

PERIOVIVE™

Hyaluronic Acid for Veterinary Dental Applications

March 2025

EXECUTIVE SUMMARY

Major unmet need persists in veterinary periodontal disease

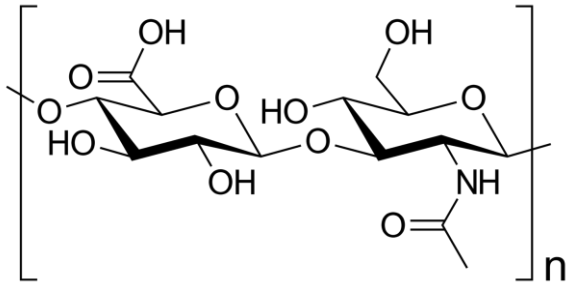
- Contemporary estimates suggest that **6.4% of gross veterinary revenue is generated from dentistry** (AVMA 2023).
- Periodontal disease remains one of the most common health issues in veterinary medicine, but there are **limited options to accelerate tissue healing and recovery** in connection with dental prophylaxis or surgery

Introducing PERIOVIVE

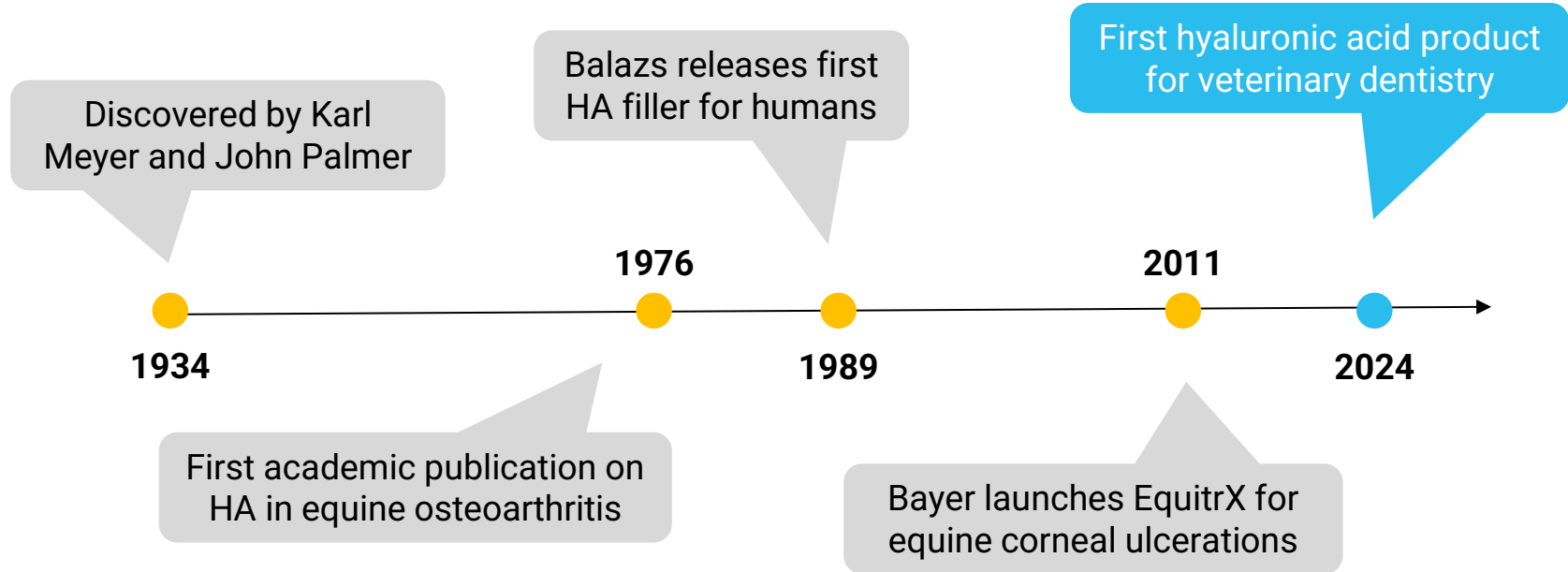
A simple, cost-effective hyaluronic gel formulation to facilitate periodontal tissue recovery after routine prophylaxis or other dental procedures, such as tooth extraction or gingival surgery.

- Hyaluronic acid (HA) is a naturally occurring biomaterial that has been proven safe and effective in both humans and dogs for a variety of indications
- Periodontal applications have shown statistically significant efficacy across at least 5 studies, including improvements in bone, cementum, and ligament formation
- Surrogate endpoints suggest halting of progression to more severe periodontal disease and reduction in required tooth extractions
- The PerioVive medical device consists of a pre-filled tissue applicator containing HA for convenient and precise delivery to tissues.
- Reasonably priced at \$65 per dose.

Hyaluronic acid: a longstanding therapeutic biomaterial



HYALURONIC ACID THROUGH THE YEARS

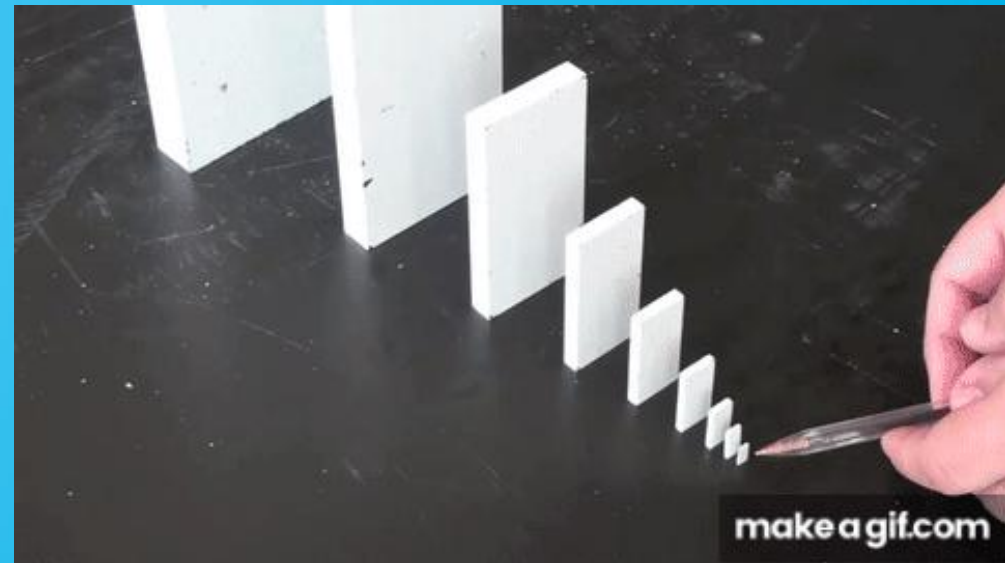


Note: FDA has approved human versions of every veterinary HA product – but not vice versa!

Hyaluronic acid drives catalytic healing in new wounds



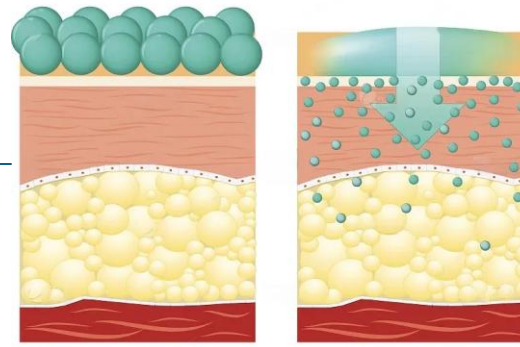
Hyaluronic acid is naturally generated by platelets in response to trauma. It triggers the healing cascade, driving sustained effects long after it has gone.



Hyaluronic acid (HA) is produced endogenously in response to trauma; its action is important for the acute phase of healing (initial 2-3 days)



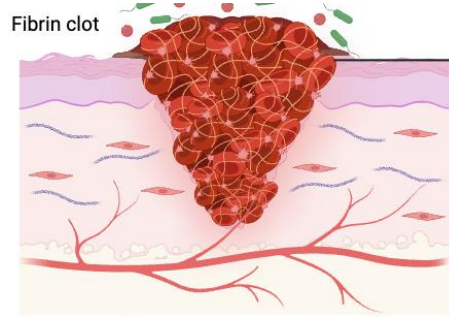
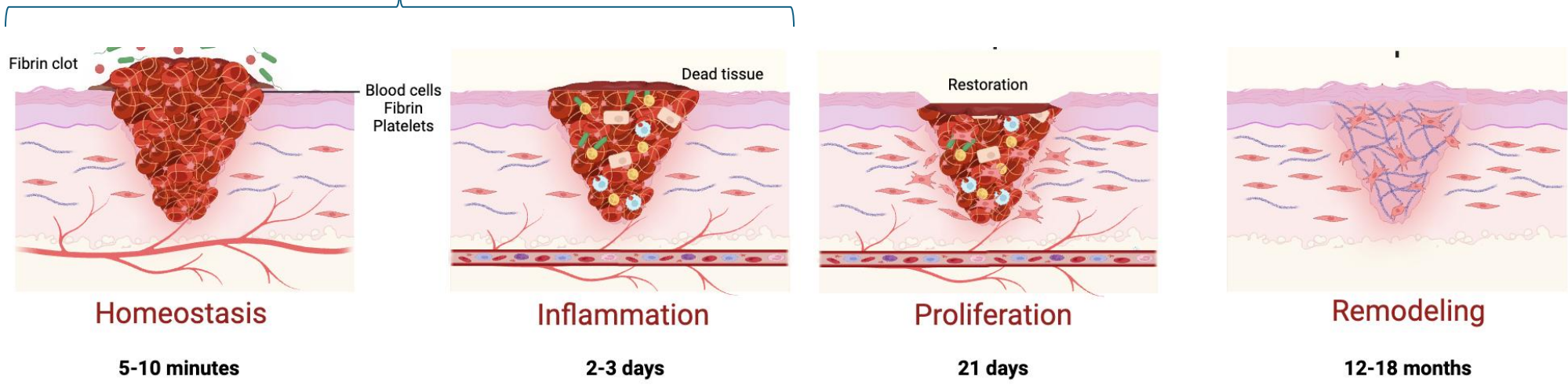
Hyaluronic acid



High molecular

Low molecular

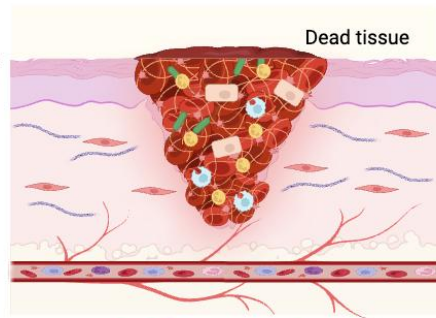
- HMW HA: binds fibrinogen for clot formation, facilitates leukocyte access to the wound site for removal of dead tissue, debris, and bacteria
- LMW HA: drives angiogenesis, endothelial cell proliferation



Homeostasis

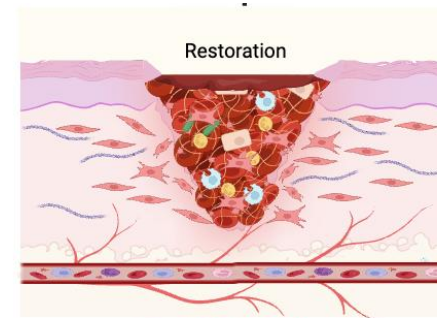
5-10 minutes

Blood cells
Fibrin
Platelets



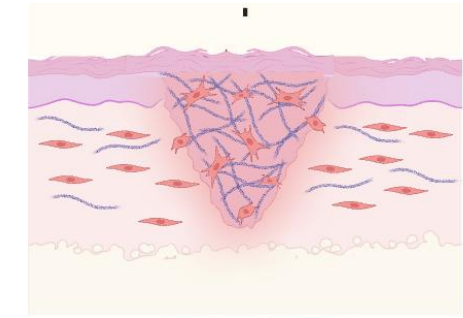
Inflammation

2-3 days



Proliferation

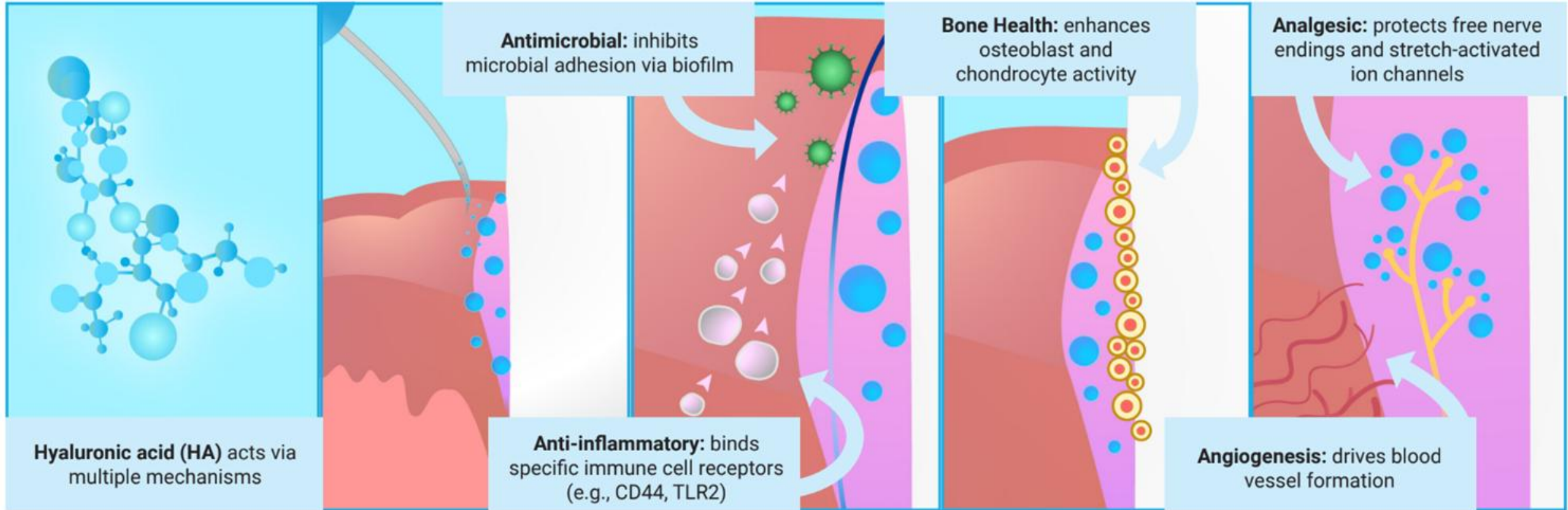
21 days



Remodeling

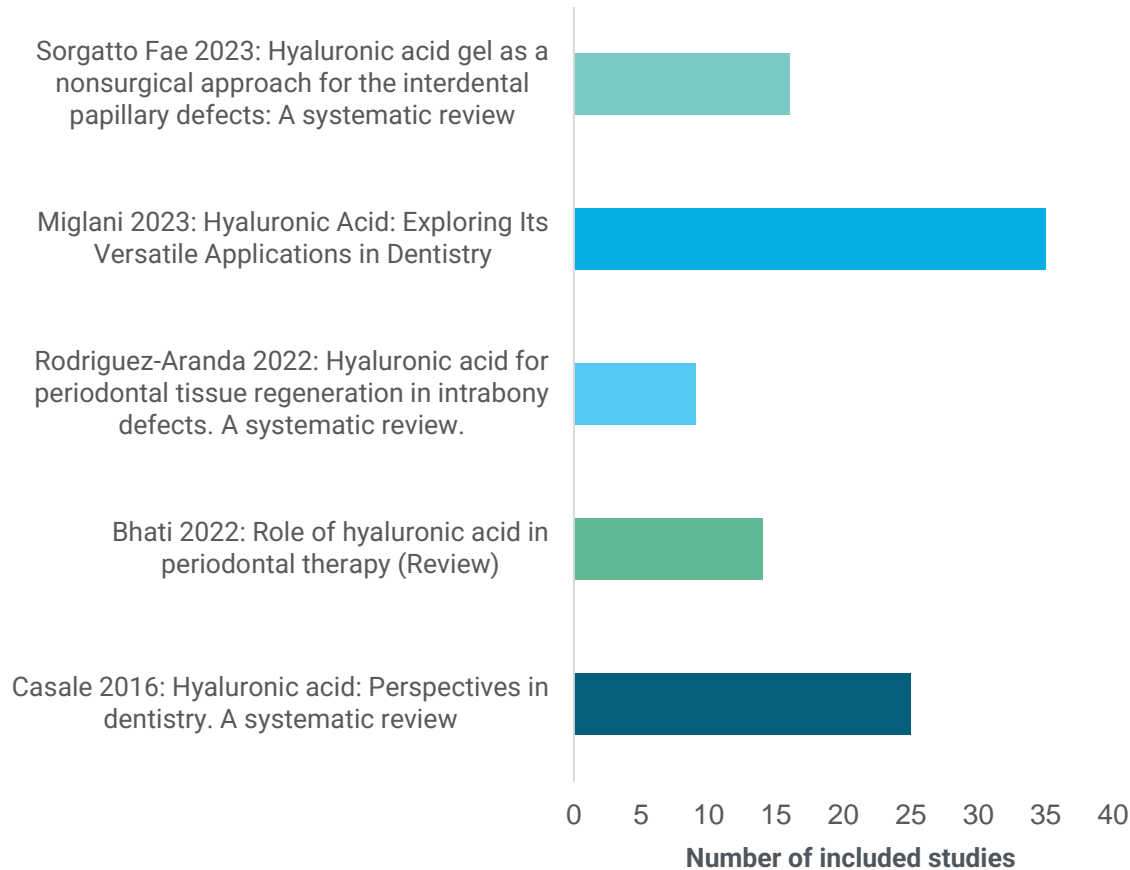
12-18 months

Hyaluronic acid (HA) acts as an extracellular scaffold, amplifying beneficial activity of endogenous cells across a variety of effects



Hyaluronic acid in human dentistry: therapeutically beneficial in a variety of settings and applications

Selected HA review articles and number of included studies



Key findings

- ▶ *“All included studies reported promising results on the reconstruction of the deficient interdental papilla after injection of HA.”*
- ▶ *“[HA’s]... function in periodontal treatment, implant dentistry, endodontics, facial aesthetics, oral surgery, and orthodontics has been thoroughly researched. Because of its biocompatibility, regenerative qualities, and antibacterial characteristics, it is an appealing material for use in a variety of dental treatments*
- ▶ *“Every group resulted in a statistically significant improvement in clinical attachment level (CAL) and probing pocket depth after 6–12 months of follow-up. Three studies showed significant results for bone defect filling on using HA.”*
- ▶ *“Treatment with HA leads to clinical improvement in patients with gingivitis, periodontitis, implants and periodontal defects. Treatment with HA accelerates wound healing, resulting in improved postoperative results and high levels of patient comfort.”*
- ▶ *“Not only does topical administration of HA play a pivotal key role in the postoperative care of patients undergoing dental procedures, but positive results were also generally observed in all patients with chronic inflammatory gingival and periodontal disease and in patients with oral ulcers.”*

Hyaluronic acid (HA) in canine dentistry: identified studies demonstrate substantial efficacy for a single application of HA in a variety of settings

Author and year	Indication
Tella et al., 2023	Class II furcations
Shirakata et al., 2022	Class III furcations
Shirakata et al., 2021	Gingival recessions
Shirakata et al., 2021	Two-wall intrabony defects
Kim et al., 2016	Infected extraction sockets



Endpoints with statistical improvement after single application of HA	
✓ Decreased gingival recession	✓ Increased bone formation
✓ Decreased probing pocket depth	✓ Increased cementum formation
✓ Decreased epithelial down growth	✓ Increased connective tissue attachment
✓ Decreased pain post periodontal therapy and tooth extraction	✓ Increased ligament attachment
✓ Decreased bleeding on probing	✓ Increased pocket filling post extraction
	✓ Increased rate of wound healing

All studies conducted via split-mouth design (i.e., self-control)

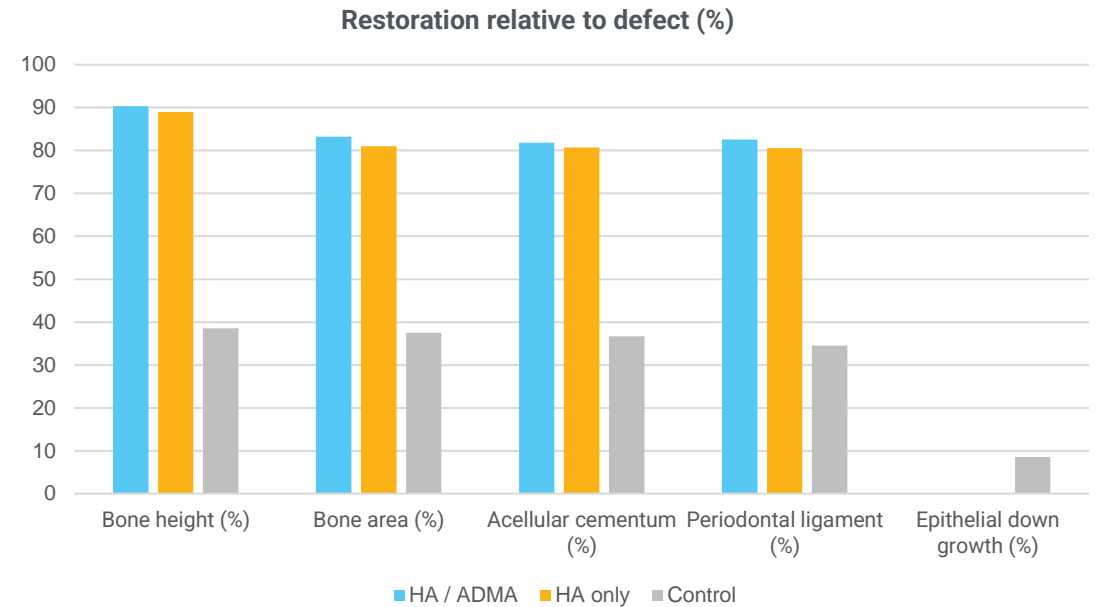
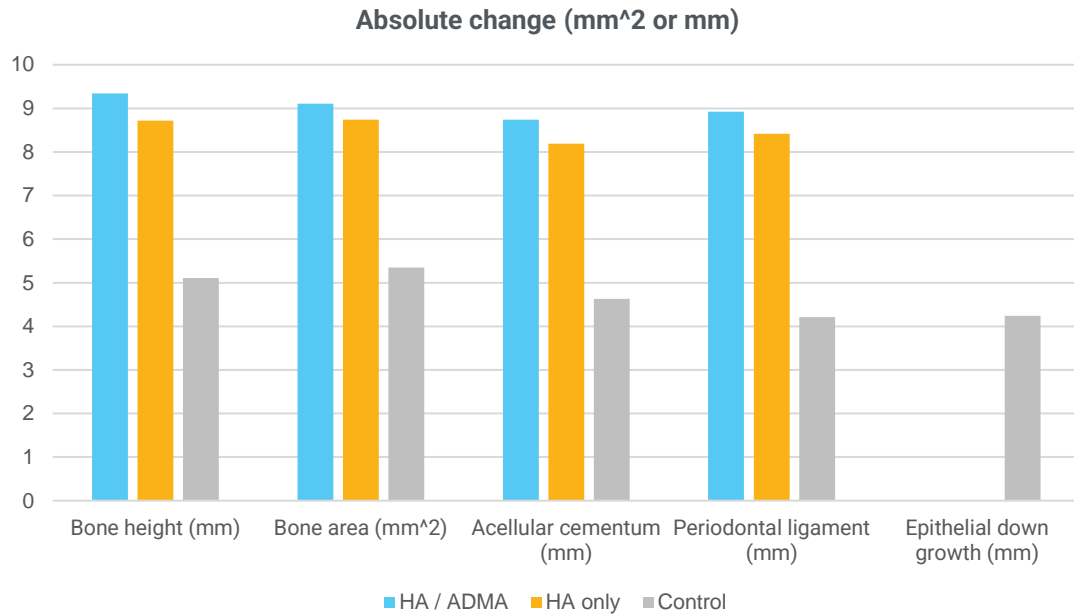
Hyaluronic acid can drive meaningful impacts as early as 10 weeks



[Shirakata et al., 2021](#)

Tella, et al., showed HA drove over >80% restoration of bone height, bone area, acellular cementum, and periodontal ligament formation vs. self-control (open flap debridement, ~35%) in Class II furcations

Results (3 months)



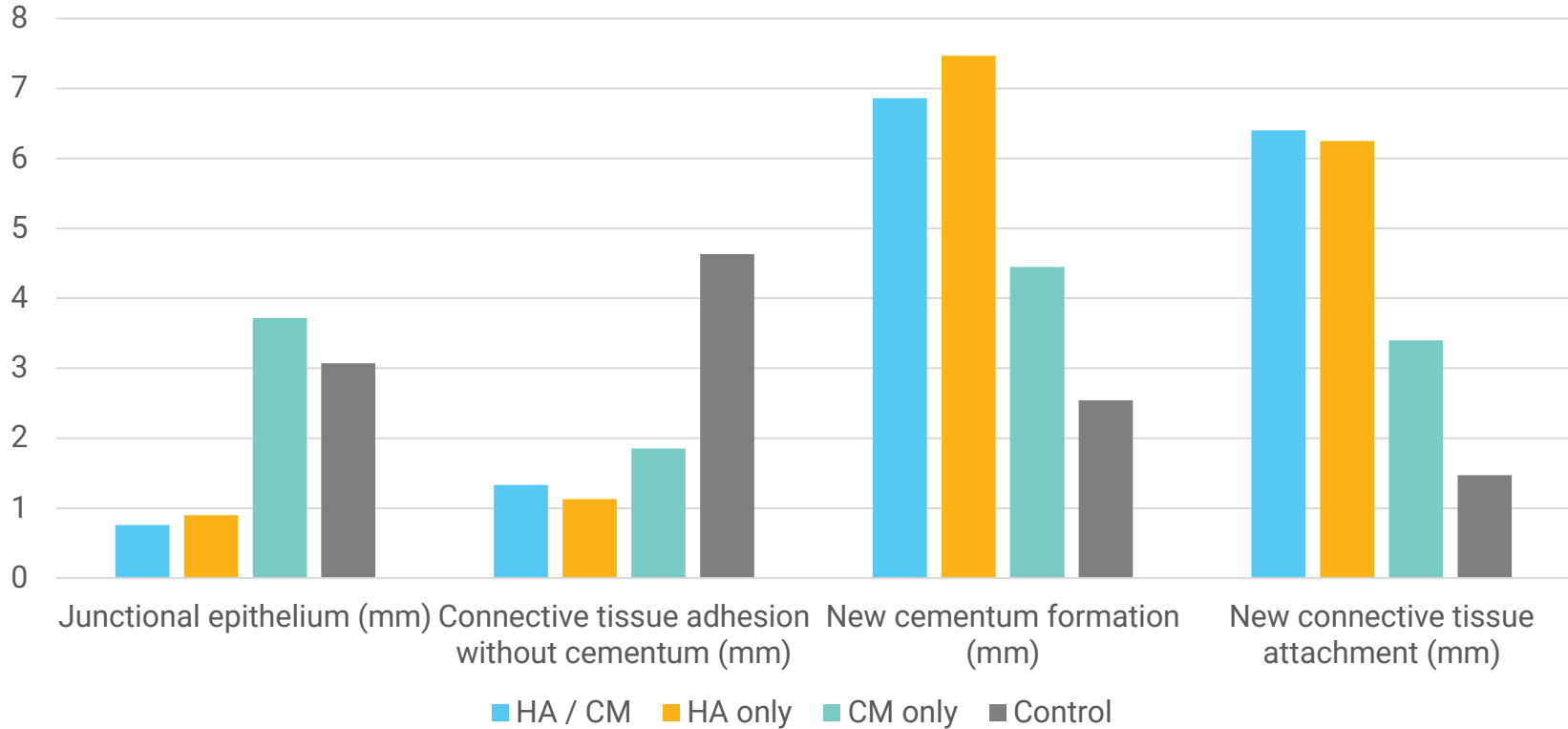
Conclusion

HA (and HA + ADMA) positively affects the **periodontal regeneration and wound healing in Class II furcation defects**

Source: [Tella et al., 2023](#)

Shirakata, et al., showed HA promoted periodontal healing in Class III furcation defects, highlighted by nearly tripling of new cementum formation (7.47mm) vs. control (2.54)

Results (10 weeks)*



*Statistically significant results only; non-significant results in bone defect area, collagen matrix, connective tissue area, epithelial tissue area, new bone area, defect height, defect width, length of root surface, tissue-free defect length
 CM = collagen matrix

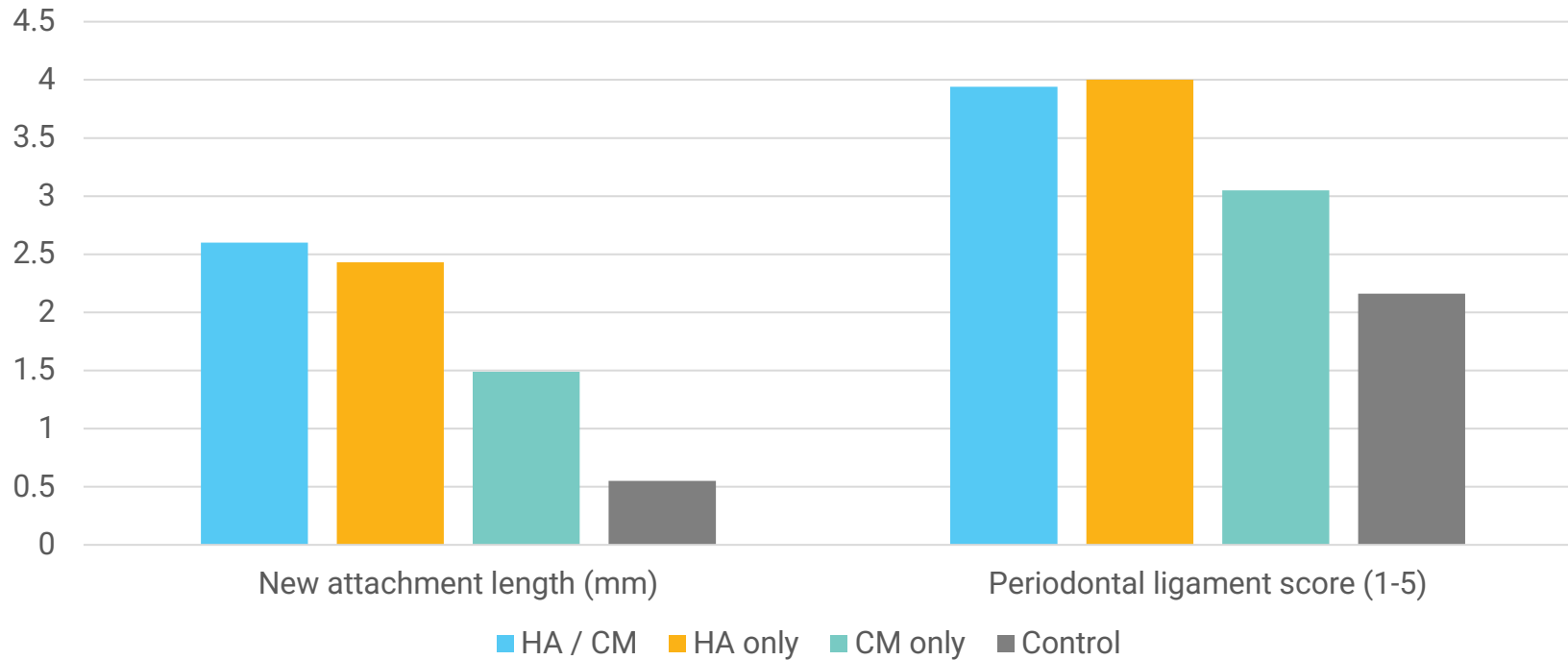
Conclusion

The application of HA with or without CM promoted **periodontal healing in class III furcation defects**, although complete furcation closure was not achieved

Source: Shirakata et al., 2022

Shirakata, et al., showed HA promotes periodontal wound healing / regeneration in two-wall intrabony defects, highlighted by a ~5x improvement in new attachment length

Results (8 weeks)*



*Statistically significant results only; non-significant results in defect height, junctional epithelium length, connective tissue adhesion, new cementum length, new bone length, new bone area
CM = collagen matrix

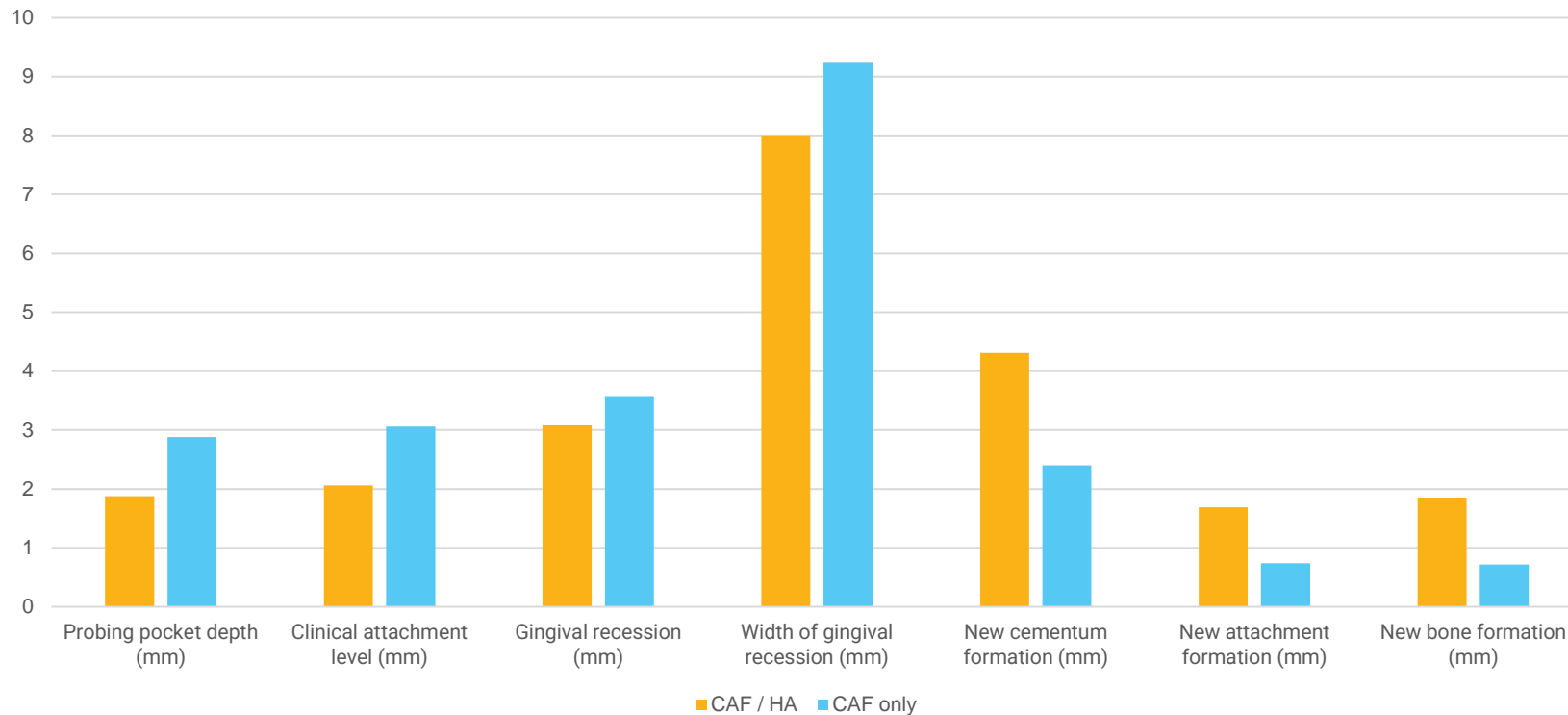
Conclusion

HA with/without CM effectively promotes periodontal regeneration in two-wall intrabony defects in dogs

Source: Shirakata et al., 2021

Shirakata, et al., showed HA promoted periodontal healing in conjunction with coronally advanced flap (CAF) for cases of gingival recession, including >2x increases in new bone and attachment formation

Results (10 weeks)*



*Statistically significant results only; non-significant results in width of keratinized tissue, defect height, histomorphometric gingival recession, epithelial length, connective tissue adhesion (without cementum), soft tissue height, soft tissue thickness
CAF = coronally advanced flap

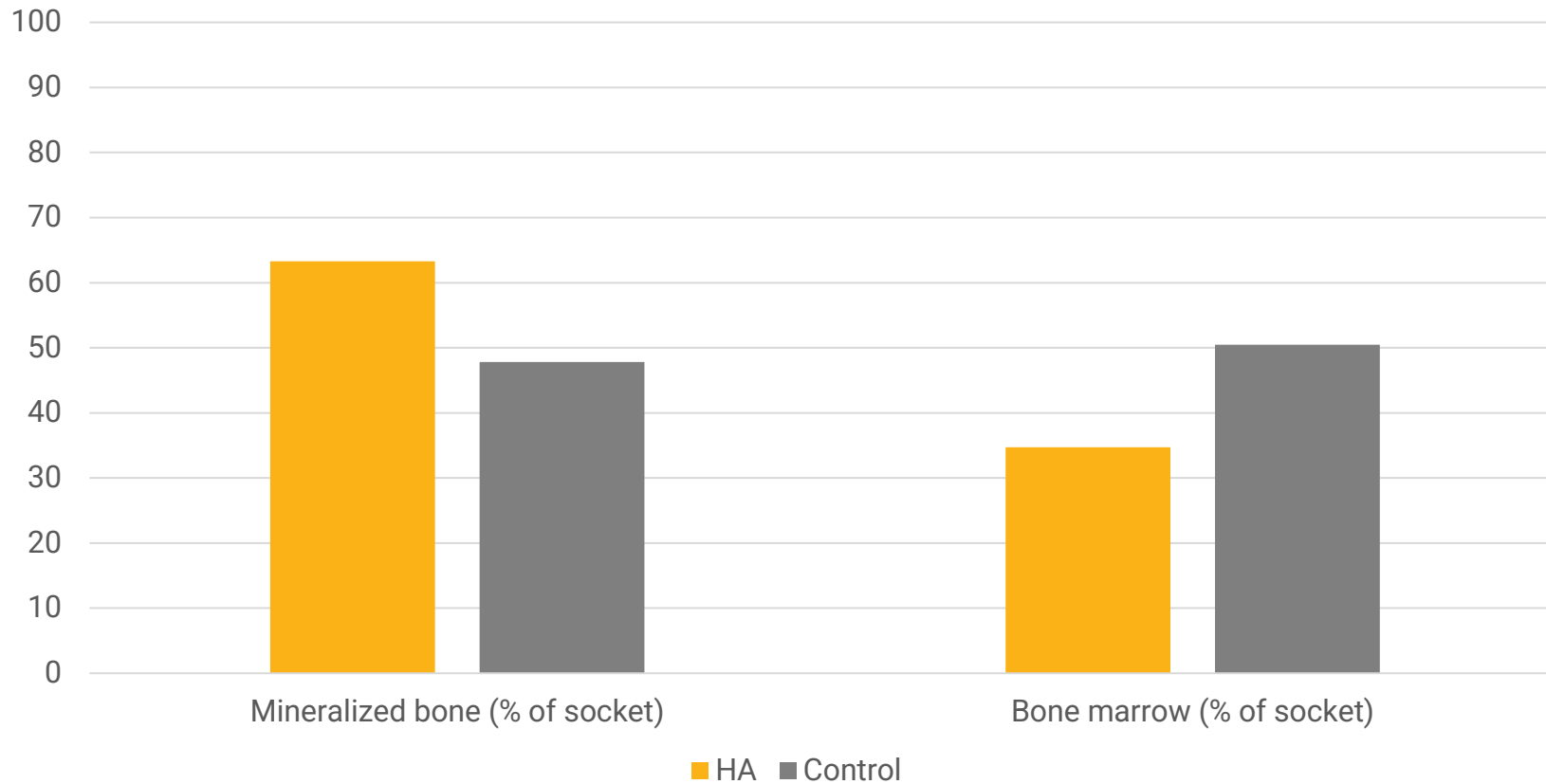
Conclusion

The application of HA in conjunction with CAF promotes **periodontal wound healing/regeneration** in gingival recession defects

Source: Shirakata et al., 2021

Kim, et al., showed HA promoted wound healing in infected sockets, highlighted by 63% restoration of mineralized bone in tissue vs. 47.8% for the control

Results (3 months)



Conclusion

HA due to its osteoinductive, bacteriostatic and anti-inflammatory properties may **improve bone formation and accelerate wound healing in infected sockets.**

Source: [Kim et al., 2016](#)

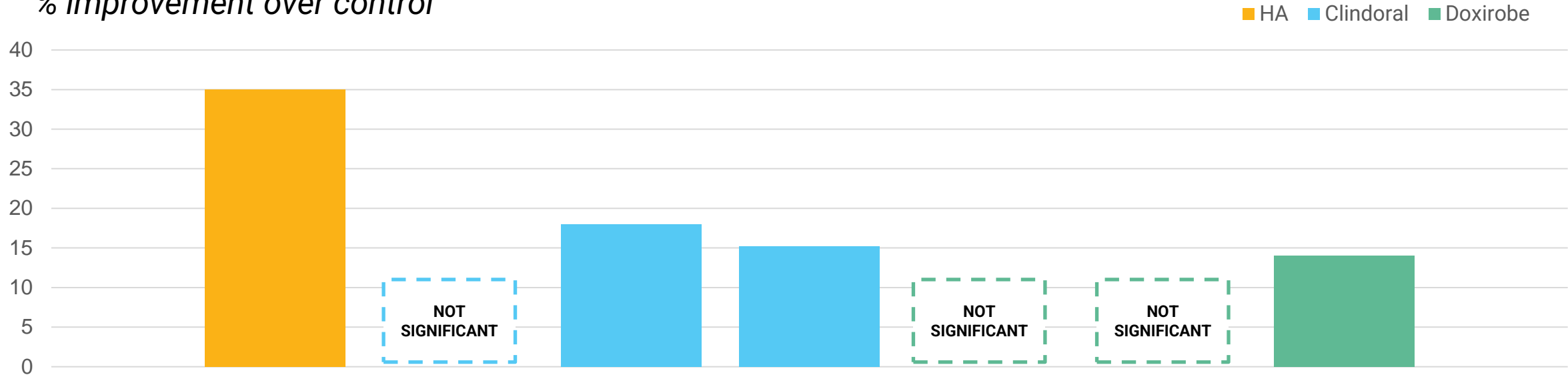
Hyaluronic acid has been studied extensively and across a range of endpoints; Clindoral and Doxirobe have been studied in similar numbers with mixed results and fewer endpoints

Treatment	Total studies	Total N	Statistically significant endpoints	Citations
Hyaluronic acid	5 (+ multiple combo studies)	34	<ul style="list-style-type: none"> ✓ Probing pocket depth ✓ Bone height ✓ Bone area ✓ Acellular cementum ✓ Periodontal ligament ✓ Epithelial downgrowth ✓ Periodontal ligament score ✓ Gingival recession ✓ Width of gingival recession ✓ Mineralized bone ✓ Bone marrow 	<ul style="list-style-type: none"> Tella et al., 2023 Shirakata et al., 2022 Shirakata et al., 2021 Shirakata et al., 2021 Kim et al., 2016
Clindoral	3	50	<ul style="list-style-type: none"> ✓ Probing pocket depth ✓ Bleeding sites ✓ Suppurating sites ✓ Bacterial burden 	<ul style="list-style-type: none"> Martel et al., 2019 Trilogic Pharma 2016 Johnston et al., 2011
Doxirobe	3	24	<ul style="list-style-type: none"> ✓ Probing pocket depth ✓ Bacterial burden ✓ Periodontal ligament attachment ✓ Gingival crevicular fluid 	<ul style="list-style-type: none"> Martel et al., 2019 Trilogic Pharma 2016 Zetner et al., 2002

In a cross-study comparison, HA demonstrated ~2x greater improvement in probing pocket depth vs. antibiotic-based gels; the most recent study from Martel et al. showed no improvement vs. control

Probing Pocket Depth Across Therapies

% improvement over control

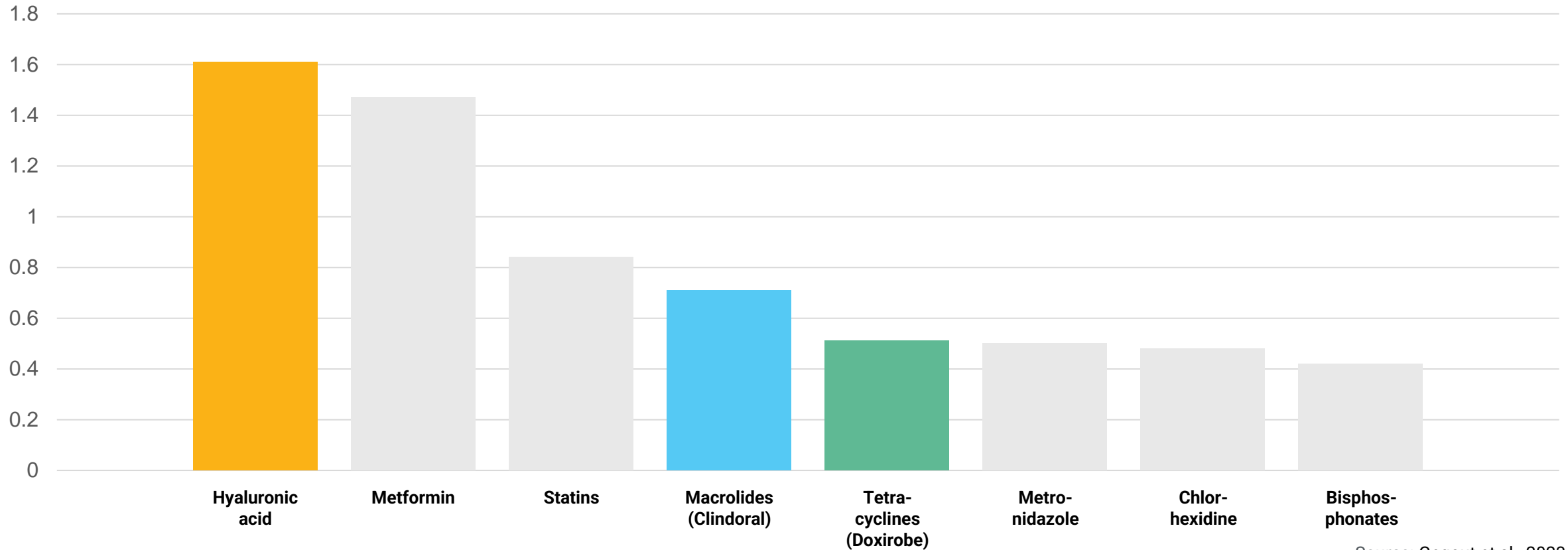


N	8 (lab; self-control)	12 (client-owned)	6 (client-owned)	32 (client-owned)	12 (client-owned)	6 (client-owned)	6 (lab; self-control)
Original PPD	2.5mm	3.5-5.5mm	4.2mm	3.6mm	3.5-5.5mm	4.2mm	3mm
Timepoint	70 days	84 days	90 days	90 days	84 days	90 days	84 days
Source	Shirakata 2021	Martel 2019	Trilogic Pharma 2016	Johnston 2011	Martel 2019	Trilogic Pharma 2016	Zetner 2002

Meta-analysis of 77 human randomized clinical trials numerically supports cross-trial comparisons in canine studies, with hyaluronic acid more than doubling improvement demonstrated by macrolides (Clindoral)

Probing Pocket Depth Across Therapies – Human Meta-analysis


Weighted mean difference in millimeters vs. scaling / root planing



Source: [Gegout et al., 2023](#)

When is it applied?

PerioVive can be used in a broad range of settings strictly as an adjunct to standard of care. Given surrogate endpoints suggest halting / delaying of progression, it should be used across early and late stage disease.

	INCREASING SEVERITY 				
	Gingival recession	Class II furcations	Class III furcations	Two-wall intrabony defects	Post-extraction sockets
Probing Pocket Depth (mm)	2.5	5	5	5.5	N/A
Recommended Intervention	Conservative management	Closed root planing or Open flap debridement	Extraction	Extraction	Extraction
HA as an adjunct?	✓	✓	✓	✓	✓
Source	Shirakata et al., 2021	Tella et al., 2023	Shirakata et al., 2022	Shirakata et al., 2021	Kim et al., 2016

How is it applied?

PerioVive comes conveniently packaged in a pre-filled luer-lock syringe with two applicator tips. PerioVive does not require premixing or excessive drying before or after application. Any remaining product can be used in other patients, but should be used within the same week as unsealed.

For closed root planing, PerioVive should be generously applied to the subgingival space until full. The gel should be visualized overflowing from the gingival margin.

For open flap debridement or in post extraction sockets, PerioVive should be generously applied just before final suturing.

[Click for video](#)

Hyaluronic acid vs. retention-based therapies: HA does not require sustained retention to achieve efficacy, minimizing application errors

	Hyaluronic acid	Clindoral	Doxirobe	Sanos
Retention claims	24 hours	7-10 days	45 days	6 months
Additional instructions	Fill to alveolar ridge	Completely and thoroughly dry; wait to form pliable matrix	Pre-mix 100x; wait 30-60 seconds to harden	Completely and thoroughly dry; "paint" onto tooth and gingival margins
Post-application restrictions	None	Resume homecare at 1 week	Resume homecare at 2 weeks	Resume homecare at 1 week

How does it stick?

Hyaluronic acid is extremely hydrophilic, capable of binding to and absorbing 1000x its weight in water. It forms a gel-like structure when it comes into contact with water, giving it viscoelastic qualities. It also possesses a significant negative charge, enabling specific binding to a wide range of molecules, including proteins, lipids, and carbohydrates. Finally, it can be chemically changed to improve its stability, extending its stay in the body, and enhancing cell adhesion.

PERIOVIVE™

- *Hyaluronic Acid for Canine Dental Applications*

PerioVive provides a novel, specially designed formulation of hyaluronic acid for easy administration to pets in conjunction with all dental procedures



Comprehensive, well-established safety and efficacy



Designed specifically for veterinarians by veterinarians



Optimized route of administration for expedient application



Reasonably priced at \$65 / dose

PERIOVIVE™

Periodontal gel (0.8% hyaluronic acid gel)
Veterinary Medical Device

Contents: 1 unit, comprised of a 2.0 mL prefilled luer-lock syringe containing 1.0 mL of 0.8% hyaluronic acid gel with separate applicator tip.

PERIOVIVE™
0.8% hyaluronic acid gel
Veterinary Medical Device



For Periodontal Application in Dogs and Cats Only.
Not for use in animals intended for human consumption.



Store at room temperature. Do not freeze.
Refer to package insert for additional information.



Thank you