	10.25	12.92	9.00	-12	34

Table 8. Descriptive statistics for ΔSpO_2 (Effort – Recovery).

Diastolic blood pressure (*DBP*) increased modestly following exercise in all groups. Descriptive statistics are summarized in Table 9. Traditional smokers showed the highest average increase (4.30 mmHg), followed by e-cigarette users (2.40 mmHg) and non-smokers (0.80 mmHg).

Group	Mean [s]	SD [s]	Median [s]	Min [s]	Max [s]
Non-smokers	0.80	6.44	2.00	-14	10
E-cigarette users	2.40	5.44	2.00	-8	14
Traditional smokers	4.30	6.97	2.00	-12	14

Table 9. Descriptive statistics for ΔDBP (Effort – Rest).

However, an ANOVA test revealed no statistically significant differences between the groups ($p = 0.223$). The distribution of post-exercise *DBP* changes is shown in Figure 8.

To evaluate the recovery of diastolic blood pressure following exercise, the difference between post-effort and recovery values was calculated ($\Delta DBP = \text{Effort} - \text{Recovery}$). Mean recovery was greatest in the traditional smokers group (5.75 mmHg), followed by e-cigarette users (3.75 mmHg) and non-smokers (1.70 mmHg). Full details are shown in Table 10.

However, an ANOVA test revealed no statistically significant differences between the groups ($p = 0.199$). The distribution of recovery *DBP* changes is shown in Figure 9.

The change in mean arterial pressure (*MAP*) from resting to post-exercise values was assessed as an integrated indicator of cardiovascular load. Descriptive statistics are provided in Table 11. All groups showed a moderate *MAP* increase, with the highest mean observed among e-cigarette users (5.95 mmHg).

However, a Kruskal–Wallis test found no statistically significant differences between groups ($p = 0.843$). Figure 10 illustrates ΔMAP distributions across the study groups.

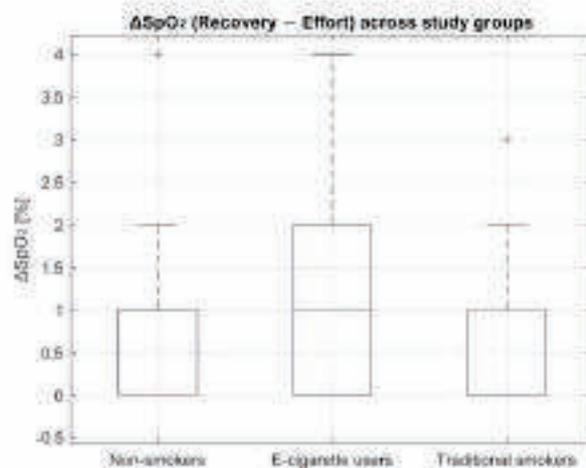


Figure 5. Boxplot of ΔSpO_2 (Recovery – Effort) across study groups. E-cigarette users showed the greatest improvement in SpO_2 during recovery. The trend approached statistical significance ($p = 0.0700$, Kruskal–Wallis test).

Group	Mean [s]	SD [s]	Median [s]	Min [s]	Max [s]
Non-smokers	1.70	5.86	3.00	-10	9
E-cigarette users	3.75	7.61	4.00	-12	17
Traditional smokers	5.75	7.49	5.00	-9	17

Table 10. Descriptive statistics for $\Delta MA_{effort-Recovery}$.

Post-exercise recovery of MAP was evaluated by comparing values between the effort and recovery phases. As summarized in Table 12, e-cigarette users demonstrated a slightly greater MAP reduction than the other groups (mean = 7.60 mmHg), although this difference was not statistically significant ($p = 0.426$). The data are visualized in Figure 11.

To explore the relationship between physiological reactivity and recovery efficiency, Pearson correlation analyses were conducted between recovery time and other cardiovascular or oxygenation markers (Table 13). Among all assessed parameters, only the increase in heart rate from resting to post-exercise ($\Delta HR_{effort-Post}$) showed a statistically significant correlation with recovery time ($r = 0.264$, $p = 0.0417$). This suggests that individuals exhibiting greater acute HR response to effort also required longer durations to return to baseline. Other examined variables such as ΔSpO_2 , ΔSYS , or ΔMAP demonstrated non-significant trends and did not reach statistical significance.

To evaluate between-group differences in physiological responses to exertion and recovery, pairwise comparisons were conducted using Welch's t-test (Table 14). Significant differences were observed for recovery time; with e-cigarette users showing significantly prolonged recovery compared to both non-smokers ($p < 0.0001$) and traditional smokers ($p < 0.0001$). Although the difference between non-smokers and traditional smokers did not reach statistical significance ($p = 0.1173$), the effect was directionally consistent. A statistically significant difference was also observed in $\Delta HR_{effort-Post}$ between non-smokers and e-cigarette users ($p = 0.01525$), and between e-cigarette users and traditional smokers ($p = 0.01658$), indicating a more pronounced acute HR response among e-cigarette users. No significant differences were found for $\Delta HR_{effort-Recovery}$, ΔSpO_2 , ΔSYS , ΔMA , or ΔMAP parameters between any of the groups.

The analysis of statistical significance received support from effect size calculations using Cohen's d for all significant and trend-level pairwise comparisons. The results are summarized in Table 15. The effect sizes for recovery time comparisons were very large between non-smokers and e-cigarette users ($d = 4.03$) and between e-cigarette users and traditional smokers ($d = 3.19$) which indicates a significant practical difference in post-exercise recovery duration. The heart rate reactivity to effort ($\Delta HR_{effort-Post}$) produced large effects when comparing non-smokers to e-cigarette users ($d = 0.81$) and e-cigarette

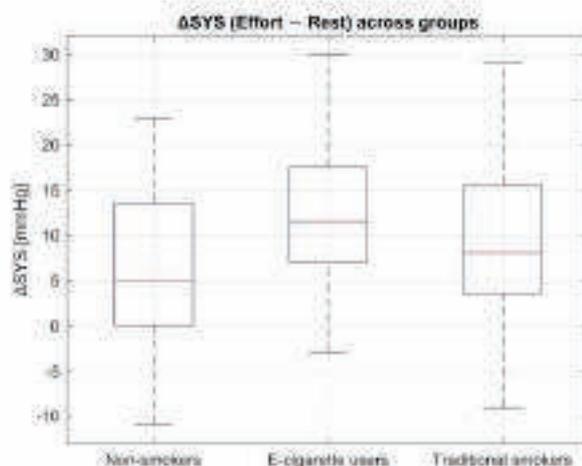


Figure 6. Boxplot of $\Delta SYS_{(Effort-Rest)}$ across study groups. Although e-cigarette users exhibited a greater mean increase in systolic blood pressure following exercise, the group differences were not statistically significant ($p = 0.161$, ANOVA test).

Group	Mean [s]	SD [s]	Median [s]	Min [s]	Max [s]
Non-smokers	4.10	8.87	4.50	-13	26
E-cigarette users	5.95	6.85	6.00	-6	26
Traditional smokers	4.10	5.72	5.00	-13	14

Table 11. Descriptive statistics for $\Delta MAP_{(Effort-Rest)}$

users to traditional smokers ($d = 0.90$). The results demonstrate that the detected differences have both statistical significance and substantial practical importance particularly for recovery-related outcomes.

A multiple linear regression model (Table 16) was used to evaluate the relationship between selected physiological parameters and recovery time. The overall model did not reach statistical significance ($F(4, 55) = 1.95$, $p = 0.115$), with an R^2 of 0.124 and an adjusted R^2 of 0.0606. Among the predictors, ΔHR showed a trend toward significance ($p = 0.076$), while other variables (ΔSpO_2 , ΔSYS , ΔMAP) were not significant.

A logistic regression model was trained to distinguish e-cigarette users from other participants based on ΔHR , ΔSpO_2 , ΔSYS , and ΔMAP . The model achieved an overall accuracy of 76.67%, with an AUC of 0.681. Only ΔHR was a statistically significant predictor ($p = 0.012$), confirming its role as the most informative feature. Despite decent discrimination performance, the model produced a relatively high $\log - loss$ of 0.5318, indicating imperfect probability calibration. The confusion matrix (Figure 12) revealed 11 false negatives, where e-cigarette users were misclassified as non-users.

A decision tree classifier (Figure 13) showed improved performance, achieving 85.00% accuracy and a lower $\log - loss$ of 0.3296. ΔHR remained the most important feature (Figure 14) followed by ΔSYS and ΔMAP .

The confusion matrix (Figure 15) showed strong sensitivity, with only 3 false negatives, demonstrating the model's ability to reliably identify e-cigarette users.

To evaluate generalization, both models were assessed using 5-fold cross-validation. That confirmed the stability of the models, with the decision tree again outperforming logistic regression in both accuracy and discrimination. The relatively close AUC values (0.681 vs. 0.756) suggest that while both models perform similarly at the probabilistic level, the tree offers slightly improved classification at the default decision threshold. The results are shown in Table 17.

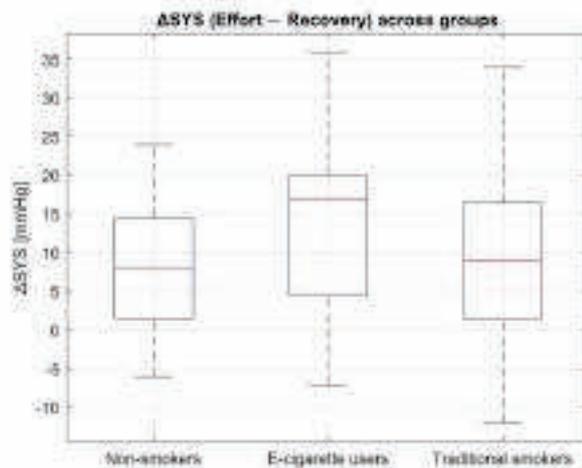


Figure 7. Boxplot of $\Delta SYS_{Effort-Recovery}$ across study groups. E-cigarette users showed the greatest reduction in systolic blood pressure during recovery, but no significant differences were observed between groups ($p = 0.291$, ANOVA).

Group	Mean [s]	SD [s]	Median [s]	Min [s]	Max [s]
Non-smokers	5.50	7.00	6.00	-6	26
E-cigarette users	7.60	6.85	6.50	-2	25
Traditional smokers	4.90	4.02	4.50	-4	12

Table 12. Descriptive statistics for $\Delta MAP_{Effort-Recovery}$.

Variable	Pearson r	p -value	Interpretation
$\Delta HR_{Effort-Rest}$	0.264	0.0417	Significant positive correlation
$\Delta HR_{Effort-Recovery}$	0.083	0.531	Not significant
$\Delta SpO_2_{Rest-Effort}$	0.204	0.119	Not significant
$\Delta SpO_2_{Effort-Rest}$	0.173	0.186	Not significant
$\Delta SpO_2_{Effort-Recovery}$	0.097	0.462	Not significant
$\Delta MA_{Effort-Rest}$	-0.128	0.331	Not significant
$\Delta MA_{Effort-Recovery}$	-0.080	0.545	Not significant
$\Delta MAP_{Effort-Rest}$	0.143	0.271	Not significant
$\Delta MAP_{Effort-Recovery}$	0.226	0.073	Trend, not significant

Table 13. Pearson correlations between recovery time and physiological response variables.

Variable	Comparison	t -statistics	p -value	Interpretation
Recovery time	Non-smokers vs E-cigarette users	-12.758	< 0.0001	Significant
Recovery time	E-cigarette users vs Traditional smokers	10.096	< 0.0001	Significant
$\Delta HR_{Effort-Rest}$	Non-smokers vs E-cigarette users	-2.546	0.0152	Significant
$\Delta HR_{Effort-Rest}$	E-cigarette users vs Traditional smokers	2.521	0.0166	Significant
Recovery time	Non-smokers vs Traditional smokers	-1.666	0.1173	Not significant (trend)
$\Delta MAP_{Effort-Recovery}$	Non-smokers vs E-cigarette users	-1.391	0.1716	Not significant (trend)

Table 14. Welch's t -test for selected pairwise comparisons of key variables (statistically significant or trend-level results).

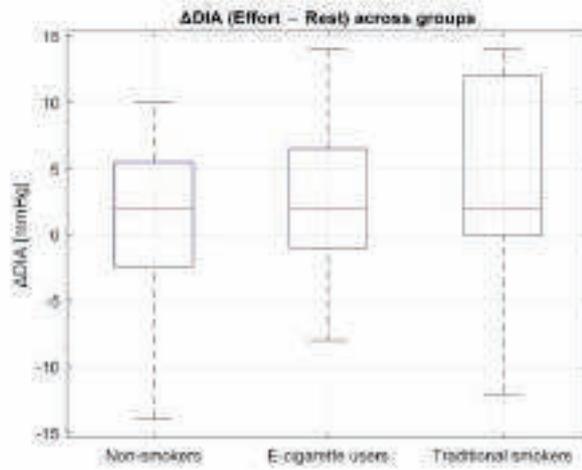


Figure 8. Boxplot of $\Delta DIA_{(Effort-Rest)}$ across study groups. Slight increases in diastolic blood pressure were observed in all groups following exercise, with no significant differences between them ($p = 0.223$, ANOVA test).

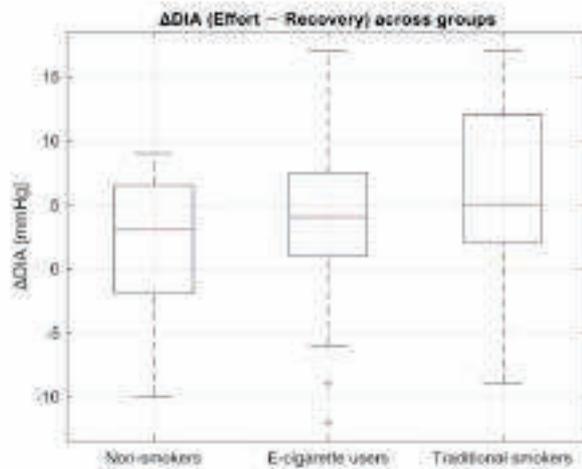


Figure 9. Boxplot of $\Delta DIA_{(Effort-Recovery)}$ across study groups. Diastolic pressure reductions during recovery were comparable among groups, and no statistically significant differences were found ($p = 0.199$, ANOVA test).

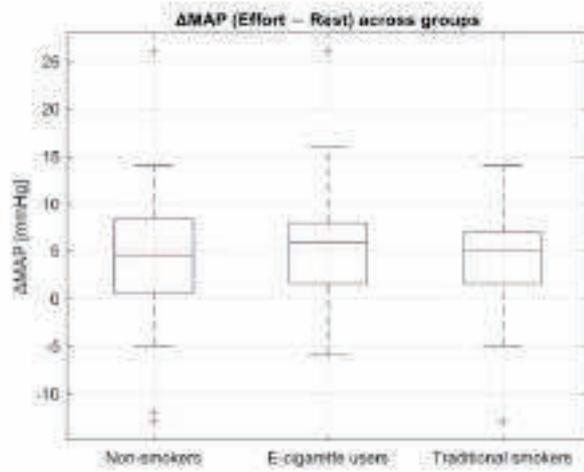


Figure 10. Boxplot of $\Delta\text{MAP}_{(\text{Effort}-\text{Rest})}$ across study groups. Mean arterial pressure increased after exercise in all groups, with no significant group differences observed ($p = 0.843$, Kruskal-Wallis test).

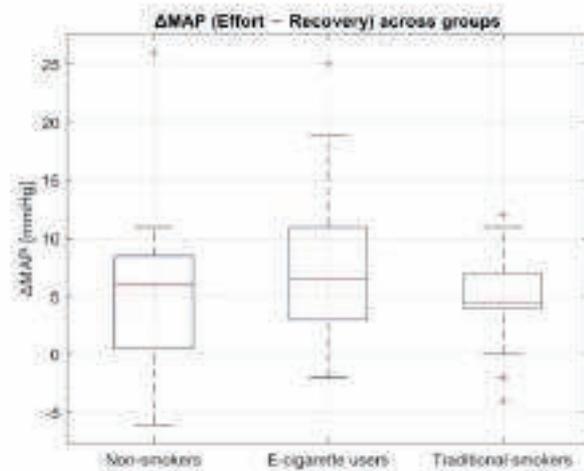


Figure 11. Boxplot of $\Delta\text{MAP}_{(\text{Effort}-\text{Recovery})}$ across study groups. Although e-cigarette users showed a slightly greater MAP decrease during recovery, differences between groups were not statistically significant ($p = 0.426$, Kruskal-Wallis test).

Variable	Comparison	Cohen's <i>d</i>	Interpretation
Recovery time	Non-smokers vs E-cigarette users	-4.03	Very large effect
Recovery time	E-cigarette users vs Traditional smokers	3.19	Very large effect
$\Delta HR_{effort-free}$	Non-smokers vs E-cigarette users	-0.81	Large effect
$\Delta HR_{effort-free}$	E-cigarette users vs Traditional smokers	0.90	Large effect
Recovery time	Non-smokers vs Traditional smokers	-0.51	Medium effect (trend)

Table 15. Cohen's *d* effect sizes for selected pairwise comparisons between study groups (for statistically significant or near-significant results from *t*-tests).

Variable	Estimate	Standard Error	<i>t</i> -statistics	<i>p</i> -value
Intercept	51.7900	14.6150	3.5436	0.00081
ΔHR	1.0423	0.5755	1.8112	0.07557
ΔSpO_2	4.7345	3.3661	1.4065	0.16520
ΔSI^2	0.4540	0.4698	0.9662	0.33815
ΔMAP	0.0825	0.6243	0.1322	0.89531

Table 16. Multiple linear regression coefficients for recovery time prediction.

[†] The root mean squared error of the model was 29.1 seconds.

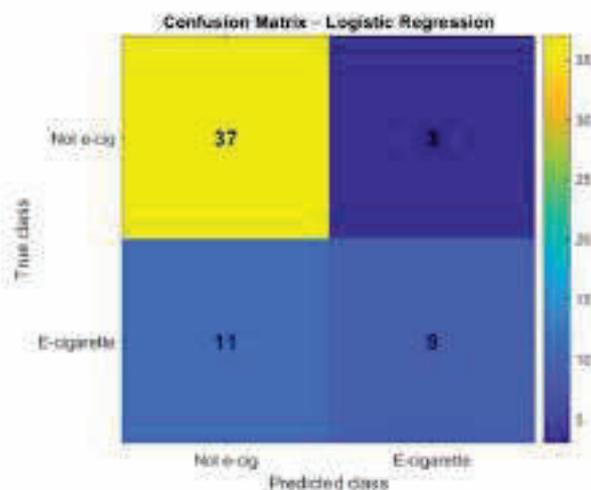


Figure 12. Confusion matrix for logistic regression.

Model	Accuracy [%]	AUC	log-loss
Logistic Regression	76.67	0.681	0.5318
Decision Tree	85.00	0.756	0.3296

Table 17. Model performance comparison (accuracy, AUC, log-loss).

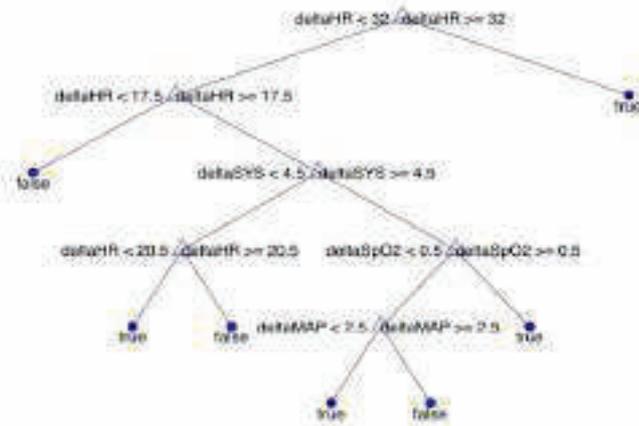


Figure 13. Visualized decision tree structure.

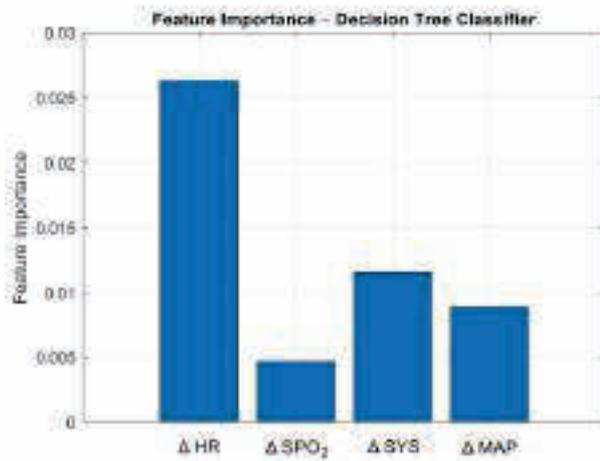


Figure 14. Feature importance scores from the tree model.

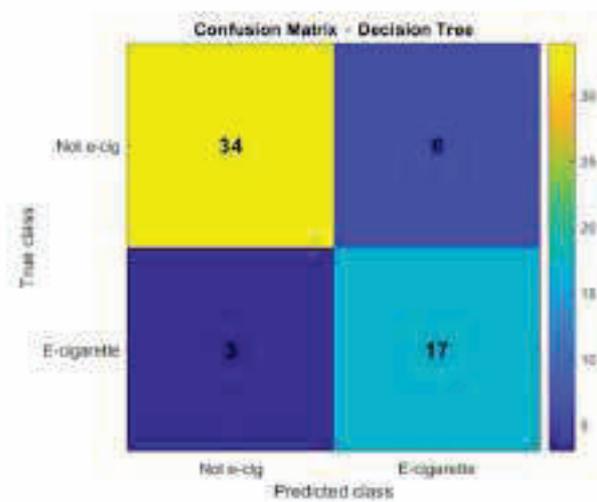


Figure 15. Confusion matrix for decision tree.

Discussion

Our study found that e-cigarette users had a markedly higher heart rate response to exercise and a slower post-exercise heart rate recovery compared to both traditional smokers and non-smokers. This heightened cardiac reactivity aligns with reports that nicotine exposure from e-cigarettes can acutely stimulate the sympathetic nervous system similarly to tobacco cigarettes. Multiple controlled studies have shown that vaping rapidly elevates heart rate, an effect largely attributable to nicotine's sympathomimetic action²¹. For example, Dimitriadis et al. observed that in habitual smokers, the acute "unfavorable" sympathetic and blood pressure responses to an e-cigarette were indistinguishable from those provoked by a tobacco cigarette²². Our finding that e-cigarette users' heart rate reactivity even exceeded that of regular smokers is noteworthy – it suggests that chronic vaping may confer no autonomic advantage over smoking, and perhaps reflects high nicotine intake or altered autonomic regulation in this group. Consistent with this, Mohebbani et al. documented increased cardiac sympathetic activity in habitual e-cigarette users²³, indicating a shift toward sympathetic dominance that could underlie the exaggerated heart rate response and delayed recovery we observed. Traditional cigarette smokers are already known to have impaired autonomic recovery – for instance, heavy smokers exhibit significantly slower heart rate recovery after exercise than non-smokers²⁴.

The e-cigarette group's similar (or greater) impairment suggests that long-term vaping, like smoking, blunts vagal reactivation post-exercise. Additionally, changes in cardiac rhythm dynamics have been reported with vaping; one study noted that e-cigarette use (with nicotine) acutely reduces heart rate variability and prolongs the QTc interval^{25,26}, reinforcing the concept that nicotine-containing vapes evoke autonomic perturbations comparable to cigarettes. These converging findings support the interpretation that our e-cigarette users' pronounced heart rate and autonomic responses are not anomalous, but rather parallel those seen with combustible tobacco, underscoring that e-cigarettes can significantly stress the cardiovascular system akin to traditional smoking.

Despite clear differences in heart rate dynamics, our study found no significant group differences in blood pressure (BP) response or recovery following exercise. All three cohorts – vapers, smokers, and non-smokers – showed a similar return of blood pressure to baseline during recovery. This contrasts with the acute effects literature, where both smoking and vaping are well-documented to raise blood pressure transiently via sympathetic activation. For instance, a recent meta-analysis confirmed that e-cigarette inhalation causes significant increases in systolic, diastolic, and mean arterial pressure, much like conventional cigarettes²¹. Dimitriadis et al. likewise reported that e-cigarette puffing in smokers acutely boosts arterial pressure to levels comparable with smoking a tobacco cigarette²². Our exercise-based protocol, however, assessed BP after a period of recovery rather than immediately post-inhalation, which may explain the discrepancy – any acute nicotine-induced pressor effect likely subsided by the time BP restitution was evaluated. In terms of chronic exposure, our results are consistent with observations that long-term e-cigarette use does not drastically differ from smoking in its impact on resting BP. A comprehensive review by La Rosa et al. found that in nearly two-thirds of comparisons, e-cigarette use showed no significant difference from tobacco smoking on heart rate or blood pressure outcomes²⁷. This suggests that the overall hemodynamic burden of habitual vaping is on par with smoking, at least in young adults without established cardiovascular disease. Notably, some studies even suggest slight cardiovascular benefits when smokers switch to e-cigarettes – for example, hypertensive smokers who transitioned to vaping experienced a reduction in systolic BP after one year²⁸. While our cross-sectional design did not capture such longitudinal effects, the absence of BP differences between groups in our data aligns with the notion that both smoking and vaping exert similar chronic influences on blood pressure regulation, with neither group showing overt BP dysregulation at rest or after exercise compared to non-smokers. In summary, the dissociation between heart rate and blood pressure findings in our study (significant HR effects but uniform BP recovery) may indicate that autonomic cardiac control is more sensitive to smoking/vaping status than vascular tone is, echoing the idea that being "less harmful" than cigarettes does not mean e-cigarettes are benign for all cardiovascular parameters²¹.

We observed only subtle differences in blood oxygen saturation (SpO_2) dynamics among the groups. During the six-minute walk exercise, all participants showed a slight drop in SpO_2 (a normal physiological response to exertion), and e-cigarette users had the largest mean desaturation – but this trend did not reach statistical significance. By the end of recovery, oxygen saturation returned toward baseline in all groups, with no clear impairment in the vaping or smoking cohorts. These findings align with much of the existing literature, which generally reports minimal acute changes in oxygen saturation from e-cigarette use. A recent review¹⁶ noted that in four studies examining SpO_2 before and after vaping, three found no significant change in oxygen levels, and only one²⁹ observed a slight decrease in SpO_2 following e-cigarette use in smokers. In our study, any exercise-induced desaturation was quickly reversible, and the lack of group difference suggests that neither chronic vaping nor smoking induced a severe gas exchange deficit under moderate exercise conditions. It is worth mentioning that chronic cigarette smokers often have marginally lower resting oxygen saturation compared to non-smokers³⁰, likely due to subtle ventilation-perfusion mismatches or elevated carboxyhemoglobin from smoke inhalation. The fact that our traditional smokers did not significantly differ from non-smokers in SpO_2 may reflect the relatively young, healthy status of our sample and their normal lung function. For e-cigarette users, some emerging evidence indicates vaping can affect pulmonary function in ways not immediately reflected by SpO_2 .

Kizhakké Puliyakode et al.²⁷ showed that while pulse oximetry oxygen saturation remained unchanged, a single vaping session in daily vapers acutely increased heart rate and caused measurable ventilation-perfusion mismatch in the lungs. This implies that a standard SpO_2 reading might be too coarse to capture early vape-related pulmonary impairments. In our data, the e-cig group's slightly greater (though non-significant) exercise desaturation could hint at such subtle impairment in oxygen exchange or delivery. However, overall oxygenation profiles during exercise and recovery were comparable across e-cig users, smokers, and non-smokers in our study. This suggests that, in the absence of overt lung disease, habitual vaping has no pronounced effect on oxygen saturation at rest or with mild exercise, paralleling findings from acute trials where even nicotine-rich vaping had limited immediate impact on SpO_2 ¹⁶. Any small deviations we noted remain below clinical significance, yet they underscore the importance of investigating long-term respiratory consequences of e-cigarettes with more sensitive measures (e.g. diffusion capacity or exercise blood gases).

When contextualizing our results with broader health outcomes, a consistent picture emerges: chronic e-cigarette use mirrors many of the deleterious effects of traditional smoking on cardiopulmonary function. Our finding that vapers have prolonged cardiovascular recovery times and elevated exercise heart rates is in line with recent evidence on exercise capacity. Notably, a study by Simovic et al.²⁸ showed that young adult e-cigarette users had significantly reduced exercise tolerance (peak exercise capacity), comparable to age-matched cigarette smokers, and markedly worse than never-smokers. Both vapers and smokers in that study exhibited impaired blood vessel function and greater muscle fatigue during exercise, suggesting that habitual vaping may induce cardiovascular limitations akin to long-term tobacco use. These data resonate with our observations of slow post-exercise recovery in e-cig users, pointing to a potential subclinical decrement in fitness or circulatory efficiency. In essence, although e-cigarettes eliminate combustion byproducts, they still deliver nicotine and other chemicals that can negatively impact cardiovascular physiology over time²¹.

Our results contribute to the growing consensus that switching from combustible to electronic cigarettes does not fully safeguard users from cardiovascular strain. In some metrics (like heart rate recovery), e-cig users in our study even fared worse than smokers, highlighting individual variability and the possibility that certain vaping behaviors (e.g. frequent high-nicotine puffs) might exacerbate autonomic stress. It is also important to note the role of advanced analytical approaches in uncovering these effects. We applied a multimodal physiological signal analysis and even achieved a moderate accuracy in classifying individuals by smoking status based on their vital-sign response patterns. Similarly, other researchers have employed statistical and machine-learning techniques on biosignals to differentiate smoking behaviors. For instance, Yu et al.²⁹ used wearable ECG data and machine learning to detect smoking events with about 69% accuracy. Such approaches underscore that there are discernible physiological signatures associated with chronic smoking and vaping. In our case, the ability to classify e-cig users from their recovery profiles reinforces the idea that the autonomic and cardiorespiratory deviations we observed are systematic. Taken together, the current findings align with published evidence that e-cigarette use, much like traditional smoking, is linked to elevated heart rate, acute blood pressure spikes, and reduced exercise performance, all of which raise concerns about long-term cardiovascular risk²⁰.

Where our results diverge slightly is in the magnitude and context of these effects—for example, the unexpectedly pronounced heart rate impairment in vapers versus smokers, which contrasts with some literature suggesting e-cigarettes might be a “lesser evil” on the heart³⁰. This discrepancy invites further research but also cautions against complacency regarding e-cigarette health effects. In summary, our study's cardiovascular and respiratory findings are largely consistent with peer-reviewed studies of similar outcomes in smokers and vapers, reinforcing that e-cigarettes share many of the physiological burdens of combustible cigarettes.

The overall evidence indicates that regular vaping produces effects on autonomic function and hemodynamics and exercise capacity which match those of conventional smoking thus disproving the notion that e-cigarettes are harmless alternatives²¹. The findings from these studies enhance our knowledge about how both e-cigarette and tobacco cigarette users develop quantifiable cardiovascular and respiratory system problems while non-smokers retain better physiological health. The discussion emphasizes the need for ongoing comparative research that employs advanced signal analysis and machine learning techniques to determine the complete risks of new nicotine delivery products against traditional smoking.

The research contains multiple limitations that need to be recognized. The cross-sectional research design prevents researchers from establishing cause-and-effect relationships between e-cigarette use and changes in physiological responses. The observed group differences cannot establish whether these differences stem from long-term vaping exposure or pre-existing individual traits that lead to nicotine use and autonomic imbalance. The small sample size restricts statistical power to detect minor effects especially in secondary measurements such as oxygen saturation and blood pressure when the sample is divided into three groups. The study results show meaningful clinical differences but some trends failed to achieve statistical significance. The study results are not applicable to older populations or individuals with cardiovascular or respiratory conditions because all participants were young adults aged 18–25 who were generally healthy. The lack of objective verification for smoking and vaping behavior through biomarkers such as cotinine levels or carbon monoxide testing introduces classification bias into the study. The results could have been affected by unmeasured confounding factors including fitness status and vaping intensity.

and dual-use patterns despite the age and physical activity level matching between groups. The physiological data collection occurred through short-term controlled exertion rather than real-world stressors or prolonged activity. Although the chosen exercise protocol was standardized and reproducible, it may not fully capture the long-term cardiopulmonary burden of habitual nicotine use.

Conclusions

The research demonstrates that regular electronic cigarette use leads to observable changes in cardiovascular and respiratory reactions during submaximal physical exercise among young adults. The results indicate that e-cigarette users experience delayed cardiovascular recovery after physical activity. The consistency of this effect across participants, as indicated by the narrow interquartile range and large effect sizes, highlights a potentially systematic alteration in autonomic recovery mechanisms within this group.

E-cigarette users demonstrated significantly larger heart rate responses to exercise which indicates their sympathetic nervous system activation or reduced vagal control when compared to traditional smokers and non-smokers. The increased reactivity of the autonomic system most likely caused the longer recovery times seen in the vaping group. The blood pressure recovery rates showed no significant differences between groups but the heart rate recovery rates demonstrated substantial variations between groups. The different effects of smoking and vaping behaviors on autonomic processes that control heart rate and vascular function become apparent through this dissociation. The oxygen saturation changes in e-cigarette users remained small and failed to achieve statistical significance yet they showed patterns of altered saturation during and after exercise. The combined results show that e-cigarette users have a unique physiological pattern which includes increased heart rate responses and delayed recovery and possible minor impairments in cardiorespiratory control. The multimodal physiological signal analysis using phase-specific measures and machine learning-based classification demonstrated that these differences follow specific patterns rather than random occurrences. The parameter ΔHR proved to be the most useful feature for identifying autonomic responses in individuals exposed to nicotine.

The overall pattern showed clear distinctions between e-cigarette users and both smokers and non-smokers even though some differences were not statistically significant. The findings indicate that regular e-cigarette use does not result in neutral physiological effects and produces cardiovascular strain at a level similar to traditional smoking. The increasing youth adoption of e-cigarettes makes it essential to continue studying vaping health risks through education programs. Future research should implement machine learning and multi-modal data fusion to create predictive models which can identify vaping-related cardiovascular or respiratory dysfunction at its early stages.

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Author contributions statement

Conceptualization, J.C. and P.S.K.; methodology, J.C., H.Z., A.F. and P.S.; software, J.C., R.D.; validation, R.J.D., R.M. and P.S.K.; formal analysis, J.C. and P.S.K.; investigation, J.C., H.Z., A.F. and P.S.; resources, H.Z., P.S., A.F. and J.C.; data curation, R.D.; writing—original draft preparation, J.C.; writing—review and editing, P.S.K., R.J.D., R.D. and R.M.; visualization, J.C.;

supervision, P.S.K. and R.M.; project administration, J.C.; funding acquisition, P.S.K. All authors have read and agreed to the published version of the manuscript.

Additional information

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee for Research Involving Human Participants at the Silesian University of Technology, Gliwice, Poland, resolution No. 3/2025 dated March 11, 2025.

Informed consent

Informed consent was obtained from all subjects involved in the study.

Data availability

The authors confirm that the data supporting the findings of this study are available upon request. The dataset is not publicly accessible, but it can be shared with interested researchers upon reasonable request.

Conflicts of interest

The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

HR	Heart Rate
BP	Blood Pressure
SpO_2	Saturation of Peripheral Oxygen
FEV_1	Forced Expiratory Volume in 1 second
NIBP	Non-invasive Blood Pressure
ECG	Electrocardiogram
PR	Pulse Rate
PPG	Photoplethysmogram
SYS	Systolic Blood Pressure
DIA	Diastolic Blood Pressure
MAP	Mean Arterial Pressure
ANOVA	Analysis of Variance
TP	True Positive
TN	True Negative
FP	False Positive
FN	False Negative
SD	Standard Deviation
bpm	Beats per Minute
CI	Confidence Interval
log-loss	logarithmic loss

Opinia Komisji Bioetycznej



UCHWAŁA NR 3/2025

Komisji ds. etyki badań naukowych prowadzonych z udziałem ludzi
z dnia 11.03.2025 r.

w sprawie wydania opinii przez Komisję ds. etyki badań naukowych prowadzonych z udziałem ludzi o badaniu naukowym, opisanym we wniosku przez mgr inż. Joannę Chwał nt. „Wpływ palenia papierosów elektronicznych i tradycyjnych na wybrane parametry układu oddechowego i sercowo-naczyniowego pacjentów, na podstawie analizy wektorów danych, uzyskanych z rejestracji wielomodalnych sygnałów biomedycznych”
(dot. badań: praca doktorska).

Na podstawie § 5 ust. 4 pkt Zarządzenia Nr 209/2024 Rektora Politechniki Śląskiej z dnia 12 listopada 2024 r. w sprawie powołania i zasad działania Komisji ds. etyki badań naukowych prowadzonych z udziałem ludzi, Komisja ds. etyki badań naukowych prowadzonych z udziałem ludzi postanawia, co następuje:

§ 1

Komisja potwierdza spełnienie warunków rzetelności badawczej i wymogów etycznych stawianych badaniom naukowym.

Komisja wyraża pozytywną opinię na temat badania naukowego z udziałem ludzi, opisanego przez Panią mgr inż. Joannę Chwał afiliowaną przy Wspólnej Szkole Doktorskiej działającej przy Politechnice Śląskiej oraz przy Akademii Śląskiej, Katedrze Inżynierii Klinicznej, we wniosku z dnia 05.03.2025 r.

§ 2

Uchwała wchodzi w życie z dniem podjęcia.

Przewodnicząca Komisji
ds. etyki badań naukowych
prowadzonych z udziałem ludzi

Podpisała Katarzyna Krukiewicz
(podpis odręczny)

Gliwice, 14.03.2025 r.

Oświadczenia współautorów publikacji

Zgodnie z obowiązującymi zasadami dotyczącymi rozpraw doktorskich przygotowanych w formie cyklu publikacji, do każdej pracy wchodzącej w skład niniejszej rozprawy zostały sporządzone i podpisane przez wszystkich współautorów oświadczenia dotyczące wkładu merytorycznego. Oświadczenia, obejmują szczegółowe wyszczególnienie ról autorskich, takich jak: konceptualizacja, metodologia, oprogramowanie, walidacja, analiza formalna, badania, wizualizacja, opracowanie oryginalnej wersji manuskryptu, recenzja i edycja manuskryptu oraz nadzór naukowy. Dodatkowo, w każdym oświadczeniu wskazano procentowy udział doktorantki w powstaniu danej publikacji. Wkład ten został określony przez współautorów i potwierdzony ich własnoręcznymi podpisami.

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Niniejszym oświadczam, że w publikacji:

Chwał Joanna, Filipowska Anna, Antonowicz Magdalena, Lisicki Dawid, Kostka Paweł, Doniec Rafał, "Elemental Composition of Vaping and Smoking Aerosols: Influence of Liquid Type and Tank Conditions"

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Oświadczenie współautorów publikacji

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Potwierdzenia przyjęcia artykułów do druku



CERTIFICATE

We hereby certify that the paper

"Comparative Pharmacokinetics of Nicotine from ECigarettes and Traditional Cigarettes: A PBPK Modeling and Machine Learning Approach"
Joanna Chwał, Arkadiusz Banasik, Radosław Dzik, Piotr Pańtak, Ewaryst Tkacz

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Stowarzyszenie Wychowanków
Politechniki Śląskiej
Oddział przy Wydziale Organizacji
i Zarządzania

Zabrze, dn. 20.09.2025 r.

mgr inż. Joanna Chwał
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Artykuł nt. „PHYSIOLOGICALLY-BASED PHARMACOKINETIC MODELING OF NICOTINE”, którego autorkami są: Joanna Chwał, Radosław Dzik, Arkadiusz Banasik, Piotr Pańtak i Ewaryst Tkacz.

Praca została zaprezentowana na Konferencji Naukowej Strategie w podejmowaniu decyzji w sytuacjach konfliktu i współpracy. W chwili obecnej artykuł został pozytywnie zrecenzowany przez dwóch recenzentów i przechodzi proces wydawniczy. Publikacja artykułu w Zeszytach Naukowych Politechniki Śląskiej, seria: Organizacja i Zarządzanie, ISBN 1641-3466, jest przewidziana na koniec roku 2025. Zeszyty Naukowe Politechniki Śląskiej, seria Organizacja i Zarządzanie według wykazu czasopism punktowanych MNiSW z roku 2024 posiadają 70 punktów.

Z poważaniem

Przewodnicząca Komitetu Organizacyjnego

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Konferencja Naukowa
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Artykuł nt. „P. MODELING THE IMPACT OF TOBACCO CONTROL POLICIES ON SMOKING PREVALENCE: A DYNAMIC SIQ+P+E+H+X FRAMEWORK”, którego autorkami są: Joanna Chwał, Radosław Dziłk, Arkadiusz Benasik, Karol Piotrowski, Marcin Wawryszczuk, Mateusz Zapotoczny, Wojciech M. Kempa, Piotr Pkiewicz i Ewaryst Tkacz.

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Mgr inż. Joanna Chwał w październiku 2015 roku rozpoczęła studia inżynierskie na Wydziale Inżynierii Biomedycznej Politechniki Śląskiej w Zabrzu, na specjalności Informatyka i Aparatura Medyczna. W styczniu 2019 roku uzyskała tytuł inżyniera, a następnie kontynuowała naukę na studiach magisterskich na tym samym wydziale, wybierając specjalność Przetwarzanie i Analiza Informacji Biomedycznych. W lipcu 2020 roku obroniła pracę magisterską, uzyskując tytuł magistra inżyniera. W październiku 2020 roku rozpoczęła kształcenie w ramach Wspólnej Szkoły Doktorskiej Politechniki Śląskiej w dyscyplinie inżynieria biomedyczna, realizując rozprawę doktorską pt.: „Wpływ palenia papierosów elektronicznych i tradycyjnych na wybrane parametry układu oddechowego i sercowo-naczyniowego pacjentów, na podstawie analizy wektorów danych, uzyskanych z rejestracji wielomodalnych sygnałów biomedycznych”, pod opieką promotora dr. hab. inż. Pawła Kostki, prof. PŚ oraz promotora pomocniczego dr. hab. inż. Rafała Dońca.

Doktorantka jest autorką i współautorką publikacji naukowych, w tym artykułów w czasopismach z listy JCR, rozdziałów w monografiach oraz wystąpień konferencyjnych krajowych i międzynarodowych. Do jej dorobku należą m.in. prace w czasopismach Healthcare, Journal of Clinical Medicine, Applied Sciences oraz w wydawnictwie Springer, dotyczące m.in. modelowania 3D w medycynie, analizy sygnałów biologicznych oraz wykorzystania algorytmów uczenia maszynowego w diagnostyce i profilaktyce zdrowotnej. Brała udział w licznych konferencjach naukowych, takich jak International Summer School on BioX (Chania, Grecja), 6th Polish Conference on Artificial Intelligence, NBC & PCBBE, czy MaST & Majówka Młodych Biomechaników.

Doktorantka prowadzi zajęcia dydaktyczne w języku polskim i angielskim z zakresu inżynierii biomedycznej. Była promotorem pomocniczym pracy dyplomowej oraz sprawowała opiekę nad projektami studenckimi, w tym nad inicjatywą „Silesian Wheels” w Studenckim Kole Naukowym Biomechatroniki „BIOKREATYWNI”. Aktywnie angażuje się w popularyzację nauki, m.in. poprzez prowadzenie korepetycji dla studentów, reprezentowanie Wydziału Inżynierii Biomedycznej podczas wydarzeń otwartych Politechniki Śląskiej, a także zdobywając III miejsce w konkursie Three Minute Thesis® w 2021 roku. Jej dorobek obejmuje także działalność recenzencką – wykonała pięć recenzji dla czasopism Quantitative Imaging in Medicine and Surgery (QIMS) oraz SAGE Digital Health.