2. Materials and Methods

2.3. Literature search

Table S1. Literature search strategies.

Databases (Start date)	Search strategies (Search end date: April 31, 2023)
PubMed (1946)	((((("saliva"[MeSH Terms]) OR ("saliva"[All Fields])) OR ("salivary"[All Fields])) **AND** (((((("proteomics"[MeSH Terms]) OR ("proteome"[MeSH Terms])) OR ("mass spectrometry"[MeSH Terms])) OR ("proteomics"[All Fields])) OR ("proteomic"[All Fields])) OR ("proteome"[All Fields])) OR ("mass spectrometry"[All Fields]))) **AND** (("periodontitis"[MeSH Terms]) OR ("periodontitis"[All Fields]))
Web of Science (1956)	(((TS=(proteomics)) OR TS=(proteome)) OR TS=(mass spectrometry)) **AND** TS=(periodontitis) **AND** ((TS=(saliva)) OR TS=(salivary))

Table S2. Case and control definition for all shortlisted case-control studies (n = 13).

Study	Case	Control
Wu et al. 2009 [32]	**AP:** Age < 30 years; ≥ 3 teeth affected in addition to first molar and incisor; generalized interproximal attachment loss on affected teeth.	< 10% BOP; PPD < 3 mm; < 1% of sites with CAL > 2mm; no radiographic bone loss.
Gonçalves et al. 2010 [39]	**CP:** > 35 years; ≥ six sites on different teeth with BOP, PPD > 6 mm, and CAL > 5 mm.	< 10% BOP; PPD < 3 mm.
Kim et al. 2010 [40]	**AP:** CAL > 5 mm in ≥ 8 teeth; ≥ 3 teeth affected in addition to first molar and incisor. **CP:** CAL > 5 mm with BOP in all four quadrants; no evidence of rapid progression.	No evidence of CAL, BOP, or radiographic bone loss.
Salazar et al. 2013 [33]	**CP:** BOP > 10%; PPD ≥ 5 mm at ≥ 2 sites; PPD ≥ 4 mm at ≥ 40% teeth.	BOP < 30%; maximum PPD ≤ 3 mm.
Mertens et al. 2018 [41]	American Academy of Periodontology classification criteria, no details reported.	
Bostanci et al. 2018 [42]	**AP:** CAL > 5 mm and PPD > 6 mm in ≥ 8 teeth; ≥ 3 teeth affected in addition to first molar and incisor. **CP:** CAL > 5 mm and PPD > 6 mm in ≥ 4 non-adjacent teeth; > 50% radiographic bone loss in ≥ two quadrants.	No sites with PPD > 3 mm and CAL > 2 mm; no evidence of radiographic bone loss.
Grant et al. 2019 [43]	**Periodontal disease:** Radiographic bone loss ≥ 1/3 of the root length and/or PPD > 5 mm, and BOP > 20%.	No tooth with PPD > 5 mm or Radiographic bone loss ≥ 1/3 of the root length.
Tang et al. 2019 [44]	**CP:** CAL ≥ 1 mm; PPD ≥ 4 mm; radiographic bone lone; > 30% of teeth involved.	No sites with CAL or PPD > 3 mm; BOP ≤ 20%; no radiographic bone loss.
Shin et al. 2019 [45]	**Periodontitis:** Presence of proximal bone of ≥ 3 mm in ≥ 2 non-adjacent teeth.	No proximal bone of ≥ 3 mm in ≥ 2 non-adjacent teeth.
Hartenbach et al. 2020 [46]	**CP:** > 10% of teeth with PPD and/or CAL ≥ 5 mm and BOP.	< 10% sites with BOP, no PPD or CAL > 3 mm; < 5% sites of PPD or CAL = 4 mm without BOP was allowed.
Antezack et al. 2020 [47]	**Periodontitis:** Inter-dental CAL detectable at ≥ 2 non-adjacent teeth or buccal or oral CAL ≥ 3 m with PPD ≥ 3 mm at ≥ 2 teeth.	BOP < 10%; PPD < 3 mm; no CAL.
Grant et al. 2022 [27]	**Birmingham cohort:** Stage I/II periodontitis: interproximal CAL of 2-4 mm at > 8 teeth with PPD of 5-7 mm; Stage III/IV: interproximal CAL > 5 mm at 12 teeth and PPD > 7 mm. **Newcastle cohort:**	**Birmingham cohort:** No sites of interproximal CAL; no sites with PPD > 3 mm; < 10% sites with GI of 1 and no sites with GI of 2 or 3; < 10% sites with BOP.

	Stage I/II periodontitis: interproximal PPD of 5-7 mm (equating to approximately 2-4 mm CAL) at ≥ 8 teeth; Stage III/IV: interproximal PPD > 7 mm (equating to approximately ≥ 5 mm CAL) at ≥ 12 teeth, BOP scores > 30%.	**Newcastle cohort:** No sites with interproximal CAL; PPD ≤ 3 mm in all sites (but would allow up to four 4 mm pockets at distal of last standing molars); ≤ 10% sites with mGI of ≥ 2.0; < 10% sites with BOP.
Casarin et al. 2023 [34]	< 35 years; PPD ≥ 5 mm at ≥ 8 teeth and PPD ≥ 7 mm at ≥ 2 teeth; CAL > 5 mm in three teeth other than the first molars and incisors.	No history of CAL, PPD < 4 mm, no radiographic bone loss, ≥ 20 teeth present.

AP: aggressive periodontitis; BOP: bleeding on probing; CAL: clinical attachment loss; CP: chronic periodontitis; GI: gingival index; PPD: probing pocket depth.

2.5. Risk of bias assessment

Table S3. Quality assessment by the Newcastle Ottawa Scale for all shortlisted case-control studies (n = 13).

Study	Selection				Comparability	Exposure		Total score
	Case definition	Representativeness of the cases	Selection of controls	Definition of controls		Ascertainment of exposure	Non-response rate	
Wu et al. 2009 [32]	*	*	*	*	*		*	6
Gonçalves et al. 2010 [39]	*		*	*	*		*	6
Kim et al. 2010 [40]	*		*	*	**		*	6
Salazar et al. 2013 [33]	*	*	*	*	**		*	7
Mertens et al. 2018 [41]	*	*	*	*	*		*	6
Bostanci et al. 2018 [42]	*		*	*	*		*	5
Grant et al. 2019 [43]	*		*	*	*		*	5
Tang et al. 2019 [44]	*	*	*	*	*		*	6
Shin et al. 2019 [45]	*	*	*	*	**		*	7
Hartenbach et al. 2020 [46]	*		*	*	*		*	5
Antezack et al. 2020 [47]	*	*	*	*	*		*	6
Grant et al. 2022 [27]	*		*	*	**		*	6
Casarin et al. 2023 [34]	*		*	*	**		*	6

Table S4. Risk of bias assessment by QUADAS-2 for all shortlisted diagnostic studies (n = 13).

Study	Risk of bias			
	Patient selection	Index test	Reference standard	Flow and timing
Wu et al. 2009 [32]	High	High	Low	Low
Gonçalves et al. 2010 [39]	High	High	Low	Low
Kim et al. 2010 [40]	High	High	Low	Low
Salazar et al. 2013 [33]	High	High	Low	Low
Mertens et al. 2018 [41]	High	High	Low	Low
Bostanci et al. 2018 [42]	High	Low	Low	Low
Grant et al. 2019 [43]	High	High	Low	Low
Tang et al. 2019 [44]	High	High	Low	Low
Shin et al. 2019 [45]	High	High	Low	Low
Hartenbach et al. 2020 [46]	High	High	Low	Low
Antezack et al. 2020 [47]	High	Low	Low	Low
Grant et al. 2022 [27]	High	High	Low	Low
Casarin et al. 2023 [34]	High	High	Low	Low

Table S5. Quality assessment by NIH quality assessment tool for before-after (pre-post) studies with no control group (n = 2).

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Total score
Haigh et al. 2010 [48]	Y	Y	N	Y	N	Y	Y	N	Y	Y	N	NA	7
Yuan et al. 2022 [49]	Y	Y	N	Y	N	Y	Y	N	Y	Y	N	NA	7

N: no; NA; not applicable; NIH, National Institutes of Health; Y: yes.

Q1. Was the study question or objective clearly stated?

Q2. Were eligibility/selection criteria for the study population prespecified and clearly described?

Q3. Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?

Q4. Were all eligible participants that met the prespecified entry criteria enrolled?

Q5. Was the sample size sufficiently large to provide confidence in the findings?

Q6. Was the test/service/intervention clearly described and delivered consistently across the study population?

Q7. Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?

Q8. Were the people assessing the outcomes blinded to the participants' exposures/interventions?

Q9. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?

Q10. Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes?

Q11. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e., did they use an interrupted time-series design)?

Q12. If the intervention was conducted at a group level (e.g., a whole hospital, a community, etc.) did the statistical analysis take into account the use of individual-level data to determine effects at the group level?

Table S6.. Differentially expressed (descending order of absolute fold change) unstimulated or stimulated whole salivary proteins detectable by mass spectrometry-based proteomics.