
RESEARCH REVIEW • ISSUE 01 • 6 JUNE 2026

Frontiers of Dental Research

The week in dental science, graded for what it actually proves — from the lab bench to the chairside, every claim cited and weighed.



12

FIELDS REVIEWED

150+

STUDIES SCANNED

7

CLAIMS FACT-CHECKED

What's inside

01 Periodontology

Peri-implant disease, host modulation, and where regeneration evidence actually holds

02 Endodontics

Endodontics: biology overtakes mechanics, with the evidence still maturing

03 Implantology & Oral Surgery

Survival is solved; peri-implant disease and precision are the open problems

04 Cariology & Prevention

Hydroxyapatite, silver diamine fluoride, and AI are widening the caries-prevention toolkit, but the proof for most new tools stays thin

05 Oral-Systemic Health

One infected pocket, four organs: where the oral-systemic evidence is real and where it is only a hypothesis

06 Oral Oncology & Oral Medicine

Oral cancer caught too late: the race to find it sooner and less invasively

07 Pediatric Dentistry

Minimally invasive caries management: SDF, the Hall Technique, and the cautious evidence behind the hype

08 Orthodontics

Four frontiers, one pattern: routine cases are solved, the hard problems stay open

09 **Biomaterials Research**

Bioactive and regenerative materials, from evidence-backed pulp capping to still-preclinical scaffolds and implant coatings

10 **AI & Technology Research**

AI & technology: strong headline numbers, weak methodology underneath

11 **Featured Paper**

CariedAway: a one-dollar drop of silver diamine fluoride matched the full sealant-plus-ART toolkit across 7,418 high-risk NYC children

12 **Evidence Updates: Reviews & Guidelines**

Evidence recalibrated: when dentistry's bedrock tools meet modern GRADE

Periodontology

Peri-implant disease, host modulation, and where regeneration evidence actually holds

Two stories run through periodontology's research frontier right now. One is a hard reckoning: peri-implant disease is common, and the strongest recent surgical trials for failing implants are negative or borderline. The other is more hopeful, with host-modulation biology and graft-supported regeneration producing measurable, if modest, gains. The organizing event is the 2024 AO/AAP Consensus, published in 2025 and backed by eight commissioned systematic reviews.

46%

IMPLANT PATIENTS
WITH PERI-IMPLANT
MUCOSITIS

21%

IMPLANT PATIENTS
WITH PERI-
IMPLANTITIS

58%

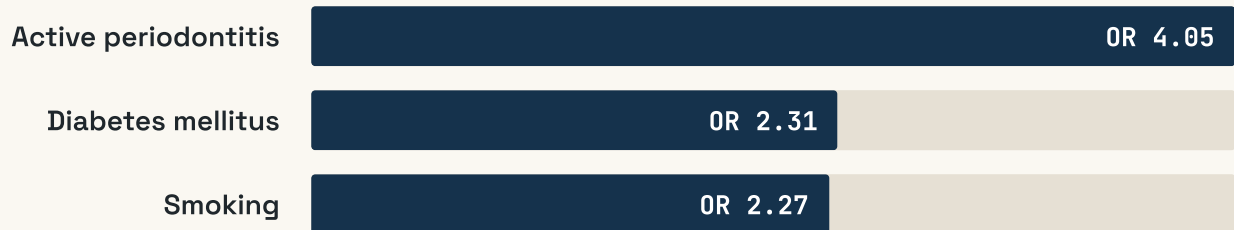
MUCOSITIS AT 10-20
YEARS

The companion prevalence meta-analysis is the largest of its kind to date, pooling 102 studies covering 13,030 patients and 39,991 implants. Patient-level peri-implant mucositis sits at 46% (95% CI 41-51) and peri-implantitis at 21% (95% CI 17-24), with mucositis rising to 58% (95% CI 51-65) in implants followed 10 to 20 years. One caveat belongs in any headline figure: peri-implantitis prevalence ranges roughly 12-25% at the patient level depending on diagnostic threshold, and the 2017 World Workshop criteria yield higher numbers than older definitions. The same review quantified who is at risk.¹

EXHIBIT 1

What drives peri-implantitis risk

Odds ratios from the AO/AAP prevalence meta-analysis (102 studies)



DENTAL NATION RESEARCH

SOURCE: J PERIODONTOL 2025, DOI 10.1002/JPER.24-0154

That risk picture explains the consensus's central message. The 2024 AO/AAP Consensus, convened in Oak Brook with 46 experts, built a unified flow-diagram framework that prioritizes early risk-factor identification, tailored protocols, and ongoing maintenance. It acknowledged possible benefit from surgery but did not crown any regenerative approach. The trial data make that caution look earned.

Surgery for failing implants: the unsentimental verdict

The two most rigorous recent peri-implantitis surgical RCTs both came back negative or equivocal on their primary regenerative comparisons. Adding bone-substitute material to access-flap surgery did not reliably rebuild bone, and composite treatment success was low in both arms regardless of grafting.

Bone Substitute Material in the Surgical Therapy of Peri-Implantitis: 3-Year Outcomes of an RCT

ALIBEGOVIĆ ET AL. • CLIN ORAL IMPLANTS RES • 2024

In a 6-center trial (120 subjects, 127 implants), adding bone substitute to access-flap surgery gave no clear benefit at 3 years: marginal bone gain 1.1 vs 1.3 mm ($p=0.576$), composite success only 8.3% vs 19.4% ($p=0.086$), disease resolution 30.0% vs 46.3% ($p=0.081$). Bleeding reduction actually favored the no-graft control.

Reconstructive therapy in surgical management of peri-implantitis: 3-year follow-up of an RCT

RENVERT ET AL. • J CLIN PERIODONTOL • 2024

Guided bone regeneration vs open-flap debridement (50 completers) showed no significant clinical superiority. GBR trended toward more bone fill (2.13 vs 1.64 mm, $p=0.18$) and higher composite success (46.2% vs 20%, $p=0.053$), but probing depth, bleeding, and suppuration did not differ between groups.

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The takeaway that gets oversold

The narrative that grafting reliably regrows bone around a failing implant is not supported by current high-level evidence. Composite success stayed in the 8-46% range across these trials, and recurrence happened even in initially successful cases. The strongest endorsement in the field today goes to prevention and early risk-factor control, not salvage surgery.

The biologics that work around teeth perform far more weakly around implants. A meta-analysis of five RCTs found enamel matrix derivative gave only 0.59 mm of surgical bone-level gain for peri-implant disease (95% CI -0.01 to 1.19, $p=0.05$), a borderline result. That tooth-versus-implant asymmetry is clinically important and easy to forget.²

Host modulation and regeneration: where the gains are real

Host modulation has moved past sub-antimicrobial doxycycline, still the only FDA-approved host-modulating drug, working by inhibiting matrix metalloproteinases rather than killing bacteria. The current excitement is around specialized pro-resolving mediators (resolvins, lipoxins, maresins), active at picogram-to-nanogram doses with osteogenic potential and no immunosuppressive downside. Some SPM formulations are already on certain European markets. The fair framing: preclinical and mechanistic evidence currently outpaces clinical proof, and large human periodontitis RCTs are still lacking.^{3,4}

Omega-3 supplementation tells a similar measured story. A 40-patient RCT in stage III-IV periodontitis paired high-dose omega-3 PUFA (2.6 g EPA plus 1.8 g DHA daily) with scaling and found real 3-month gains: closed pockets 59.9% vs 49.8% ($p=0.02$), bleeding 13.1% vs 19.0% ($p=0.004$), attachment 4.39 vs 5.04 mm ($p=0.03$). Probing-depth differences were non-significant, and most benefit faded by 6 months. It reads as a short-term adjunct, not a standalone therapy.⁵

On natural teeth, regeneration is where the evidence is most encouraging. The most rigorous 2025 synthesis pooled 21 RCTs (739 patients, 828 intrabony defects) and found that pairing a biologic agent with bone graft beat the biologic alone for radiographic bone gain (+0.81 mm, $p=0.003$) and pocket reduction (+0.38 mm, $p=0.02$), though attachment gain was not significantly different (+0.30 mm, $p=0.22$). The subgroups matter: PRF and growth factors benefit from a graft scaffold, while EMD performs comparably with or without one. Growth-factor regeneration is the mature end of this field, with rhFGF-2 plus deproteinized bovine bone reaching 3.5 mm of attachment gain at four years versus 2.7 mm for the control.

Periodontal regeneration with biologic agents alone vs combined with graft for intrabony defects

SYSTEMATIC REVIEW AND META-ANALYSIS • PERIODONTOLOGY • 2025

Across 21 RCTs, biologic plus graft gave significantly greater radiographic bone gain (+0.81 mm, $p=0.003$) and pocket reduction (+0.38 mm, $p=0.02$); attachment gain favored combination but was not significant.

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One adjacent diagnostic frontier dovetails with the host-modulation theme: chairside aMMP-8 testing of crevicular and peri-implant fluid for earlier detection. Lasers and implantoplasty (Er:YAG, around 3 mm probing-depth reduction) look promising but rest on small, heterogeneous studies, so they belong in the emerging category rather than standard of care.^{6,7}

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SECTION 02

Endodontics

Endodontics: biology overtakes mechanics, with the evidence still maturing

For a century the operating logic of endodontics was mechanical: remove the inflamed pulp, shape the canal, seal it. The 2024-2026 literature describes a slow inversion of that logic. Biology is winning. Regenerative protocols are coaxing immature roots to keep growing, calcium-silicate cements are letting inflamed pulps survive that would once have been extirpated, and bioceramic sealers are displacing resin as the default fill. The qualifier running through all of it is plain: the evidence is young, heterogeneous, and short on long follow-up.

Regenerative endodontics: high success, low-confidence evidence

The clearest signal in regenerative endodontic therapy (RET) is also the most carefully hedged. A 2024 network meta-analysis pooling 9 RCTs across 6 scaffold interventions found clinical and radiographic success above 85% in immature necrotic permanent teeth, with continued root lengthening and dentin-wall

thickening that apexification cannot produce. The same paper graded its own evidence as very-low-to-low confidence across every outcome. Both facts belong in the same sentence.

Treatment outcomes of regenerative endodontic therapy in immature permanent teeth with pulpal necrosis: a systematic review and network meta-analysis

SABETI ET AL. • INTERNATIONAL ENDODONTIC JOURNAL • 2024

RET success exceeds 85% in immature necrotic teeth and drives continued root development. PRP scaffolds gave the greatest early root lengthening (MD 4.2 mm at 6-12 months, SUCRA 89%); coronal discoloration occurred in roughly 15% of cases, largely tied to minocycline/triclosan medicaments. Overall evidence confidence: very low to low.

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Scaffold choice is not settled. Platelet-rich plasma and fibrin outperformed the blood clot for early outcomes, while enhanced blood-clot variants did better beyond 12 months. The 15% discoloration rate is a real clinical cost that traces back to the medicament rather than to regeneration itself.

Vital pulp therapy crosses into mature teeth

A more provocative shift is indication-creep. Calcium-silicate pulpotomy is being tested in mature teeth with pulpitis, including frank irreversible pulpitis, territory that traditionally meant root canal treatment. One-year clinical success in recent RCTs lands at 90.4-98%. Partial pulpotomy for carious exposure in adult teeth pools lower, around 86.8%. The strongest long-term data still sit with immature teeth and reversible cases, so this remains a paradigm to watch rather than a settled standard of care.

Clinical influencing factors of vital pulp therapy on pulpitis permanent teeth with two calcium silicate-based materials: a randomized clinical trial

PMC11062667 · 2024

Pulpotomy with calcium-silicate cements in mature pulpitis teeth reached 90.4-98% one-year clinical success (TheraCal LC vs iRoot BP Plus 90.4%; premixed injectable calcium silicate 94.4%), challenging the long-held rule that inflamed exposed pulp must be removed.

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Bioceramic sealers: non-inferiority plus simpler workflow

On materials the story is convergence. Premixed bioceramic single-cone obturation is clinically non-inferior to warm vertical compaction with resin sealers. The 2024 Zamparini meta-analysis found no significant difference in treatment outcome, a small non-significant reduction in extrusion, and slightly less 24-hour pain for bioceramics. Read honestly, that is a workflow advantage and less early discomfort, with no claim of dramatically higher long-term success.

The efficacy of premixed bioceramic sealers versus standard sealers on root canal treatment outcome, extrusion rate and post-obturation pain

ZAMPARINI ET AL. · INTERNATIONAL ENDODONTIC JOURNAL · 2024

Premixed bioceramic sealers are non-inferior to standard resin sealers: no significant outcome difference, a small non-significant lower extrusion risk, and slightly less post-op pain within 24 hours. Evidence is short-term with reporting inconsistencies.

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Early pain is where bioceramics show a measurable edge. A double-blind RCT in 90 patients found Bio-C Sealer Ion+ produced significantly less post-obturation pain at 6 hours ($p < 0.001$) and 24 hours ($p = 0.028$), with lower analgesic intake ($p = 0.022$), versus AH Plus epoxy resin. In 240 older patients, C-Root SP delivered 91.2-93.0% one-year success across techniques, statistically indistinguishable from the iRoot SP control (94.8%, $p = 0.892$).^{1,2}

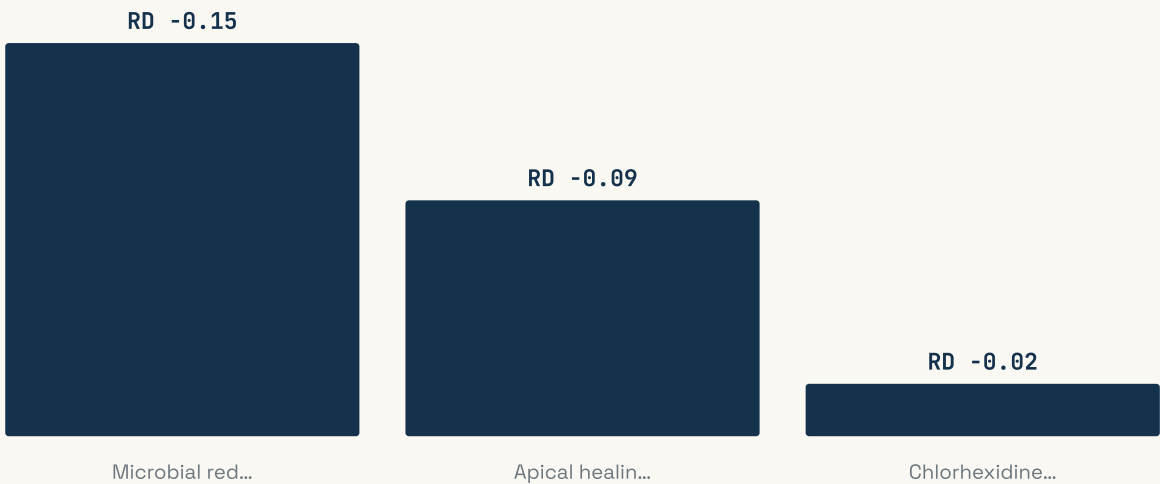
Disinfection: hypochlorite holds, activation helps

A 2025 umbrella review of 13 systematic reviews confirmed sodium hypochlorite as the irrigant of choice and quantified the benefit of activation. Passive ultrasonic irrigation beat conventional needle irrigation for both microbial reduction and apical healing. Chlorhexidine showed no significant antimicrobial advantage over NaOCl.

EXHIBIT 2

Passive ultrasonic irrigation vs conventional needle irrigation

Risk differences favoring PUI (negative = better with ultrasonic activation)



DENTAL NATION RESEARCH

SOURCE: OROZCO-GALLEGO ET AL., DENT J 13(6):273 (2025), 10.3390/DJ13060273

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Two operator-level findings reinforce the chemistry. Extended NaOCl exposure with periodic renewal after preparation cut bacterial CFUs more than standard continuous irrigation, and heated NaOCl improves tissue dissolution. Multisonic disinfection (GentleWave) reports 97.3% 12-month healing, though that headline figure comes from a 2016 prospective study and reviewers flag the broader evidence as industry-linked and heterogeneous.^{3,4}

The CBCT reality check

The most uncomfortable finding of the period is a measurement story. A 2025 CBCT-based meta-analysis put pooled nonsurgical success at roughly 42% under strict criteria, against roughly 88% under loose criteria (retreatment 39% vs 80%). The gap does not mean treatment got worse; it tracks detection sensitivity, because 3D imaging finds periapical lesions that 2D films miss. The profession's familiar 90%-plus success narrative is partly an artifact of how it has been measured.⁵

Pulp status and preoperative lesions remain the dominant prognostic factors. A 2025 meta-analysis of undergraduate-performed treatment quantified the spread: 87.8% success for vital versus 65.6% for necrotic pulp, and 86.8% without versus 56.3% with a preoperative radiolucency.⁶

Read the success rate with the imaging method attached

Strict-criteria CBCT success (~42%) and loose-criteria CBCT success (~88%) describe the same treatments scored on different yardsticks. Long-term tooth survival stays high either way: 97%, 81%, 76% and 68% cumulative survival at 10, 20, 30 and 37 years after primary treatment.

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AI: adjunctive and experimental, not established

AI for working-length and apical-landmark assessment shows accuracy of 0.70-0.95 in vitro, with one model reaching 96% against 76% for endodontists; some CBCT canal-detection models report accuracy above 90% in the same experimental setting. The 2026 systematic review rates the certainty low and classifies these tools as adjunctive and experimental, pending prospective multicenter validation. The defensible reading is that AI may help operators check their own work; it has not been shown to replace clinical judgment.

Performance of artificial intelligence models as adjuncts for determining working length and apical landmark assessment in endodontics: a systematic review

FRONTIERS IN DENTAL MEDICINE • 2026

Across 6 studies (2012-2024): sensitivity 0.85-1.00, accuracy 0.70-0.95, with one model at 96% vs 76% for endodontists. Certainty graded low; AI judged adjunctive and experimental until prospective multicenter trials confirm clinical value.

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The throughline for the field is steady. Biologic and bioceramic approaches are promising and increasingly mainstream, the early-pain and workflow gains are documented, and the long-term, CBCT-validated, standardized RCTs that would settle the headline numbers have not yet been done.

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Implantology & Oral Surgery

Survival is solved; peri-implant disease and precision are the open problems



For three decades the research question in implant dentistry was whether the bone would accept the titanium. That question is largely closed. Survival now sits between roughly 95% and 98% across loading protocols, materials, and lengths, and the differences between them have shrunk below statistical significance. The frontier has moved to two harder problems: keeping the tissue around a successful implant healthy, and placing the implant more accurately with less surgery.

The clearest sign that survival is settled comes from an umbrella review of 24 systematic reviews covering 18,373 implants in 8,063 patients. Immediate loading produced survival of 92 to 97.8%, non-immediate loading 95 to 99%, and the two were

statistically indistinguishable on survival, marginal bone loss, and prosthetic complications. The multi-month staged protocol is now optional rather than default.¹

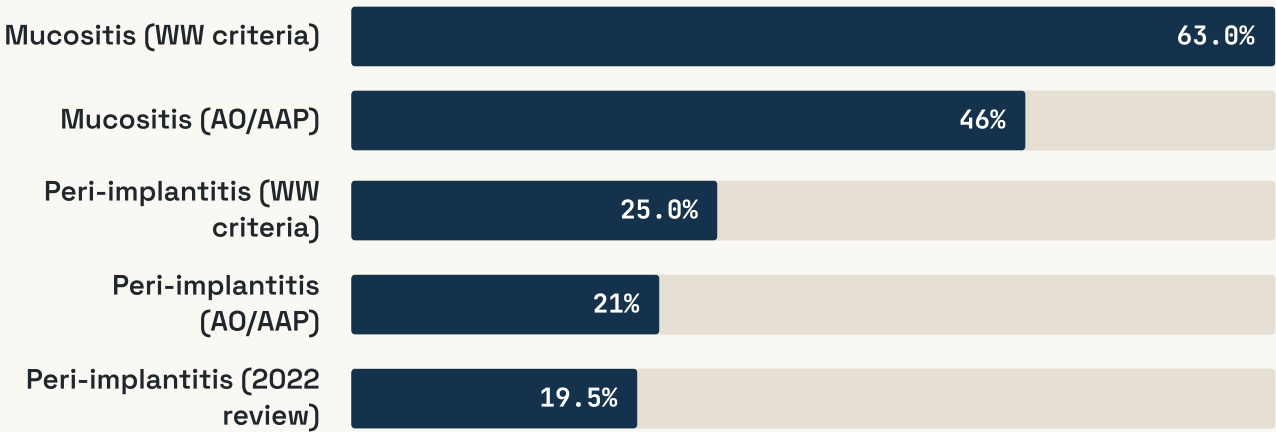
The real problem: the tissue, not the implant

If the metal survives, the gum and bone around it often do not. Three independent syntheses converge on a hard number: roughly one in four to five implant patients develops peri-implantitis, the inflammatory bone loss that no treatment reliably reverses. A global meta-analysis using 2017 World Workshop criteria put patient-level peri-implantitis at 25.0% and mucositis at 63.0%. An AO/AAP review of 102 studies and 13,030 patients landed at 21% and 46%. An earlier 57-article meta-analysis found 19.5%. The thresholds differ; the burden is the same.

EXHIBIT 3

Peri-implant disease is common across diagnostic thresholds

Patient-level prevalence from three independent meta-analyses (2022-2025)



DENTAL NATION RESEARCH

SOURCE: J DENT 2025 (PMID 40523497); J PERIODONTOL 2025; BMC ORAL HEALTH 2022

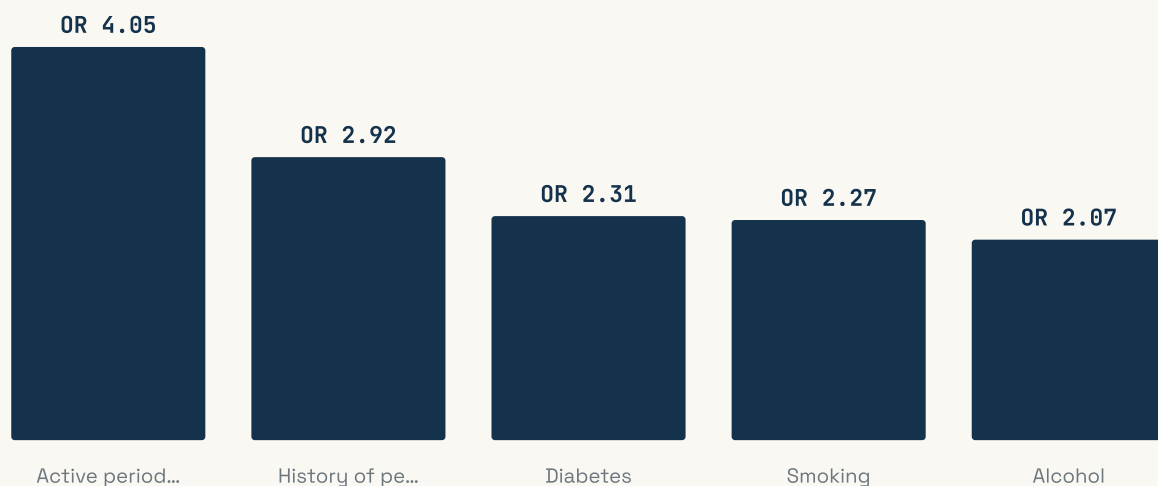
Risk is now quantified well enough to guide patient selection. The AO/AAP analysis reported odds ratios for the dominant drivers: active periodontitis carries roughly

four times the risk, with diabetes, smoking, and alcohol each roughly doubling it. Periodontal control before placement is the strongest lever a clinician holds.

EXHIBIT 4

What raises peri-implantitis risk

Odds ratios for patient-level risk factors (AO/AAP meta-analysis, 102 studies)



DENTAL NATION RESEARCH

SOURCE: GALARRAGA-VINUEZA ET AL., J PERIODONTOL 2025 (10.1002/JPER.24-0154)

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Treatment, by contrast, is humbling. Systemic antibiotics improved surgical success at one to two years (OR 2.33) but the benefit faded at three years or more (OR 0.69), while 21% of recipients got diarrhea. Enamel matrix derivative produced only a non-significant bone-level gain of 0.59 mm ($p=0.05$). No reliable cure exists, which is the strongest argument for prevention over rescue.^{2,3}

The reframing

Survival metrics are excellent and stable. The unsolved problem is a biological one: peri-implant disease is common, risk-stratified, and poorly treatable. Patient selection and periodontal control matter more than any new surface or robot.

Precision: the case for robots and AI is still directional

The second frontier is getting the implant into the right place with smaller incisions. Pooled clinical data place robot-assisted placement at the top of an accuracy hierarchy: 0.81 mm coronal, 0.77 mm apical, and 1.71 degrees of angular deviation, roughly half the angular error of static and dynamic guides at about 3.5 degrees. The ranking of robot over guided over freehand holds up well. The absolute robotic numbers do not yet: they rest on 2 studies and 44 implants. AI is following a similar curve, present in 89.2% of 120 implant studies but judged underdeveloped, with high risk of bias in 11 of them.

Accuracy of static, dynamic, and robot-assisted implant placement

KHAOHOEN ET AL. • BMC ORAL HEALTH • 2024

Robot-assisted placement showed the lowest deviations (0.81 mm coronal, 0.77 mm apical, 1.71 deg angular), roughly halving angular error versus guided systems, but robotic data came from only 2 studies and 44 implants.

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The role of artificial intelligence in implant dentistry

VAZQUEZ-SEBRANGO ET AL. • INT J ORAL MAXILLOFAC SURG • 2025

Across 120 papers (2018-2024), deep learning appeared in 89.2% of implant-AI studies spanning guided surgery, implant identification, and prognosis, but the field was rated relatively underdeveloped with high risk of bias in 11 studies.

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Materials and biologics: fewer trade-offs, less surgery

Three findings point toward less invasive care. Short implants matched long implants with sinus floor elevation on survival (OR 0.96) while showing less marginal bone loss and fewer biological complications, a real argument against grafting the atrophic posterior maxilla. L-PRF reduced horizontal ridge resorption by 0.8 mm after extraction and cut early pain. Zirconia matched titanium survival at 12 months

($P=0.094$) with better esthetic scores, though that result rests on 4 articles and 199 implants, so read it as promising rather than proven.

Short implants vs long implants with sinus floor elevation

ALENEZI ET AL. • CUREUS • 2025

Seven RCTs (474 implants) found no survival difference (OR 0.96), but short implants had less marginal bone loss (-0.26 mm) and fewer biological complications (OR 0.39), supporting them as a less invasive option.

9

Autologous platelet concentrates in alveolar ridge preservation

SIAWASCH ET AL. • PERIODONTOLOGY 2000 • 2025

Across 35 papers, L-PRF reduced horizontal ridge resorption by 0.8 mm and vertical buccal height loss by 0.6 mm versus spontaneous healing, increased socket fill, and lowered post-extraction pain in the first three days.

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Survival and success of zirconia compared with titanium implants

PADHYE ET AL. • CLIN ORAL INVESTIG • 2023

Zirconia and titanium showed no significant 12-month survival difference ($P=0.094$) and zirconia scored higher on pink esthetics, but the result rests on only 4 articles and 199 implants with short follow-up.

11

The pattern across the section is consistent. The large meta-analyses cover survival, prevalence, and risk. The thinner, shorter-follow-up work covers the things everyone is excited about: robotics, AI, and zirconia. The next decade of trials needs to extend duration and standardize outcomes before the exciting numbers can be called established.

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SECTION 04

Cariology & Prevention

Hydroxyapatite, silver diamine fluoride, and AI are widening the caries-prevention toolkit, but the proof for most new tools stays thin

For a century, caries prevention meant one molecule and one verb: fluoride, and drilling. The 2023-2025 literature complicates both. Hydroxyapatite now has real clinical evidence behind it, silver diamine fluoride is being read more soberly than its reputation suggests, and AI is moving faster than its own evidence base. The honest summary is that the toolkit is widening while the proof for most of the new tools stays thin.

Hydroxyapatite: the first credible challenge to fluoride

Two well-designed trials moved hydroxyapatite from marketing claim to clinical candidate. The result that matters most is non-inferiority, not superiority, and the

distinction is worth holding onto.

Caries-preventing effect of a hydroxyapatite toothpaste in adults: an 18-month double-blinded RCT

PASZYNSKA ET AL. • FRONTIERS IN PUBLIC HEALTH • 2023

In 189 adults, fluoride-free hydroxyapatite toothpaste was statistically non-inferior to 1,450 ppm fluoride for caries prevention. The difference was -1.93% with an upper 95% CI of 6.84%, well inside the pre-set 20% non-inferiority margin.

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Hydroxyapatite-fluoride toothpastes on caries activity: a triple-blind RCT

COCCO, CAMPUS ET AL. • INTERNATIONAL DENTAL JOURNAL • 2025

Among 610 children aged 4-7, a hydroxyapatite-fluoride paste inactivated 58 of 78 baseline active enamel lesions (~74%) versus roughly half for standard sodium monofluorophosphate ($p=.04$). Here hydroxyapatite plus fluoride beat fluoride alone for reversing early lesions.

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Read together, these say something genuinely new. Fluoride's monopoly is contested for the first time on rigorous evidence. They do not say hydroxyapatite is better as a standalone agent, and the adult trial's whole point was equivalence, so patient counselling should reflect a real alternative rather than a replacement.

Silver diamine fluoride: strong against decay, even against fluoride

SDF arrests active caries in a single brushed-on application, costs little, and can be delivered by non-dentists, which makes it a serious equity tool for pediatric and low-resource settings. Reported arrest rates span 25% to 99%. The nuance that marketing tends to lose is what happens when you compare SDF against active treatment instead of against doing nothing.

EXHIBIT 5

SDF vs active comparators: the gap is small and not significant

Caries-arrest, SDF vs fluoride varnish/restorations across 20 RCTs (12 meta-analysed)



DENTAL NATION RESEARCH SOURCE: FRONTIERS IN ORAL HEALTH 2024, DOI 10.3389/FROH.2024.1492762

The individual-level difference (58% vs 49%) carries a p-value of 0.28. It is not statistically significant, and GRADE certainty sits at low-to-moderate. SDF earns its place; it just is not clearly superior to fluoride varnish or restorations once the comparison is fair. Its main barrier to anterior use, the black stain, is being addressed by adding potassium iodide (SDF+KI), an active research front through 2023-2024.^{1,2}

AI caries detection: fast, but ahead of its proof

AI is the fastest-moving area in this section, and also the one where the evidence most undercuts the headlines. On bitewings, pooled performance is good. The catch is where it works and how it was tested.

0.87

POOLED SENSITIVITY
ON BITEWINGS

0.89

POOLED SPECIFICITY
ON BITEWINGS

0.71

SENSITIVITY ON
EARLY ENAMEL
LESIONS

Sensitivity drops to 0.71 for early enamel lesions versus 0.84 for advanced dentinal ones. AI is weakest at exactly the early caries a preventive screening tool most needs

to catch. Nearly every study is retrospective and internally validated; only one of 14 had low risk of bias across all domains, and externally validated, prospective, multi-center trials are essentially absent.

So the claim that "AI now detects cavities more accurately than dentists" should be presented as unsettled. The finding that holds up is assistive: AI helps dentists beat their own baseline, and unaided dentists have genuinely poor sensitivity on early lesions (~0.25-0.36), which is where AI adds clearest value. Standalone superiority is not established.^{3,4}

What still holds, and what is still immature

The evidence-based core has not moved. Cochrane data put fluoride varnish at roughly 43% caries-increment reduction in permanent teeth and 37% in primary teeth, on moderate-quality, mostly high-risk-of-bias evidence. CPP-ACP (MI Paste) is the cautionary tale: after 20-plus years, the 2025 systematic review of 14 studies could not even pool data and found it no better than fluoride in most head-to-heads.

APPROACH	KEY NUMBER	VERDICT
Fluoride varnish	~43% / ~37% reduction (perm / primary)	Gold-standard professional preventive
CPP-ACP for white-spot lesions	Data unpoolable; WSL prevalence 55.06% (ortho) vs 29.1%	Clinically inconsistent
Salivary microbiome risk model	AUC ~0.78 at 12 months	Promising, immature
Arginine + probiotic lozenge	No significant benefit vs placebo	Unproven

7 8

The conceptual frontier is the reframing of caries as ecological dysbiosis rather than a single-pathogen *S. mutans* disease. Salivary microbiome assembly at 12 months predicts future early childhood caries (AUC ~0.78) before *S. mutans* is detectable,

and a 16-species metagenomic signature reaches AUC ~0.905 for severe caries. The interventions built on that model are not there yet: an arginine+probiotic lozenge added to fluoride showed no significant caries-increment benefit over placebo in 343 children.

The throughline

The prevention toolkit is diversifying and fluoride's monopoly is genuinely contested. But most alternatives still rest on small, heterogeneous, or biased evidence. Fluoride, diet, and professional varnish remain the proven core; the rest is promising and worth watching, not yet settled.

9 10

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Oral-Systemic Health

One infected pocket, four organs: where the oral-systemic evidence is real and where it is only a hypothesis

The mouth is not sealed off from the rest of the body. Severe periodontitis is a chronically ulcerated infection that, in advanced cases, exposes a wound surface the size of a palm to the bloodstream. Whether this matters systemically is one of dentistry's most active research frontiers, and the honest summary is uneven. The epidemiological association with cardiovascular disease, diabetes, dementia, and adverse pregnancy outcomes is consistent. The shared inflammatory mechanism is plausible. But intervention proof exists for only one of the four links.

Scale is what makes the question worth asking. Roughly 1.07 billion people worldwide had severe periodontitis in 2021, an age-standardized prevalence of 12,498 per 100,000, with South Asia highest at 17.57%. Even a modest per-person systemic risk, multiplied across a billion people, becomes a large absolute public-health burden.¹

Diabetes: the one proven win

The periodontitis-diabetes axis is the only link with randomized-controlled-trial proof that treatment helps. The 2022 Cochrane review pooled 33 studies and 2,443 analyzed participants and found that non-surgical periodontal treatment lowered HbA1c by an absolute 0.43% at 3 to 4 months, with moderate certainty. That is clinically comparable to adding a second glucose-lowering drug. It improves control without curing the disease, and the report frames it that way. The benefit narrowed but held over time, around 0.5% at 12 months in the EFP/WONCA summary.

The relationship runs both ways. Poorly controlled diabetes, with HbA1c above 7%, is associated with roughly 2.8-fold higher periodontal disease risk and about 4.2-fold

more alveolar bone resorption. In 2023 the EFP and WONCA Europe elevated this to a formal recommendation: family doctors should tell patients that periodontal care improves glycemic control.

Treatment of periodontitis for glycaemic control in people with diabetes mellitus

SIMPSON ET AL. • COCHRANE DATABASE OF SYSTEMATIC REVIEWS • 2022

Across 33 studies and 2,443 participants, scaling and root planing cut HbA1c by an absolute 0.43% (95% CI -0.59 to -0.28) at 3-4 months — moderate-certainty, the strongest oral-systemic intervention evidence to date.

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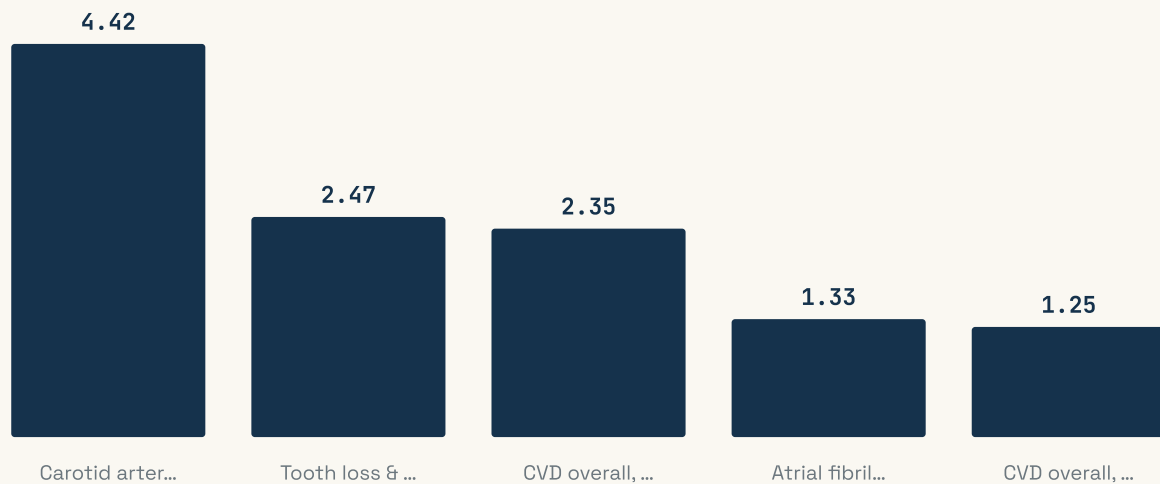
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Cardiovascular disease: association, not proof

The heart link is where the epidemiology is loudest and the causal evidence is weakest. A 2024 umbrella review of 41 systematic reviews, drawing on roughly 839 primary studies with 26 rated high-confidence on AMSTAR-2, reported overall periodontitis-CVD odds ratios in the range of 1.25 to 2.35, with specific signals elevated across several conditions.

How strong is the cardiovascular signal?

Reported risk estimates from the 2024 umbrella review (odds ratio, except where noted)



DENTAL NATION RESEARCH

SOURCE: ARBILDO-VEGA ET AL., BMC ORAL HEALTH (2024), PMC11520879

8

The temptation is to read those numbers as causation. The data do not support it. A 2024 review found 28 of 32 epidemiological studies positive, yet Mendelian-randomization studies, which use genetics to test for cause, found no causal signal. No trial has shown that treating gum disease reduces actual heart attacks or strokes. The PAVE secondary-prevention trial was null. Periodontal therapy reliably moves surrogate markers like CRP, IL-6, and flow-mediated dilation, but not hard outcomes. The accurate framing is that periodontitis and CVD share risk factors and inflammatory pathways, with no evidence that one causes the other.

The framing that survives the evidence

"Treating gum disease reduces the risk of heart attack and stroke" is not yet supported. This is absence of proof, not proof of absence: the association and mechanism are real, but no randomized trial has cut cardiovascular events. State it as a hypothesis, never a finding.

9 10

Alzheimer's: a striking mechanism, an underwhelming trial

The brain link is the most provocative and the most contested. A 2019 Science Advances paper detected the periodontal keystone pathogen *Porphyromonas gingivalis* and its toxic gingipain enzymes in Alzheimer's brains, where gingipain levels tracked tau pathology (Spearman $r = 0.674$, $p < 0.0001$). In mice, small-molecule gingipain inhibitors cut brain bacterial load by about 90% and rescued hippocampal neurons. It was the first concrete infectious mechanism for the oral-brain hypothesis.

***P. gingivalis* in Alzheimer's disease brains: evidence for disease causation and treatment with small-molecule inhibitors**

DOMINY ET AL. • SCIENCE ADVANCES • 2019

Gingipain proteases in Alzheimer's brains correlated with tau ($r=0.674$) and ubiquitin ($r=0.786$) pathology; inhibitors reduced brain bacterial load ~90% and rescued neurons in mice.

11

The clinical translation was a cautionary arc. The GAIN trial of the gingipain inhibitor atuzaginstat (COR388), enrolling 643 participants, failed its primary cognitive and functional endpoints overall. In the 242 patients who were *P. gingivalis*-positive, it showed dose-dependent slowing of decline, up to 57% on ADAS-Cog11 at the 80mg dose, but dose-related liver-enzyme elevations and an FDA hold complicated the program. Suggestive, unresolved.

Here is the genuine tension worth flagging. A 2025 umbrella review found 14 of 16 reviews positive for a periodontitis-Alzheimer’s association (OR 1.03 to 6.87, rising to 4.89-6.87 for severe disease). Yet the 2024 Lancet Commission, the field’s authority on dementia prevention, declined to add oral health to its 14 modifiable risk factors, citing insufficient high-quality evidence. The dental and neurology literatures disagree, and that disagreement is the most honest thing this section can report.^{2,3,4}

Pregnancy: strongest where dental access is weakest

A 2024 meta-analysis of 35 studies covering more than 2.5 million women linked periodontitis to low birth weight at OR 2.48 and, more weakly, to preterm birth at OR 1.87. A 2022 meta-analysis of 30 studies found a preeclampsia odds ratio of 3.18, climbing to 6.70 in lower-middle-income countries. That gradient matters: the burden lands hardest where dental care is least available. As with CVD, intervention has not followed association. Treating periodontitis during pregnancy has not reliably reduced preterm birth in trials.

2.48

OR, LOW BIRTH
WEIGHT

3.18

OR, PREECLAMPSIA

6.70

OR, PREECLAMPSIA
IN LMICS

12 13

One pocket, four destinations

The unifying mechanism is biologically plausible. A chronically inflamed periodontal pocket leaks bacteria into the bloodstream, with bacteremia detectable in 49.4% of patients after periodontal procedures, alongside pro-inflammatory cytokines such as IL-6, TNF-alpha, and CRP. These can reach the coronary vessels, the pancreas and insulin signaling, the placenta, and the brain. One local infection, four systemic

destinations. The throughline of the whole frontier: consistent association and a credible mechanism everywhere, but intervention proof only for diabetes.⁵

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SECTION 06

Oral Oncology & Oral Medicine

Oral cancer caught too late: the race to find it sooner and less invasively

Oral and oropharyngeal cancer is a disease caught at the wrong moment. More than half of cases still surface at advanced stage, where five-year survival drops below 50%, against more than 90% for localized disease that is found early. Almost the entire research frontier follows from that single fact: the work is about finding cancer, and the lesions that precede it, sooner and with less cutting.

The first thing the recent literature forces is a split. What used to be filed under "oral cancer" is now two epidemiologically distinct diseases that need different strategies. Oral-cavity squamous cell carcinoma remains roughly 90% attributable to tobacco and alcohol, with HPV transcriptionally active in only about 3.0 to 4.4% of cases, and

it is rising fastest in low- and medium-HDI countries. Oropharyngeal cancer is now an HPV-driven epidemic in high-income countries, where the virus accounts for around 70% of cases and has overtaken cervical cancer as the most common HPV-related malignancy in the US. Conflating the two obscures the fact that one is answered mainly by visual screening, biomarkers and behavior change, the other by vaccination and viral-DNA surveillance.¹

The burden behind all of this is growing. Between 1990 and 2021 the global age-standardized incidence climbed from 3.26 to 5.34 per 100,000, and mortality from 1.83 to 2.64 per 100,000. GLOBOCAN 2022 counted 188,438 oral-cavity and lip cancer deaths, about seven in ten of them male. Modeling projects incidence rising roughly 65% by 2050, and as much as 147.8% in low-HDI countries.

5.34

INCIDENCE PER
100,000, 2021 (UP
FROM 3.26 IN 1990)

188,438

ORAL-CAVITY / LIP
CANCER DEATHS,
2022

~65%

PROJECTED
INCIDENCE RISE BY
2050

2

AI image screening: strong on paper, softer in the clinic

Deep learning has matured fast against curated image sets. A meta-analysis of 18 studies put pooled sensitivity at 87%, specificity at 81% and summary AUC at 0.976 for AI detecting oral potentially malignant disorders and cancer, with CNNs reaching roughly 95% on both axes and histopathology images near 97% sensitivity. Then the picture changes. When the same task is judged on real clinical photographs rather than histology, specificity falls to 67%, which in practice means a high false-positive and over-referral rate. External validation and prospective trials are the gap the field keeps naming.

Diagnostic performance of AI in detecting OPMDs and oral cancer on medical imaging

SYSTEMATIC REVIEW AND META-ANALYSIS • FRONTIERS IN ORAL HEALTH • 2024

Across 18 studies, AI reached 87% sensitivity, 81% specificity and AUC 0.976; CNNs and histopathology images performed best, but the datasets were largely curated and retrospective.

3

Automated detection of oral malignant lesions using deep learning

SCOPING REVIEW AND META-ANALYSIS • ORAL DISEASES • 2024

On clinical images, pooled sensitivity held at 86% but specificity dropped to 67% (95% CI 0.58–0.75), a more sober read of real-world performance than histopathology studies suggest.

4

Liquid biopsy: the most clinic-ready non-invasive frontier

For oropharyngeal cancer, circulating tumor HPV-DNA is the closest thing the field has to a clinical-grade blood test. Pooled sensitivity is about 81% with specificity near 98%, and individual studies have reached 95 to 100%. Chera and colleagues reported detection roughly 3.9 months before clinical or radiographic evidence of recurrence, which is the kind of lead time that makes minimal-residual-disease monitoring plausible. Salivary biomarkers for oral-cavity cancer lag behind. The molecular signals are real, but no large prospective validation exists yet.

Circulating biomarkers in HPV-associated oropharyngeal cancer

REVIEW OF LIQUID BIOPSY APPLICATIONS • THE JOURNAL OF LIQUID BIOPSY • 2025

Pooled ctHPV-DNA sensitivity 81% / specificity 98%, with some studies near-perfect, and recurrence detected about 3.9 months before clinical evidence.

5

Salivary biomarkers for oral cancer detection

EXPLORATORY SYSTEMATIC REVIEW (62 STUDIES) • INT. J. MOLECULAR SCIENCES • 2024

IL-8, TNF-alpha, IL-1beta, IL-6 and MMP-9 were the most promising salivary markers; IL-1beta AUC ran 0.729–0.772, but larger cohorts are still needed before clinical use.

6

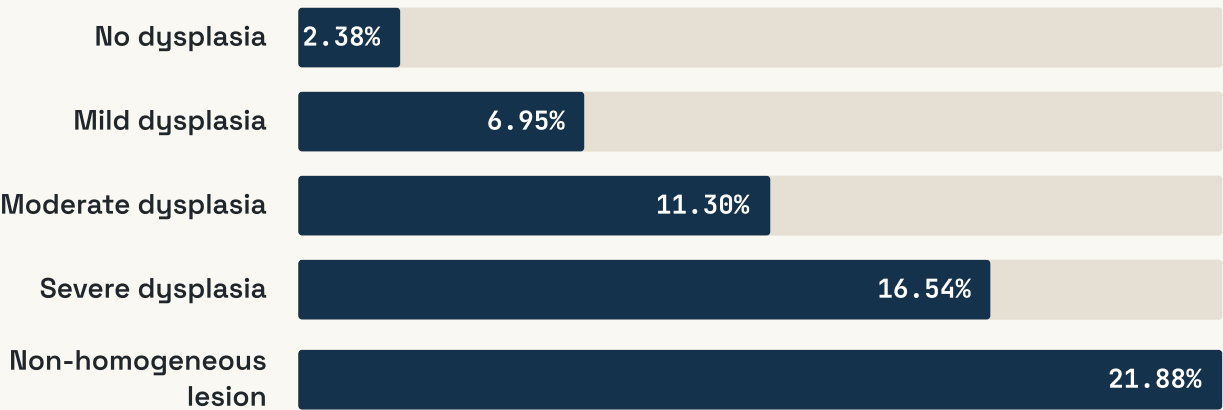
Prevention and risk stratification

On the prevention side, Gardasil 9 received FDA accelerated approval on June 12, 2020 for preventing HPV-related oropharyngeal and other head-and-neck cancers (types 16, 18, 31, 33, 45, 52, 58). For lesions already present, malignant-transformation risk is now quantified well enough to set surveillance intensity. Oral leukoplakia transforms in about 6.6% of cases overall, but the figure tracks dysplasia grade and clinical subtype sharply.

EXHIBIT 7

Malignant transformation of oral leukoplakia, by grade and subtype

Pooled rates from 55 studies (41,231 patients) — risk rises with dysplasia and non-homogeneous appearance



DENTAL NATION RESEARCH

SOURCE: ORAL DISEASES (2025), PMC11808172

The gap nobody has closed

For all the new tools, the strongest hard-outcome evidence in the field is twenty years old. The Kerala cluster-randomized trial showed visual screening cut oral cancer mortality by about 34% in tobacco and alcohol users (rate ratio 0.66) and 43% in male users (0.57), and authors estimated it could prevent at least 37,000 deaths worldwide. The overall effect across the trial was non-significant, and no AI tool, optical adjunct or liquid biopsy has yet shown a mortality benefit in a comparably powered trial.

The unsolved problem

Detection technology is advancing quickly, but the field's central question is still open: turning sensitive new tools into validated, equitable, mortality-reducing screening at scale. The Kerala RCT remains the only strong proof that screening saves lives, and only in high-risk subgroups. A 2025 Taiwan trial (NCT06862414) testing a smartphone-based deep-learning screen is the kind of prospective study that could finally move the field past retrospective accuracy claims.

9 10

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Pediatric Dentistry

Minimally invasive caries management: SDF, the Hall Technique, and the cautious evidence behind the hype

Pediatric dentistry is converging on a single idea: arrest or seal childhood caries with minimal trauma rather than drill it out. Two agents now anchor that shift. Silver diamine fluoride (SDF), a brush-on liquid that stops active decay without anesthesia or drilling, and the Hall Technique (HT), a preformed metal crown sealed over a carious primary molar with no caries removal. The 2024-2026 evidence is large enough to make the approach defensible. It is also more cautious than the marketing around it.

The most important document in the field is also the most sobering. The 2024 Cochrane review pooled 29 randomized trials and 13,036 participants. It confirms SDF is safe and equivalent to fluoride varnish for preventing caries in primary teeth, with a mean difference of 0.00 (95% CI -0.26 to 0.26). But it rates much of the caries-arrest evidence in primary dentition as low certainty, and prevention of new caries as very uncertain. The honest framing is that SDF is safe, useful, and equal to fluoride varnish. It is not a miracle agent.

Topical silver diamine fluoride for preventing and managing dental caries in children and adults

COCHRANE ORAL HEALTH GROUP • COCHRANE DATABASE OF SYSTEMATIC REVIEWS • 2024 • CD012718

29 RCTs, 13,036 participants. SDF is safe and as effective as fluoride varnish for prevention, but the caries-arrest and new-caries-prevention evidence is graded low to very low certainty. A deliberate cooling of earlier single-trial enthusiasm.

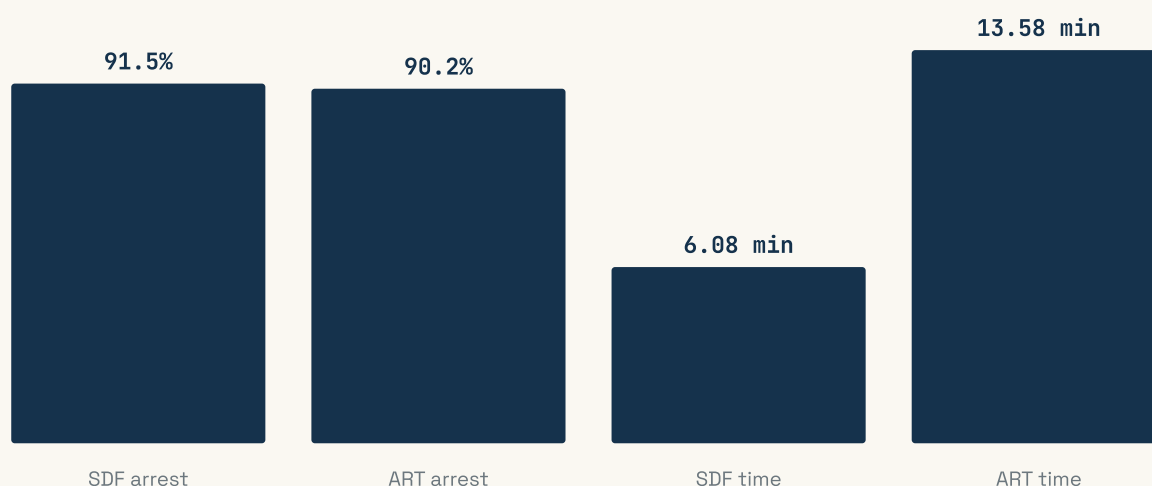
SDF's real selling point is chair time

Head-to-head trials keep showing the same thing. SDF arrests roughly 90% of dentin lesions at 12 months, which matches atraumatic restorative treatment (ART). The difference is the chair. In a trial of 118 preschoolers, SDF and ART arrested lesions almost identically (91.5% vs 90.2%, $p=1.000$), but SDF took 6.08 minutes versus 13.58 for ART. For a very young, fearful, or special-needs child, that gap is the whole argument: no drilling, no anesthesia, and less than half the time in the chair.¹

EXHIBIT 8

SDF and ART arrest caries equally, but SDF is twice as fast

Preschoolers, 12-month caries arrest and mean treatment time per lesion



DENTAL NATION RESEARCH

SOURCE: CLIN ORAL INVESTIG 2024;29(1):3

How often you apply SDF matters as much as the choice to use it. A 12-month trial in 80 Indian preschoolers found arrest rose sharply with frequency: 80.5% with four applications a year, 78.2% twice a year, and 58.4% with a single annual application ($P<0.001$). The protocol design drives the result as much as the agent does.²

Scalability is where SDF earns its place in public health. The CariedAway school-based RCT enrolled 2,998 children and found SDF noninferior to glass-ionomer

sealants at two years: caries arrest 56% (SDF) vs 46% (sealants), and caries prevention 81% vs 82%. That validates SDF for large school programs that cannot lean on a dentist for every child. One caution worth keeping in view: only 46.6% of participants completed the two-year follow-up.³

The staining problem and a stain-free contender

SDF leaves arrested lesions permanently black. That single drawback drives the next research wave. Nano-silver fluoride (NSF) is the most-watched stain-free candidate. In an Egyptian RCT of 360 children under four, NSF out-arrested SDF (71.3% vs 56.3% at 12 months) and avoided the staining, with higher parental aesthetic satisfaction. NSF remains experimental, not FDA-cleared, and rests on small single-center trials, so this is a promising signal rather than a settled finding.

Effectiveness of nanosilver fluoride and silver diamine fluoride in arresting early childhood caries

RANDOMIZED CONTROLLED CLINICAL TRIAL • BMC ORAL HEALTH • 2024

In 360 children under 4, NSF arrested more lesions than SDF (71.3% vs 56.3% at 12 months) without black staining and with better parental acceptance. Early, single-center evidence.

⁶

The Hall Technique: seal it in, don't drill it out

The Hall Technique applies the same biological logic to restoration. Cement a preformed metal crown over the carious molar, no caries removal, no anesthesia, and the sealed-in bacteria are starved. The evidence is among the strongest in pediatric dentistry. A meta-analysis of five studies and 1,775 teeth found a pooled risk ratio of 5.55 (95% CI 3.31-9.30) for success over conventional restorations. More recent reviews put 12-month success near 98% (95% CI 97-99%).

~98%

HALL TECHNIQUE
SUCCESS AT 12
MONTHS

5.55×

RISK RATIO FOR
SUCCESS VS
CONVENTIONAL
FILLINGS

92.8%

MODIFIED HT
SUCCESS AT 24
MONTHS

7 8

It holds up over time. A two-year RCT of 268 molars in 189 children found standard and modified Hall both highly successful at 24 months (86.6% vs 92.8%, $p=0.121$, not significant). The trial also names the one thing operators control: crown fit. Insufficient fit predicted 40% major failure versus 7.3% with adequate fit ($p=0.005$).⁴

Behaviour management: where evidence and hype part ways

Virtual reality (VR) distraction is heavily promoted and heavily studied, and the data are genuinely mixed. A meta-analysis of 76 RCTs and 6,723 participants found distraction reduced procedural pain versus tell-show-do (SMD -0.43, 95% CI -0.76 to -0.10) but not anxiety (SMD -0.34, 95% CI -0.71 to 0.04). VR specifically was not statistically superior to traditional techniques for anxiety (SMD -0.47, 95% CI -0.96 to 0.02). Heterogeneity ran high (I^2 71-97%), so individual positive trials sit inside a noisy literature.

The honest read on VR

Distraction reliably cuts procedural pain. It does not reliably cut anxiety. The largest meta-analysis to date finds VR no better than plain tell-show-do for dental anxiety, even as smaller trials report relaxed children and lower pain scores. Useful, but oversold.

Analyzing nonpharmacological behavior management in children with dental anxiety

SYSTEMATIC REVIEW AND META-ANALYSIS • HEALTH SCIENCE REPORTS • 2025 • 8(8):E71176

76 RCTs, 6,723 participants (1985-2024). Distraction reduces procedural pain but not anxiety; VR is not statistically superior to tell-show-do for anxiety. High heterogeneity throughout.

9

The synthesis is straightforward and a little deflationary. The tools to treat childhood caries without trauma now exist, work about as well as drilling, and are well tolerated. What remains open is durability beyond three to five years, the aesthetics of staining, and the gap between what the strongest reviews show and what the marketing promises.

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SECTION 08

Orthodontics

Four frontiers, one pattern: routine cases are solved, the hard problems stay open

Four frontiers are reshaping orthodontics in the 2024–2026 literature: clear aligner therapy, accelerated tooth movement, AI-driven planning, and the still-unsettled question of long-term retention. The honest

summary is that aligners and AI have closed the gap with conventional care for routine cases, while the hard problems remain open. Read the most recent reviews closely and a pattern repeats: enthusiasm is running ahead of the randomized-trial base.

Clear aligners: parity on simple cases, predictability still the weak point

For simple non-extraction malocclusions, aligners now finish about as well as fixed appliances. A 2025 meta-analysis pooling 21 randomized trials (970 patients) found no significant difference in ABO grading, Little Irregularity Index, or PAR scores, with aligners showing significantly better periodontal indices and better six-month quality of life. The catch is the evidence quality: only one of the 21 trials was rated at low risk of bias.

Effectiveness of clear orthodontic aligners in correcting malocclusions: a systematic review and meta-analysis

BANESHI ET AL. • J EVID BASED DENT PRACT • 2025;25(1):102081

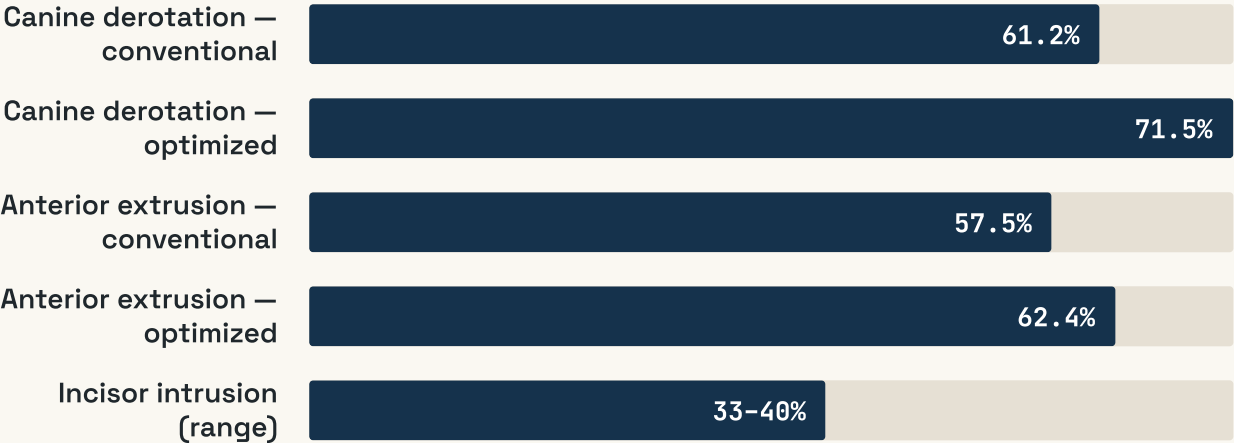
Across 21 RCTs and 970 patients, aligners matched fixed appliances on finish quality for simple cases and won on periodontal health and quality of life, though the pooled evidence was low quality.

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Where aligners still struggle is predictability of difficult movements. Pooled accuracy falls well short of the digital prescription, and optimized attachments do not reliably close the gap.

Aligners deliver only a fraction of the prescribed movement

Pooled tooth-movement accuracy (achieved vs predicted), conventional vs optimized attachments



DENTAL NATION RESEARCH

SOURCE: PANDIAN ET AL., J ORAL BIOL CRANIOFAC RES 2025;15(5):1123-1133

7

Vertical control is a relative bright spot. A 2024 review of sequential aligner distalization reported roughly 87% efficacy (about 2 mm of maxillary molar movement) with only 0.26 mm of unwanted first-molar intrusion and no significant skeletal change. All 11 included studies carried medium-to-high risk of bias, so the finding is encouraging rather than settled.¹

One regulatory note belongs here. The efficacy data above come almost entirely from dentist-supervised treatment. Aligners are a capable device, but that evidence does not transfer to unsupervised direct-to-consumer use; the two settings are not equivalent on safety.

Accelerating tooth movement: MOPs lead, lasers lag on evidence

Micro-osteoperforation (MOPs) currently has the strongest case among acceleration methods. A 2026 meta-analysis of 16 RCTs (n=459) found a real but modest effect, and importantly no clinically significant root resorption.

+0.20 mm

EXTRA MOVEMENT
PER MONTH WITH
MOPS (16 RCTS)

+0.67 mm

TOTAL ADDED
MOVEMENT

+0.19 mm

ROOT RESORPTION
(95% CI -0.14 TO
0.51), NOT
CLINICALLY
SIGNIFICANT

Micro-osteoperforation for accelerating orthodontic tooth movement: a meta-analysis of short-term efficacy, safety, and optimal application parameters

CHING ET AL. • FRONTIERS IN DENTAL MEDICINE • 2026;7

MOPs added 0.67 mm of total movement and 0.20 mm per month of rate with non-significant root resorption, making it the freshest and highest-certainty acceleration evidence retrieved, at moderate certainty.

8

Photobiomodulation (low-level laser) probably accelerates movement too, with effective parameters clustering around 780–810 nm and roughly 5.3 J/cm², but the evidence is shakier. An umbrella review of six systematic reviews rated half at uncertain-to-high risk of bias and three as critically low quality, with no standardized protocol to point clinicians to.²

AI: strong on the mechanical task, thin on clinical judgment

AI's clearest win is narrow and well-evidenced. On automated cephalometric landmarking, a deep-learning model trained on 1,600 cephalograms hit a corrected mean error of 1.75–2.10 mm across 48 landmarks and tracked more consistently than two human examiners, in 0.43 seconds per image. That is a repetitive measurement task, and machines now do it more reliably than people.

Automated cephalometric landmark detection (48 landmarks, deep learning)

BAGDY-BÁLINT ET AL. • J DENT SCI • 2024;20(2):830-843

AI placed 48 landmarks with 1.75–2.10 mm corrected error and beat human examiner consistency (inter-examiner 2.02 mm) in under half a second per image.

9

Clinical treatment planning is a different claim, and the data are thinner. A single-center RCT (n=100) reported AI-assisted planning cut mean treatment time (14.6 vs 18.9 months) and appointments (10.2 vs 12.8) and raised satisfaction (9.2 vs 8.1, all $p<0.001$), at slightly higher cost. One small trial does not establish AI planning superiority, so the result is best read as promising rather than settled.³

Retention: still scientifically unsettled

For all the progress upstream, the question of how to hold the result remains open. The 2023 Cochrane review (47 studies, 4,377 participants) found fixed and removable retainers give clinically similar stability and could not endorse any single approach. Certainty was low to very low, and the authors called for two-year-plus, high-quality trials. The practical takeaway is a biology-versus-compliance trade-off rather than a winner.

Retention procedures for stabilising tooth position after treatment with orthodontic braces

MARTIN ET AL. • COCHRANE DATABASE SYST REV • 2023;5(5):CD002283

Across 47 studies and 4,377 patients, no retention method was demonstrably superior; fixed and removable retainers performed similarly, on low-to-very-low certainty evidence.

10

Adjacent frontiers worth watching

Two manufacturing and anchorage shifts are maturing alongside the headline frontiers. Directly 3D-printed aligners are now more dimensionally true than

thermoformed ones (RMS 0.140 mm printed vs 0.188 mm Zendura FLX and 0.209 mm Essix ACE), pointing to printing as the next production step. And orthodontic mini-implants (TADs) succeed roughly 87–95% of the time, with failure driven less by patient demographics than by site and operator experience (15% failure for experienced operators vs 31% for inexperienced).^{4,5}

The open frontiers

Routine cases are largely solved. What remains genuinely unsettled, and flagged as low-quality or high-risk by the most recent reviews, is the predictability of difficult movements (rotation, extrusion, intrusion, extraction-space closure), a standardized acceleration protocol, and high-certainty long-term retention evidence. A 2026 review of aligners in extraction-based treatment confirms extraction cases as one of those active frontiers.

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Biomaterials Research

Bioactive and regenerative materials, from evidence-backed pulp capping to still-preclinical scaffolds and implant coatings



Dental biomaterials are shifting from passive, bioinert fillers toward systems engineered to do biological work. The newest materials release calcium and other ions, stimulate repair, and fight bacteria on their own surfaces. The 2024–2026 literature clusters around five fronts: regenerative pulp materials, high-translucency ceramics, durable adhesives, printable resins, and nano-engineered implant surfaces. The evidence is uneven across them. It is strong for calcium-silicate pulp capping and for the material physics of zirconia and adhesives. It is

largely preclinical for regenerative scaffolds and many implant nano-coatings, which is the field's central translational gap.

Bioactive pulp materials: the strongest clinical signal

The clearest clinical win is in vital pulp therapy. Calcium-silicate cements (MTA, Biodentine) release Ca^{2+} that drives reparative dentin formation, and head-to-head trial data now place them well above traditional calcium hydroxide. A 2025 network meta-regression pooled 19 randomized trials covering 1,733 patients and ranked the materials by probability of clinical success.

Comparative clinical success of direct pulp capping materials: a network meta-regression of randomized clinical trials

JOURNAL OF DENTISTRY • 2025

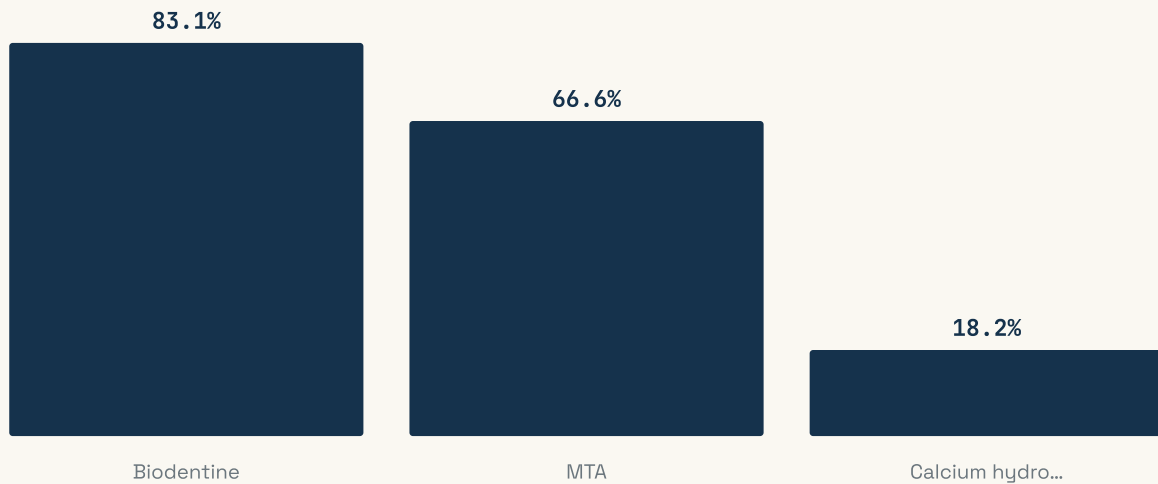
Across 19 RCTs (1,733 patients), Biodentine ranked first (SUCRA 83.1%) and MTA second (66.6%), both far above calcium hydroxide (18.2%). Biodentine odds ratio was 4.41 [95% CrI 1.40–17.66] versus $\text{Ca}(\text{OH})_2$. The authors graded certainty as low and the credible intervals are wide.

5

The durability gap explains why clinicians are migrating to bioceramics. MTA direct pulp capping success exceeds 90%, while calcium hydroxide starts at 80–90% but falls to 58.7–76.3% by ten years as its weak seal degrades.

Direct pulp capping: success probability by material

SUCRA ranking from a network meta-regression of 19 RCTs (1,733 patients)



DENTAL NATION RESEARCH SOURCE: JOURNAL OF DENTISTRY (2025), DOI 10.1016/J.JDENT.2025.106073

Beyond capping sits the more ambitious goal of true pulp-dentin regeneration. A 2025 review frames the agenda around the “holy trinity” of a cell source, signaling molecules, and a scaffold, then surveys the new generation of candidates: GelMA hydrogels, chitosan, hyaluronic acid, amnion-chorion membranes, platelet-rich fibrin (PRF), and demineralized dentin matrix (DDM). The early numbers are encouraging. DDM reached 92.86% apexification success, and PRF beat MTA at 12 months (82.6% versus 61.9%). These results come from small studies and animal models, not confirmatory RCTs, so they should be read as promising rather than proven.

Next-generation biomaterials for vital pulp therapy: biological properties and dentin regeneration mechanisms

BIOENGINEERING (BASEL) • 2025

MTA capping success exceeds 90% and Ca(OH)_2 declines to 58.7–76.3% at ten years. Regenerative scaffolds (GelMA, chitosan, PRF, DDM) show early promise: DDM 92.86% apexification, PRF 82.6% versus MTA 61.9% at 12 months, but remain largely confined to lab and animal models.

6

Ceramics: the strength-versus-translucency trade-off, now quantified

Zirconia’s evolution is the cleanest engineering trade-off in the section. Adding yttria to raise the translucent cubic phase makes restorations more lifelike but weaker. The numbers are specific. Tough 3Y-TZP delivers 1,000–1,200 MPa, while highly esthetic 5Y-PSZ drops to 600–800 MPa, roughly a 50% strength loss for about a 30% translucency gain. The market’s answer is the composition-gradient multilayer disk: durable 3Y-TZP at the base, translucent 5Y-PSZ at the incisal edge.

EXHIBIT 11

Zirconia: flexural strength falls as translucency rises

Higher yttria/cubic-phase content trades strength for esthetics (upper end of reported range)



Recent advances in dental zirconia: 15 years of material and processing evolution

DENTAL MATERIALS • 2024

3Y-TZP delivers 1,000–1,200 MPa; 4Y-PSZ around 900–1,000 MPa with 4.1 MPa·√m fracture toughness; 5Y-PSZ 600–800 MPa, a roughly 30% translucency gain for a roughly 50% strength loss. Gradient multilayer disks combine a 3Y-TZP base with a 5Y-PSZ top.

7

Additive manufacturing is closing the gap with milled ceramics. A systematic review of 40 in vitro studies found 3D-printed 3Y-TZP spanning 320–1,519 MPa against milled 915–1,507 MPa, with essentially equivalent density (5.90–6.03 g/cm³). The mechanics have come close, but porosity, microcracks, and surface roughness still cap reliability.

Additive-manufactured ceramics for dental restorations: a systematic review on mechanical perspective

FRONTIERS IN DENTAL MEDICINE • 2025

Printed 3Y-TZP reached 320–1,519 MPa versus milled 915–1,507 MPa with comparable density and toughness; printed lithium disilicate hit 431 MPa at optimal orientation. Processing defects, not chemistry, remain the limiting factor.

8

Adhesives: chemistry over technique

Bond durability comes down to two levers. The first is monomer chemistry. A meta-analysis of 206 in vitro studies across 64 systems found 10-MDP adhesives, which form stable calcium-phosphate complexes at the apatite surface, bond significantly better than other acidic monomers, with a dentin effect size of 6.98 and enamel of 2.79 (both $p < 0.00001$). The second lever is protecting the bond from enzymatic breakdown. A separate review of 61 studies found prior MMP-inhibitor application significantly improves universal-adhesive bond strength to dentin ($p < 0.001$).

Polyphenols such as myricetin and resveratrol, along with chlorhexidine, are the active research front here.^{1,2}

Printable resins and engineered implant surfaces

3D-printable photopolymers are moving from provisionals toward permanent crowns, dentures, aligners, and guides, with additive manufacturing saving roughly 95–98% of material versus milling. Biocompatibility is not automatic. It hinges on post-processing, an isopropanol wash followed by a UV cure, to clear cytotoxic residual monomers. On implants, nano-engineered titanium surfaces are designed to do two jobs at once. Nano-modification raised the osteoblast-to-fibroblast affinity ratio to 3:1 (versus 1:1 for conventional surfaces), and TiO₂-nanotube plus silver-nanoparticle coatings inhibited bacterial adhesion for up to 30 days, a direct engineering response to peri-implantitis. These implant findings remain at the literature-review and in vitro stage.^{3,4}

Read the evidence by stage, not by hype

Antibacterial function is becoming a design requirement rather than a bonus. It is now built into implant coatings, ion-doped bioactive glasses, and chitosan pulp materials in response to peri-implantitis and secondary caries. But the maturity ladder is steep. Calcium-silicate pulp capping and the physics of zirconia and adhesives rest on RCTs and large meta-analyses. Regenerative scaffolds, nano-implant coatings, and bioactive-glass remineralization remain dominated by in vitro and animal work. Even the strong pulp-capping trial data carries a low-certainty warning from its own authors. The promising-but-unproven label belongs on the regenerative claims until confirmatory trials arrive.

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SECTION 10

AI & Technology Research

AI & technology: strong headline numbers, weak methodology underneath



Between 2021 and 2026, AI in dentistry crossed from proof-of-concept into measurable clinical performance. The headline numbers look strong. The methodology behind them often does not. Almost every domain shares one weakness: studies are retrospective, single-center, internally validated, and heavy with statistical heterogeneity. Read the accuracy figures with that caveat attached.

Caries detection: the most mature use case

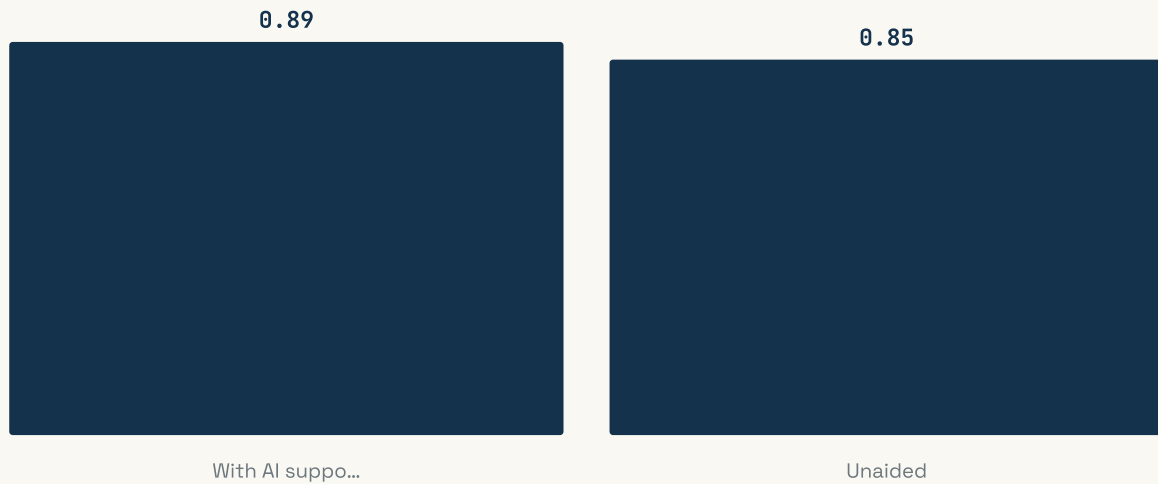
Radiographic caries detection is where the evidence base is deepest. A 2025 systematic review and meta-analysis pooled accuracy across a wide band of 73.3% to 98.8%, with individual-study AUCs from 0.87 to 0.99. That spread is not a detail to wave away. Heterogeneity ran very high (I^2 of 86–96%), and the authors flagged moderate-to-high risk of bias on patient selection and reference standard. A single optimistic accuracy number lifted from this literature would misrepresent it.¹

The most decision-relevant finding is not a benchmark score. It is a trial. A cluster-randomized cross-over study had 22 dentists assess proximal caries on bitewings both with and without AI support. The same clinicians, aided by the tool, reached a higher mean ROC-AUC than they did unaided. This is the honest framing the evidence supports: AI helps dentists beat their own baseline, particularly on early lesions where unaided sensitivity is genuinely poor. The claim that AI standalone is simply more accurate than dentists remains unsettled.

EXHIBIT 12

AI assistance lifts dentists' caries reading

Mean ROC-AUC for the same 22 dentists, with vs without AI support (proximal caries, bitewings)



DENTAL NATION RESEARCH SOURCE: MERTENS ET AL., J DENT 2021 (DOI 10.1016/J.JDENT.2021.103849)

Architecture also matters. A modality-stratified meta-analysis of 17 studies found that on radiographs, Mask R-CNN markedly outperformed the older Faster R-CNN: sensitivity 86.3% versus 67.2%, specificity 96.5% versus 85.0%, AUC 0.97 versus 0.86. Newer model design closed real gaps rather than shaving decimals.

Deep Learning-Based Dental Caries Diagnosis: A Modality-Stratified Systematic Review and Meta-Analysis of Faster R-CNN and Mask R-CNN

DIAGNOSTICS (BASEL) • 2026 • 17 STUDIES

On radiographs, Mask R-CNN reached AUC 0.97 against Faster R-CNN's 0.86. Model architecture drives the performance gap as much as data volume does.

8

Beyond caries: lesions and oral cancer

For periapical lesions, a review of 28 studies reported accuracy from 70% to 99.65% across panoramic, intraoral, and CBCT imaging. Every included study was

retrospective, and roughly 32% carried high risk of bias on the reference standard. When the ground truth itself is uncertain, apparent AI performance inflates.²

In oral cancer, deep learning is statistically comparable to human experts on image-based diagnosis (DL median sensitivity 0.901 versus experts' 0.878; specificity 0.902 versus 0.945) and beats postgraduate students. But none of the eight studies had low risk of bias, all were retrospective and photo-based, and the GRADE rating is low. Image-only benchmarks omit the clinical context, the history and palpation that a real consultation uses.

Diagnosis of Oral Cancer With Deep Learning: A Comparative Test Accuracy Systematic Review

NIERI ET AL. • ORAL DISEASES • 2025 • 8 STUDIES (3 META-ANALYZED)

Deep learning matches human experts on photo-based diagnosis, but evidence is GRADE-low: every study was retrospective and image-only.

⁹

Robotics: sub-millimeter precision, marginal clinical gain

Implant robotics has reached clinically meaningful precision. A meta-analysis of 16 clinical studies covering 908 implants pooled global platform deviation at 0.69 mm, apex deviation at 0.72 mm, and angular deviation at 1.62 degrees, with high heterogeneity across studies.³

A pilot study of an autonomous robot in 74 patients (86 implants) reported similar figures, mean coronal deviation 0.61 mm, apical 0.79 mm, angular 2.56 degrees, with no intraoperative complications. Head-to-head, robotic surgery beat dynamic navigation on linear accuracy (platform 0.91 versus 1.26 mm, $p < 0.01$), though the angular difference was not significant.⁴

ACCURACY METRIC	ROBOT	DYNAMIC NAVIGATION
Platform deviation	0.91 mm	1.26 mm
Apex deviation	1.06 mm	1.51 mm
Angular deviation	3.07°	3.71° (n.s.)

10

The real robotic advantage may be time, not tenths of a millimeter

Authors themselves note the sub-half-millimeter gaps over navigation may be clinically marginal. The more tangible edge is workflow: vendor clinical data for the Yomi system reports roughly 45% procedure-time reduction in partial implant cases. Precision is already good enough; throughput is where robots may earn their place.

Scanners and language models

Digital workflows have quietly become reliable. In vitro, the best full-arch scanners reach clinically acceptable trueness: Primescan at 30.5 micrometres, with iTero Lumina showing the lowest relative trueness error (0.04%). Both scanner figures come from search-result abstracts rather than full-text confirmation, so treat them as indicative.^{5,6}

Large language models are the least mature domain. ChatGPT reached about 80% accuracy in a pediatric diagnosis-and-planning pilot, equivalent to two of four pediatric dentists, but every study cautions against clinical reliance and flags unresolved ethical, legal, and hallucination concerns. Frame LLMs as decision support, not autonomous diagnosis.⁷

The frontier is the same across all of it: prospective, multi-center, externally validated studies with patient-outcome data. Internal benchmarks have peaked. Generalizability is the metric that still has the most room to move.

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Featured Paper

CariedAway: a one-dollar drop of silver diamine fluoride matched the full sealant-plus-ART toolkit across 7,418 high-risk NYC children

For decades, protecting a high-risk child's teeth meant a chairside ritual: seal the molars, place atraumatic restorations on the cavities, paint on fluoride varnish, and repeat. The CariedAway trial asked a blunt question. What if a single 60-second drop of an inexpensive liquid did the same job? Across 48 New York City Title-I primary schools and nearly four years of follow-up, the answer came back: yes, more or less.

Noninferiority of Silver Diamine Fluoride vs Sealants for Reducing Dental Caries Prevalence and Incidence: A Randomized Clinical Trial

RUFF RR, BARRY GODÍN TJ, NIEDERMAN R • JAMA PEDIATRICS • 2024;178(4):354-361

In 7,418 high-risk children aged 5–13, twice-yearly 38% silver diamine fluoride (SDF) plus fluoride varnish prevented cavities as well as glass-ionomer sealants plus atraumatic restorative treatment (ART) over a mean 3.7 years. SDF was statistically noninferior on both prevalence and incidence.

4

Why this is the featured paper

This is a pragmatic, cluster-randomized, double-arm noninferiority trial (ClinicalTrials.gov NCT03442309), and the scale is the point. Schools were block-randomized to one of two arms. The "simple" arm received 38% SDF (2.24 mg fluoride-ion per dose) brushed onto cavitated lesions and the pits and fissures of premolars and molars, then 5% sodium fluoride varnish, reapplied every six months. The "complex" arm received the conventional package: glass-ionomer sealants, ART on cavities, and varnish. The contrast is one cheap liquid against the entire standard preventive-and-restorative toolkit. Funding came from the Patient-Centered

Outcomes Research Institute (PCORI grant PCS-160936724), not a materials maker, though one author’s disclosures (below) deserve a footnote.

7,418

CHILDREN ENROLLED
ACROSS 48 NYC
TITLE-I SCHOOLS

3.7 yr

MEAN FOLLOW-UP
(SD 0.32)

OR 0.94

CONTROL VS SDF
PREVALENCE (95% CI
0.80–1.11)

The headline: roughly ten cavities per 1,000 tooth-years, in both arms

Caries incidence was almost indistinguishable. The SDF arm logged 10.2 new lesions per 1,000 tooth-years; the sealant/ART arm logged 9.8. The rate ratio was 1.05 (95% CI 0.97–1.12), and the adjusted incidence rate ratio was 0.92 (95% CI 0.83–1.04). Odds of decay fell over time in both groups (OR 0.79, 95% CI 0.75–0.83), so both interventions worked. They simply worked about equally well.

EXHIBIT 13

One drop matched the full toolkit, tooth for tooth

New caries lesions per 1,000 tooth-years over a mean 3.7 years of follow-up



DENTAL NATION RESEARCH

SOURCE: RUFF ET AL., JAMA PEDIATRICS 2024 (RATE RATIO 1.05, 95% CI 0.97–1.12)

On the primary noninferiority outcome, the control-versus-SDF odds ratio for longitudinal prevalence was 0.94 (95% CI 0.80–1.11; 90% CI 0.82–1.08). The confidence interval sat outside the prespecified noninferiority margin (a 0.10 risk difference, equivalent to an odds-ratio bound of 0.63), so noninferiority was met, and the test for a difference returned p=0.47. What that means in plain terms: the trial detected

no meaningful difference between the two arms, which is not the same as showing SDF is superior. Noninferior is the word the data support.

Two trials in one

CariedAway carried a second, workforce-shifting result. SDF applied by registered nurses was noninferior to application by dental hygienists (prevalence OR 0.89, 95% CI 0.67–1.19). A treatment that already drops the dentist from the chair can, on this evidence, also drop the dental professional from the room. Lead author Ryan Ruff framed nurses as “an untapped resource for addressing oral health inequities.”

The frontier, and its honest limits

This is high-strength evidence: a large, multi-year cluster RCT in a flagship general-pediatrics journal, deliberately run in the children conventional sealant programs reach least (schools with at least 50% Black or Hispanic enrollment and at least 80% free or reduced-price lunch). Baseline untreated decay sat near 26.7% in both arms, so neither group started easy. The trial also survived a real-world stress test, running straight through the COVID-19 NYC school closure, a roughly two-year gap from March 2020 to September 2021. A restricted pre-COVID cohort and a Cox proportional-hazards sensitivity analysis both reproduced the headline.

The caveats are real and the authors name them. Only 4,100 of 7,418 children (55%) completed follow-up, so attrition ran near 45%. Patients could not be blinded because SDF stains arrested lesions black, and clinicians could not be blinded because the two arms used visibly different procedures. The analysis pooled children with and without baseline untreated decay. And the population is specific: external validity to suburban or single-clinic settings should be argued, not assumed. The black staining is itself an acceptability trade-off worth stating plainly, especially on front teeth.^{1,2,3}

One transparency note for the record: senior author Niederman disclosed nonfinancial support from Colgate, GC America, and Elevate Oral Care (all SDF or

dental-materials companies) and consulting fees from Delta Dental Washington. The trial was PCORI-funded and the disclosures are stated openly. The conclusion stands on its own numbers: a roughly one-dollar, 60-second liquid, deliverable by a school nurse, held its own against the full conventional standard for nearly four years. For a field trying to close pediatric oral-health gaps at scale, that is the frontier worth watching.

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SECTION 12

Evidence Updates: Reviews & Guidelines

Evidence recalibrated: when dentistry's bedrock tools meet modern GRADE

The recent wave of dental evidence has not been about miracle interventions. It has been about recalibration. When long-trusted measures like water fluoridation and fast-adopted tools like silver diamine fluoride are re-graded under modern GRADE standards, many land at low or very-low certainty. The most confident guidance now clusters around minimally invasive, prevention-first care.

Water fluoridation: a smaller effect in the toothpaste era

The 2024 Cochrane update is the single most consequential primary source of the period. Across 21 studies of fluoridation initiation, the post-1975 trials show a mean difference of just 0.24 fewer decayed primary teeth, with a confidence interval that crosses zero. The authors are explicit that benefits "may be smaller than they were before the widespread addition of fluoride to toothpaste." The ADA continues to

state that community water fluoridation prevents at least 25% of tooth decay across the lifespan, working alongside fluoride toothpaste. Both positions are defensible. The gap between them is a live evidence-versus-policy debate, not a settled number.

Water fluoridation for the prevention of dental caries

IHEOZOR-EJIOFOR ET AL. • COCHRANE DATABASE OF SYSTEMATIC REVIEWS • 2024

Across 21 fluoridation-initiation studies, post-1975 trials show only ~0.24 fewer decayed baby teeth (dmft MD 0.24, 95% CI -0.03 to 0.52). Effect on permanent teeth is uncertain. Low to very-low certainty.

3

Silver diamine fluoride gets its first definitive review

SDF spread quickly through pediatric and geriatric practice before the evidence caught up. The November 2024 Cochrane review pooled 29 RCTs and 13,036 participants (12,020 children plus 1,016 older adults). The headline is narrow and honest: SDF likely prevents new root caries in permanent teeth at moderate certainty, while the evidence stays inconclusive for crowns and baby teeth and for SDF versus fluoride varnish or sealants. A widely used tool, in other words, has one well-supported indication and several open questions.

Topical silver diamine fluoride for preventing and managing dental caries in children and adults

WORTHINGTON ET AL. • COCHRANE DATABASE OF SYSTEMATIC REVIEWS, ISSUE 11 • 2024

29 RCTs, 13,036 participants. SDF likely prevents new root caries in permanent teeth (moderate certainty). Effects on crowns, primary teeth, and versus varnish/sealants remain uncertain (low/very-low certainty).

4

Guidelines turn conservative

The 2023 ADA restorative caries guideline made selective carious-tissue removal the default. Across 16 evaluated treatments for vital, non-endodontically-treated teeth,

it prioritizes leaving some affected dentin in place over complete or non-selective excavation for moderate-to-advanced lesions, which lowers pulp-exposure risk.¹

The January 2026 ADA imaging guideline, the first patient-selection update in over a decade, points the same direction: order X-rays only when clinically justified, follow ALARA, and retire routine thyroid collars and lead aprons given low modern doses. It is also the first ADA guidance to formally cover CBCT selection.²

Two forces, one cause

Regulators are loosening some precautions (routine lead aprons retired in 2026) while tightening others (X-rays and antibiotics only when justified). Both moves trace back to better evidence, not less caution.

Periodontology's operating system

The EFP S3-level guidelines are now the reference framework. The stage I-III guideline carries 62 recommendations built on 15 commissioned systematic reviews and organized as a step-wise (Step 1-4) protocol. Stage IV (2022) extends that model to splinting, orthodontic repositioning, and prosthetic rehabilitation. The 2023 peri-implant guideline, informed by 13 commissioned systematic reviews, adds 55 recommendations for mucositis and peri-implantitis. The UK BSP adaptation operationalizes the step-wise process for NHS practice.

GUIDELINE	SCALE	SOURCE
EFP stage I-III periodontitis	62 recommendations (Steps 1-4)	Sanz et al., J Clin Periodontol 2020
EFP stage IV periodontitis	Extends Steps 1-4 to splinting, ortho, prosthetics	Herrera et al., J Clin Periodontol 2022
EFP peri-implant diseases	55 clinical recommendations	Herrera et al., J Clin Periodontol 2023
ADA restorative caries	16 treatments evaluated	JADA 2023
Cochrane SDF review	29 RCTs, 13,036 participants	Worthington et al. 2024

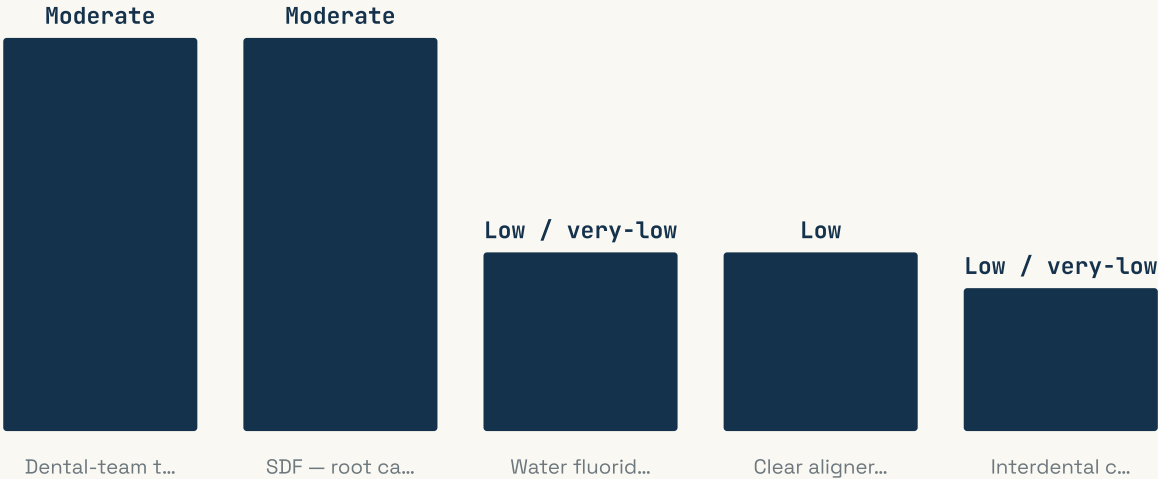
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Where the certainty is, and where it isn't

One finding ties this clinical guidance to behavior. A 2021 Cochrane review of 20 trials and 14,897 participants found that behavioural support plus NRT or e-cigarettes from dental teams roughly tripled quit rates (RR 2.76). That is moderate certainty, a notably firmer footing than most flagship reviews of the period. By contrast, the 2025 aligner meta-analysis (21 RCTs, 970 participants) found no difference in objective alignment quality versus fixed appliances, with better periodontal indices and 6-month quality of life favouring aligners, but rated the overall evidence LOW. Fixed appliances retain advantages for complex cases.

GRADE certainty across flagship reviews

How confident the evidence base actually is



DENTAL NATION RESEARCH

SOURCE: COCHRANE CD005084.PUB4, CD012718.PUB2, CD010856.PUB3, CD012018.PUB2; BANESHI ET AL. 2025

The pattern is the frontier itself. Water fluoridation, SDF, interdental cleaning, and aligners all carry low or very-low certainty in their flagship reviews. Much of routine practice still awaits high-quality RCT confirmation. The honest reading is methodological humility, and the period’s most durable contribution may be naming exactly how much we do not yet know.

SOURCES

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About this report

Researched against peer-reviewed journals, Cochrane, the ADA, NHS, FDI World Dental Federation and named industry sources via the Dental Nation deep-research engine, with the contentious claims independently fact-checked. Source numbers in the text correspond to the Sources list at the foot of each section.

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