

Nicotine Vaping, Oral Microbiome Dysbiosis, and Periodontal Inflammation in Adolescents: Mechanistic Evidence to Inform U.S. School-Based Prevention Policy and the National Interest — A Narrative Review

Gissele Lima Ribeiro¹

¹Specialist in Family Health, Universidade do Estado do Rio de Janeiro (UERJ), Rio de Janeiro, RJ, Brazil.
ORCID: 0009-0009-1763-7140.

Dayane Rosevics Saran Chagas²

²Specialist in Implant Dentistry, Faculdade São Leopoldo Mandic, Campinas, SP, Brazil.
ORCID: 0009-0003-0739-8808

Suzana Carolina Ramos Silva³

³Specialist in Periodontology, Instituto Nacional de Pesquisa e Ensino Odontológico (INPEO), Cuiabá, MT, Brazil. ORCID: 0009-0008-3771-9365

Adrielen Henrique Picoli⁴

⁴Specialist in Orthodontics, FAIPE, Cuiabá, MT, Brazil.
ORCID: 0009-0009-5864-171X

Caroline Weinert Marçal⁵

⁵Specialist in Orthodontics, São Leopoldo Mandic, Vila Velha, ES, Brazil; Specialist in Implant Dentistry, Instituto de Ensino Superior Blauro Cardoso de Mattos, Serra, ES, Brazil.
ORCID: 0009-0001-8786-7613

Taís Rocha⁶

⁶Master's Degree in Pediatric Dentistry, Faculdade São Leopoldo Mandic, Campinas, SP, Brazil.
ORCID: 0000-0003-1477-8633

Thaís Abrunhosa Peres Magri⁷

⁷Specialist in Orthodontics, Universidade Cidade de São Paulo – Instituto Vellini, São Paulo, SP, Brazil.
ORCID: 0009-0005-9682-0795

Sara Renata Pereira Borges⁸

⁸Graduated in Dentistry, Universidade São Francisco, Bragança Paulista, SP, Brazil.
ORCID: 0009-0000-8735-4474

Abstract

Background: Electronic cigarettes remain the most commonly used tobacco product among U.S. middle and high school students, and a substantial share of adolescents who vape do so frequently, with flavored disposable devices. Meta-analyses comparing adult e-cigarette users with smokers and non-smokers report an intermediate and heterogeneous periodontal profile, and often lower bleeding on probing, which has encouraged the perception that vaping is periodontally benign. This review asks whether the mechanistic evidence supports that perception.

Materials and Methods: Narrative review of PubMed-indexed literature (2016-2026) on electronic nicotine delivery systems and the oral microbiome, host inflammation and oxidative stress, periodontal cell biology, microvascular function and clinical periodontal outcomes, together with U.S. youth surveillance data and school-based prevention evaluations. Three recent mechanistic reviews on oxidative stress, platelet-rich fibrin biology and implant-surface cell biology were used as an interpretive framework. Findings were graded by model (in vitro, animal, human) and by whether adolescents were actually studied.

Results: Vaping is consistently associated with a distinct subgingival community that is enriched in inflammation-associated taxa and that, according to the available longitudinal and cross-sectional data, lies between the communities of smokers and non-smokers. Aerosol constituents are metabolized by oral biofilms into dense, exopolysaccharide-rich structures, and the oral mycobiome is also remodelled. In host cells, e-cigarette aerosol and flavorings induce carbonyl and oxidative stress, receptor for advanced glycation end-products (RAGE) up-regulation and pro-senescence signalling, which converge on the same AGE-RAGE-NF- κ B axis that drives diabetes-associated periodontitis. Nicotine impairs the proliferation, migration and osteogenic differentiation of periodontal ligament stem cells through a miR-1305/RUNX2 mechanism, while e-cigarette aerosol reduces gingival fibroblast function on titanium surfaces. Nicotine vaping acutely increases thrombogenicity and impairs microvascular function, which offers a plausible explanation for the reduced bleeding on probing reported in meta-analyses. Almost no study enrolled adolescents.

Conclusion: The mechanistic evidence does not support the view that vaping is periodontally neutral. It suggests instead a pattern of subclinical dysbiosis and inflammation that conventional periodontal indices may under-detect. Because exposure begins in adolescence, school-based prevention, routine screening during dental visits and flavor-access policy are biologically justified. Adolescent-specific longitudinal studies with microbial and inflammatory endpoints are required.

Key Word: Electronic nicotine delivery systems; Vaping; Adolescent; Oral microbiome; Dysbiosis; Periodontitis; Oxidative stress; Periodontal ligament stem cells; School health; Public health policy.

Date of Submission: 15-10-2026

Date of Acceptance: 28-10-2026

I. Introduction

Nearly all tobacco and nicotine use begins during adolescence, and in the United States the dominant product of initiation is no longer the combustible cigarette but the electronic cigarette. The 2024 National Youth Tobacco Survey (NYTS), conducted by the Centers for Disease Control and Prevention and the Food and Drug Administration, found that e-cigarettes were the most commonly used tobacco product among middle and high school students (5.9% of all students), well ahead of nicotine pouches (1.8%) and cigarettes (1.4%), with an estimated 1.63 million students reporting current use [1]. The 2025 NYTS confirmed a continued decline in prevalence, with an annual percent change of -18.1 for e-cigarette use between 2022 and 2025, but it also showed that 5.2% of middle and high school students still vaped, that 41.2% of current users vaped on 20 or more days per month and that 66.3% used disposable devices [2]. A smaller population of adolescents is therefore vaping more intensely, which is the exposure profile most relevant to chronic local effects in the mouth.

The oral cavity is the first tissue exposed to e-cigarette aerosol, which carries nicotine, humectants (propylene glycol and glycerol), flavoring chemicals and thermal degradation products such as carbonyls. Yet the periodontal consequences of vaping are often discussed only in comparison with combustible smoking. Systematic reviews of mainly adult, cross-sectional data place e-cigarette users at an intermediate position between smokers and non-smokers, and several report lower bleeding on probing in e-cigarette users than in non-smokers [3-5]. Read uncritically, these findings can be taken to mean that vaping is periodontally benign. That reading is especially consequential for adolescents, whose periodontal tissues are usually clinically healthy, whose disease, if it develops, will become clinically evident only years later, and for whom the relevant comparator is not smoking but non-use.

The aim of this narrative review is therefore mechanistic and translational. It synthesizes the evidence on four biological pathways through which nicotine vaping may affect the periodontium (microbial ecology, host inflammation and oxidative stress, the behaviour of repair cells, and microvascular function; Figure 1); it examines why conventional clinical indices may under-detect these effects; and it translates the findings into recommendations for U.S. school-based prevention and dental practice. The review deliberately draws on three recent mechanistic syntheses published by our research network, on oxidative stress in the periodontitis-diabetes axis [6], on the molecular biology of platelet-rich fibrin (PRF) [7] and on the cellular mechanisms that govern responses at implant surfaces [8], because together they describe the oxidative, regenerative and immunological machinery that nicotine aerosol appears to disturb.

II. Materials and Methods

This is a narrative (non-systematic) review. PubMed/MEDLINE was searched in October 2026 using combinations of "electronic cigarette", "electronic nicotine delivery systems", "vaping" and "e-cigarette aerosol" with "periodontal", "periodontitis", "oral microbiome", "subgingival", "mycobiome", "gingival fibroblasts", "periodontal ligament stem cells", "oxidative stress", "macrophage", "thrombogenicity" and "adolescent". Targeted searches retrieved the 2024 and 2025 NYTS reports, studies of flavors and flavor policy among adolescents, studies of platelet-rich fibrin in smokers, and evaluations of school-based vaping prevention

curricula. Priority was given to studies published from 2016 to 2026 and to systematic reviews and meta-analyses; foundational studies were retained regardless of date.

Each finding was classified by model (in vitro, animal or human) and by population (adolescent, young adult or adult), because extrapolation from adult or cellular data to adolescents is the central inferential step of this review and must remain visible to the reader (Table 1). The three mechanistic reviews mentioned above [6-8] were not used as sources of primary data on vaping, which they do not address, but as an interpretive framework for oxidative stress, regenerative signalling and macrophage polarization. No predefined protocol, dual independent screening or formal risk-of-bias assessment was applied; the conclusions are a critical synthesis, not a pooled estimate of effect. All bibliographic metadata were verified against PubMed records.

Table 1. Evidence map: domains, key findings, models and applicability to adolescents

Domain	Key findings	Model / population	Adolescent data?
Youth exposure	E-cigarettes most used product; 41.2% of current users vape frequently; 66.3% use disposables; flavors drive willingness to try [1, 2, 9]	National surveys; adolescent DCE	Yes (behavioural only)
Microbial ecology	Distinct, stable subgingival community; Porphyromonas/Veillonella ↑; EPS-rich biofilm; microbiome remodeling [10-13]	Human cross-sectional and longitudinal; in vitro biofilm	No (adults/young adults)
Inflammation / oxidative stress	Carbonyl stress, RAGE ↑, COX-2/PGE2 ↑, DNA damage; MPO and MMP-9 differences [14, 15]	In vitro; human pilot	No
Repair cells	Fibroblast function ↓ on titanium; PDLSC miR-1305 ↑/RUNX2 ↓; mixed results in other models [16-18]	In vitro	No
Microvasculature	Thrombogenicity ↑, microvascular function ↓ after nicotine vaping [19]	Human RCT (healthy adults)	No
Clinical indices	Intermediate, heterogeneous profile; BOP often lower [4, 5, 20, 21]	Meta-analyses of adult observational studies	No
Prevention	Knowledge gains and high reach; limited effect on use [22, 23]	School-based program evaluations	Yes

Abbreviations: BOP, bleeding on probing; PI, plaque index; PD, probing depth; CAL, clinical attachment loss; MBL, marginal bone loss; NMA, network meta-analysis; RCT, randomized controlled trial; DCE, discrete choice experiment; EPS, exopolysaccharide; PDLSC, periodontal ligament stem cell.

III. The Adolescent Exposure: Prevalence, Intensity and Flavors

Three features of adolescent vaping matter biologically. The first is intensity. Prevalence has fallen since 2022, but the 2025 NYTS shows that two in five adolescents who currently vape do so frequently [2]; and in a young-adult cohort the oral microbiome changes associated with vaping were more pronounced among high-puff-volume users, who also had lower microbial diversity [24]. Prevalence alone therefore underestimates the biological dose received by the most exposed adolescents.

The second feature is flavor. In a discrete-choice experiment among California adolescents aged 12-17 who did not use e-cigarettes or cannabis, the predicted willingness to try a nicotine vape was 21% when the product was fruit or sweet-flavored and 4% when it was tobacco-flavored or unflavored [9]. After California's 2022 statewide ban on the retail sale of most flavored tobacco products, flavored use declined among adolescents who used cigarettes, cigars and smokeless tobacco, but not among those who vaped: 91.0% of adolescent e-cigarette users used flavored products before the ban and 90.7% afterwards [25]. Flavors are not only a marketing issue. As discussed in Section V, flavored aerosols produced greater oxidative, inflammatory and pro-senescence responses in periodontal cells than unflavored aerosols [14].

The third feature is the absence of oral health data in adolescents. National cohort data on oral outcomes come from adults. In the Population Assessment of Tobacco and Health (PATH) Study, e-cigarette use among U.S. adults was associated with a higher incidence of self-reported bleeding after brushing or flossing (adjusted hazard ratio 1.27; 95% CI 1.04-1.54) [26], and daily e-cigarette use was associated with greater odds of xerostomia (adjusted odds ratio 1.8; 95% CI 1.5-2.2) [27]. Both outcomes are plausible early markers of periodontal and salivary disturbance, but neither has been measured clinically in a representative adolescent sample.

IV. Microbial Dysbiosis: A Distinct Subgingival Ecology

The most consistent finding in the literature is that vaping is associated with an oral microbial community of its own, rather than a diluted version of the smoker's community. In a cohort of 119 participants, e-cigarette users showed significantly altered beta-diversity compared with both never-smokers and cigarette smokers, a higher abundance of Porphyromonas and Veillonella, and elevated interleukin (IL)-6 and IL-1β; epithelial cells exposed to e-cigarette aerosol were also more susceptible to infection by Porphyromonas gingivalis and

Fusobacterium nucleatum in vitro [10]. A six-month longitudinal study of 84 participants then showed that this vaping-associated subgingival microbiome was stable over time and occupied a heterogeneous position between those of smokers and non-smokers, with considerably more in common with the smokers' microbiome [11].

Newer studies have moved from composition to function. In 70 adults aged 18-35, vaping was associated with fewer beneficial taxa and more inflammation-associated bacteria, together with an enrichment of microbial pathways related to lipid metabolism, inflammation and xenobiotic degradation; salivary metabolomics and analysis of the volatile organic compounds emitted by participants' own devices supported these functional shifts [24]. Metabolomic and metatranscriptomic work has shown that oral biofilms metabolize e-cigarette aerosol, triggering a quorum-sensing-regulated stress response that produces dense, exopolysaccharide-rich biofilms in health-compatible communities and amplifies antimicrobial resistance and virulence in disease-associated communities [12]. The fungal compartment is affected as well. In 123 periodontally and systemically healthy adults, e-cigarette users had a more diverse subgingival mycobiome than smokers and never-smokers and showed 5- to 10-fold higher bacterial-fungal network connectivity [13]. In young adults, red-complex pathogens were found more frequently and in larger quantities among both smokers and vapers than among non-smokers [28].

The certainty of this evidence must be stated plainly. A 2026 systematic review in the *Journal of Clinical Periodontology* found that beta-diversity more consistently separated e-cigarette users from never-smokers and smokers, with some enrichment of *Veillonella*, *Leptotrichia* and *Fusobacterium*, but rated the certainty of evidence as very low because most studies were cross-sectional and heterogeneous [29]. A second systematic review, of 18 studies and 1,418 participants, reached a similar conclusion and pointed out that most studies relied on self-reported exclusive vaping [30], and an umbrella review of ten systematic reviews concluded that e-cigarette use may promote dysbiosis and biofilm accumulation [31]. The direction of the evidence is therefore consistent, even though its precision is low.

V. Host Inflammation and Oxidative Stress: Convergence on the RAGE Axis

At the cellular level, e-cigarette aerosol is not inert. In human periodontal ligament fibroblasts, gingival epithelial progenitors and three-dimensional gingival epithelium, e-cigarette aerosols increased oxidative and carbonyl stress and inflammatory cytokine release; they up-regulated cyclooxygenase-2, prostaglandin E2 and the receptor for advanced glycation end-products (RAGE); and they induced DNA damage and a reduction in histone deacetylase 2 through RAGE-dependent mechanisms, all of which are features of stress-induced premature senescence. Flavored aerosols elicited stronger responses [14]. In a clinical pilot study, e-cigarette users differed from non-smokers in salivary and crevicular myeloperoxidase and matrix metalloproteinase-9, markers of neutrophil activity and matrix degradation [15]. Beyond the mouth, e-cigarette aerosol impairs neutrophil chemotaxis, phagocytosis and oxidative burst, increases macrophage and dendritic-cell activation, and disrupts epithelial barriers [32].

These findings take on additional meaning when read alongside the periodontitis-diabetes literature. In our review of antioxidant therapy in type 2 diabetes, oxidative stress was described as the central mechanistic hub of the bidirectional relationship: advanced glycation end-products bind RAGE on immune and periodontal cells, activate nuclear factor kappa-B (NF- κ B) and drive the release of TNF- α , IL-6 and IL-18; AGE accumulation impairs the osteogenic differentiation of periodontal ligament stem cells; and diabetic patients show a blunted anti-inflammatory response to identical non-surgical periodontal therapy [6]. E-cigarette aerosol up-regulates the same receptor through a different trigger, carbonyl stress rather than hyperglycemia [14]. The convergence matters for adolescents in two ways. First, adolescents living with type 1 or type 2 diabetes who also vape would receive two independent inputs into the same inflammatory axis, a combination that has not been studied. Second, antioxidant adjuncts with demonstrated benefit in the diabetic periodontal model, of which melatonin was the most consistent [6], become a rational, although still untested, research target for nicotine-exposed periodontal tissues.

VI. Repair Cells Under Nicotine: Fibroblasts, Stem Cells and Macrophages

The periodontium of an adolescent is not only a tissue to be protected but also a tissue whose capacity for repair will be needed for decades, including after orthodontic treatment, periodontal therapy, extractions and implant placement. Evidence on how vaping affects repair cells is mixed, and the reasons for that inconsistency are informative.

Several in vitro studies found little or no damage. E-cigarette vapor was markedly less harmful than cigarette smoke to human gingival fibroblasts and did not increase reactive oxygen species [33], and e-cigarette aerosol, unlike cannabis and cigarette smoke, did not significantly reduce the colony formation or viability of gingival fibroblasts/mesenchymal stem cells [18]. By contrast, when gingival fibroblasts were cultured on titanium alloy and titanium nitride implant disks and exposed twice daily to aerosol containing 12 mg/mL nicotine, adhesion, proliferation, migration and collagen contraction all decreased, and the apoptotic fraction rose from

0.75% to 5.25% [16]. These results are compatible. Exposure models, nicotine concentrations and substrates differ, and the more realistic designs, with repeated exposure on a clinically relevant surface, tend to show harm.

Nicotine itself acts on periodontal ligament stem cells (PDLSCs) through specific regulatory pathways. It up-regulates miR-1305, which directly targets the osteogenic transcription factor RUNX2; nicotine-exposed PDLSCs proliferate, migrate and differentiate less, and restoring miR-1305 reverses the effect [17]. Inflammation up-regulates the $\alpha 7$ nicotinic acetylcholine receptor on PDLSCs, so that nicotine and inflammation act synergistically to reduce osteogenic differentiation and to increase the cells' capacity to induce osteoclast formation [34]. This is the same post-transcriptional layer of control that our review of platelet-rich fibrin identified as a key mediator of regeneration: PRF contains stable microRNAs such as miR-21 and miR-146a, its extracellular vesicles promote M2 macrophage polarization and suppress NF- κ B activation, and it promotes mesenchymal stem cell recruitment through TGF- β /Smad, PDGF/Akt and BMP2 signalling [7]. Nicotine therefore appears to act on the same targets that regenerative therapies aim to activate, but in the opposite direction.

Clinical regenerative data in tobacco users are limited and come from smokers rather than vapers. In a split-mouth randomized trial in 25 smokers with stage II-III, grade C periodontitis, subgingival injectable PRF added to scaling and root planing produced greater probing-depth reduction and attachment gain at one and three months than scaling and root planing alone [35]. An ex vivo study found that PRF prepared from smokers had altered platelet indices and higher FGF and TGF- β 1 concentrations, of uncertain clinical significance [36]. Macrophage behaviour adds a further dimension. Our review of implant-surface biology described how a transient early M1 response supports debris clearance and stem-cell recruitment, whereas a prolonged M1 state is associated with fibrotic encapsulation and impaired bone formation, and how reactive-oxygen-species mechanisms are not cell-type-selective [8]. Because e-cigarette aerosol increases macrophage activation and oxidative stress [14, 32], a vaping-related shift of the M1/M2 balance in periodontal and peri-implant tissues is biologically plausible, although it has not been demonstrated. Umbrella-level evidence already identifies e-cigarette use as a potential risk factor for implant healing and peri-implant outcomes [37]. For today's adolescents, the relevance lies in their future implant and regenerative needs, not in their present ones.

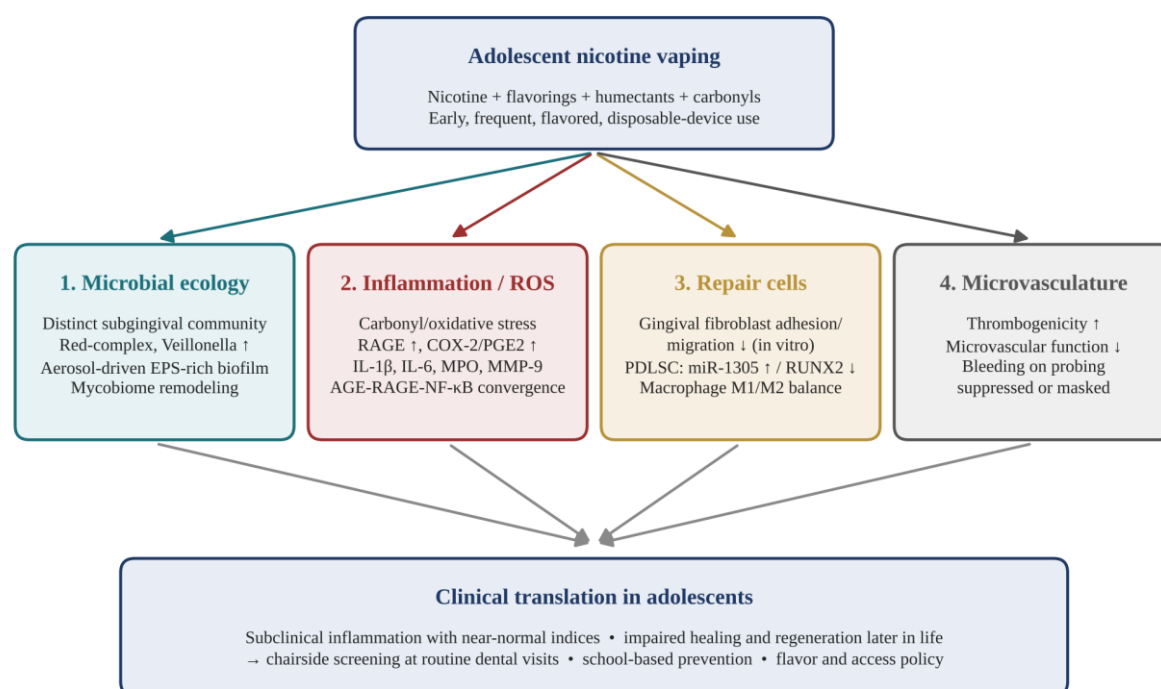


Figure 1. Conceptual framework of the four biological pathways linking adolescent nicotine vaping to periodontal change, and their clinical and policy translation. Arrows indicate proposed relationships synthesized from in vitro, animal and adult human data; none has been confirmed in adolescent cohorts.

VII. The Clinical Paradox: Why Periodontal Indices Under-Read Vaping Harm

If vaping produces dysbiosis, oxidative stress and impaired repair, why do meta-analyses so often find e-cigarette users clinically similar to, or even "better" than, non-smokers? The pooled data are summarized in Table 2. A 2024 meta-analysis of 12 studies found lower bleeding on probing in e-cigarette users than in non-users (pooled mean difference -14.2) and no significant differences in plaque index, probing depth, clinical attachment loss or marginal bone loss [5]. A network meta-analysis found bleeding on probing reduced in both e-cigarette

users and smokers compared with non-smokers, but all five included studies came from Saudi Arabia and 99% of participants were adult men [4]. In contrast, a 2025 meta-analysis of ten studies described a risk gradient (non-smokers lowest, e-cigarette users intermediate, smokers highest), with lower probing depth in non-smokers than in e-cigarette users [20], and a 40-study systematic review found higher plaque scores and higher pro-inflammatory markers in users of electronic nicotine delivery systems than in non-smokers, with no difference in probing depth or marginal bone loss [21].

Three explanations, not mutually exclusive, reconcile these findings. The first is vascular. In a randomized, double-blind crossover trial in healthy volunteers, inhaling nicotine-containing e-cigarette aerosol increased thrombus formation and impaired microvascular function [19]. Nicotine-induced vascular change is also the mechanism commonly invoked to explain suppressed gingival bleeding in smokers, and it means that low bleeding on probing in a vaping adolescent may reflect vasoconstriction rather than health. The second is temporal. Attachment loss and bone loss are cumulative outcomes that take years to appear, whereas most e-cigarette cohorts have short exposure histories; the early signals (dysbiosis, cytokine shifts, neutrophil activation) are precisely the ones that standard indices do not capture. A 2026 narrative review that integrated clinical, inflammatory and microbiome outcomes concluded that biological alterations in users of electronic nicotine delivery systems were not consistently reflected in traditional clinical indices, and that vaping should be treated as a distinct exposure rather than a predictable intermediate between smoking and non-use [38]. The third is methodological. Most studies are cross-sectional, rely on self-reported exclusive use, include dual users or former smokers and do not adjust for key confounders [29, 30, 39].

For clinical practice, the conclusion is that a periodontal chart within normal limits does not rule out vaping-related harm in an adolescent. In the staging-and-grading framework of the 2017 World Workshop, tobacco exposure modifies the grade of periodontitis [40]; whether nicotine vaping should be treated as an equivalent grade modifier is an open question that adolescent cohort data could answer. Until then, the history (product, frequency, flavor and device) carries more diagnostic value than bleeding scores, and consistent with professional guidance, dental practitioners should discourage e-cigarette use except where it replaces a more harmful habit in an adult smoker [41].

Table 2. Clinical periodontal findings in e-cigarette users: pooled evidence and interpretation

Source	Main pooled finding	Interpretation for adolescents
Shabil et al., 2024 (12 studies) [5]	BOP lower in e-cigarette users vs non-users; no significant difference in PI, PD, CAL, MBL	Low BOP is compatible with nicotine-induced microvascular change [19]; does not exclude inflammation
Pesce et al., 2022 (NMA, 5 studies) [4]	BOP reduced in both e-cigarette users and smokers vs non-smokers	All studies from one country, 99% adult men; not generalizable to adolescents
Thiem et al., 2023 (16 studies) [3]	Smokers worse than e-cigarette users; lower chance of BOP in e-cigarette users	Comparator is smoking, not non-use; harmful ENDS effects also noted
Alkattan et al., 2025 (10 studies) [20]	Risk gradient: non-smokers < e-cigarette users < smokers	Supports vaping as a risk exposure relative to non-use
Tattar et al., 2025 (40 studies) [21]	Higher plaque and pro-inflammatory markers vs non-smokers; no PD/MBL difference	Early biological signals precede destructive changes
Park et al., 2026 (narrative) [38]	Inflammatory and microbial changes not mirrored in clinical indices	Clinical charting alone under-detects vaping-related change

Abbreviations: BOP, bleeding on probing; PI, plaque index; PD, probing depth; CAL, clinical attachment loss; MBL, marginal bone loss; NMA, network meta-analysis; RCT, randomized controlled trial; DCE, discrete choice experiment; EPS, exopolysaccharide; PDLSC, periodontal ligament stem cell.

VIII. From Mechanism to Policy: Implications for U.S. School-Based Prevention

The mechanistic evidence has practical consequences for prevention because it changes what adolescents can be told. Prevention messages based only on nicotine addiction or lung injury do not connect with what an adolescent sees in the mirror. The oral findings reviewed here (a different bacterial and fungal community, inflamed gums that may not bleed, slower tissue repair and dry mouth) are visible, personal and immediate, and they can be integrated into existing curricula.

School-based programs provide the platform for this. In eight Central Appalachian counties in West Virginia and Kentucky, the CATCH My Breath curriculum reached 6,217 students in 25 middle and high schools between 2019 and 2023; knowledge improved, about 84% of students reported being less likely to use e-cigarettes, and current use fell from 5.1% to 4.4% between pre-test and post-test [22]. The program was then scaled statewide. In its first two years it reached 13,734 students in 94 schools across 39 counties, with large knowledge gains and high acceptability but no significant pre-post change in ever-use or 30-day use [23]. These results show both the

reach of school-based delivery and the limits of knowledge-based messaging, which supports adding concrete, health-specific content such as oral effects.

Dental practice is a second platform. Adolescents attend routine dental visits, and dental practitioners in the South Texas Oral Health Network have already co-designed a practice-based e-cigarette education and cessation program after identifying gaps in practitioner knowledge and in patient awareness [42]. The mechanistic framework of this review suggests three chairside elements: a structured vaping history (product, frequency, flavor, device), interpretation of low bleeding scores in vaping patients with caution, and brief advice that links vaping to visible oral effects. At the policy level, flavor restrictions are justified on two grounds, the adolescents' preference for flavored products [9] and the greater biological toxicity of flavored aerosols [14], but the California experience shows that restrictions need enforcement and attention to online sales before they change vaping behaviour [25].

IX. National Interest and Significance

Youth tobacco prevention is a long-standing federal public health priority in the United States, as reflected in the joint CDC-FDA surveillance of tobacco use among middle and high school students through the NYTS [1, 2]. This review contributes to that priority in four ways that extend beyond dentistry.

First, it identifies a biological rationale, independent of addiction, for preventing adolescent vaping: the oral microbiome, periodontal inflammation and the capacity for tissue repair. That rationale strengthens prevention messaging in schools, where knowledge-based curricula have shown wide reach but limited behavioural effect [23]. Second, it positions the dental visit as an underused point of early detection. Because low bleeding on probing can coexist with dysbiosis and inflammation in vaping patients [19, 38], a structured vaping history allows dental teams to identify at-risk adolescents years before attachment loss appears, at very low cost. Third, it links vaping to the AGE-RAGE-oxidative stress axis shared with diabetes-associated periodontitis [6, 14], a convergence of direct relevance to adolescents living with diabetes and to the long-term costs of periodontal and metabolic disease. Fourth, it identifies a research agenda (adolescent cohorts with microbial, inflammatory and vascular endpoints) that federal surveillance and research programs are well placed to support, and whose results would directly inform FDA product regulation, state flavor policies and school health programs.

Preventing a single generation of adolescents from establishing a dysbiotic, inflamed periodontal environment is likely to reduce future demand for periodontal treatment, regenerative procedures and implant therapy, which are costly to individuals and to public programs. The argument does not depend on vaping being as harmful as smoking; it depends only on vaping not being harmless, which is what the mechanistic evidence currently indicates.

X. Limitations and Research Agenda

The principal limitation of this review is the evidence gap it describes: almost no mechanistic or clinical study has enrolled adolescents, so every inference about the adolescent periodontium is extrapolated from young adults, adults or cell culture (Table 1). Most clinical studies are cross-sectional, rely on self-reported exclusive vaping and include dual users and former smokers, and several key meta-analyses draw on geographically narrow samples [4, 29, 30]. In vitro studies differ widely in device, e-liquid, nicotine concentration and exposure protocol, which explains part of their inconsistency [16, 18, 33]. The links drawn to the oxidative-stress, PRF and implant-surface literatures [6-8] are hypotheses generated by mechanistic analogy and not demonstrated effects of vaping. As a narrative review, this work is also subject to selection bias.

Five priorities follow. (1) School- or practice-based adolescent cohorts that combine periodontal examination with subgingival microbiome, crevicular-fluid inflammatory and salivary oxidative-stress endpoints, with biochemical verification of exposure. (2) Standardized exposure protocols for in vitro work, including repeated exposure on clinically relevant substrates and comparison of flavored and unflavored e-liquids. (3) Studies testing whether nicotine vaping should be recognized as a grade modifier within the current periodontitis classification [40]. (4) Trials of adjunctive antioxidant or regenerative strategies, informed by the melatonin and PRF literature [6, 7, 35], in nicotine-exposed periodontal tissues. (5) Evaluation of whether adding oral health content to school curricula such as CATCH My Breath changes behaviour, and not only knowledge [22, 23].

XI. Conclusion

Nicotine vaping is associated with a distinct and stable subgingival microbial community, with aerosol-driven biofilm and mycobiome changes, and with oxidative, carbonyl and RAGE-mediated inflammatory stress in periodontal cells. Nicotine impairs periodontal stem cell function through a defined microRNA pathway, and nicotine vaping acutely affects microvascular function in a way that can mask gingival bleeding. Together, these findings suggest that the apparently reassuring clinical indices of e-cigarette users reflect, at least in part, under-detection of subclinical disease rather than true periodontal neutrality. Because adolescents remain the main group in which vaping begins, and because almost no data exist for them, the oral effects of vaping should be added to

school-based prevention curricula, a structured vaping history should become part of adolescent dental visits, and adolescent-specific longitudinal research should be prioritized.

References

- [1]. Jamal A, Park-Lee E, Birdsey J, West A, Cornelius M, Cooper MR, et al. Tobacco product use among middle and high school students — National Youth Tobacco Survey, United States, 2024. *MMWR Morb Mortal Wkly Rep.* 2024;73(41):917-24. doi:10.15585/mmwr.mm7341a2
- [2]. Park-Lee E, Dutra LM, Cowan H, Levine B, Sawdey MD, Cooper M, et al. Tobacco product use among middle and high school students in the United States: National Youth Tobacco Survey, 2025. *Nicotine Tob Res.* 2026 [Epub ahead of print, 23 Jun 2026]. doi:10.1093/ntr/ntag116
- [3]. Thiem DGE, Donkiewicz P, Rejaey R, Wiesmann-Imilowski N, Deschner J, Al-Nawas B, et al. The impact of electronic and conventional cigarettes on periodontal health — a systematic review and meta-analysis. *Clin Oral Investig.* 2023;27(9):4911-28. doi:10.1007/s00784-023-05162-4
- [4]. Pesce P, Menini M, Ugo G, Bagnasco F, Dioguardi M, Troiano G. Evaluation of periodontal indices among non-smokers, tobacco, and e-cigarette smokers: a systematic review and network meta-analysis. *Clin Oral Investig.* 2022;26(7):4701-14. doi:10.1007/s00784-022-04531-9
- [5]. Shabil M, Khatib MN, Ballal S, Bansal P, Tomar BS, Ashraf A, et al. The impact of electronic cigarette use on periodontitis and periodontal outcomes: a systematic review and meta-analysis. *BMC Oral Health.* 2024;24(1):1197. doi:10.1186/s12903-024-05018-7
- [6]. Silva SCR, Bastos PVO, Lima PAD, Peres RRH, Castro KBL, Inácio PRS, et al. Adjunctive antioxidant therapy in the bidirectional relationship between periodontitis and type 2 diabetes mellitus: a narrative review emphasizing glycemic interaction and metabolic improvement. *South Fla J Environ Anim Sci.* 2026;6(2):1-23. doi:10.53499/sfjeasv6n2-010
- [7]. Pereira LCC. Molecular and cellular mechanisms of platelet-rich fibrin in dental implant osseointegration: emerging roles of microRNAs, exosomes, and mesenchymal stem cells. *IOSR J Dent Med Sci.* 2026;25(9 Ser. 6):17-24. doi:10.9790/0853-2509061724
- [8]. Gonçalves KS, Nóbrega SLD, Flores FW, Fernandes PL, Lima PAD, Chagas DRS, et al. Three cells, one surface: a 2026 update on the divergent cellular mechanisms driving next-generation dental implant coatings. *IOSR J Dent Med Sci.* 2026;25(9 Ser. I):67-71. doi:10.9790/0853-2509016771
- [9]. Chaffee BW, Couch ET, Wilkinson ML, Donaldson CD, Cheng NF, Ameli N, et al. Flavors increase adolescents' willingness to try nicotine and cannabis vape products. *Drug Alcohol Depend.* 2023;246:109834. doi:10.1016/j.drugalcdep.2023.109834
- [10]. Pushalkar S, Paul B, Li Q, Yang J, Vasconcelos R, Makwana S, et al. Electronic cigarette aerosol modulates the oral microbiome and increases risk of infection. *iScience.* 2020;23(3):100884. doi:10.1016/j.isci.2020.100884
- [11]. Thomas SC, Xu F, Pushalkar S, Lin Z, Thakor N, Vardhan M, et al. Electronic cigarette use promotes a unique periodontal microbiome. *mBio.* 2022;13(1):e0007522. doi:10.1128/mbio.00075-22
- [12]. Beverly ML, Chaudhary PP, Dabdoub SM, Kim S, Chatzakis E, Williamson K, et al. Toxic cultures: e-cigarettes and the oral microbial exposome. *NPJ Biofilms Microbiomes.* 2025;11(1):66. doi:10.1038/s41522-025-00709-7
- [13]. Nikam R, Kalani K, Beverly M, Kumar PS. The vape, the mouth, and the mycobiome: a comparative metagenomic analysis. *J Dent Res.* 2026 [Epub ahead of print, 18 Jul 2026]. doi:10.1177/00220345261450182
- [14]. Sundar IK, Javed F, Romanos GE, Rahman I. E-cigarettes and flavorings induce inflammatory and pro-senescence responses in oral epithelial cells and periodontal fibroblasts. *Oncotarget.* 2016;7(47):77196-204. doi:10.18632/oncotarget.12857
- [15]. Ye D, Gajendra S, Lawyer G, Jadeja N, Pishey D, Pathagunti S, et al. Inflammatory biomarkers and growth factors in saliva and gingival crevicular fluid of e-cigarette users, cigarette smokers, and dual smokers: a pilot study. *J Periodontol.* 2020;91(10):1274-83. doi:10.1002/JPER.19-0457
- [16]. Choueiri ME, Laaboudi FZ, Zhang Z, Chmielewski W, Rouabhia M. Evaluation of the effect of electronic cigarette aerosol on normal and diabetic human fibroblast interaction with dental implant materials. *Int J Oral Maxillofac Implants.* 2025 [Epub ahead of print, 31 Oct 2025]. doi:10.11607/jomi.11435
- [17]. Chen Z, Liu HL. Restoration of miR-1305 relieves the inhibitory effect of nicotine on periodontal ligament-derived stem cell proliferation, migration, and osteogenic differentiation. *J Oral Pathol Med.* 2017;46(4):313-20. doi:10.1111/jop.12492
- [18]. El-Mouelhy ATM, Nasry SA, Abou El-Dahab O, Sabry D, Fawzy El-Sayed K. In vitro evaluation of the effect of the electronic cigarette aerosol, Cannabis smoke, and conventional cigarette smoke on the properties of gingival fibroblasts/gingival mesenchymal stem cells. *J Periodontol Res.* 2022;57(1):104-14. doi:10.1111/jre.12943
- [19]. Lyytinen G, Brynedal A, Anesäter E, Antoniewicz L, Blomberg A, Wallén H, et al. Electronic cigarette vaping with nicotine causes increased thrombogenicity and impaired microvascular function in healthy volunteers: a randomised clinical trial. *Cardiovasc Toxicol.* 2023;23(7-8):255-64. doi:10.1007/s12012-023-09802-9
- [20]. Alkattan R, Tashkandi N, Mirdad A, Ali HT, Alshibani N, Allam E. Effects of electronic cigarettes on periodontal health: a systematic review and meta-analysis. *Int Dent J.* 2025;75(3):2014-24. doi:10.1016/j.identj.2024.12.036
- [21]. Tattar R, Jackson J, Holliday R. The impact of e-cigarette use on periodontal health: a systematic review and meta-analysis. *Evid Based Dent.* 2025;26(2):117-8. doi:10.1038/s41432-025-01119-6
- [22]. Burchfield K, Doyle D, Mantey D, Bennett T, Baus A. The CATCH My Breath vaping prevention curriculum: an evaluation of impacts in Central Appalachian middle and high schools, 2019-2023. *J Prim Care Community Health.* 2024;15:21501319241277393. doi:10.1177/21501319241277393
- [23]. Baus A, Burchfield K, Chill C, Litton A, Bolen S, Barclay CT, et al. Statewide youth vaping prevention in West Virginia: two-year outcomes of CATCH My Breath. *J Prim Care Community Health.* 2026;17:21501319261428032. doi:10.1177/21501319261428032
- [24]. Yang I, He X, Jeon J, Claussen H, Arthur R, Cushenan P, et al. The impact of vaping behavior on functional changes within the subgingival microbiome. *Sci Rep.* 2025;15(1):34374. doi:10.1038/s41598-025-17121-y
- [25]. Chaffee BW, Donaldson CD, Couch ET, Guerra Castillo C, Farooq O, Cheng NF, et al. Flavored tobacco product use among California adolescents before and immediately after a statewide flavor ban. *Nicotine Tob Res.* 2025;27(6):1035-42. doi:10.1093/ntr/ntae261
- [26]. Silveira ML, Everard CD, Sharma E, Lauten K, Alexandridis AA, Duffy K, et al. Tobacco use and incidence of adverse oral health outcomes among US adults in the Population Assessment of Tobacco and Health Study. *JAMA Netw Open.* 2022;5(12):e2245909. doi:10.1001/jamanetworkopen.2022.45909
- [27]. Chaffee BW. Associations of current cigarette, e-cigarette, and cannabis use with xerostomia. *JDR Clin Trans Res.* 2026;11(3):484-92 [Epub 2025 Sep 5]. doi:10.1177/23800844251364158
- [28]. Mociu M, Pușcașu CG, Buștiuc SG, Bartok-Nicolae C, Raftu G, Briceag R, et al. Subgingival microbiome in young adult cigarette smokers, e-cigarette users, and non-smokers. *Medicina (Kaunas).* 2026;62(8):1544. doi:10.3390/medicina62081544

- [29]. La Rosa GRM, Samaranayake LP, Zaura E, Sun A, Fuochi V, Furneri PM, et al. Impact of electronic cigarette use on the oral microbiota: a systematic review. *J Clin Periodontol*. 2026;53(6):956-85. doi:10.1111/jcpe.70111
- [30]. Sidhom J, Balla SB, Tadakamadla SK, Tadakamadla J. The association between self-reported vaping and the human oral microbiome: a systematic review. *Nicotine Tob Res*. 2026;28(9):1480-8. doi:10.1093/ntr/ntag103
- [31]. Panariello B, Dias Panariello F, Misir A, Barboza EP. An umbrella review of e-cigarettes' impact on oral microbiota and biofilm buildup. *Pathogens*. 2025;14(6):578. doi:10.3390/pathogens14060578
- [32]. Zima K, Bogucka A, Wojtas M, Zabielska-Kaczorowska M. Immunological effects of electronic cigarette use: a review of current evidence. *Clin Rev Allergy Immunol*. 2025;68(1):9. doi:10.1007/s12016-025-09026-5
- [33]. Vermehren MF, Wiesmann N, Deschner J, Brieger J, Al-Nawas B, Kämmerer PW. Comparative analysis of the impact of e-cigarette vapor and cigarette smoke on human gingival fibroblasts. *Toxicol In Vitro*. 2020;69:105005. doi:10.1016/j.tiv.2020.105005
- [34]. Zhou Z, Liu F, Wang L, Zhu B, Chen Y, Yu Y, et al. Inflammation has synergistic effect with nicotine in periodontitis by up-regulating the expression of $\alpha 7$ nAChR via phosphorylated GSK-3 β . *J Cell Mol Med*. 2020;24(4):2663-76. doi:10.1111/jcmm.14986
- [35]. Çağırır Gürbüz T, Meracı Yıldırım B. The clinical efficacy of injectable platelet-rich fibrin (i-PRF) as an adjunct to nonsurgical periodontal therapy in smokers with periodontitis. *BMC Oral Health*. 2025;25(1):618. doi:10.1186/s12903-025-06019-w
- [36]. Kayhan HG, Ozcan M, Totik N, Alkaya B, Ucak Turer O, Haytac MC. Effect of smoking on growth factors in platelet-rich fibrin: ex-vivo pilot study. *J Vis Exp*. 2026;(231). doi:10.3791/70997
- [37]. Fathi A, Salehi S, Sadeghi S, Atash R, Monirifard R, Farahmand S. Electronic cigarettes and peri-implantitis: an umbrella review. *J Oral Implantol*. 2024;50(6):653-8. doi:10.1563/aaid-joi-D-24-00157
- [38]. Park SH, Yaung J, Yaghamai S, Bezerra B. A narrative review on the impact of ENDS use on clinical, inflammatory and microbiological periodontal-related parameters. *Dent J (Basel)*. 2026;14(7):452. doi:10.3390/dj14070452
- [39]. Kruthika K, Aishwarya MU, Vaishnavi K, Shetty KP, Divyadharshini J. Electronic cigarette use and periodontal tissue damage: a scoping review and an evidence-informed conceptual framework. *Front Dent Med*. 2026;7:1956724. doi:10.3389/fdmed.2026.1956724
- [40]. Tonetti MS, Greenwell H, Kornman KS. Staging and grading of periodontitis: framework and proposal of a new classification and case definition. *J Periodontol*. 2018;89(Suppl 1):S159-72. doi:10.1002/JPER.18-0006
- [41]. Robson G, Lim XC, Chaudhari I, Hurley J, Khalil S, Amin V, et al. Trying to clear the air: e-cigarette use and periodontal disease. *Br Dent J*. 2025;239(10):687-92. doi:10.1038/s41415-025-8919-5
- [42]. Mungia R, Case K, Valerio MA, Mendoza M, Taverna M, de la Rosa EM, et al. Development of an e-cigarettes education and cessation program: a South Texas Oral Health Network study. *Health Promot Pract*. 2021;22(1):18-20. doi:10.1177/1524839920914870