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RESEARCH ARTICLE

Role of oral health in heart and vascular health: A population-based study

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Abstract

Background and aim

Conditions such as hypertension, cardiovascular diseases, and hypercholesterolemia, are a major public health challenge. This study investigates the influence of oral health indicators, including gum bleeding, active dental caries, tooth mobility, and tooth loss, on their prevalence in Hungary, considering socioeconomic, demographic, and lifestyle factors.

Materials and methods

Data from the 2019 Hungarian European Health Interview Survey with 5,603 participants informed this analysis. Data were accessed from the records maintained by the Department of Health Informatics at the University of Debrecen between September and November 2023. Variable selection employed elastic net regularization and k-fold cross-validation, leading to high-performing predictors for weighted multiple logistic regression models. Sensitivity analysis confirmed the findings' validity.

Results

Significant links were found between poor oral health and chronic cardiac conditions. Multiple teeth extractions increased hypertension risk (OR = 1.67, 95% CI: [1.01-2.77]); dental prosthetics had an OR of 1.45 [1.20-1.75]. Gum bleeding was associated with higher cardiovascular disease (OR = 1.69 [1.30-2.21]) and hypercholesterolemia risks (OR = 1.40 [1.09-1.81]).

Conclusions

Oral health improvement may reduce the risk of cardiac conditions. This underscores oral health's role in multidisciplinary disease management.

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1. Introduction

1.1 Impact of heart and vascular conditions globally and in Hungary

Chronic non-communicable diseases (NCDs) remain a major challenge in global public health, responsible for 74% of all deaths in 2019. Among these, heart and vascular conditions such as hypertension and cardiovascular diseases (CVDs) are increasingly prevalent and significant. Ischemic heart disease, a key CVD, accounted for 16% of global fatalities. The rising incidence of heart and vascular conditions, also reflected in conditions like stroke and chronic obstructive pulmonary disease, underscores the critical need for targeted public health strategies [1–3].

Within this context, hypercholesterolaemia presents as a variable of particular significance, contributing to the plot of CVDs. Characterized by perturbations in lipid profiles—be it elevated total cholesterol, low-density lipoprotein cholesterol (LDL-c), or triglycerides (TG)—hypercholesterolaemia has long been implicated in cardiovascular pathology [4, 5].

Europe leads with a 53.7% prevalence of hypercholesterolemia, contrasted by much lower rates in regions like Southeast Asia and Africa [6].

Hypertension affects an estimated 1.28 billion adults worldwide, particularly in low- and middle-income countries. Interestingly, only 46% of these individuals are aware of their condition, and just 21% effectively manage their hypertension. The etiological landscape is further complicated by many of factors, including genetic predispositions and lifestyle choices such as obesity and excessive sodium intake. CVDs, including coronary and cerebrovascular diseases, are the leading global cause of death, accounting for 17.9 million fatalities in 2019. Once again, low- and middle-income countries bear the brunt of this condition. While traditional risk factors have been heavily studied, evidence posits a compelling link between oral health and the onset or exacerbation of CVDs [7–10].

In Hungary, NCDs present an alarming public health situation, with 40% of adults reporting at least one chronic condition, surpassing the EU average of 36%. The nation leads the EU in preventable mortality rates at 326 per 100,000 individuals, primarily due to lung cancer, ischaemic heart disease, and lifestyle risks like smoking. CVDs account for one-third of all deaths, and hypertension prevalence stands at 34% for women and 29% for men [11–13].

1.2 Oral health: The overlooked factor in chronic cardiac conditions

Globally, oral health conditions, affecting about 3.5 billion individuals, exceed the combined prevalence of the top five non-communicable diseases. Nearly 19% of adults, or over 1 billion people, suffer from severe periodontal diseases, while dental caries in permanent teeth impact 2 billion [14–16].

In Hungary, the oral health situation presents notable challenges linked to chronic diseases. Leading in dental caries prevalence in Europe, Hungary also grapples with significant rates of edentulism among the elderly; 30% of those aged 65 and above, and 40% of those over 75, have experienced complete tooth loss. This reflects not only poor oral health but also broader social and economic disparities. Additionally, gingivitis and periodontitis affect about a third of the population. These issues highlight the critical need to address Hungary's unique oral health concerns within the broader European context [17–22].

1.3 The link between oral health and heart-related conditions

Previous research has highlighted the link between periodontal health, CVDs, and hypercholesterolemia, with a focus on Porphyromonas gingivalis (P. gingivalis) [23, 24]. This pathogen is implicated in atherosclerosis development by oxidizing HDL and LDL, damaging vascular endothelial cells, and contributing to endothelial dysfunction. P. gingivalis also promotes the proliferation of smooth muscle cells, formation of foam cells, and destabilization of atherosclerotic plaques, exacerbating cardiovascular outcomes [25]. A key mechanism involves the secretion of gingipains, cysteine proteases that degrade host proteins, incite inflammation, impair vascular function, and promote clot formation through platelet activation and fibrinogen degradation. These proteases also activate matrix metalloproteinases (MMPs), which contribute to plaque destabilization. Additionally, P. gingivalis invades endothelial cells, inducing oxidative stress and elevated reactive oxygen species (ROS) levels, further aggravating endothelial dysfunction and increasing cardiovascular risk [26–30].

As the preceding discussion predominantly emphasized the links between periodontitis and cardiovascular diseases, it is imperative to consider the early-stage oral health markers that constitute the focal point of this study. Dental caries, as identified by Folayan et al. (2021), not only serve as plaque retention factors but also foster biofilm proliferation, conducive to anaerobic bacteria growth and gingival inflammation [31]. Further, Sabharwal et al. (2021) linked dental caries to an increased risk of metabolic diseases [32]. These findings highlight the potential role of chronic oral inflammation and salivary biomarkers in mediating the link between dental caries and systemic metabolic disorders.

Gingival bleeding serves as both a primary symptom and an initial clinical indicator of periodontal disease [33]. It is frequently used by clinicians as a hallmark of active disease, highlighting its relevance in diagnosing the inflammatory state of the periodontium [34]. Additionally, the progression of periodontal disease can lead to tooth mobility, resulting from the degradation of the tooth's supporting structures like the periodontal ligament and alveolar bone. This process typically involves bone resorption and gingival recession, further destabilizing teeth [35].

Tooth loss and edentulism are recognized as markers for chronic conditions. Sara Hag Mohamed and Wael Sabbah's 2023 study identified tooth loss as an early indicator of chronic diseases in working-age adults, linked to shared risk factors affecting both oral and general health [36]. Similarly, Yuqing Zhang et al. (2022) found a strong association between edentulism, tooth loss, and multiple chronic diseases. Their research suggests that individuals with multiple chronic conditions are more likely to be edentulous than those with fewer or no chronic diseases, underscoring the significance of tooth loss and edentulism in evaluating the relationship between oral health and systemic health [37].

In Central Eastern Europe, especially in Hungary, there is a notable lack of research that simultaneously considers a large, representative sample and a broad set of oral health variables, such as gum bleeding, dental caries, tooth mobility, and tooth loss, to investigate the relation-ship between oral health and heart related conditions. While Hungary faces high rates of car-diovascular diseases and their related conditions, and some of Europe's worst oral health indicators, previous studies have not fully explored how social, demographic, economic, and lifestyle factors might confound this relationship. This study, utilizing data from the 2019 Hungarian instalment of the European Health Interview Survey (EHIS), aims to fill this gap. It explores the connections between oral health and heart and vascular health, considering the influence of a range of confounding variables.

2. Materials and methods

2.1 Study design

The EHIS is a representative survey conducted every five years in each member state of the EU, and covers a range of health variables, extending from lifestyle habits to chronic diseases, with a specific segment on oral health metrics [38].

To account for non-response bias and maintain a representative sample, individualized weighting was applied. This method followed Eurostat recommendations to synchronize the sample's demographic profile with the general population [39].

Managed by the Hungarian Central Statistical Office under Eurostat's supervision, the dataset was obtained using a rigorous stratified sampling technique, ensuring its generalizability to Hungary's adult populace residing in households.

This research is confined to data from the 2019 EHIS cycle, and was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of the University of Debrecen (5609–2020). All data used in this study were fully anonymized before access.

2.2 Sample population and data collection

The survey targeted a representative sample from across Hungarian municipalities, achieving a final response rate of approximately 47% from the intended 12,002 participants. Additional data were collected for children residing in sampled households. Data acquisition, detailed in [40] combined electronic and in-person methods using a standardized Eurostat questionnaire, ensuring consistency and cross-national comparability. The data collection period spanned from September 16 to December 31, 2019. The dataset for this study was accessed from the records maintained by the Department of Health Informatics at the Faculty of Health Sciences, University of Debrecen. Data retrieval was conducted over a period from September to November 2023.

2.3 Data treatment and variable specification

The study utilized key oral health indicators, including self-perceived oral health (categorized as 'Average,' 'Good,' or 'Bad'), number of unreplaced teeth extracted due to decay ('None,' '1 to 5,' '6 to 19,' 'More than 20'), filled teeth, active dental caries, tooth mobility, and gingival bleeding. Overall oral health was assessed as 'Optimal' or 'Suboptimal,' and the timing of the last dental visit was noted. Sociodemographic variables (age, gender, residence area, employment status, and education level) and lifestyle factors (alcohol consumption, smoking, BMI) were also included. Participants' financial standing was evaluated both subjectively and within quintiles. Composite variables were created for CVDs (encompassing stroke, myocardial infarction, arrhythmia, and coronary artery diseases) and cardiovascular risk profile (combining hyper-tension, CVDs, and hypercholesterolemia) to provide a comprehensive assessment of cardiac health. The main outcomes investigated were binary classifications of these conditions [41].

2.4 Variable selection method and statistical analysis

A two-stage variable selection strategy was employed to optimize model reliability and accuracy. The initial stage involved applying weighted Pearson's Chi-square tests to potential predictor variables to assess their association with each chronic disease outcome, alongside obtaining weighted proportions. Variables were chosen based on their documented impact on the outcomes studied within the scientific literature, ensuring a solid theoretical foundation. This selection was further supported by empirical evidence, underscoring the relevance and significance of each variable included in the analysis. Subsequently, a penalized regression approach was employed using Elastic Net regularization, a hybrid of Lasso and Ridge regression techniques. Elastic Net incorporates a hyperparameter α set at 0.5, allowing for a balanced compromise between Lasso's variable selection properties and Ridge's ability to handle multicollinearity. This approach effectively mitigates the risks of overfitting and multicollinearity while facilitating more accurate variable selection [42–44].

K-fold cross-validation was conducted to iteratively partition the dataset and gauge the predictive accuracy of the penalized model across multiple data folds. Variables that consistently exhibited high predictive performance were selected for inclusion in the final model. It is noteworthy that the hybrid Lasso-Ridge approach was compared against a stepwise logistic regression model and was found to surpass it in terms of model fit and strength, as evidenced by lower values in information criteria such as the Akaike Information Criterion (AIC) and the Bayesian Information Criterion (BIC).

Upon finalization of the predictor set, weighted multiple logistic regression models were constructed. Their performance was subsequently validated through a series of diagnostic tests, confirming both their goodness-of-fit using the Hosmer–Lemeshow test, and predictive strength.

The level of statistical significance was set at a p-value below 0.05. This criterion was applied across all analytical procedures to ascertain the meaningfulness of relationships between variables. Results stemming from logistic regression were expressed in terms of odds ratios (ORs), accompanied by 95% confidence intervals (CIs). The entirety of the statistical evaluations was executed using STATA IC Version 17.0 software [45].

2.5 Sensitivity analysis

Robustness tests were conducted through bootstrapping with 1,000 repetitions and comprehensive subpopulation analyses. The bootstrapping process involved applying the logistic regression model across various demographic, lifestyle, and oral health variables to assess the stability of the findings under varied sampling conditions. Concurrently, subpopulation analyses were performed across different demographic groups defined by age, gender, educational status, employment status, area of residence, and income levels. These analyses aimed to evaluate the consistency of the associations identified in the primary analysis within diverse segments of the study population.

3. Results

3.1 Data completeness

The study analyzed a total sample of 5,603 participants. The completeness of data for each variable of interest varied as follows:

- Variables with complete data (5,603 observations): Age groups, Gender, Area of residence, Educational attainment, Employment, Smoking status, Alcohol use, Oral health, Income quintiles, Cardiovascular risk profile.
- Variables with high data availability: Self-perceived health (5,570), Hypertension (5,556), Last dental checkup (5,520), BMI (5,537), and Presence of prosthetic tooth replacement (5,534).
- Variables with moderate data availability: Financial status (5,467), Hypercholesterolemia (5,462), CVDs (5,594), Presence of chronic disease (5,489), Has filled teeth (5,486), Has permanent teeth missing due to decay (extracted) and not replaced (5,476), Has mobile Teeth (5,457), Gum bleeding (5,443), and Self-perceived oral health (5,562).
- Variables with lower data Availability: Has active caries (5,320) and Number of permanent teeth missing due to extraction (4,444).

This overview indicates a high level of data completeness across most variables. Notable exceptions include presence of active caries and missing teeth except wisdom, where a

relatively larger proportion of data was missing. The potential impact of these missing data on the study's findings is discussed further in the 'Limitations' section.

3.2 Sociodemographic and lifestyle characteristics

As seen in Table 1, gender differences were significant, with women exhibiting higher prevalence rates for hypertension (17.71%) and CVDs (8.7%), and a notable prevalence of hypercholesterolemia (7.66%; all p<0.05). Among age groups, the 65+ demographic showed increased prevalence in hypertension (15.32%) and CVDs (7.87%; p<0.001), as well as a noticeable rate in hypercholesterolemia (6.02%; p<0.001).

Socioeconomic factors, such as educational attainment and employment status, also had a marked impact. Lower educational attainment was linked to higher rates of hypertension (16.54%) and CVDs (7.93%), while unemployment correlated with higher prevalence in all three conditions (hypertension: 19.85%, CVDs: 10.42%, hypercholesterolemia: 7.77%; p<0.001). Lifestyle factors, specifically non-smoking status and overweight/obese condition consistently showed higher prevalence rates across all outcomes (hypertension: 24.35% and 24.83%, CVDs: 10.27%, hypercholesterolemia: 10.16% and 10.53%; p<0.001). Alcohol consumption showed marginal significance in hypercholesterolemia (8.94%; p = 0.049).

3.3 Comparative oral health profiles

Results in <u>Table 2</u> showed significant links between hypertension, self-perceived oral health, dental checkup frequency, and presence of filled teeth (all p < 0.001). Hypertensive individuals reported worse self-perceived oral health and had fewer dental checkups compared to their non-hypertensive counterparts. In the context of CVDs, individuals with CVDs were more likely to report poor oral health, have fewer dental checkups, have a higher number of teeth missing due to extraction, and more likely to have prosthetic replacements (all p < 0.001).

Hypercholesterolemia was significantly associated with suboptimal self-perceived oral health, gum bleeding, infrequent dental checkups, fewer filled teeth, and higher mobility and number of missing teeth (p values ranging from <0.001 to 0.038).

3.4 Multiple logistic regression models

Tables 3 and 4 present multiple logistic regression analysis for the key outcomes of interest. For hypertension, younger age groups (15-34: OR = 0.14 [0.09-0.21]; 35-64: 0.45 [0.35-0.57]) and higher educational attainment (secondary: 0.73 [0.60-0.90]; tertiary: 0.63 [0.48-0.83]) were associated with lower odds. Normal BMI (0.42 [0.35-0.51]) and non-drinking (0.80 [0.66-0.97]) also reduced odds, whereas oral health factors like 6 to 19 extracted teeth (1.67 [1.00-2.77]) and prosthetic replacements (1.45 [1.20-1.75]) increased them.

For CVDs, younger ages $(15-34: 0.40 \ [0.23-0.70]; 35-64: 0.64 \ [0.49-0.84])$ and employment $(0.69 \ [0.52-0.91])$ were protective, while chronic disease presence $(4.34 \ [3.18-5.92])$, poor self-perceived health $(2.70 \ [2.12-3.45])$, gum bleeding $(1.69 \ [1.30-2.21])$, and prosthetic teeth $(1.35 \ [1.07-1.70])$ increased risks.

In hypercholesterolemia, younger age (15-34: 0.27 [0.15-0.50]; 35-64: 0.63 [0.48-0.83]), urban residence (1.28 [1.03-1.59]), and tertiary education (1.40 [1.03-1.89]) showed significant associations. Normal BMI (0.51 [0.40-0.65]) was protective, while chronic disease (3.16 [2.39-4.17]), poor self-perceived health (1.67 [1.29-2.16]), gum bleeding (1.40 [1.09-1.81]), prosthetic teeth (1.51 [1.19-1.92]), and recent dental checkups (1.51 [1.19-1.93]) correlated with increased risks. Key associations with cardiovascular risk profile outcomes were also identified. Younger age groups (15-34: 0.12 [0.09-0.17], 35-64: 0.41 [0.33-0.52]) had significantly lower odds than those 65+. Normal BMI (0.47 [0.40-0.56]) reduced odds and the presence of a

Variable	Category		Hypertension	_		Cai	Cardiovascular diseases	nr disease	S	Hy	Hypercholesterolaemia		
		Without hypertension (n, %)	With hypertension (n, %)	Total (n, %)	P value	Without heart disease $(n, \%)$	With heart disease (n, %)	Total (n, %)	P value	Without hypercholesterolaemia (n, %)	With hypercholesterolaemia (n, %)	Total (n, %)	P value
Gender	Male	1702 (33.32)	843 (13.79)	2545 (47.11)	<0.001	2187 (41.44)	380 (5.77)	2567 (47.21)	<0.001	2171 (41.4)	321 (5.52)	2492 (46.92)	0.004
	Female	1884 (35.18)	1127 (17.71)	3011 (52.89)		2478 (44.09)	549 (8.7)	3027 (52.79)		2510 (45.42)	460 (7.66)	2970 (53.08)	
Age groups	65+	542 (7.84)	1077 (15.32)	1619 (23.15)	<0.001	1070 (15.23)	557 (7.87)	1627 (23.1)	<0.001	1188 (17.17)	406 (6.02)	1594 (23.19)	<0.001
	15-34	1214 (25.97)	49 (1.06)	1263 (27.02)		1232 (26.23)	42 (0.85)	1274 (27.08)		1229 (26.72)	26 (0.62)	1255 (27.34)	
	35-64	1830 (34.7)	844 (15.12)	2674 (49.82)		2363 (44.07)	330 (5.76)	2693 (49.82)		2264 (42.93)	349 (6.54)	2613 (49.47)	
Area of residence	Rural	1166 (20.03)	634 (9.71)	1800 (29.74)	0.232	1511 (25.1)	299 (4.59)	1810 (29.69)	0.17	1571 (26.64)	200 (3.14)	1771 (29.78)	<0.001
	Urban	2420 (48.47)	1336 (21.79)	3756 (70.26)		3154 (60.42)	630 (9.89)	3784 (70.31)		3110 (60.18)	581 (10.04)	3691 (70.22)	
Educational attainment	Primary	1436 (25.71)	1059 (16.54)	2495 (42.25)	<0.001	1975 (34.18)	528 (7.93)	2503 (42.11)	<0.001	2119 (36.87)	341 (5.53)	2460 (42.4)	0.184
	Secondary	1247 (24.2)	577 (9.48)	1824 (33.68)		1601 (29.91)	241 (3.84)	1842 (33.75)		1553 (29.61)	245 (4.17)	1798 (33.77)	
	Tertiary	903 (18.59)	334 (5.48)	1237 (24.07)		1089 (21.44)	160 (2.71)	1249 (24.14)		1009 (20.34)	195 (3.49)	1204 (23.83)	
Employment	Unemployed	1445 (25.4)	1336 (19.85)	2781 (45.25)	<0.001	2085 (34.72)	709 (10.42)	2794 (45.14)	<0.001	2239 (37.66)	504 (7.77)	2743 (45.43)	<0.001
	Employed	2141 (43.1)	634(11.65)	2775 (54.75)		2580 (50.81)	220 (4.05)	2800 (54.86)		2442 (49.15)	277 (5.42)	2719 (54.57)	
Financial status	Average	1890 (36.14)	1225 (19.79)	3115 (55.93)	<0.001	2582 (47.24)	550 (8.66)	3132 (55.9)	<0.001	2596 (48.02)	464 (7.87)	3060 (55.89)	<0.001
	Good	1230 (25.19)	435 (7.41)	1665 (32.6)		1476 (29.3)	194 (3.2)	1670 (32.5)		1466 (29.47)	183 (3.39)	1649 (32.86)	
	Bad	381 (.7.07)	275 (4.41)	656 (11.47)		497 (8.97)	168 (2.63)	665 (11.6)		522 (9.38)	113 (1.87)	635 (11.25)	
Income quintiles	First	699 (12.81)	449 (7.29)	1148 (2.01)	<0.001	928 (16.56)	225 (3.49)	1153 (20.05)	<0.001	990 (17.86)	142 (2.29)	1132 (20.14)	0.013
	Second	673 (12.43)	496 (7.67)	1169 (20.1)		937 (16.46)	236 (3.57)	1173 (20.03)		953 (16.87)	190 (3.14)	1143 (20.01)	
	Third	710 (13.4)	414 (6.5)	1124 (19.9)		942 (16.91)	196 (3.11)	1138 (20.02)		960 (17.42)	152 (2.59)	1112 (20.01)	
	Fourth	837 (15.72)	420 (6.75)	1257 (22.46)		1069 (19.51)	197 (2.97)	1266 (22.48)		1040 (19.28)	197 (3.2)	1237 (22.48)	
	Fifth	667 (14.15)	191 (3.29)	858 (17.44)		789 (16.09)	75 (1.33)	864 (17.42)		738 (15.39)	100 (1.96)	838 (17.35)	

Variable	Category		Hypertension			Car	Cardiovascular diseases	r diseases		Hy	Hypercholesterolaemia		
		Without hypertension $(n, \%)$	WithTotalhypertension $(n, \%)$ $(n, \%)$	Total (n, %)	P value	Without heart disease	With heart disease	Total P value (n, %)	P value	Without hypercholesterolaemia (n, %)	With hypercholesterolaemia (n, %)	Total (n, %)	P value
Smoking	Smoker	1098 (20.85)	426 (7.14)	1524 (28)	<0.001	(n, %) 1324 (24.58)	(n, %) 213 (3.45)	1537 (28.02)	0.004	1350 (25.37)	148 (2.65)	1498 (28.02)	<0.001
	Non-smoker	2488 (47.65)	1544 (24.35)	4032 (72)	1	3341 (60.95)	716 (11.03)	4057 (71.98)	1	3331 (61.45)	633 (10.53)	3964 (71.98)	
BMI	Overweight and Obese	1781 (33.4)	1532 (24.83)	3313 (58.23)	<0.001	2676 (47.93)	655 (10.27)	3331 (58.2)	<0.001	2642 (47.7)	598 (10.16)	3240 (57.86)	<0.001
	Normal	1770 (35.11)	420 (6.66)	2190 (41.77)		1938 (37.59)	266 (4.22)	2204 (41.8)		1996 (39.12)	175 (3.02)	2171 (42.14)	
Alcohol use Drinker	Drinker	2590 (50.52)	1273 (20.54)	3863 (71.06)	<0.001	3352 (62.6)	545 (8.61)	3897 (71.21)	<0.001	3265 (62.01)	527 (8.94)	3792 (70.95)	0.049
	Non-drinker	996 (17.98)	697 (10.96)	1693 (28.94)		1313 (22.92)	384 (5.86)	1697 (28.79)		1416 (24.81)	254 (4.25)	1670 (29.05)	

Bold values indicate statistical significance, p<0.05 based on weighted Pearson's chi-squared test.

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Table 1. (Continued)

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Table 2. Cor	

Variable	Category		Hypertension			Car	Cardiovascular diseases	ur disease	s	H	Hypercholesterolaemia		
		Without hypertension (n, %)	With hypertension (n, %)	Total (n, %)	P value	Without heart disease (n, %)	With heart disease (n, %)	Total (n, %)	P value	Without hypercholesterolaemia (n, %)	With hypercholesterolaemia (n, %)	Total (n, %)	P value
Presence of active caries	No	2402 (48.16)	1386 (22.94)	3788 (71.1)	0.065	3172 (60.71)	631 (10.33)	3803 (71.04)	0.82	3191 (61.59)	544 (9.62)	3735 (71.21)	0.1654
	Yes	1019 (20.35)	488 (8.55)	1507 (28.9)		1264 (24.82)	253 (4.14)	1517 (28.96)		1282 (25.33)	193 (3.47)	1475 (28.79)	
Self-perceived oral health	Average	1023 (18.92)	791 (12.43)	1814 (31.35)	<0.001	1489 (26.05)	341 (5.35)	1830 (31.4)	<0.001	1475 (26.29)	299 (4.84)	1774 (31.13)	<0.001
	Good	1976 (39.77)	607 (10.3)	2583 (50.07)		2346 (45.87)	249 (4.13)	2595 (50)		2301 (45.74)	256 (4.71)	2557 (50.44)	
	Bad	567 (9.8)	562 (8.78)	1129 (18.58)		802 (13.62)	334 (4.99)	1136 (18.6)		881 (14.8)	221 (3.63)	1102 (18.43)	
Has gum bleeding when	No	2925 (56.99)	1622 (26.56)	4547 (83.55)	0.196	3852 (72.23)	718 (11.3)	4570 (83.53)	<0.001	3870 (73.19)	610 (10.52)	4480 (83.71)	0.012
brushing teeth	Yes	577 (11.59)	291 (4.86)	868 (16.45)		688 (13.32)	185 (3.14)	873 (16.47)		699 (13.72)	147 (2.57)	846 (16.29)	
Last dental checkup	More than a year ago	1835 (34.01)	1253 (19.8)	3088 (53.8)	<0.001	2486 (44.23)	621 (9.6)	3107 (53.83)	<0.001	2601 (46.66)	436 (7.17)	3037 (53.83)	0.007
	Less than 6 months ago	963 (19.71)	395 (6.74)	1358 (26.45)		1192 (23.57)	175 (2.91)	1367 (26.48)		1126 (22.56)	212 (3.92)	1338 (26.48)	
	less than a year but more than 6 months ago	750 (14.88)	292 (4.87)	1042 (19.75)		926 (17.76)	119 (1.93)	1045 (19.69)		903 (17.65)	120 (2.04)	1023 (19.69)	
Has filled teeth	No	1057 (19.47)	838 (13.13)	1895 (32.61)	<0.001	1458 (25.71)	439 (6.73)	1897 (32.44)	<0.001	1585 (28.09)	288 (4.72)	1873 (32.81)	0.038
	Yes	2472 (49.15)	1087 (18.24)	3559 (67.39)		3122 (59.9)	467 (7.66)	3589 (67.56)		3020 (58.91)	470 (8.29)	3490 (67.19)	
Has mobile teeth	No	3283 (64.59)	1709 (27.91)	4992 (92.5)	<0.001	4231 (79.88)	787 (12.6)	5018 (92.48)	<0.001	4255 (81.2)	662 (11.45)	4917 (92.66)	<0.001
	Yes	225 (3.96)	211 (3.54)	436 (7.5)		321 (5.65)	118 (1.87)	439 (7.52)		325 (5.69)	96 (1.66)	421 (7.34)	
Number of permanent	None	154 (4.08)	40 (0.99)	194 (5.08)	<0.001	174 (4.6)	20 (0.46)	194 (5.05)	<0.001	171 (4.59)	17 (0.45)	188 (5.03)	<0.001
teeth missing due to	1 to 5	1514 (38.42)	533 (11.92)	2047 (50.34)		1854 (45.86)	206 (4.55)	2060 (50.4)		1768 (44.67)	245 (5.68)	2013 (50.36)	
extraction	6 to 19	556 (12.38)	666 (13.61)	1222 (25.99)		918 (19.89)	310 (6.14)	1228 (26.03)		960 (20.82)	246 (5.27)	1206 (26.1)	
	More than 20	376 (7.28)	586 (11.31)	962 (18.59)		636 (12.3)	326 (6.21)	962 (18.51)		733 (14.33)	208 (4.18)	941 (18.52)	

Variable	Category		Hypertension			Car	Cardiovascular diseases	nr disease	s	Η	Hypercholesterolaemia		
		Without hypertension (n, %)	With hypertension (n, %)	Total (n, %)	P value	Without heart disease $(n, \%)$	With heart disease (n, %)	Total (n, %)	Total P value (n, %)	Without hypercholesterolaemia (n, %)	With hypercholesterolaemia (n, %)	Total (n, %)	P value
Has permanent	No	1636 (33)	685 (11.2)	2321 (44.21)	<0.001	2032 (39.24)	302 (4.97)	2334 (44.21)	<0.001	2024 (39.65)	267 (4.76)	2291 (44.41)	<0.001
teeth missing due to decay (extracted) and not replaced	Yes	1891 (35.62)	1236 (20.17)	3127 (55.79)		2544 (46.41)	601 (9.38)	3145 (55.79)		2577 (47.29)	491 (8.3)	3068 (55.59)	
Presence of prosthetic	No	2232 (45.09)	610 (10.33)	2842 (55.42)	100.0>	2563 (50.63)	298 (4.84)	2861 (55.47)	<0.001	2574 (51.39)	223 (4.12)	2797 (55.52)	<0.001
replacement (bridge, denture, or implant)	Yes	1319 (23.41)	1339 (21.17)	2658 (44.58)		2054 (34.93)	619 (9.6)	2673 (44.53)		2060 (35.39)	552 (9.1)	2612 (44.48)	
Oral health	Optimal	800 (16.64)	171 (2.91)	971 (19.55)	<0.001	915 (18.55)	68 (1.09)	983 (19.64)	<0.001	884 (18.28)	78 (1.44)	962 (19.73)	< 0.001
	Suboptimal	2786 (51.87)	1799 (28.59)	4585 (80.45)		3750 (66.97)	861 (13.39)	4611 (80.36)		3797 (68.53)	703 (11.74)	4500 (80.27)	

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Table 2. (Continued)

Character	istics	Hypertensi	on	Cardiovascular	diseases
		OR (95% CI)	P value	OR (95% CI)	P value
Gender	Male				
	Female	1.13 [0.94–1.35]	0.192	1.02 [0.83-1.26]	0.828
Age groups	65+				
	15-34	0.14 [0.09-0.21]	<0.001	0.40 [0.23-0.70]	0.001
	35-64	0.45 [0.35-0.57]	<0.001	0.64 [0.49-0.84]	0.001
Area of residence	Rural				
	Urban				
Educational attainment	Primary				
	Secondary	0.73 [0.60-0.90]	0.003	0.91 [0.72-1.16]	0.459
	Tertiary	0.63 [0.48-0.83]	0.001	1.28 [0.95–1.73]	0.105
Employment	Unemployed				
1 7 7	Employed	0.89 [0.71-1.12]	0.318	0.69 [0.52-0.91]	0.009
Financial status	Average				
	Good	0.94 [0.76-1.15]	0.524	1.16 [0.91–1.48]	0.231
	Bad	0.93 [0.71-1.21]	0.593	1.10 [0.84–1.45]	0.491
Income quintiles	First		01070		01171
income quintiles	Second	0.81 [0.63-1.04]	0.101		
	Third	0.70 [0.54-0.91]	0.008		
	Fourth	0.93 [0.70–1.23]	0.616		
	Fifth	0.74 [0.53-1.03]	0.073		
moking	Smoker		0.075		
onioning	Non-smoker	1.08 [0.89–1.32]	0.434		
BMI	Overweight and Obese	1.00 [0.09 1.52]	0.131		
	Normal	0.42 [0.35-0.51]	<0.001		
Alcohol use	Drinker	0.12 [0.33 0.31]	<0.001		
Alcohol use	Non-drinker	0.80 [0.66-0.97]	0.02	1.04 [0.84–1.28]	0.749
Has Chronic disease	No	0.00 [0.00-0.97]	0.02	1.04 [0.04-1.20]	0.747
Thas Chrome disease	Yes	5.85 [4.80-7.13]	<0.001	4.34 [3.18-5.92]	<0.001
Self-perceived health	Average	5.85 [4.80-7.15]	<0.001	4.54 [5.16-5.92]	<0.001
Sen-perceived hearth	Good	0.74 [0.60-0.90]	0.003	0.45 [0.35-0.59]	<0.001
	Bad	1.11 [0.85–1.43]	0.446	2.70 [2.12-3.45]	
Solf noncoived and health		1.11 [0.85-1.45]	0.440	2.70 [2.12-3.43]	<0.001
Self-perceived oral health	Average Good	0.86 [0.71, 1.05]	0.141	1.01 [0.70, 1.20]	0.947
		0.86 [0.71-1.05]		1.01 [0.79–1.29]	
NT	Bad	0.86 [0.69–1.08]	0.198	1.12 [0.88–1.42]	0.367
Number of permanent teeth extracted due to decay, not	None	1.00 [0.67, 1.77]	0.74	1 10 [0 50 0 10]	0.722
replaced	1 to 5	1.09 [0.67–1.77]	0.74	1.12 [0.59-2.12]	0.732
	6 to 19	1.67 [1.01-2.77]	0.049	1.49 [0.79-2.84]	0.221
IT Cll. J 441	More than 20	1.35 [0.80-2.29]	0.264	1.31 [0.69–2.51]	0.407
Has filled teeth	No				0.000
	Yes			0.81 [0.64–1.03]	0.088
Presence of active caries	No				0.1.5
	Yes			1.09 [0.86–1.39]	0.463
Has mobile teeth	No				
	Yes	1.14 [0.85–1.54]	0.38	1.01 [0.73–1.39]	0.959

Table 3. Weighted multiple logistic regression analysis of factors affecting hypertension and cardiovascular diseases.

(Continued)

Characterist	ics	Hypertensi	on	Cardiovascular	diseases
		OR (95% CI)	P value	OR (95% CI)	P value
Has gum bleeding when	No				
brushing teeth	Yes	0.91 [0.72-1.15]	0.433	1.69 [1.30-2.21]	<0.001
Has permanent teeth missing	No				
due to decay (extracted) and not replaced	Yes	1.00 [0.78-1.28]	0.989	0.94 [0.75-1.18]	0.607
Oral health	Optimal				
	Suboptimal			1.50 [0.88-2.55]	0.141
Presence of prosthetic tooth	No				
replacement	Yes	1.45 [1.20-1.75]	<0.001	1.35 [1.07-1.70]	0.01
Last dental Checkup	More than a year ago				
	Less than 6 months ago	1.03 [0.83-1.27]	0.798	1.11 [0.86–1.44]	0.415
	less than a year but more than 6 months ago	0.97 [0.77–1.22]	0.795	0.88 [0.67–1.17]	0.391

Table 3. (Continued)

Bold values indicate statistical significance at p < 0.05. Adjusted ORs account for other variables within the model. Variables that were excluded by elastic net regularization are shaded with grey.

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chronic disease (5.20 [4.36–6.20]) elevated it. Good self-perceived health also reduced the odds while bad health elevated it. Certain oral health conditions increased cardiovascular risk profile odds (mobility: 1.49 [1.10–2.02], prosthetics: 1.69 [1.41–2.03], and recent dental visits 1.30 [1.06–1.60]).

3.5 Sensitivity analysis

The results from both bootstrapping and subpopulation analyses consistently affirmed the robustness of the original model. Across various demographic groups and under repeated sampling conditions, the associations originally identified remained stable and unchanged, underscoring the reliability and generalizability of the primary findings.

4. Discussion

In light of the study's aim to assess the impact of oral health indicators on hypertension, CVDs, and hypercholesterolemia, findings indicated that certain dental health factors, such as the number of extracted teeth and prosthetic tooth use, were associated with the aforementioned cardiovascular conditions. Poor self-perceived oral health and gum bleeding also emerged as risk factors.

In alignment with findings by Se-Yeon Kim et al. (2018), which advocated for the utility of self-perceived oral health as a reliable indicator of clinical oral health status, particularly in relation to periodontal conditions, the present study provided additional support for the accuracy of self-assessed oral health measures [46]. Furthermore, the work of D. Locker et al. (2000) substantiated the concurrence of poor self-perceived oral health with lower psychological well-being and diminished life satisfaction, particularly among older adults [47]. While these prior studies established the validity of self-perceived oral health as a proxy metric for oral health, they did not explore its relationship with the prevalence of chronic cardiac conditions.

While chi-squared tests indicated significant associations between self-perceived oral health and chronic cardiac conditions, these associations diminished in multiple logistic regression

Character	ristics	Hypercholester	olaemia	Cardiovascula profile	ır risk
		OR (95% CI)	P value	OR (95% CI)	P value
Gender	Male				
	Female	1.13 [0.92-1.40]	0.242	1.10 [0.93-1.30]	0.257
Age groups	65+				
	15-34	0.27 [0.15-0.50]	<0.001	0.12 [0.09-0.17]	<0.001
	35-64	0.63 [0.48-0.83]	0.001	0.41 [0.33-0.52]	<0.001
Area of residence	Rural				
	Urban	1.28 [1.03-1.59]	0.025	1.13 [0.95-1.35]	0.153
Educational attainment	Primary				
	Secondary	1.10 [0.86-1.39]	0.458	0.87 [0.71-1.07]	0.183
	Tertiary	1.40 [1.03-1.89]	0.031	1.02 [0.79–1.31]	0.872
Employment	Unemployed				
	Employed	1.18 [0.89-1.56]	0.24	0.97 [0.78-1.20]	0.769
Financial status	Average				
	Good	0.96 [0.75-1.23]	0.75		
	Bad	1.09 [0.81–1.46]	0.559		
Income quintiles	First				
1	Second	1.15 [0.86-1.54]	0.345	0.91 [0.71-1.16]	0.439
	Third	0.97 [0.70–1.33]	0.837	0.90 [0.69–1.17]	0.422
	Fourth	1.22 [0.88-1.68]	0.226	1.09 [0.84–1.42]	0.508
	Fifth	1.24 [0.83–1.87]	0.292	0.81 [0.59–1.11]	0.19
Smoking	Smoker	1.21[0.00 1.07]	0.272	0.01 [0.09 1.11]	0.15
onioknig	Non-smoker	1.04 [0.81-1.34]	0.742		
BMI	Overweight and Obese	1.04[0.01 1.04]	0.742		
Diff	Normal	0.51 [0.40-0.65]	<0.001	0.47 [0.40-0.56]	<0.001
Alcohol use	Drinker	0.51 [0.40-0.05]	<0.001	0.17 [0.10-0.30]	<0.001
Alcohol use	Non-drinker	0.89 [0.71-1.11]	0.311		
Has Chronic disease	No	0.89 [0.71-1.11]	0.511		
rias Chronic disease	Yes	3.16 [2.39-4.17]	<0.001	5.20 [4.36-6.20]	<0.001
Self-perceived health	Average	5.10 [2.39-4.17]	<0.001	5.20 [4.30-0.20]	<0.001
Self-perceived health		0.57 [0.44.0.72]	<0.001	0.52 [0.44, 0.64]	<0.001
	Good	0.57 [0.44-0.73]	<0.001	0.53 [0.44-0.64]	< 0.001
Self-perceived oral health	Bad	1.0/ [1.29-2.10]	<0.001	1.55 [1.16-2.09]	0.003
Self-perceived oral nealth	Average	1 11 [0 07 1 40]	0.402	0.05 [0.50, 1.15]	0.505
	Good	1.11 [0.87–1.40]	0.403	0.95 [0.78–1.15]	0.595
	Bad	1.24 [0.96–1.61]	0.096	1.19 [0.94–1.50]	0.147
Number of permanent teeth extracted due to decay, not	None		0.15		
replaced	1 to 5	1.26 [0.68–2.34]	0.46		
•	6 to 19	1.26 [0.67–2.35]	0.473		
	More than 20	1.14 [0.61–2.14]	0.685		
Has filled teeth	No				
	Yes			1.01 [0.83-1.22]	0.91
Presence of active caries	No				
	Yes			0.96 [0.78–1.18]	0.693
Has mobile teeth	No				
	Yes	1.36 [1.00-1.87]	0.053	1.49 [1.10-2.02]	0.01

Table 4. Weighted multiple logistic regression analysis of factors affecting hypercholesterolaemia and cardiovascular risk profile.

(Continued)

Characterist	ics	Hypercholester	olaemia	Cardiovascula profile	ır risk
		OR (95% CI)	P value	OR (95% CI)	P value
Has gum bleeding when	No				
brushing teeth	Yes	1.40 [1.09-1.81]	0.008		
Has permanent teeth missing	No				
due to decay (extracted) and not replaced	Yes	1.00 [0.80-1.24]	0.964	0.90 [0.74-1.09]	0.264
Oral health	Optimal				
Presence of prosthetic tooth	Suboptimal			1.21 [0.90-1.61]	0.209
	No				
replacement	Yes	1.51 [1.19-1.92]	0.001	1.69 [1.41-2.03]	<0.001
Last dental Checkup	More than a year ago				
	Less than 6 months ago	1.51 [1.19-1.93]	0.001	1.30 [1.06-1.60]	0.013
	less than a year but more than 6 months ago	1.08 [0.82–1.43]	0.569	0.87 [0.70–1.09]	0.226

Table 4. (Continued)

Bold values indicate statistical significance at p < 0.05. Adjusted ORs account for other variables within the model. Variables that were excluded by elastic net regularization are shaded with grey.

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models after adjusting for confounders. This suggests that other variables may influence the relationship between oral health and chronic cardiac conditions, highlighting the complexity of oral-systemic health connections.

This study augments existing literature by showing a notable association between self-perceived oral health and chronic cardiac conditions. Generally, individuals without these conditions reported better oral health, while those with them often reported worse, supporting the concept of a bidirectional relationship between oral and systemic health.

The observed elevated odds for hypertension among individuals with 6 to 19 teeth extracted might intersect with the phenomenon related to prosthetic dental replacements increasing hypertension odds as well, in several ways.

Firstly, both conditions, multiple teeth extractions and the need for prosthetic replacements, could signify a history of chronic oral infections, tooth decay and periodontal disease. These conditions can induce a state of systemic inflammation, which is in line with what Ramadan et al. (2020), and Passarelli et al. (2020), have concluded on the given topic [48, 49]. The bioactive molecules released during this chronic low-grade inflammation, such as cytokines, can adversely affect vascular endothelial function, setting the stage for increased arterial stiffness and hypertension [50].

Secondly, multiple teeth extractions often necessitate prosthetic replacements for functional reasons, such as chewing and speech. Research by Kim et al. (2021) found that the presence of 6–10 and 11 prosthetic crowns increased the prevalence of periodontitis by 1.24 and 1.28 times, respectively, compared to individuals without any prosthetic crowns [51]. This suggests that prosthetic replacements may serve as foci for continued bacterial infection and periodontal disease. Consequently, these localized oral health issues could perpetuate the cycle of systemic inflammation, thereby elevating hypertensive risk [52, 53].

Furthermore, severe tooth loss can impact nutrition. Kossioni (2018) highlighted that tooth loss often leads to dietary changes, with increased consumption of processed foods high in

sodium and unhealthy fats, and reduced intake of fibrous fruits and vegetables, contributing to hypertension risk [54, 55].

Lastly, these conditions may reflect healthcare-seeking behaviour. Older individuals with multiple extractions and prosthetics are likely under regular healthcare supervision and may use medications that influence blood pressure.

Oral health indicators, notably gum bleeding and the presence of prosthetic dental replacements, were significantly associated with increased CVD risk in this study. Extensive tooth loss, particularly more than 20 missing teeth, was also common among individuals with CVD, supporting the notion of systemic inflammation and endothelial dysfunction as overlapping mechanisms linking oral and cardiovascular health. Dhotre et al. (2016) highlighted how periodontitis could contribute to atherosclerotic plaque formation by allowing oral bacteria to enter the bloodstream [56]. This aligns with Ola Vedin et al. (2014), who found a correlation between periodontal disease indicators, such as gum bleeding, and elevated cardiovascular risk [57]. Prosthetic dental replacements may serve as persistent foci for bacterial accumulation, thereby contributing to atherosclerotic plaque formation. The widespread tooth loss noted in the CVD cohort may reflect a nutritional landscape marked by lipid abnormalities and diminished cardiovascular health. Collectively, these findings substantiate a complex, bidirectional interaction between oral health parameters and CVD risk, thereby augmenting current scientific discourse on the systemic implications of oral health.

The significance of these findings is particularly relevant in Hungary, where chronic conditions and heart disease-related mortality are prevalent. Given Hungary's high rates of gingivitis and periodontal disease, these results contribute to both the global understanding of CVD and offer critical insights for its management and prevention within the Hungarian context.

In accordance with the existing scientific literature, the present study delineated a statistically significant elevated risk of hypercholesterolaemia among urban residents and individuals with higher educational attainment [58–64].

The study also revealed specific oral health indicators notably influencing the risk profile for hypercholesterolaemia. Gingival bleeding was associated with elevated odds of hypercholesterolemia, as was the presence of prosthetic dental replacements. This association is supported by extant literature explaining the biological linkage between periodontal symptoms and elevated plasma cholesterol levels [65, 66]. For instance, Tahamtan et al. (2020) documented the salutary effects of statins on various dimensions of oral health, including chronic periodontitis [67]. Additionally, a 2014 study indicated that periodontal therapy ameliorated subclinical arterial thickness, implicating a correlation between atheromatous plaques and periodontal disease [68]. Fu et al. (2016) further substantiated this link, demonstrating that periodontal treatment led to improved serum lipid and proinflammatory cytokine profiles in hyperlipidaemic patients [69].

In a departure from established literature, the current study noted two interesting observations, one is the association between recent dental visits (within the last 6 months) and an elevated risk of hypercholesterolemia. Interpretation could involve the concept of "risk factor clustering". Individuals who seek dental care frequently may already be engaged in healthcare surveillance due to other comorbidities or risk factors, including dyslipidaemia. Their dental symptoms might be reflective of underlying systemic inflammation, which is also a key player in the pathophysiology of hypercholesterolemia. The elevated lipid levels could be both a cause and a consequence of inflammatory oral conditions, such as periodontitis, thus leading to a cyclical relationship between oral health and lipid metabolism. The other observation was the lack of statistically significant link between dental caries and CVDs, which was discussed in a previous review article [70]. This could potentially be attributed to factors such as the heterogeneity in dental caries progression and treatment, and the multifactorial nature of CVD, which involves various risk factors that could obscure the impact of caries alone. Additionally, the criteria for defining dental caries might not fully reflect the disease's severity or its microbial aspects, like S. mutans, suggesting the need for more focused research on the specific interactions between oral health and cardiovascular diseases.

4.1 Strengths and limitations

This study distinguishes itself not only through its robust methodological framework but also by filling a conspicuous gap in the literature on the Central and Eastern European region. To the authors' knowledge, it is the inaugural study of its kind in the Hungarian population to study the relationship between numerous chronic non-communicable diseases and oral health. The utilization of data from the EHIS lends considerable weight to the generalizability of the study's findings. Methodological rigor is further accentuated by the incorporation of multiple socioeconomic and demographic confounders, comprehensive data protocols, and innovative machine learning applications for variable selection and sensitivity analyses.

This study has limitations, primarily due to its cross-sectional design which limits causal inferences and temporal relationship establishment. Reliance on self-reported data raises concerns of recall bias, affecting metrics like comorbidities and BMI accuracy. Furthermore, the study's scope was constrained by not differentiating chronic disease severity and excluding key biochemical parameters (e.g., glycemia, HbA1c), limiting insights into metabolic and renal impacts on cardiovascular outcomes. Also, while most variables exhibited high levels of data completeness, a few had a noticeable proportion of missing values. This could potentially influence the accuracy and generalizability of the findings related to these specific aspects.

5. Conclusion

In a nationally representative sample of the Hungarian population, suboptimal oral health markers were found to be significantly associated with increased risk for negative cardiac outcomes. Conversely, improvements in oral health parameters are linked to a diminution in the risk profiles of these outcomes. Targeted oral health interventions could serve as a vital component of a multi-disciplinary approach to disease management and prevention. Future research should delve into the causal and temporal relationships between oral health and heart and vascular conditions, incorporating clinical assessments alongside self-reported data to enhance accuracy and consider medication use as a potential confounder. Additionally, examining the efficacy of oral health interventions on disease outcomes and dissecting variability across demographic groups could yield critical insights for tailored public health strategies.

Supporting information

S1 Table. Bootstrap analysis of oral health indicators and their association with cardiovascular outcomes.

(DOCX)

S2 Table. Elastic net selection results with $\alpha = 0.5$: Predictors for hypertension and cardiovascular diseases.

(DOCX)

S3 Table. Elastic net selection results with α = 0.5: Predictors for hypercholesterolaemia and cardiovascular risk profile. (DOCX) **S1** Fig. Flowchart of the study participants and variable groupings. (TIF)

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References

- The top 10 causes of death [Internet]. [cited 2023 Oct 8]. https://www.who.int/news-room/fact-sheets/ detail/the-top-10-causes-of-death
- Dattani S, Spooner F, Ritchie H, Roser M. Causes of Death. Our World in Data [Internet]. 2023 Sep 22 [cited 2023 Oct 10]; https://ourworldindata.org/causes-of-death
- FastStats [Internet]. 2023 [cited 2023 Oct 10]. https://www.cdc.gov/nchs/fastats/leading-causes-ofdeath.htm
- Pirillo A, Casula M, Olmastroni E, Norata GD, Catapano AL. Global epidemiology of dyslipidaemias. Nat Rev Cardiol. 2021 Oct; 18(10):689–700. <u>https://doi.org/10.1038/s41569-021-00541-4</u> PMID: 33833450
- Mohamed-Yassin MS, Baharudin N, Abdul-Razak S, Ramli AS, Lai NM. Global prevalence of dyslipidaemia in adult populations: a systematic review protocol. BMJ Open. 2021 Dec 3; 11(12):e049662. https://doi.org/10.1136/bmjopen-2021-049662 PMID: 34862282
- 6. Lin CF, Chang YH, Chien SC, Lin YH, Yeh HY. Epidemiology of Dyslipidemia in the Asia Pacific Region. International Journal of Gerontology. 2018 Mar 1; 12(1):2–6.
- Hypertension [Internet]. [cited 2023 Oct 10]. https://www.who.int/news-room/fact-sheets/detail/ hypertension
- Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. Nat Rev Nephrol. 2020 Apr; 16 (4):223–37. https://doi.org/10.1038/s41581-019-0244-2 PMID: 32024986
- 9. bhf-cvd-statistics-global-factsheet.pdf [Internet]. [cited 2023 Oct 8]. https://www.bhf.org.uk/-/media/ files/for-professionals/research/heart-statistics/bhf-cvd-statistics-global-factsheet.pdf?rev= e61c05db17e9439a8c2e4720f6ca0a19&hash=6350DE1B2A19D939431D876311077C7B
- Cardiovascular diseases (CVDs) [Internet]. [cited 2023 Oct 8]. https://www.who.int/news-room/factsheets/detail/cardiovascular-diseases-(cvds)
- 2021_chp_hu_english.pdf [Internet]. [cited 2023 Oct 8]. https://health.ec.europa.eu/system/files/2021-12/2021_chp_hu_english.pdf
- Kékes E, Tóth K. Kardiovaszkuláris betegségek tegnap, ma és holnap? Cardiologia Hungarica. 2019; 49(2):111–8.
- 22% of people in the EU have high blood pressure [Internet]. [cited 2023 Oct 10]. https://ec.europa.eu/ eurostat/web/products-eurostat-news/-/edn-20210929-1
- 14. Oral health [Internet]. [cited 2023 Oct 10]. https://www.who.int/news-room/fact-sheets/detail/oral-health
- Cui Y, Tian G, Li R, Shi Y, Zhou T, Yan Y. Epidemiological and sociodemographic transitions of severe periodontitis incidence, prevalence, and disability-adjusted life years for 21 world regions and globally from 1990 to 2019: An age-period-cohort analysis. Journal of Periodontology. 2023; 94(2):193–203. https://doi.org/10.1002/JPER.22-0241 PMID: 35942553
- Wen PYF, Chen MX, Zhong YJ, Dong QQ, Wong HM. Global Burden and Inequality of Dental Caries, 1990 to 2019. J Dent Res. 2022 Apr; 101(4):392–9. https://doi.org/10.1177/00220345211056247 PMID: 34852668
- 17. Jacob S. Global prevalence of periodontitis: A literarure review.

- A hazai felnőtt lakosság parodontális állapota epidemiológiai felmérés alapján | Fogorvosi Szemle. 2021 Nov 18 [cited 2023 Oct 10]; https://ojs3.mtak.hu/index.php/fogorv-szemle/article/view/5480
- 19. Borzalmas állapotban a magyarok fogazata | Glied-Berke Dental [Internet]. [cited 2023 Oct 10]. https://gbdental.hu/hir/borzalmas-allapotban-magyarok-fogazata
- 20. Fogatlanok népe? Mit mondanak el a magyar társadalomról a gyerekek szuvas fogai? | G7—Gazdasági sztorik érthetően [Internet]. [cited 2023 Oct 10]. https://g7.hu/elet/20230413/fogatlanok-nepe-mit-mondanak-el-a-magyar-tarsadalomrol-a-gyerekek-szuvas-fogai/
- Unnoticed and untreated gingivitis can also lead to serious diseases [Internet]. 2021 [cited 2023 Oct 10]. https://semmelweis.hu/english/2021/05/unnoticed-and-untreated-gingivitis-can-also-lead-toserious-diseases/
- Libicki É, Fedor AR. A telepi körülmények között élők egészségi állapotának és egészségműveltségének jellemzői. Acta Medicinae et Sociologica. 2022 May 31; 13(34):138–62.
- Mougeot JLC, Stevens CB, Paster BJ, Brennan MT, Lockhart PB, Mougeot FKB. Porphyromonas gingivalis is the most abundant species detected in coronary and femoral arteries. J Oral Microbiol. 2017 Feb 8; 9(1):1281562. https://doi.org/10.1080/20002297.2017.1281562 PMID: 28326156
- 24. Zhang J, Xie M, Huang X, Chen G, Yin Y, Lu X, et al. The Effects of Porphyromonas gingivalis on Atherosclerosis-Related Cells. Front Immunol. 2021 Dec 23; 12:766560. <u>https://doi.org/10.3389/fimmu.</u> 2021.766560 PMID: 35003080
- Czerniuk MR, Surma S, Romańczyk M, Nowak JM, Wojtowicz A, Filipiak KJ. Unexpected Relationships: Periodontal Diseases: Atherosclerosis–Plaque Destabilization? From the Teeth to a Coronary Event. Biology (Basel). 2022 Feb 9; 11(2):272. <u>https://doi.org/10.3390/biology11020272</u> PMID: 35205138
- Zardawi F, Gul S, Abdulkareem A, Sha A, Yates J. Association Between Periodontal Disease and Atherosclerotic Cardiovascular Diseases: Revisited. Front Cardiovasc Med. 2021 Jan 15; 7:625579. https://doi.org/10.3389/fcvm.2020.625579 PMID: 33521070
- 27. Beukers NGFM, van der Heijden GJMG, van Wijk AJ, Loos BG. Periodontitis is an independent risk indicator for atherosclerotic cardiovascular diseases among 60 174 participants in a large dental school in the Netherlands. J Epidemiol Community Health. 2017 Jan 1; 71(1):37–42.
- Li Y, Yuan X, Zheng Q, Mo F, Zhu S, Shen T, et al. The association of periodontal disease and oral health with hypertension, NHANES 2009–2018. BMC Public Health. 2023 Jun 12; 23(1):1122. https:// doi.org/10.1186/s12889-023-16012-z PMID: 37308938
- 29. Wojtkowska A, Zapolski T, Wysokińska-Miszczuk J, Wysokiński AP. The inflammation link between periodontal disease and coronary atherosclerosis in patients with acute coronary syndromes: case–control study. BMC Oral Health. 2021 Jan 6; 21(1):5. https://doi.org/10.1186/s12903-020-01356-4 PMID: 33407375
- Karki P, Birukov KG. Rho and Reactive Oxygen Species at Crossroads of Endothelial Permeability and Inflammation. Antioxid Redox Signal. 2019 Nov 1; 31(13):1009–22. <u>https://doi.org/10.1089/ars.2019</u>. 7798 PMID: 31126187
- Folayan MO, El Tantawi M, Chukwumah NM, Alade M, Oginni O, Mapayi B, et al. Individual and familial factors associated with caries and gingivitis among adolescents resident in a semi-urban community in South-Western Nigeria. BMC Oral Health. 2021 Mar 27; 21:166. https://doi.org/10.1186/s12903-021-01527-x PMID: 33771136
- Sabharwal A, Stellrecht E, Scannapieco FA. Associations between dental caries and systemic diseases: a scoping review. BMC Oral Health. 2021 Sep 25; 21(1):472. https://doi.org/10.1186/s12903-021-01803-w PMID: 34563194
- 33. Abe M, Mitani A, Yao A, Takeshima H, Zong L, Hoshi K, et al. Close Associations of Gum Bleeding with Systemic Diseases in Late Adolescence. Int J Environ Res Public Health. 2020 Jun; 17(12):4290. https://doi.org/10.3390/ijerph17124290 PMID: 32560147
- Pietropaoli D, Altamura S, Ortu E, Guerrini L, Pizarro TT, Ferri C, et al. Association between metabolic syndrome components and gingival bleeding is women-specific: a nested cross-sectional study. Journal of Translational Medicine. 2023 Apr 10; 21(1):252. https://doi.org/10.1186/s12967-023-04072-z PMID: 37038173
- Giargia M, Lindhe J. Tooth mobility and periodontal disease. J Clin Periodontol. 1997 Nov; 24(11):785– 95. https://doi.org/10.1111/j.1600-051x.1997.tb01190.x PMID: 9402498
- Hag Mohamed S, Sabbah W. Is tooth loss associated with multiple chronic conditions? Acta Odontol Scand. 2023 Aug; 81(6):443–8. https://doi.org/10.1080/00016357.2023.2166986 PMID: 36634031
- Zhang Y, Leveille SG, Shi L. Multiple Chronic Diseases Associated With Tooth Loss Among the US Adult Population. Front Big Data. 2022 Jul 1; 5:932618. <u>https://doi.org/10.3389/fdata.2022.932618</u> PMID: 35844965

- European Health Interview Survey (EHIS) [Internet]. [cited 2023 Oct 14]. <u>https://ec.europa.eu/eurostat/</u> cache/metadata/en/hlth_det_esms.htm
- Hintzpeter B, Finger JD, Allen J, Kuhnert R, Seeling S, Thelen J, et al. European Health Interview Survey (EHIS) 2—Background and study methodology. J Health Monit. 2019 Dec; 4(4):66–79. https://doi.org/10.25646/6228 PMID: 35146260
- 40. Európai lakossági egészségfelmérés, 2019 [Internet]. [cited 2023 Oct 14]. https://www.ksh.hu/elef
- Ulambayar B, Ghanem AS, Kovács N, Trefán L, Móré M, Nagy AC. Cardiovascular disease and risk factors in adults with diabetes mellitus in Hungary: a population-based study. Frontiers in Endocrinology [Internet]. 2023 [cited 2023 Oct 14]; 14. <u>https://www.frontiersin.org/articles/10.3389/fendo.2023.</u> 1263365 PMID: 37780630
- Xi LJ, Guo ZY, Yang XK, Ping ZG. [Application of LASSO and its extended method in variable selection of regression analysis]. Zhonghua Yu Fang Yi Xue Za Zhi. 2023 Jan 6; 57(1):107–11. https://doi.org/10. 3760/cma.j.cn112150-20220117-00063 PMID: 36655266
- Heinze G, Wallisch C, Dunkler D. Variable selection–A review and recommendations for the practicing statistician. Biom J. 2018 May; 60(3):431–49. https://doi.org/10.1002/bimj.201700067 PMID: 29292533
- 44. Kirpich A, Ainsworth EA, Wedow JM, Newman JRB, Michailidis G, McIntyre LM. Variable selection in omics data: A practical evaluation of small sample sizes. PLoS One. 2018 Jun 21; 13(6):e0197910. https://doi.org/10.1371/journal.pone.0197910 PMID: 29927942
- 45. Statistical software for data science | Stata [Internet]. [cited 2023 Oct 14]. https://www.stata.com/
- 46. Kim SY, Kim JE, Kim HN, Jun EJ, Lee JH, Kim JS, et al. Association of Self-Perceived Oral Health and Function with Clinically Determined Oral Health Status among Adults Aged 35–54 Years: A Cross-Sectional Study. International Journal of Environmental Research and Public Health. 2018 Aug; 15 (8):1681.
- Locker D, Clarke M, Payne B. Self-perceived oral health status, psychological well-being, and life satisfaction in an older adult population. J Dent Res. 2000 Apr; 79(4):970–5. <u>https://doi.org/10.1177/</u>00220345000790041301 PMID: 10831100
- Ramadan DE, Hariyani N, Indrawati R, Ridwan RD, Diyatri I. Cytokines and Chemokines in Periodontitis. Eur J Dent. 2020 Jul; 14(3):483–95. https://doi.org/10.1055/s-0040-1712718 PMID: 32575137
- 49. Passarelli PC, Pagnoni S, Piccirillo GB, Desantis V, Benegiamo M, Liguori A, et al. Reasons for Tooth Extractions and Related Risk Factors in Adult Patients: A Cohort Study. International Journal of Environmental Research and Public Health. 2020 Jan; 17(7):2575. https://doi.org/10.3390/ijerph17072575 PMID: 32283707
- Larvin H, Kang J, Aggarwal VR, Pavitt S, Wu J. The additive effect of periodontitis with hypertension on risk of systemic disease and mortality. J Periodontol. 2022 Jul; 93(7):1024–35. <u>https://doi.org/10.1002/ JPER.21-0621 PMID: 35460076</u>
- Kim YJ, Lee JY, Ku Y, Cho HJ. Association between the Number of Prosthetic Crowns and Periodontitis: The Korea National Health and Nutrition Examination Survey (KNANES VII) from 2016–2018. Int J Environ Res Public Health. 2021 Jun 2; 18(11):5957. https://doi.org/10.3390/ijerph18115957 PMID: 34199343
- Dragomir LP, Nicolae FM, Gheorghe DN, Popescu DM, Dragomir IM, Boldeanu L, et al. The Influence of Fixed Dental Prostheses on the Expression of Inflammatory Markers and Periodontal Status-Narrative Review. Medicina (Kaunas). 2023 May 13; 59(5):941. <u>https://doi.org/10.3390/medicina59050941</u> PMID: 37241173
- Knoernschild KL, Campbell SD. Periodontal tissue responses after insertion of artificial crowns and fixed partial dentures. J Prosthet Dent. 2000 Nov; 84(5):492–8. <u>https://doi.org/10.1067/mpr.2000.</u> 110262 PMID: 11105004
- Kossioni AE. The Association of Poor Oral Health Parameters with Malnutrition in Older Adults: A Review Considering the Potential Implications for Cognitive Impairment. Nutrients. 2018 Nov 8; 10 (11):1709. https://doi.org/10.3390/nu10111709 PMID: 30413041
- 55. Chauncey HH, Muench ME, Kapur KK, Wayler AH. The effect of the loss of teeth on diet and nutrition. Int Dent J. 1984 Jun; 34(2):98–104. PMID: 6588038
- 56. Dhotre SV, Davane MS, Nagoba BS. Periodontitis, Bacteremia and Infective Endocarditis: A Review Study. Arch Pediatr Infect Dis [Internet]. 2017 [cited 2023 Oct 21]; 5(3). <u>https://brieflands.com/articles/apid-55785.html#abstract</u>
- 57. Vedin O, Hagström E, Gallup D, Neely ML, Stewart R, Koenig W, et al. Periodontal disease in patients with chronic coronary heart disease: Prevalence and association with cardiovascular risk factors. Eur J Prev Cardiol. 2015 Jun; 22(6):771–8. <u>https://doi.org/10.1177/2047487314530660</u> PMID: 24721691

- 58. Reddy KKR, Rao AP, Reddy TPK. Socioeconomic status and the prevalence of coronary heart disease risk factors. Asia Pac J Clin Nutr. 2002; 11(2):98–103. https://doi.org/10.1046/j.1440-6047.2002.00267. x PMID: 12074188
- Muennig P, Sohler N, Mahato B. Socioeconomic status as an independent predictor of physiological biomarkers of cardiovascular disease: evidence from NHANES. Prev Med. 2007 Jul; 45(1):35–40. https://doi.org/10.1016/i.ypmed.2007.04.005 PMID: 17521717
- Espírito Santo LR, Faria TO, Silva CSO, Xavier LA, Reis VC, Mota GA, et al. Socioeconomic status and education level are associated with dyslipidemia in adults not taking lipid-lowering medication: a population-based study. Int Health. 2019 Nov 6; 14(4):346–53.
- Tursinawati Y, Kartikadewi A, Yuniastuti A, Susanti R. Rural-Urban Differences in Characteristic and Lipid Profile Among Javanese Ethnic of Type 2 Diabetes Patients. In Atlantis Press; 2021 [cited 2023 Oct 23]. p. 136–41. https://www.atlantis-press.com/proceedings/icosihsn-20/125951158
- 62. de Groot R, van den Hurk K, Schoonmade LJ, de Kort WLAM, Brug J, Lakerveld J. Urban-rural differences in the association between blood lipids and characteristics of the built environment: a systematic review and meta-analysis. BMJ Glob Health. 2019 Jan 24; 4(1):e001017. https://doi.org/10.1136/ bmjgh-2018-001017 PMID: 30740247
- Li H, Ge M, Pei Z, He J, Wang C. Associations of environmental factors with total cholesterol level of middle-aged and elderly people in China. BMC Public Health. 2022 Dec 23; 22(1):2423. https://doi.org/ 10.1186/s12889-022-14922-y PMID: 36564736
- 64. Adil AH. Modifiable and Non-modifiable Risk Factors Affecting Oral and Periodontal Health and Quality of Life in South Asia. The Open Dentistry Journal [Internet]. [cited 2024 Feb 20]; https://www.academia.edu/93258567/Modifiable_and_Non_modifiable_Risk_Factors_Affecting_Oral_and_Periodontal_Health_and_Quality_of_Life_in_South_Asia
- Jaramillo A, Lafaurie GI, Millán LV, Ardila CM, Duque A, Novoa C, et al. Association between periodontal disease and plasma levels of cholesterol and triglycerides. Colomb Med (Cali). 44(2):80–6. PMID: 24892452
- Khan TZ, Mobin T. Unraveling the Link Between Periodontal Disease and High Cholesterol: A Cross-Sectional Study. Cureus. 2023 Aug; 15(8):e43463. https://doi.org/10.7759/cureus.43463 PMID: 37711924
- Tahamtan S, Shirban F, Bagherniya M, Johnston TP, Sahebkar A. The effects of statins on dental and oral health: a review of preclinical and clinical studies. J Transl Med. 2020 Apr 6; 18:155. <u>https://doi.org/ 10.1186/s12967-020-02326-8 PMID: 32252793</u>
- Kapellas K, Maple-Brown LJ, Jamieson LM, Do LG, O'Dea K, Brown A, et al. Effect of periodontal therapy on arterial structure and function among aboriginal australians: a randomized, controlled trial. Hypertension. 2014 Oct; 64(4):702–8. https://doi.org/10.1161/HYPERTENSIONAHA.114.03359 PMID: 24958498
- **69.** Fu YW, Li XX, Xu HZ, Gong YQ, Yang Y. Effects of periodontal therapy on serum lipid profile and proinflammatory cytokines in patients with hyperlipidemia: a randomized controlled trial. Clin Oral Investig. 2016 Jul; 20(6):1263–9. https://doi.org/10.1007/s00784-015-1621-2 PMID: 26434651
- Nakano K, Nomura R, Ooshima T. Streptococcus mutans and cardiovascular diseases. Japanese Dental Science Review. 2008 Jul 1; 44(1):29–37.