An Roinn Sláinte
Department of Health

By e-mail only: emlsecretariat@who.int

April 8th, 2023

Dear colleagues,

On behalf of Ireland, I wish to input to the review of the WHO essential medicines list (EML) and the companion EML for children. The inclusion of fluoride varnishes, fluoride gels and fluoride mouth rinses as well as resin composites in the EML/EMLc is welcomed to enable prevention and management of dental caries. This builds on the previous additions to EML which included fluoride toothpastes, silver diamine fluoride and glass ionomers.

An estimated 70% of Ireland's population has access to fluoridated water via its public water supplies. Fluorides in this and all other forms have a valuable role to play, from a public health perspective, to reduce inequalities in oral health. Equally the availability of alternative non- mercury containing materials for restoration of teeth is supportive for the successful phase-down of dental amalgam required by the Minamata Convention on Mercury.

As Chief Dental Officer, Department of Health in Ireland, I commissioned a series of umbrella evidence reviews to inform the implementation of our policy issues in

- Smile agus Sláinte (The Irish National Oral Health Policy-2019), https://assets.gov.ie/9614/d1be290ee99743f8ba4c0ef9ac4cb401.pdf
- Ireland's Amalgam Phase Down Plan (2019), https://assets.gov.ie/19422/18299e4340394a51801dae1fb29d4ade.pdf

An umbrella review was completed initially in 2018 and updated in 2022. It relates to the **Management of Dental Caries.**
https://www.hrb.ie/fileadmin/2._Plugin_related_files/Publications/2022_Publication_files/2022_Evidence_Centre/Management_of_non-cavitated_and_cavitated_caries_2022.pdf

The second, a sister umbrella review, is the **Prevention of Dental Caries.** This is awaiting peer review and so I have attached the slide presentation that was made available to us. I have asked my colleagues in the HRB, Dr Jean Long and Dr Lisa Murphy, to liaise with you directly once the final report on **Prevention of Dental Caries** is available. They have agreed to release the non-peer reviewed version in advance to support your process.

In addition, colleagues in the Department of Environment, Climate and Communications (DECC) supported by us in the Office of the Chief Dental Officer, Department of Health, commissioned primary research in this subject area. This research was to inform the phase down of amalgam with a focus on the impact of alternative materials on the environment as well as possible related health and safety issues.

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www.health.gov.ie

Unfortunately, colleagues in the DECC are unavailable to comment presently but the publicly available links are available at https://www.epa.ie and are included below.

https://www.epa.ie/our-services/monitoring--assessment/waste/chemicals/mercury/

https://www.epa.ie/publications/research/waste/research-307.php

https://www.epa.ie/publications/research/environment--health/research-417.php

My colleagues in DECC, may wish to comment further on return from leave.

I trust these submissions will contribute to the evidence review of the WHO essential medicines. On behalf of the Department of Health and colleagues in the Health Research Board, we would be happy to facilitate further information sharing and discussion if it is helpful.

Yours with kind regards,

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Primary prevention of dental caries

An overview of reviews

Lisa Murphy, Louise Farragher, Kayleigh Clements, Annette Burns, Mary Archibald, and Jean Long

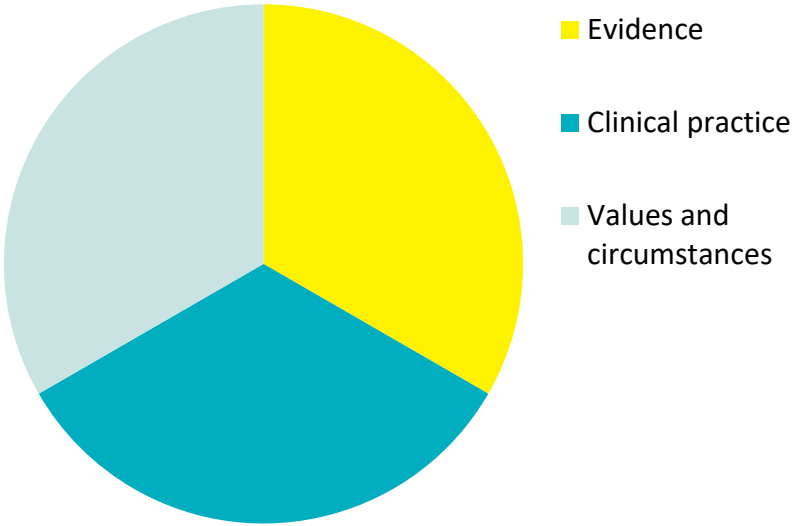
Health Research Board

Research. Evidence. Action.

Purpose

To provide evidence to assist with the development of clinical guidelines for Ireland on the prevention of caries using individual-based primary prevention interventions prior to the development of any dental decay/dental caries

- Evidence-based practice is comprised of three equal components:



Research questions

What is the evidence from systematic reviews regarding individual-based interventions to prevent caries in:

- Primary teeth
- Permanent teeth
- Mixed teeth

PICO

Population	People with some or all teeth that are caries free
Intervention	One or more of 43 possible interventions
Comparator	No treatment, a placebo, any alternative treatment/intervention
Outcome	Primary and secondary outcomes
Study Design	Systematic reviews of trials and/or prospective longitudinal cohort studies

Methods

Health Research Board

hrb.ie

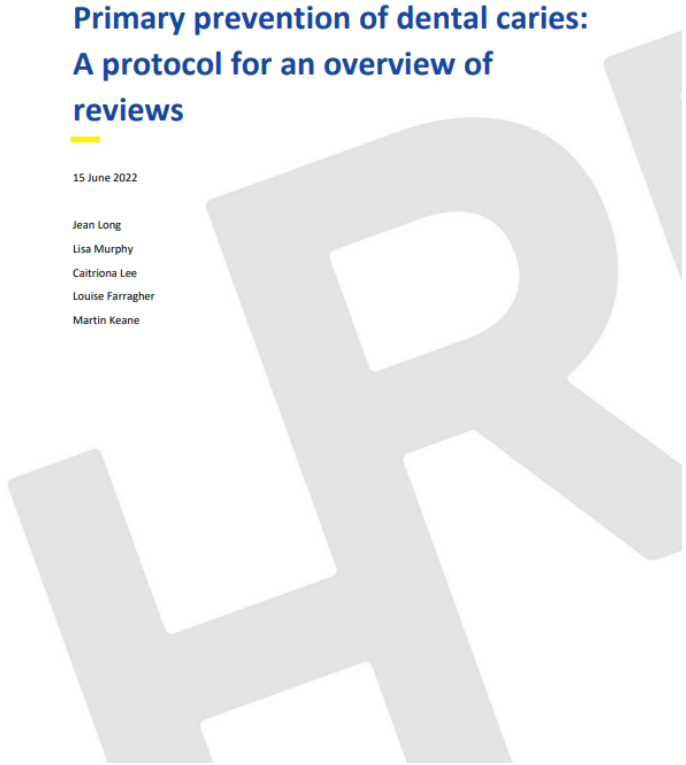
Methods

1. Developing the protocol
2. Searching
3. Screening
4. Extraction
5. Quality assessing the reviews
6. Categorising
7. Grading the certainty of evidence
8. Summarising the reviews
9. Synthesising the evidence
10. Assessing the overlap

Methods 1: Protocol

Protocol registered on PROSPERO

- CRD42022353754



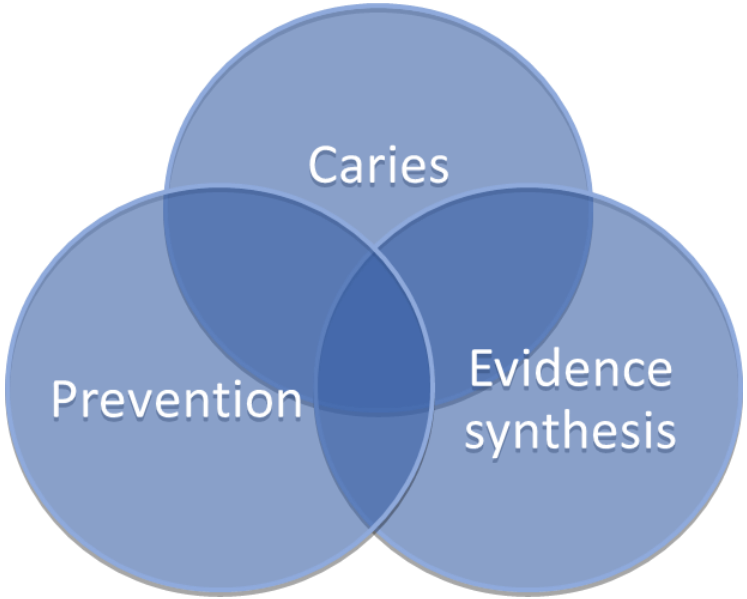
Primary prevention of dental caries: A protocol for an overview of reviews

15 June 2022

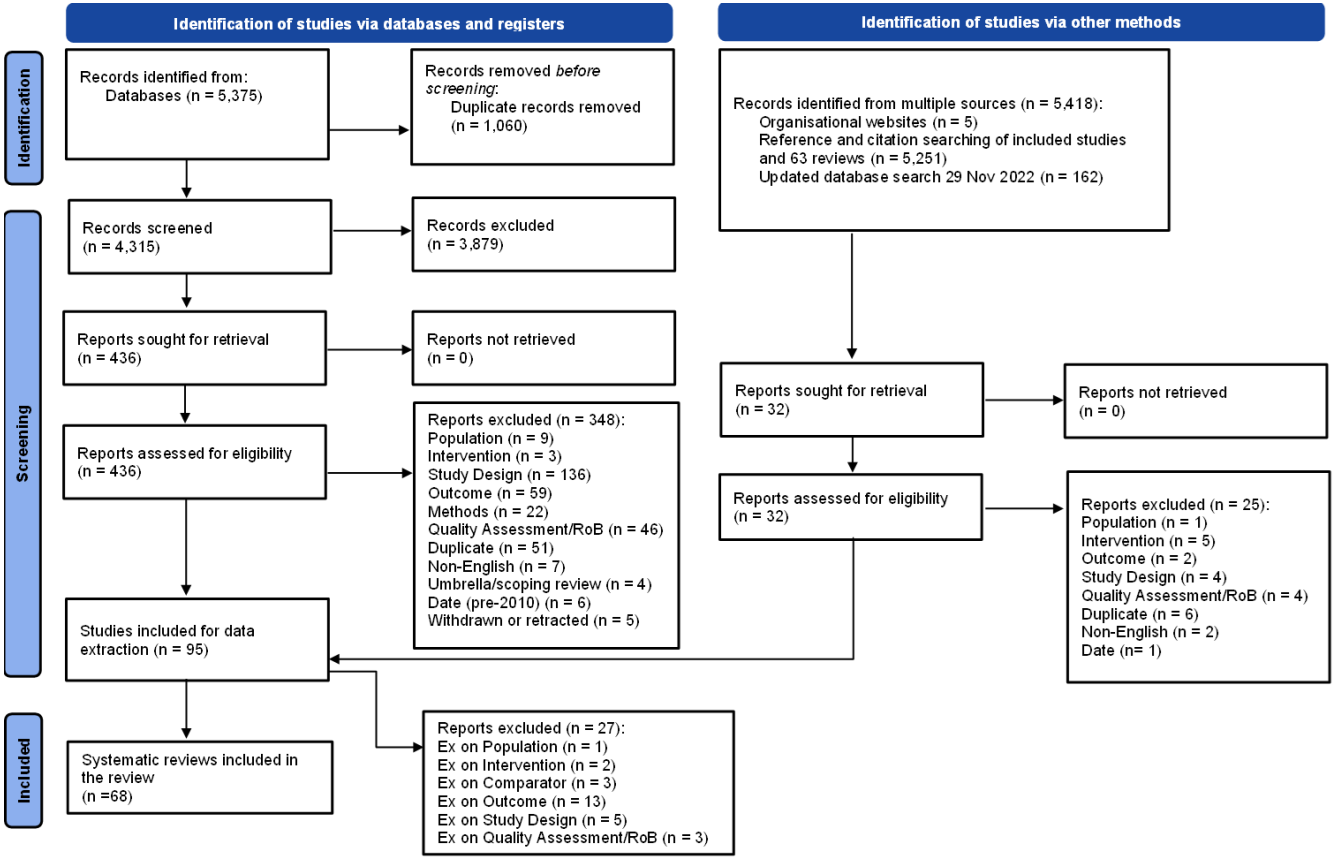
Jean Long
Lisa Murphy
Caitriona Lee
Louise Farragher
Martin Keane

Methods 2: Search

- We searched:
  - **3** clinical databases
  - **11** systematic review resources
  - **3** search engines
  - **6** resources for open access/grey/preprint material
- January 2010 to mid-June 2022



Methods 3: Screening


Identification of studies via databases and registers
Identification of studies via other methods
Identification
Screening
Included
Records identified from:
Databases (n = 5,375)
Records removed *before screening*:
Duplicate records removed
(n = 1,060)
Records identified from multiple sources (n = 5,418):
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Reference and citation searching of included studies and 63 reviews (n = 5,251)
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(n = 4,315)
Records excluded
(n = 3,879)
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Reports not retrieved
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Reports assessed for eligibility
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Reports excluded (n = 348):
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Intervention (n = 3)
Study Design (n = 136)
Outcome (n = 59)
Methods (n = 22)
Quality Assessment/RoB (n = 46)
Duplicate (n = 51)
Non-English (n = 7)
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(n = 32)
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Population (n = 1)
Intervention (n = 5)
Outcome (n = 2)
Study Design (n = 4)
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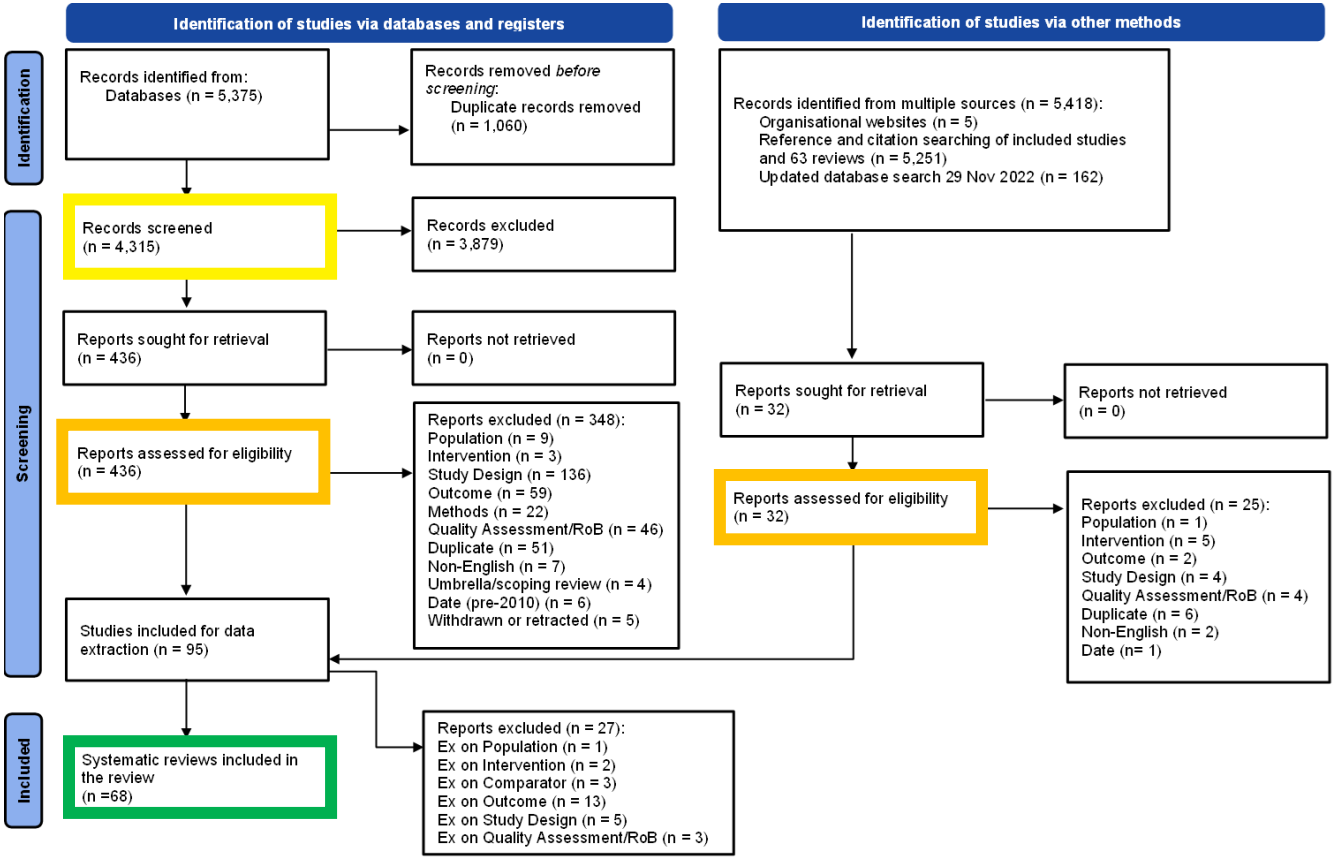
Ex on Comparator (n = 3)
Ex on Outcome (n = 13)
Ex on Study Design (n = 5)
Ex on Quality Assessment/RoB (n = 3)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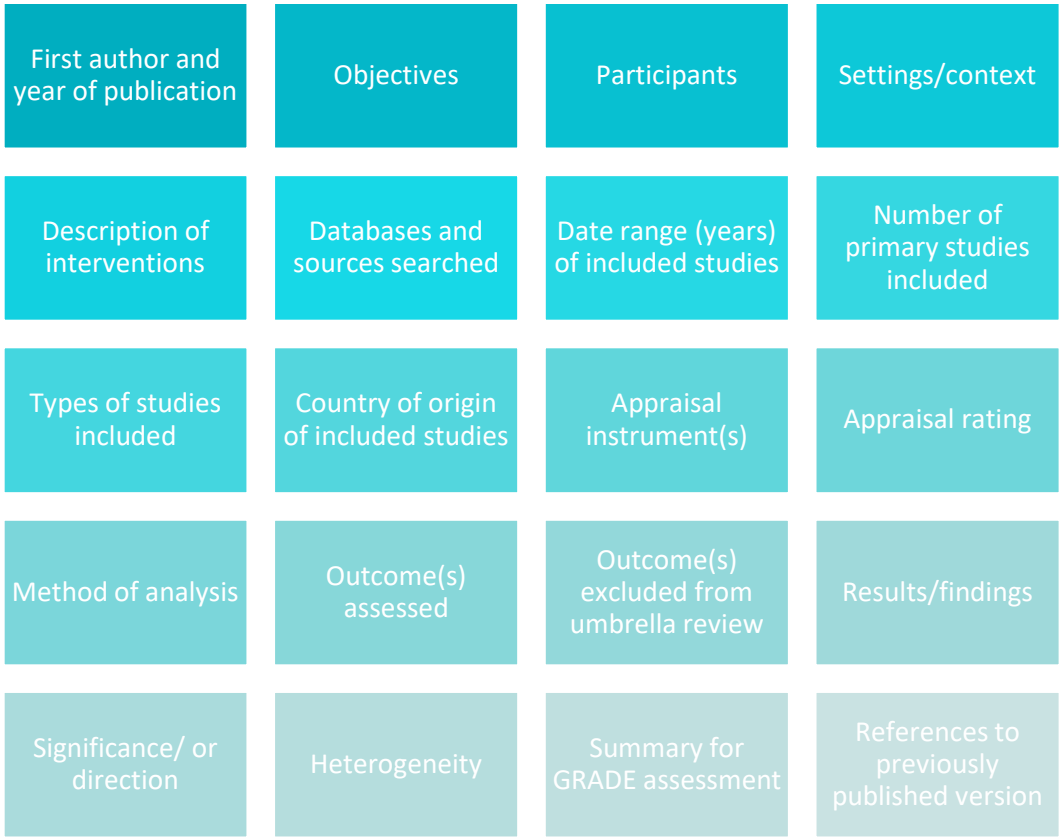
(n =68)

Methods 4: Extraction

- JBI extraction form
- Structured extraction of data from each review
- Factors that may have affected the outcome(s)



Methods 5: Quality assessment

- 16-item AMSTAR 2

- 7 critical flaws, e.g.
  - Not preparing a protocol
  - No characteristics of primary studies
  - Included high risk of bias studies
  - Did not discussed heterogeneity

Score	Criteria	No. reviews
High	No critical flaw 0 or 1 non-critical flaw	0
Moderate	No critical flaw >1 non-critical flaw	4
Low	1 critical flaw	7
Critically low	>1 critical flaw	57

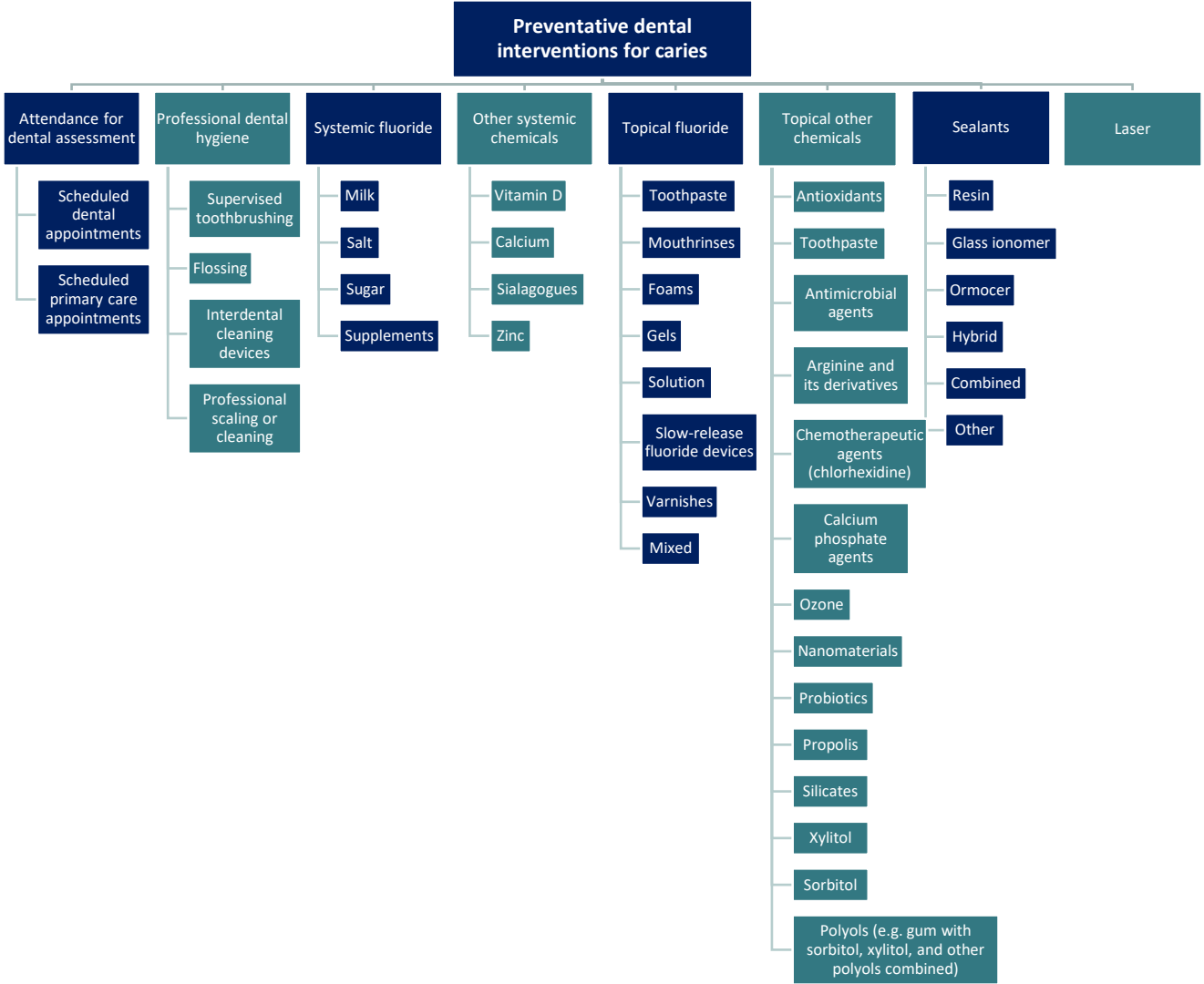
Methods 6: Categorising

- Dentition



Methods 6: Categorising

- Intervention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Attendance for dental assessment
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Professional dental hygiene
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Interdental cleaning devices
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Methods 7: Grading the certainty of evidence

- GRADE algorithm

Criteria to determine certainty
Non-RCT designs
Inadequate randomisation
Inadequate blinding
Substantial heterogeneity
Inadequate sample size
AMSTAR 2 quality rating

Methods 7: Grading the certainty of evidence

GRADE	No. reviews
High	0
Moderate	8
Low	31
Very low*	29

Methods 8 and 9: Summarising and synthesising

- Summarised the findings of individual reviews

- **Narratively synthesised** the findings from the same or similar interventions

Methods 10: Overlap

- Overlap of primary studies across systematic reviews
- Pieper et al. method known as **corrected covered area**

Methods 10: Overlap

- Outcome

Primary outcomes: general epi measures	Primary outcomes: dentistry epi measures	Secondary outcomes
Any general indicator of caries incidence on any part of the tooth – % of new carious lesions – Mean no. teeth with new caries – Cumulative survival rate	D(E/M)FT / d(e/m)ft (or variation) D(E/M)FS / d(e/m)fs (or variation) RCI	Plaque (e.g. visible plaque index) Elevated mutans streptococci levels Oral health quality of life Sealant retention Adverse effects (e.g. fluorosis)

Methods 10: Overlap

- Results of overlap assessment

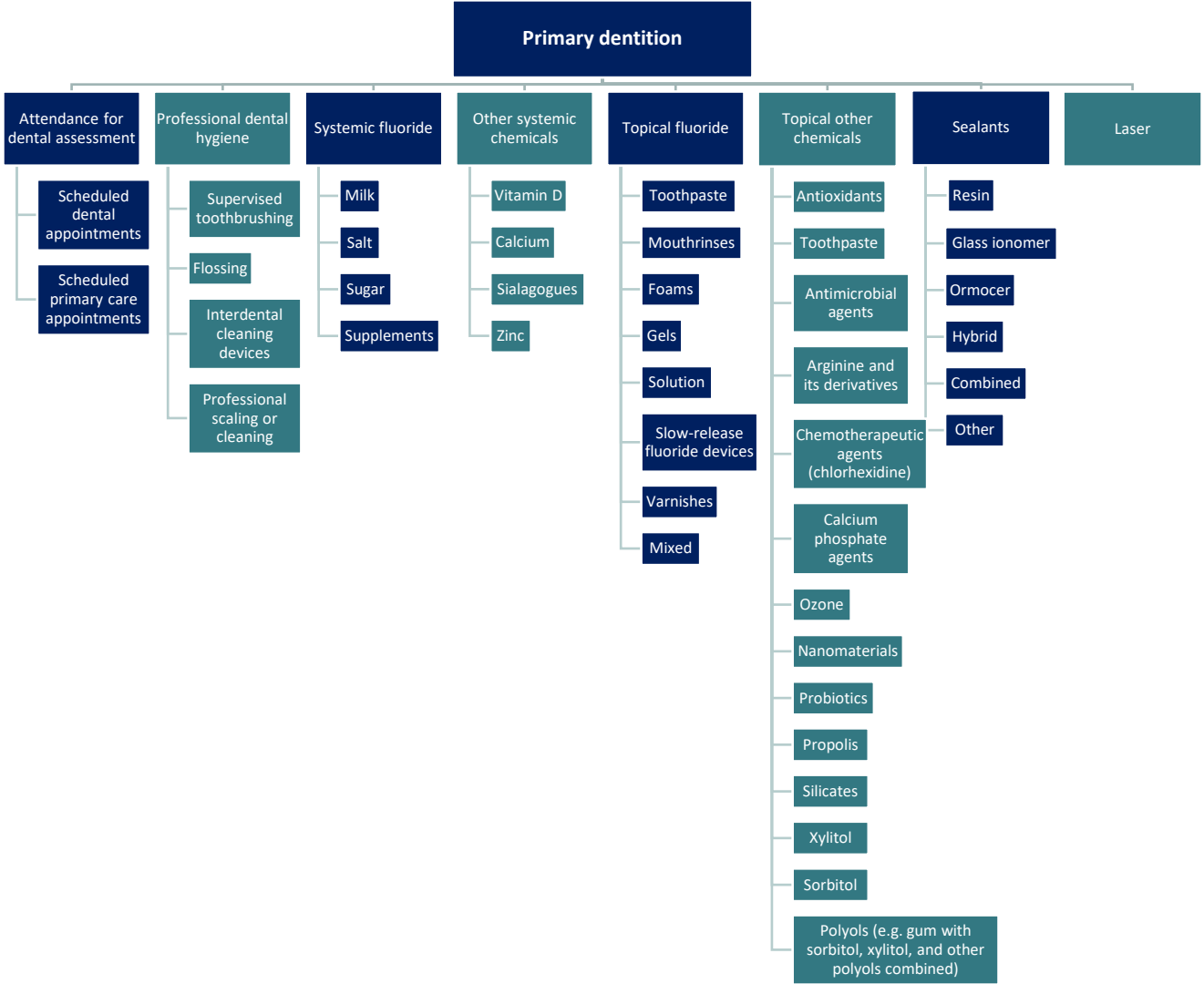
Corrected covered area	Overlap	Number
0 – 5%	Slight	4
6 – 10%	Moderate	1
11 – 14%	High	7
15% +	Very high	16

Findings

Primary dentition

Categories of findings

- Singular interventions
- Interventions delivered to pregnant women/mothers
- Combined interventions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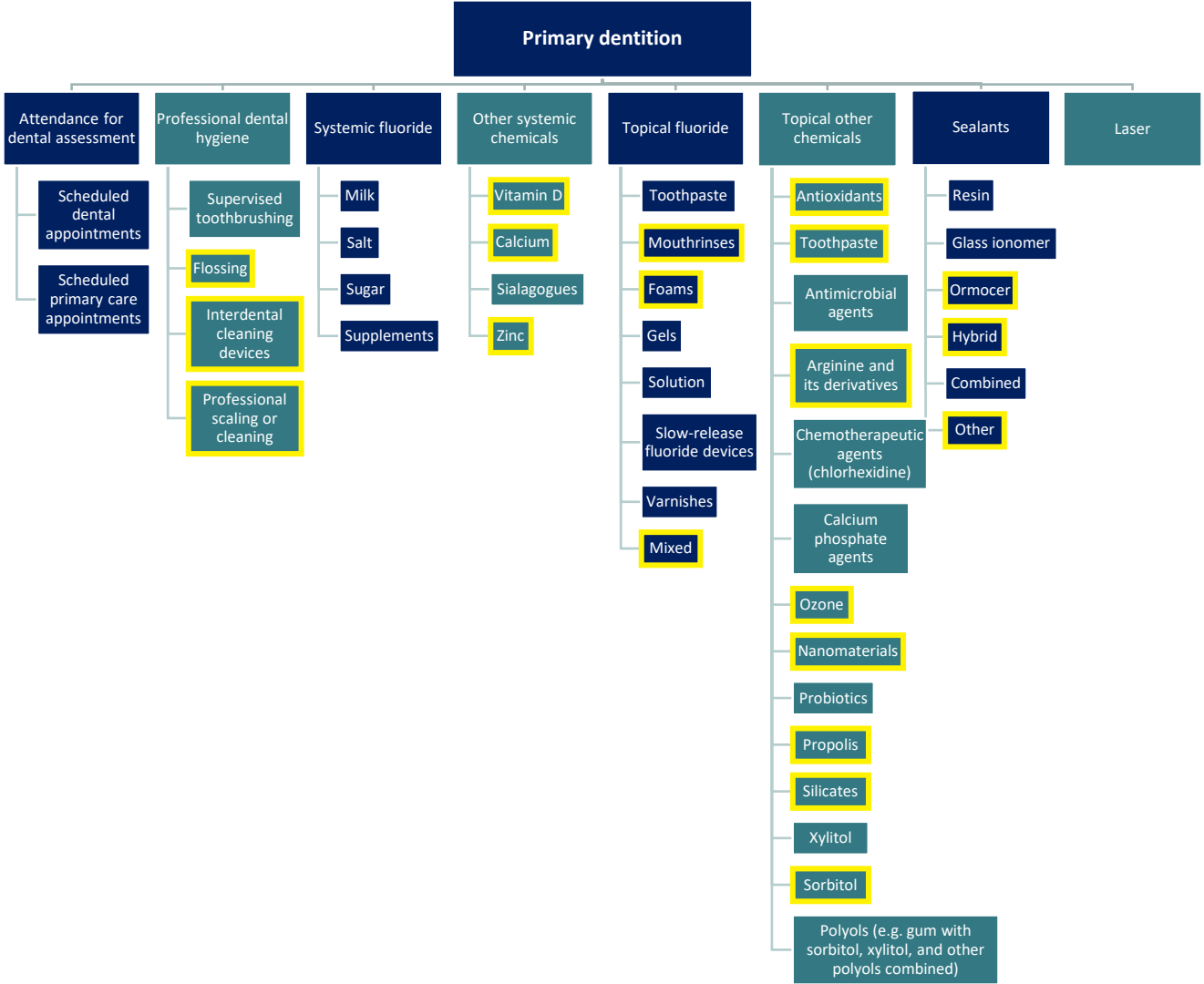
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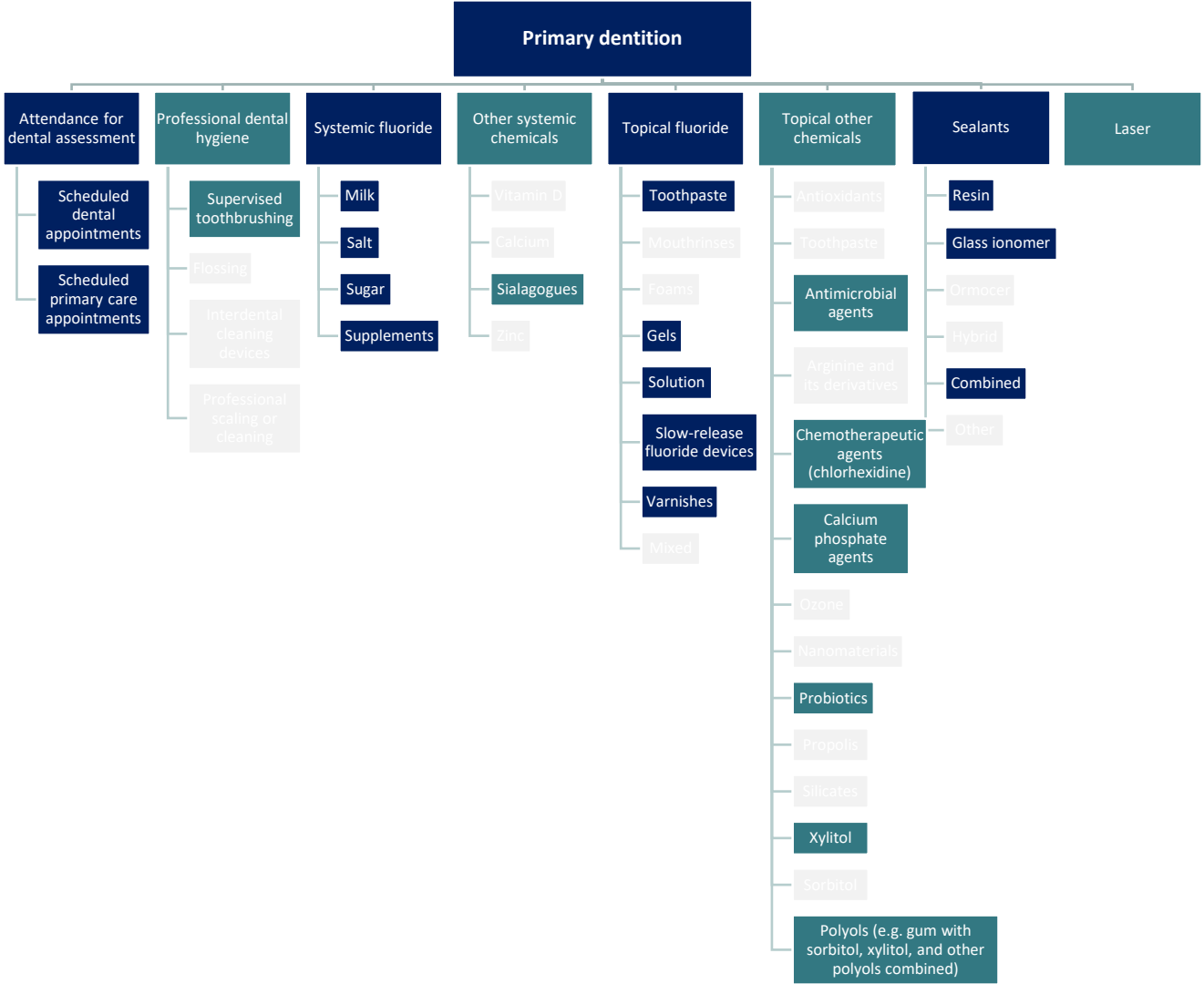
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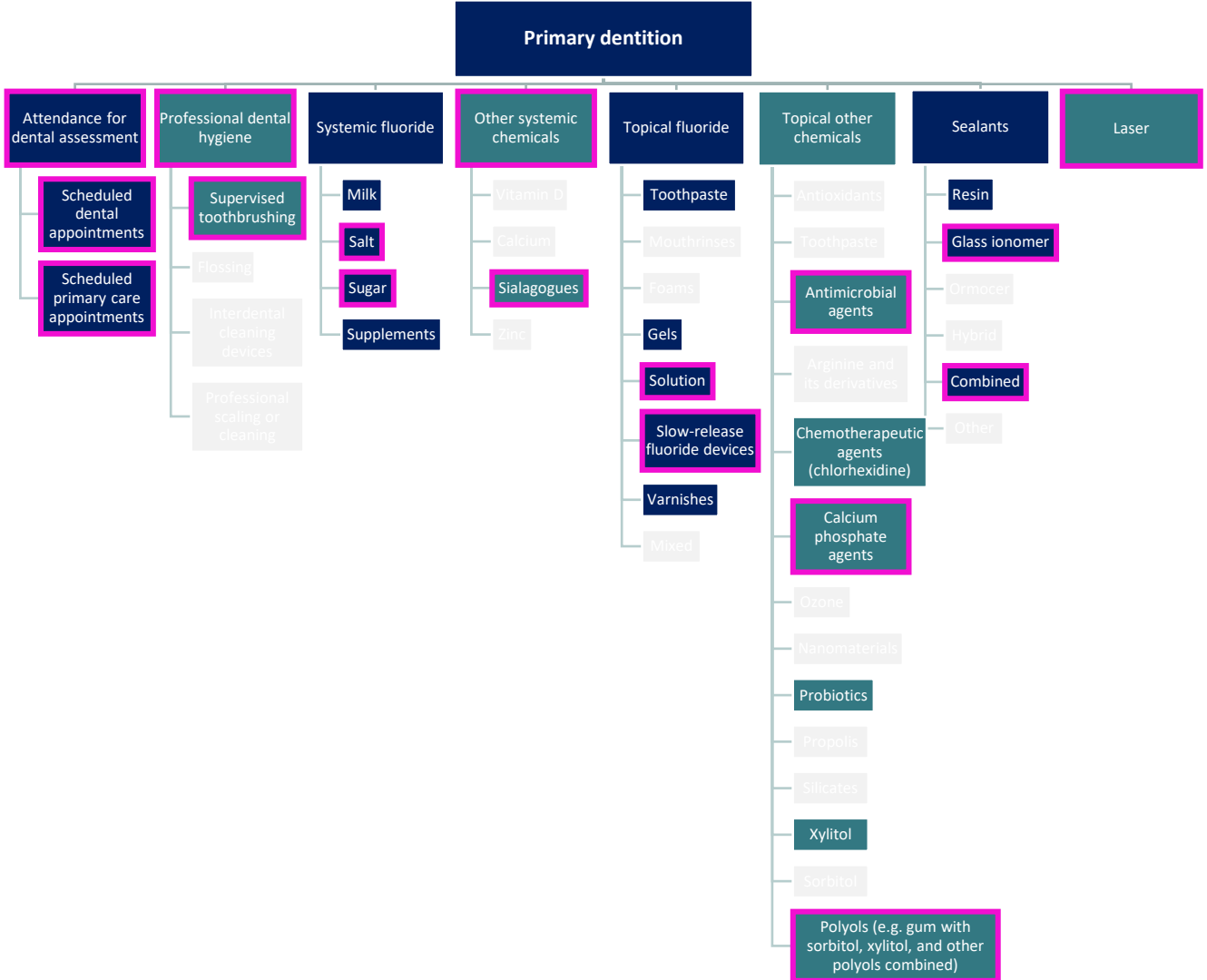
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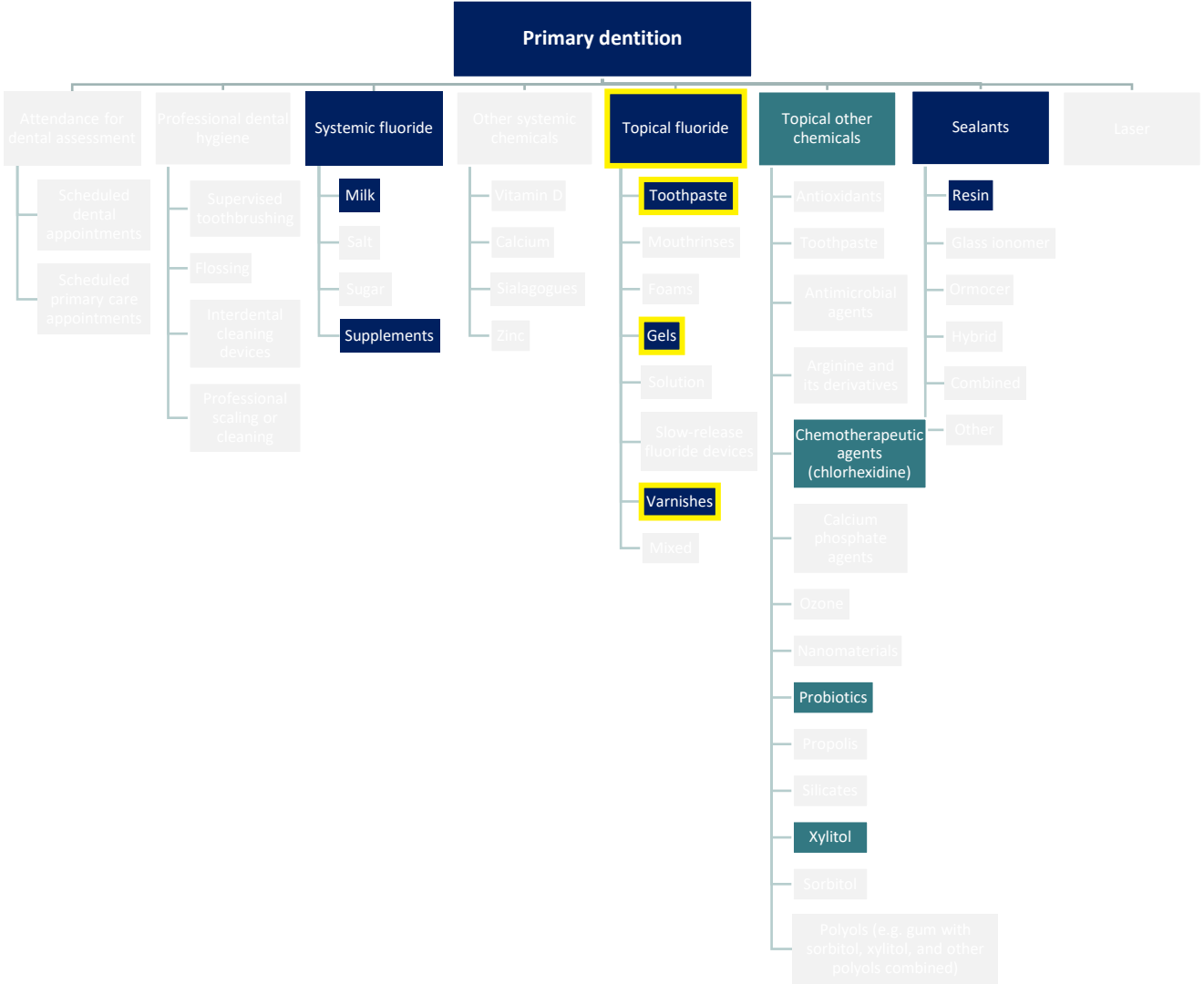
Systemic fluoride – milk

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Yeung *et al*. (2015)	180-200ml fluoridated milk per day (2.5mg fluoride per litre)	Non-fluoridated milk	**dmft**; significantly lower (1 trial)	3 years	Very low	
Cagetti *et al*. (2012)	200ml fluoridated milk per day (2.5mg fluoride per litre)	Control (unspecified)	**dmft**; significantly lower (1 trial)	21 months	Very low	
	150ml fluoridated milk (2.5mg fluoride per litre)	Standard milk	**dmfs**; significantly lower (1 trial)			
						No overlap

Systemic fluoride – supplements

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Zhou *et al.* (2019)	--	--	**Not usable**	--	--	
Tubert-Jeannin *et al.* (2011)	Fluoride tablets (1mg or 0.5mg NaF)	No tablets	**dmft**; divergent findings (2 trials, narrative summary)	2 years	Low	
	Fluoride tablets (0.5mg NaF)	No tablets	**dmfs**; significantly lower (1 trial)	2 years	Very low	
	Fluoride tablets (1mg or 0.25mg NaF)	Topical fluoride	**dmfs**; no difference (2 pooled trials)	3 years	Low	
Chou *et al.* (2021)	Supplements (unspecified)	No supplements	**dmft**; significantly lower (4 trials, narrative synthesis)	1-3 years	Very low	
	Fluoride drops/chews (0.25mg fluoride)	No drops/chews	**dmft**; significantly lower (1 trial)			
	Fluoride drops/chews (0.25mg fluoride)	No drops/chews	**dmfs**; significantly lower (same trial)			

dmfs: very high
dmft: high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Topical fluoride – toothpaste

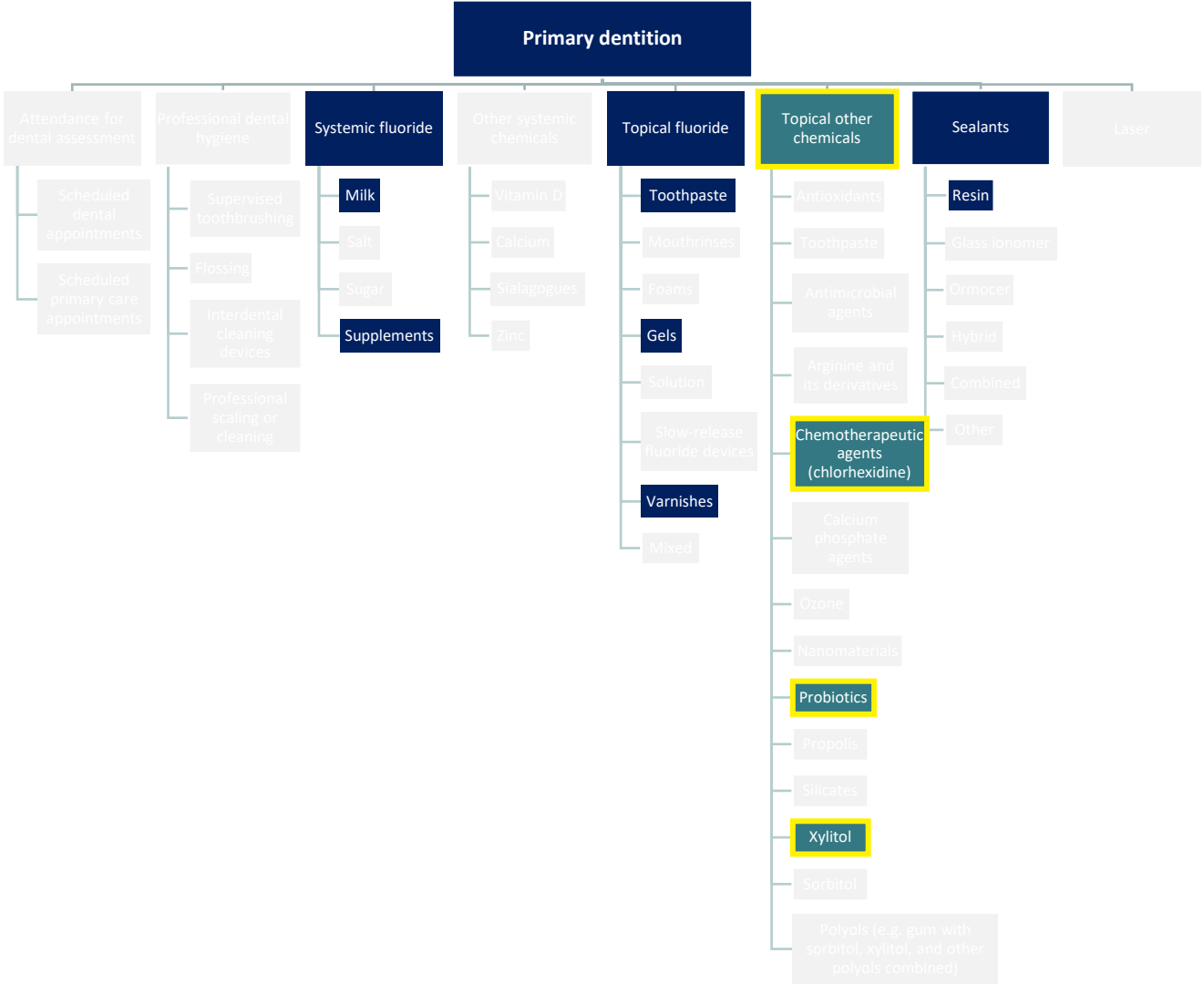
Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Walsh *et al*. (2019)	High fluoride toothpaste (1450 ppm)	Low fluoride toothpaste (440 ppm)	**% developing new caries**; significantly lower (1 trial)	5 years	Very low	
Santos *et al*. (2013)	High fluoride toothpaste (1000-1500 ppm)	Low fluoride toothpaste (<640 ppm)	**% developing new caries**; significantly lower (3 pooled trials)	2 years	Low	
						% developing new caries: very high

Topical fluoride – gel

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Marinho *et al*. (2015)	Fluoride gel (varied)	Placebo/no treatment	**d(e/m)fs**; significantly lower (3 pooled trials)	3 years	Low	
	Fluoride gel (APF 5000 ppm)	Placebo	**% not remaining caries free**; significantly lower (one of 3 pooled trials)	1.5 years	Very low	
						No overlap

Topical fluoride – varnish

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Smith *et al*. (2018)	**No trials**	--	--	--	--	
Marinho *et al*. (2013)	Fluoride varnish (varied)	No treatment or placebo varnish	**d(e/m)fs**; significantly lower (10 pooled trials)	3 years	Very low	
			d(e/m)ft; significantly lower (2 pooled trials)	3 years		
			% developing new caries; no difference (5 pooled trials)	Unspecified		
Carvalho *et al*. (2010)	Fluoride varnish (5% NaF or 1% Difluorsilano)	No treatment or oral health education	**dmfs**; significantly lower (5 trials, narrative synthesis)	2 years	Low	
	Fluoride varnish (5% NaF)	No treatment	**dmfs**; no difference (1 trial)	2 years	Very low	
						d(e/m)fs: high overlap d(e/m)ft: no overlap % new caries: no overlap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Sorbitol
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Sealants
Resin
Glass ionomer
Ormocer
Hybrid
Combined
Other
Laser

Topical other chemicals – chemotherapeutic agents

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Smith *et al*. (2018)	**No trials**	--	--	--	--	
Walsh *et al*. (2015)	Chlorhexidine varnish (1% or 40%)	No treatment/placebo varnish	**dmfs/t-molar**; no difference (3 pooled trials)	2 years	Low	
James *et al*. (2010)	Chlorhexidine varnish (40%)	Placebo varnish	**dmfs-molar**; significantly lower (1 trial)	2 years	Very low	
Rethman *et al*. (2011)	Chlorhexidine varnish (1%)	No treatment	**dft**; no difference (1 trial)	1.5 years	Very low	
Wang *et al*. (2017)	Chlorhexidine varnish or gel (1% or 40%)	No treatment/placebo varnish	**dmfs** (1 trial) **dmft** (1 trial) **dmfs-molar** (2 trials) **defs** (2 trials); significantly lower (4 trials, narrative summary)	2-3 years	Low	
						d(e/m)fs/t 1%: very high d(e/m)fs 40%: very high d(e/m)fs/t 1%: very high dmfs/t: 40% no overlap

Topical other chemicals – probiotics

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Hao *et al*. (2021)	Slow-release tablets/pacifiers containing Bifidobacterium (100g or 300g)	Placebo tablets/pacifiers	**Caries incidence**; no difference (1 trial)	2 years and 4 years	Very low	
Jorgensen *et al*. (2016)	Probiotic lozenges containing three Streptococcus-derived strains	Placebo lozenges	**ds**; significantly lower* (1 trial)	1 year	Very low	
Twetman and Jorgensen (2021)	Probiotics milk or tablets (Streptococcus/Lactobacillus/Bifidobacterium)	Placebo	**dmfs/t**; significantly lower (7 pooled trials)	6 months and 1 year	Low	
						Caries incidence: no overlap ds/dmfs/dmft: high

Topical other chemicals – xylitol

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Riley *et al*. (2015)	Xylitol syrup (8g/day)	Xylitol syrup (2.67g/day)	**No. decayed teeth**; significantly lower (1 trial)	1 year	Very low	
	Xylitol sucking tablets (0.48g-1g/day)	No sucking tablet	**dmfs (continuous)**; no difference (1 trial)	2 years		
	Xylitol tablets (200-600mg/day)	Placebo tablets	**dmfs (dichotomous)**; no difference (1 trial)	2 years		
	Xylitol wipes (4.2g/day)	Placebo wipes	**dmfs (dichotomous)**; no difference (1 trial)	1 year		
Chou *et al*. (2021)	Xylitol tablets (0.5mg/day)	No tablets	**dmfs**; no difference (1 trial)	2 years	Very low	
	Xylitol wipes (4.2g/day)	Placebo wipes	**dmfs & caries incidence**; no difference (1 trial)	1 year		
Rethman *et al*. (2011)	Xylitol syrup (8g/day)	Xylitol syrup (2.67g/day)	--	--	--	
Wang *et al*. (2017)	Xylitol wipes (4.2g/day)	No wipes	**dmfs**; no difference (1 trial)	2-2.5 years	Very low	
	Xylitol gummies (7.8g/day)	Placebo gummies	**dmfs**; no difference (1 trial)	2-2.5 years		
	Xylitol wipes (4.2g/day)	Placebo wipes	**% new caries**; significantly lower (1 trial)	1 year		
						No. decayed: none dmfs: very high Caries incidence/% new caries: complete


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Sealants – resin

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Ramamurthy *et al*. (2022)	Auto-polymerised resin-based sealant	Polymerised resin-based sealant	**Risk of developing ≥ 1 new carious lesions**; no difference (1 trial)	2-3 years	Very low	
Lam *et al*. (2020)	Resin-based sealant	Glass-ionomer based sealant or resin-modified glass-ionomer based sealant	**Caries incidence**; no difference (1 trial)	1.5 years	Very low	
	Resin-based sealant	Fluoride-containing resin-based sealant (F-RBS) or amorphous calcium phosphate-resin-based sealant (ACP-RBS)	**Caries incidence**; no difference (1 trial)	2 years		
	Auto-polymerised resin-based sealant	Light-curing resin-based sealant	**Caries incidence**; no difference (1 trial)	2 years		

Risk of new caries/caries incidence: very high

Summary

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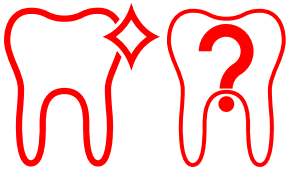
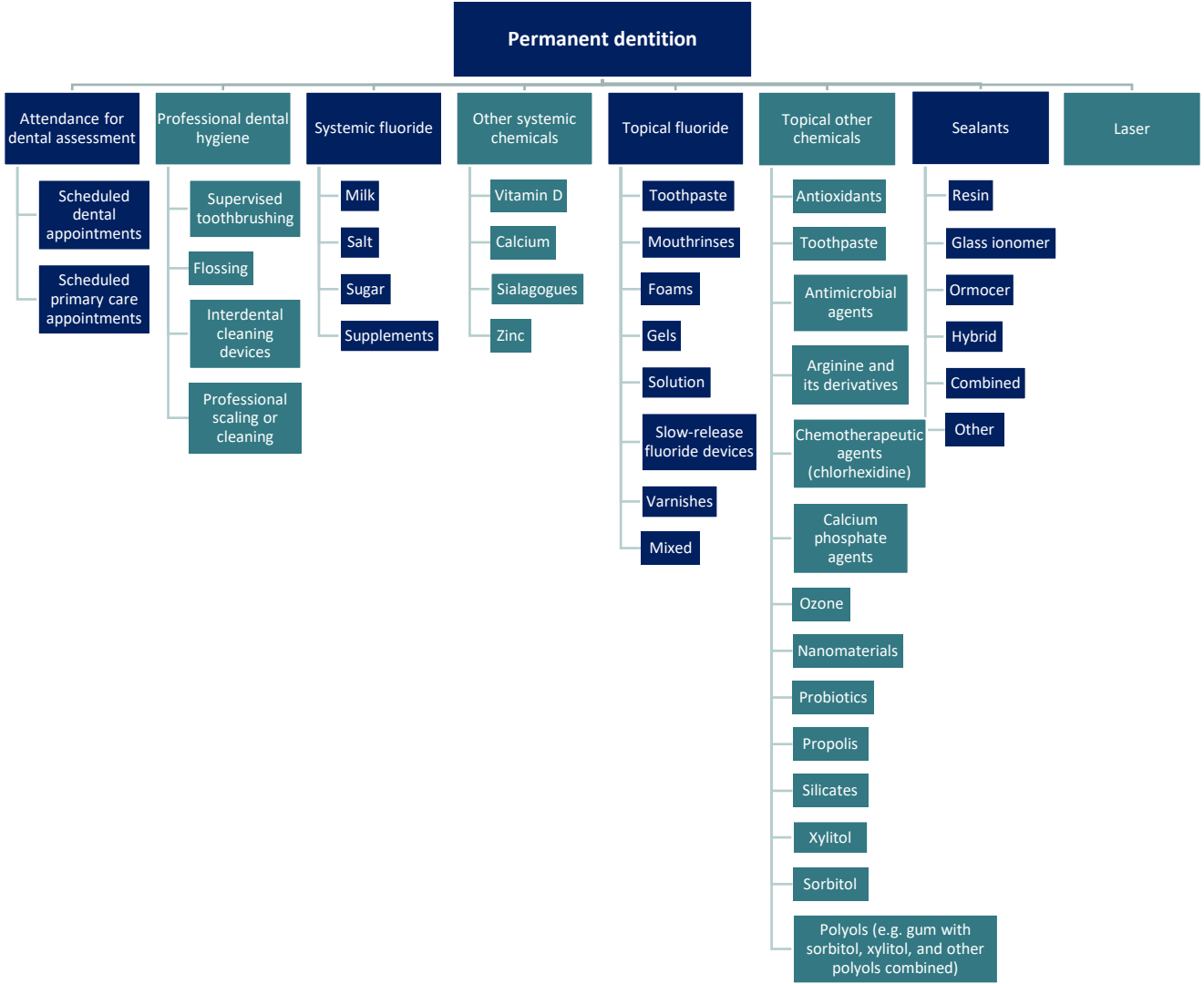
- F milk
- F supplements
- F toothpaste
- F gels
- Probiotics

- F varnish
- Chlorhexidine



- Xylitol
- Resin-based sealant

Permanent dentition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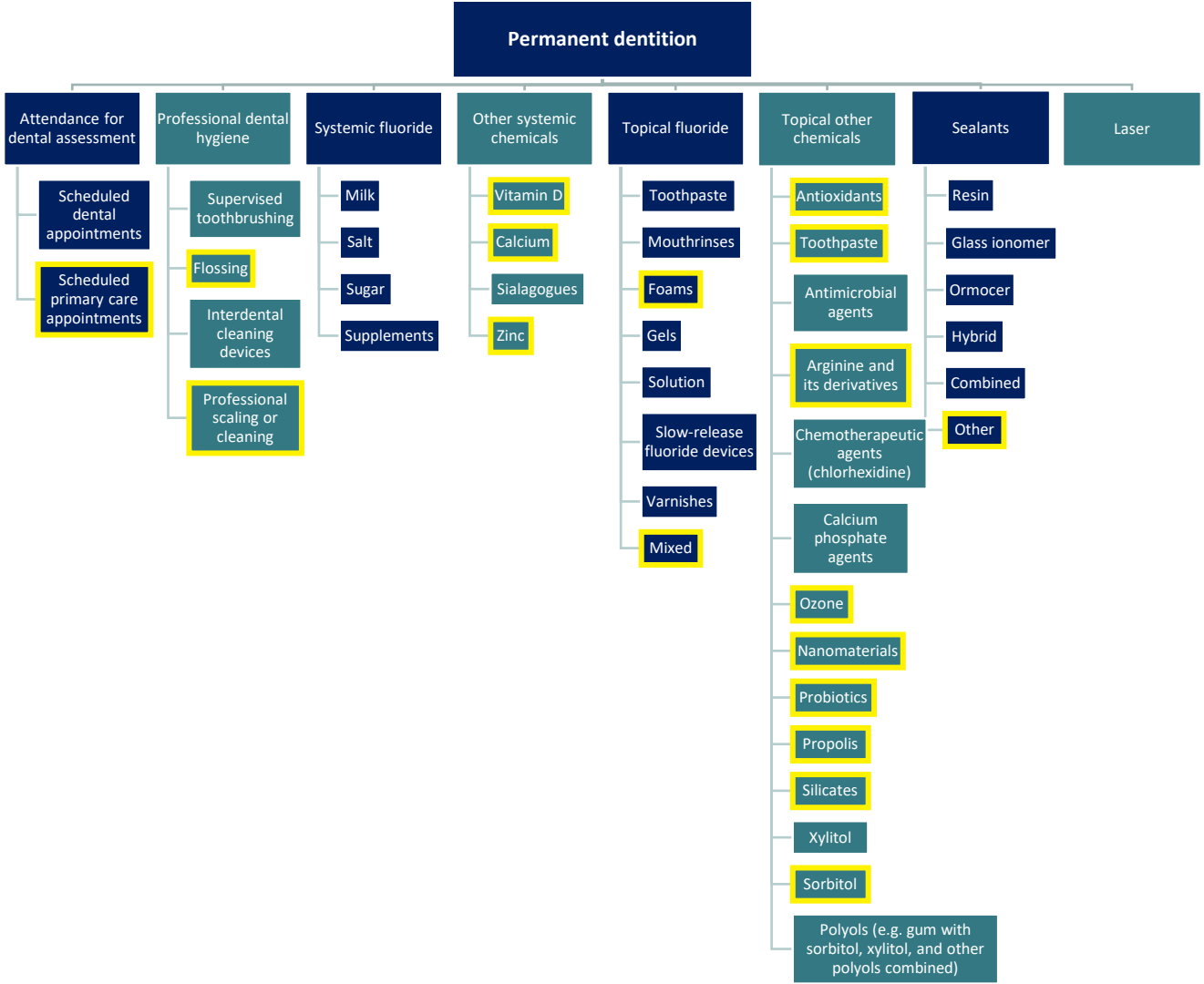
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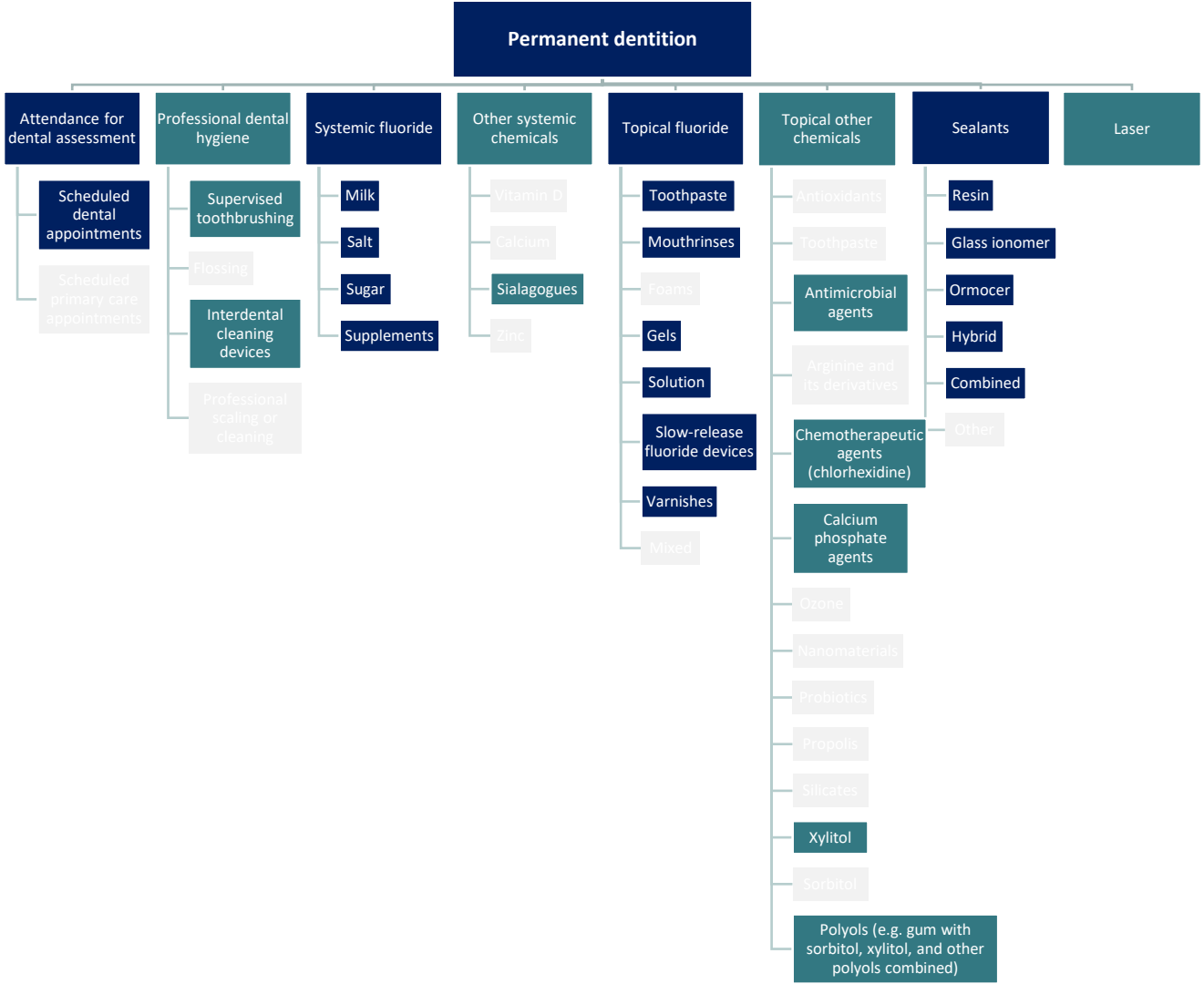
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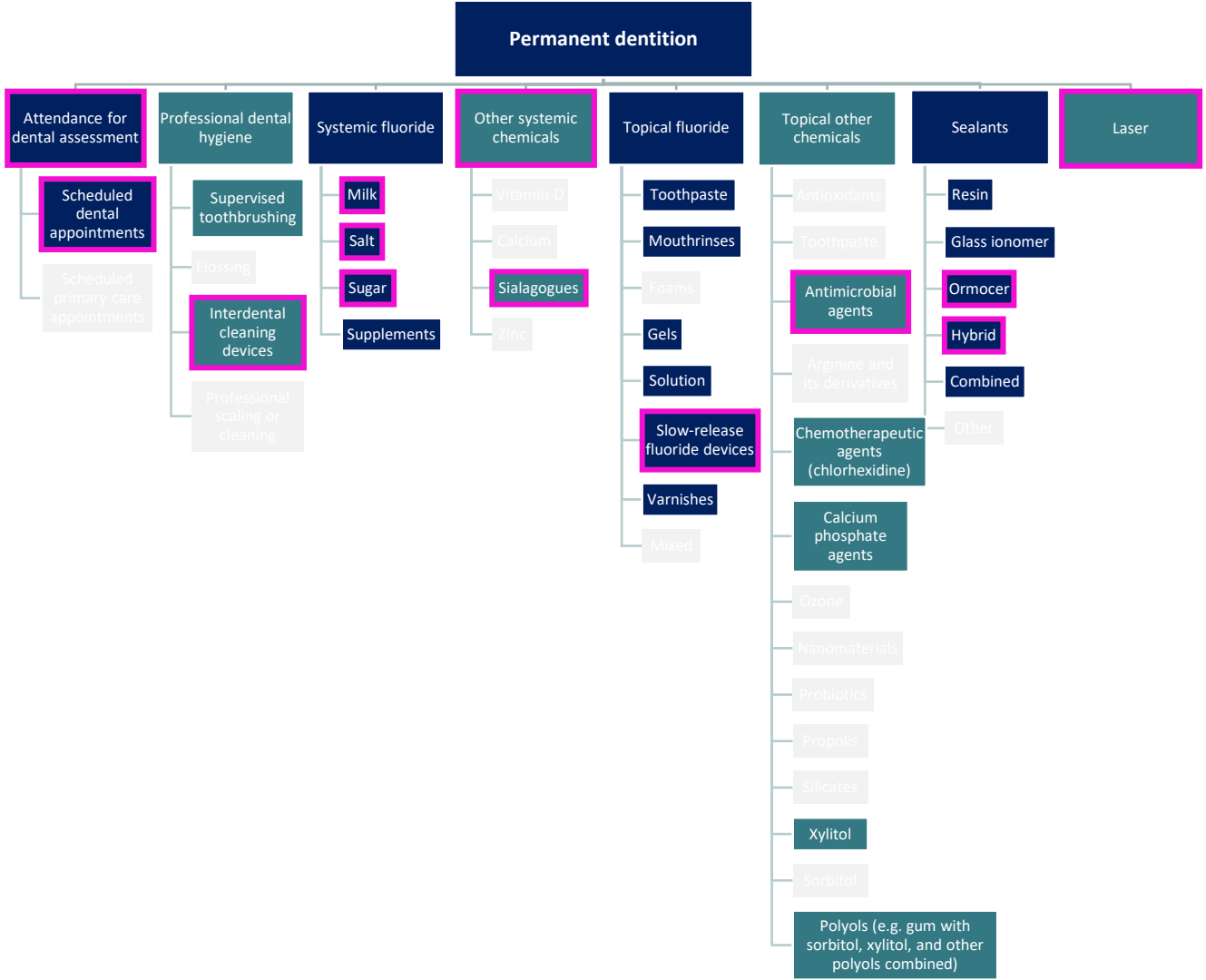
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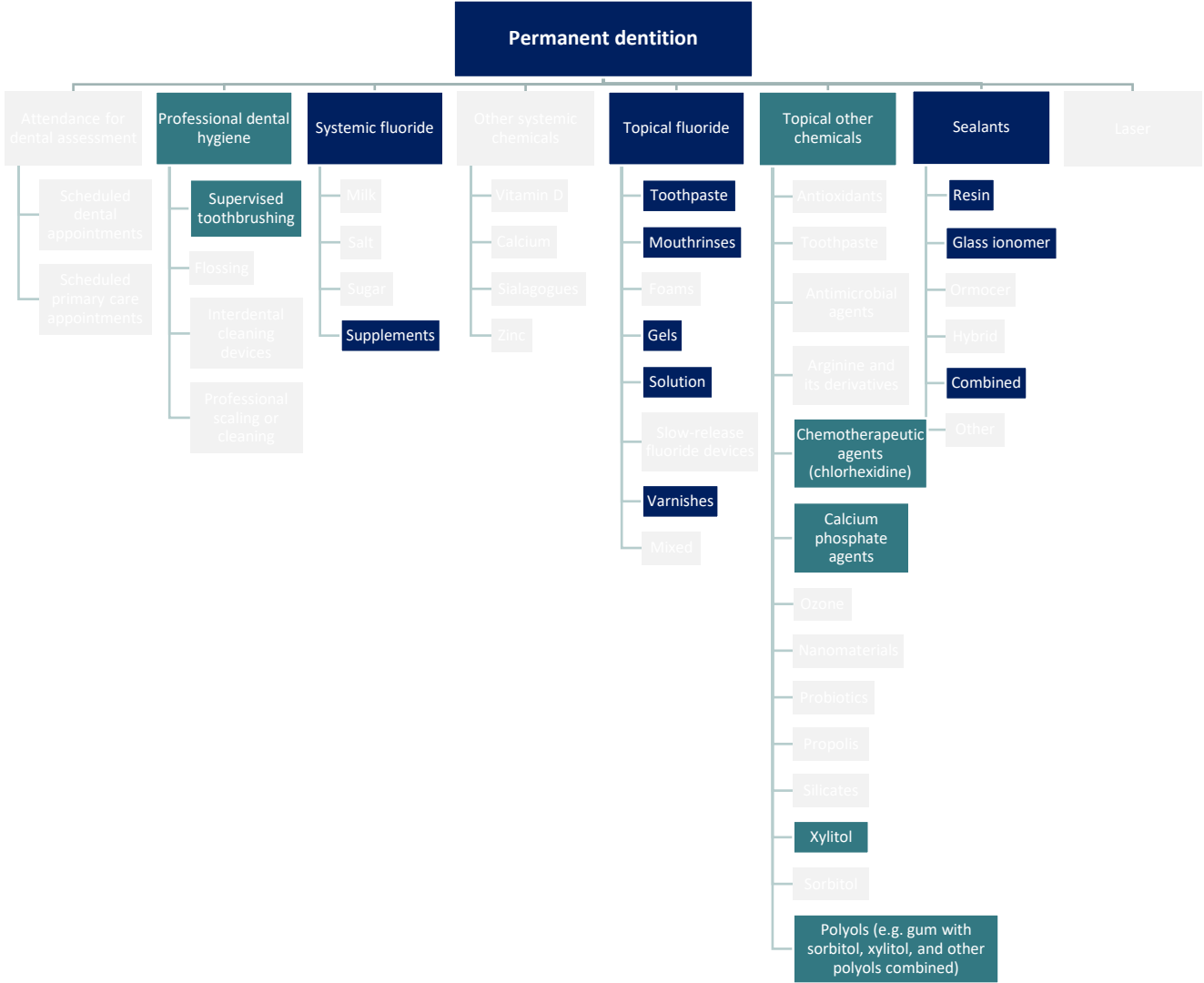
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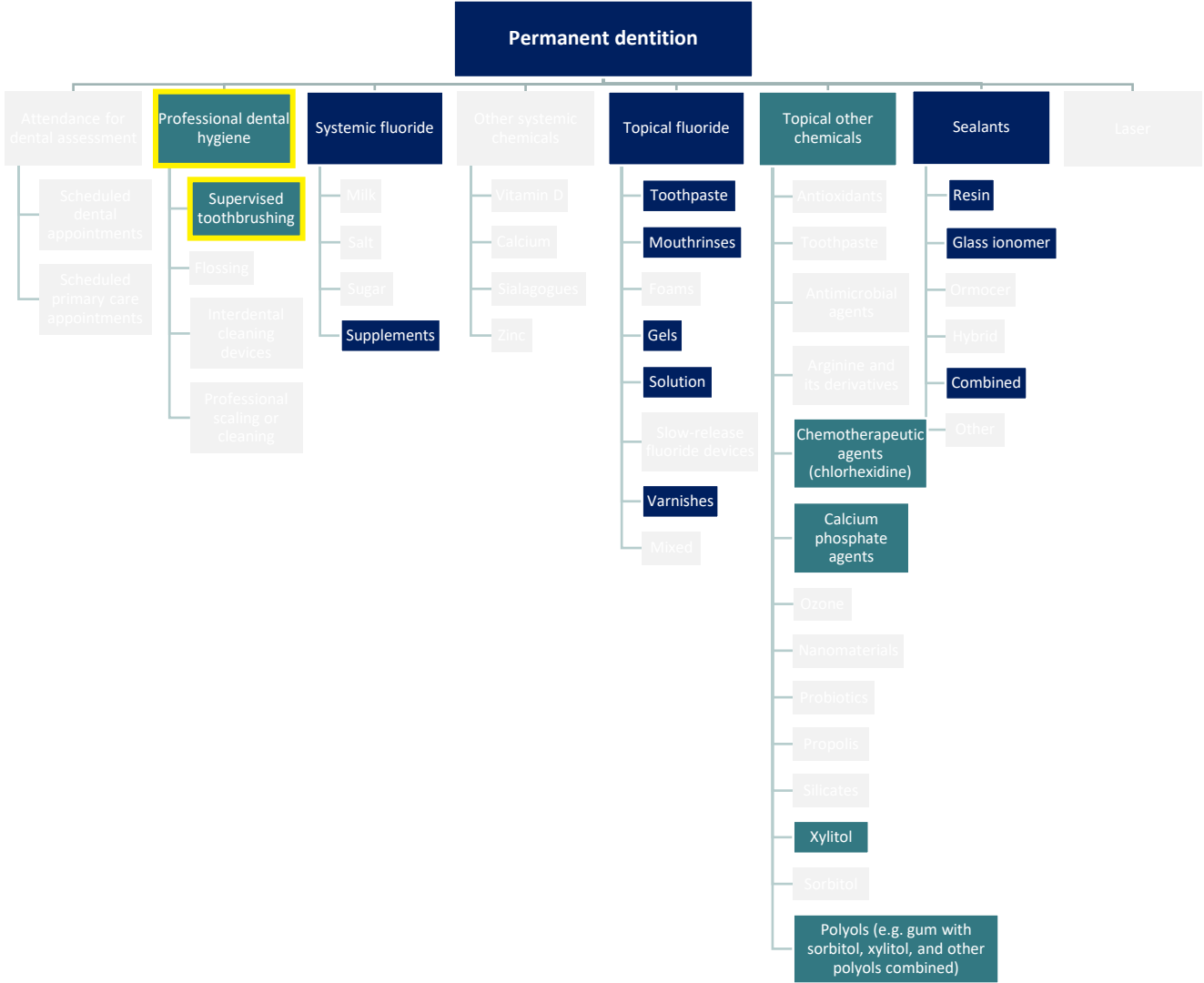
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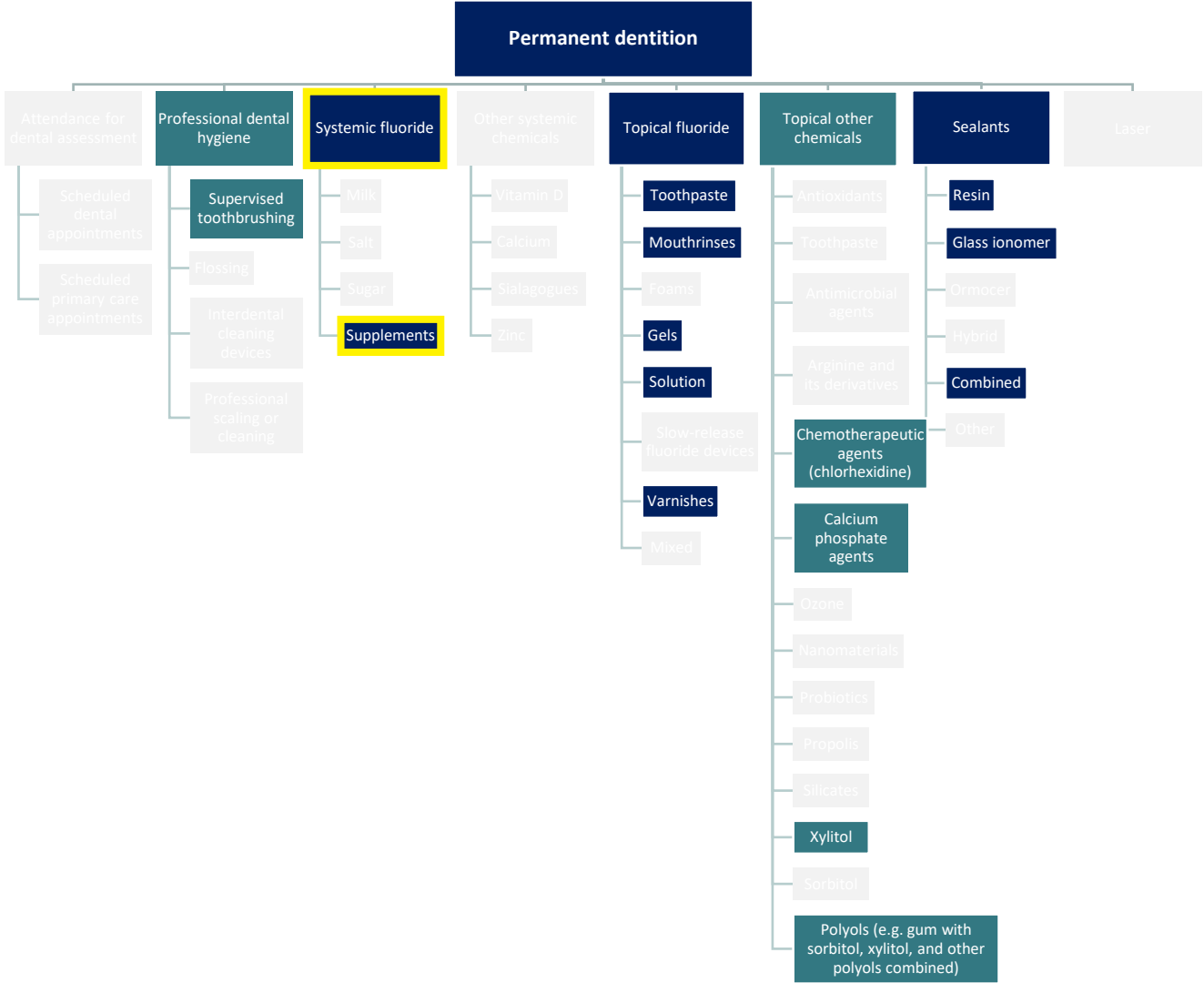
Supervised toothbrushing

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Hujoel *et al*. (2018)	Supervised toothbrushing (varied frequency), non-fluoride toothpaste	Control (unspecified)	**DMFS**; no difference (3 pooled trials)	2.5-3 years	Low	
Dos Santos *et al*. (2018)	Supervised toothbrushing (daily, school-based), non-fluoride toothpaste	No supervised toothbrushing	**DMFS**; no difference (1 trial) **DMFT**; no difference (same trial)	21 months	Very low	
						No overlap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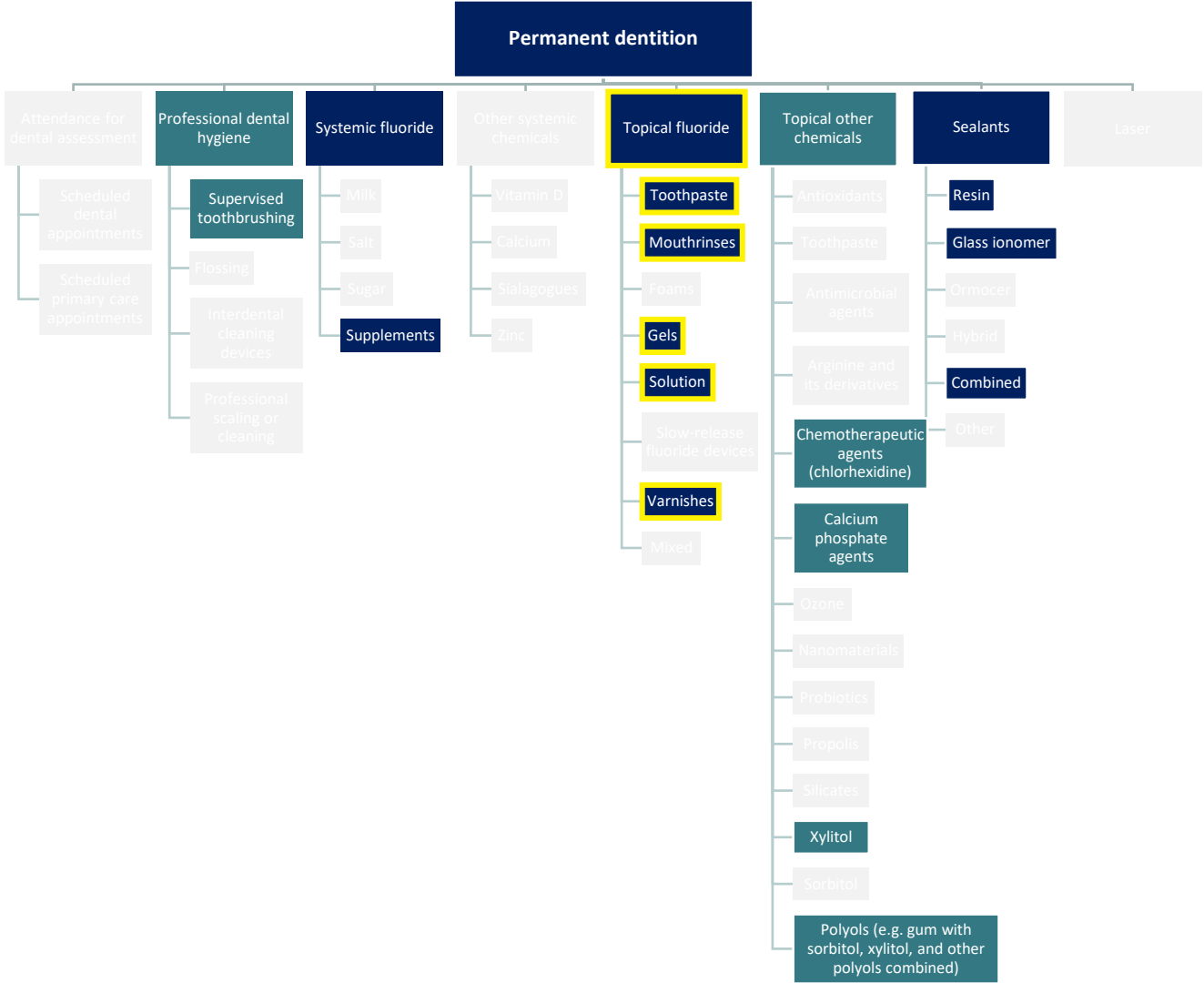
Systemic fluoride – supplements

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Zhou *et al.* (2019)	--	--	**Not usable**	--	--	
Tubert-Jeannin *et al.* (2011)	Fluoride tablets	No tablets	**DMFS**; significantly lower (3 pooled trials)	2-3 years	Low	
	Fluoride tablets	No tablets	**DMFT**; significantly lower (3 pooled trials)	2-3 years		
	Fluoride supplements (tablets and lozenges)	Fluoride mouthrinse	**DMFS**; no difference (4 pooled trials)	2-3 years		
						No overlap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Topical fluoride – toothpaste

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Walsh *et al*. (2019)	Low fluoride (250 ppm fluoride)	Non-fluoride toothpaste	**% developing new caries (immature dentition)**; no difference (2 pooled trials)	2 years	Low	
	High fluoride (1000-1250)	Non-fluoride toothpaste	**% developing new caries (immature dentition)**; no difference (7 pooled trials)	1-5 years	Low	
	High fluoride (1450-1500)	Non-fluoride toothpaste	**% developing new caries (immature dentition)**; significantly lower (1 trial)	3 years	Very low	
Zhang *et al*. (2020)	Fluoride toothpaste (1100-1500 ppm fluoride)	Control (unspecified)	**D-Root and DF-Root**; significant difference (network meta-analysis of 9 trials)	2 years	Very low	
						No overlap

Topical fluoride – mouthrinse

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Zhang *et al*. (2020)	Fluoride mouthrinse (0.05% NaF) Fluoride mouthrinse (0.2% NaF)	Control (unspecified)	**D-Root and DF-Root**; no difference (network meta-analysis of 9 trials) **D-Root and DF-Root**; significantly lower (network meta-analysis of 9 trials)	2 years	Very low	
Weirichs *et al*. (2015)	Fluoride mouthrinse (NaF, 225-900 ppm fluoride)	Placebo mouthrinse	**DMFS-root (DMFRS)**; significantly lower (4 pooled trials)	2-3 years	Very low	
						D-Root / DF-Root / DMFRS: very high

Topical fluoride – gel

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Marinho *et al*. (2015)	Fluoride gel (varied)	Placebo gel/no gel	**DMFS**; significantly lower (25 pooled trials)	3 years	Low	
	Fluoride gel (2 groups; SnF2 2425 ppm fluoride and NaF 4500 ppm fluoride)	Placebo gel	**% developing ≥ or more new caries in tooth surfaces**; significantly lower (1 of 25 pooled trials)	1.5 and 3 years	Very low	
	Fluoride gel (2 groups; SnF2 2425 ppm fluoride and NaF 4500 ppm fluoride)	Placebo gel	**Change in % not remaining caries free on tooth surfaces**; significantly lower (same trial as above)	3 years	Very low	
	Fluoride gel (varied)	Placebo gel/no gel	**DMFT**; significantly lower (10 pooled trials)	3 years	Low	
Zhang *et al*. (2022)	Fluoride gel (1.2% APF)	Control (unspecified)	**D-Root and DF-Root**; significantly lower (network meta-analysis of 9 trials)	2 years	Very low	
Chan *et al*. (2022)	Fluoride gel (1.23% APF)	Placebo gel	**Root caries incidence**; significant lower (1 trial)	2 years	Very low	

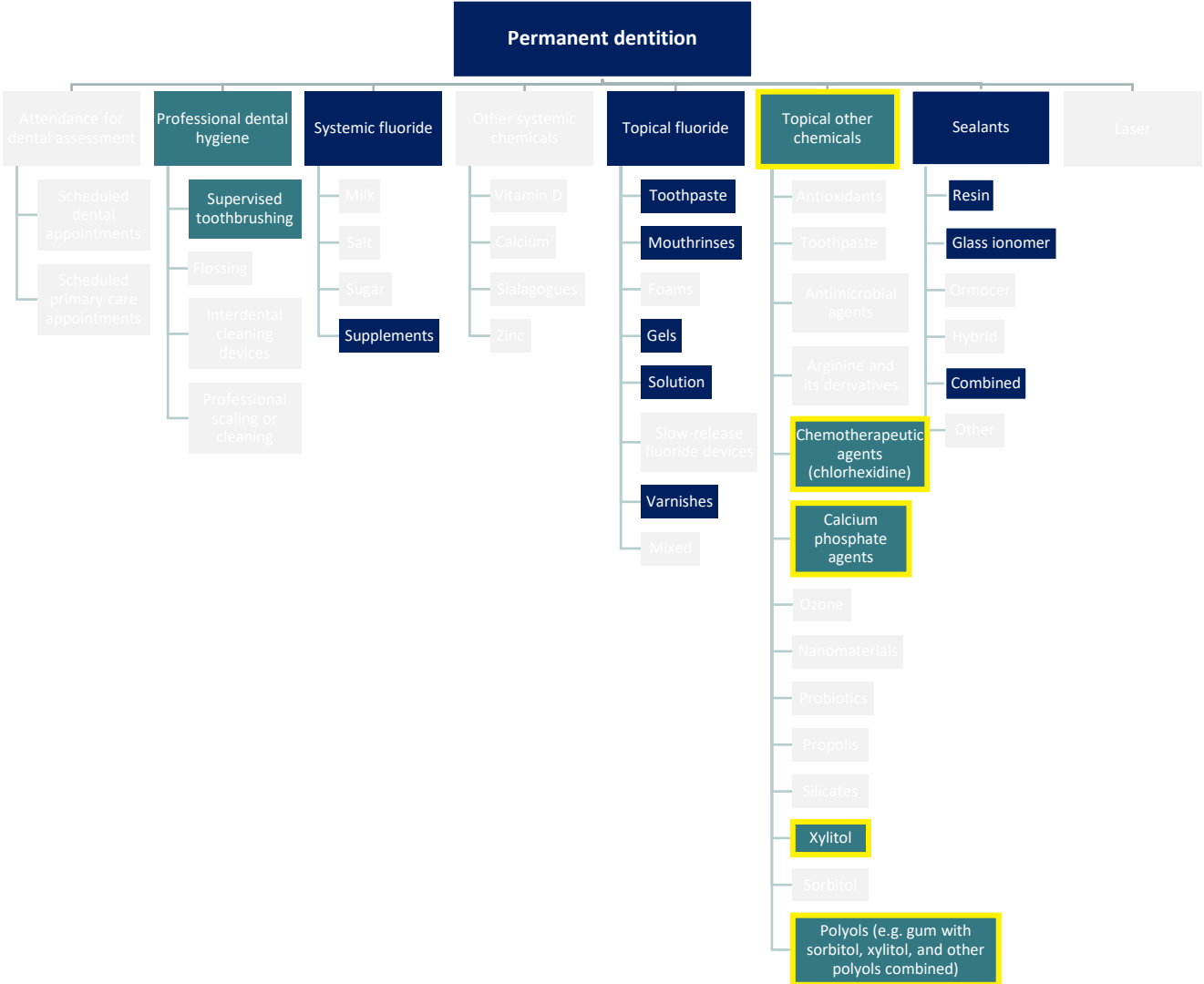
No overlap

Topical fluoride – solution

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Grandjean *et al*. (2021)	Silver diamine fluoride (concentration not reported)	Control (unspecified)	**Mean no. new root carious surfaces**; significantly lower (3 pooled trials)	2 years	Low	
Zhang *et al*. (2020)	Silver diamine fluoride (38%, professional application)	Control (unspecified)	**D-Root and DF-Root**; significantly lower (network meta-analysis of 9 trials)	2 years	Very low	
Subbiah and Gopinathan (2018)	Silver diamine fluoride (38%)	Control (unspecified), chlorhexidine, and fluoride varnish	**DMFS-root (DMFRS)**; significantly lower (1 trial)	3 years	Very low	
	Silver diamine fluoride (38%)	Control (unspecified)	**DMFS-root (DMFRS)**; significantly lower (1 trial)	2 years	Very low	
Chan *et al*. (2022)	Silver diamine fluoride (38%)	Control (unspecified)	**Mean no. new root carious lesions**; significantly lower (3 pooled trials)	2 years	Low	
						Mean no. new root caries: complete overlap D-Root / DF-Root / DMFRS: high

Topical fluoride – varnish

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Marinho *et al*. (2013)	Fluoride varnish (varied)	Placebo varnish/no treatment	**DMFS**; significantly lower (13 pooled trials)	3 years	Very low	
			DMFT; significantly lower (5 pooled trials)	3 years		
			% new caries; no difference (5 pooled trials)	Not specified		
Zhang *et al*. (2020)	Fluoride varnish (5% NaF)	Control (unspecified)	**D-Root and DF-Root**; significantly lower (network meta-analysis of 9 trials)	2 years	Very low	
Wierichs *et al*. (2015)	Fluoride varnish (38% silver diamine fluoride)	Placebo varnish	**DMFS-Root (DMFRS)**; significantly lower (2 pooled trials)	2 years	Very low	
Chan *et al*. (2022)	Fluoride varnish (5% NaF)	No treatment	**No. teeth with coronal caries**; significantly lower (1 trial)	1 year	Very low	
		Water	**Root caries incidence**; significantly lower (1 trial)	3 years		
						None, D-Root / DF-Root / DMFRS: very high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Topical other chemicals – chemotherapeutic agents

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Walsh *et al*. (2015)	Chlorhexidine varnish (10% or 40%)	No treatment/placebo product	**DMFS**; no difference (2 pooled trials)	2.5-3 years	Low	
Wierichs *et al*. (2015)	Chlorhexidine varnish (1% or 10%)	Placebo varnish	**DMFS-Root (DMFRS)**; significantly lower (3 pooled trials)	1-3 years	Very low	
James *et al*. (2010)	Chlorhexidine varnish (1%, 10% or 40%)	Placebo varnish, control (unspecified) or fluoride varnish	**DMFS**; divergent findings (11 trials, narrative synthesis)	2-3 years	Very low	
Rethman *et al*. (2011)	Chlorhexidine varnish	Placebo varnish	**RCI**; significantly lower (1 trial)	1 year	Very low	
	Chlorhexidine mouthrinse (0.12% or 0.05%)	Placebo mouthrinse or control (unspecified)	**DMFS and incidence rate**; no difference (4 pooled trials)	2-5 years		
	Chlorhexidine gel (1%)	Placebo gel	**D(E)FS**; divergent findings (4 trials, narrative summary)	1-3 years		
						No overlap

Topical other chemicals – calcium phosphate agents

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Rethman *et al*. (2011)	Casein derivative with calcium phosphate containing mouthrinse	0.05% NaF mouthrinse	**DFS**; no difference (1 trial)	1 year	Very low	
	Casein phosphopeptide toothpaste	Fluoride toothpaste	**DFS**; no difference (1 trial)			
Singal *et al*. (2022)	CPP-ACP cream	No treatment or 5% fluoride varnish	**DMFT**; significantly lower (1 trial)	1 year	Very low	
						No overlap

Topical other chemicals – xylitol

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Riggs et al. (2019)	**No trials**	--	--	--	--	
Riley *et al*. (2015)	Xylitol lozenges (5g/day or 4.7g/day)	Control lozenges or no treatment	**DMFS**; no difference (2 trials, narrative synthesis)	3-4 years	Very low	
Rethman *et al*. (2011)	Xylitol candies (2.5g/day)	Conventional care (including preventive varnish)	**DMFS**; no difference (1 trial)	2 years	Very low	
Antonio *et al*. (2011)	42.2% Xylitol lozenges	Oral health education + application of fluoride varnish	**DMFS scores and 2-year incidence of proximal enamel carious lesions**; no difference (1 trial)	2 years	Very low	

DMFS: very high

Topical other chemicals – polyols

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Rethman *et al*. (2011)	Sucrose-free polyol chewing gum	No gum	**DMFS**; significantly lower (9 pooled trials); no difference when non-randomised trials removed	2-3.5 years	Very low	
Antonio *et al*. (2011)	49% xylitol/maltitol and 49% xylitol/polydextrose candy	Control (unspecified)	**DMFS**; lowest 3-year increment* (1 trial)	3 years	Very low	
						DMFS: very high


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Supervised toothbrushing
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Professional scaling or cleaning
Systemic fluoride
Milk
Salt
Sugar
Supplements
Other systemic chemicals
Vitamin D
Calcium
Sialagogues
Zinc
Topical fluoride
Toothpaste
Mouthrinses
Foams
Gels
Solution
Slow-release fluoride devices
Varnishes
Mixed
Topical other chemicals
Antioxidants
Toothpaste
Antimicrobial agents
Arginine and its derivatives
Chemotherapeutic agents (chlorhexidine)
Calcium phosphate agents
Ozone
Nanomaterials
Probiotics
Propolis
Silicates
Xylitol
Sorbitol
Polyols (e.g. gum with sorbitol, xylitol, and other polyols combined)
Sealants
Resin
Glass ionomer
Ormocer
Hybrid
Combined
Other
Laser

Sealants – resin

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Four reviews	--	--	**Not usable**	--	--	
Alsabek *et al*. (2021)	Hydrophilic resin-based sealant	Resin-based sealant	**Caries incidence**; no difference (5 pooled trials)	1 year	Low	
Rashed *et al*. (2022)	Resin-based sealant	Fluoride varnish	**Caries incidence**; no difference (3 pooled trials) **DMFS**; no difference (2 pooled trials)	2 years	Low	
Kashbour *et al*. (2020)	Resin-based sealant	Fluoride varnish	**New carious lesions**; no difference (4 pooled trials)	2-3 years	Low	
Ahovuo-Saloranta *et al*. (2017)	Second-, third-, and fourth-generation resin-based sealants	No sealant	**New carious lesions**; significantly lower (7 pooled trials)	2 years	Moderate	
	Auto-polymerised resin-based sealants	Control (unspecified)	**DFS**; significantly lower (1 trial)		Very low	
CADTH (2016)	Resin-based sealant	No sealant	**New carious lesions**; significantly lower (1 trial)	1 year	Very low	
Li *et al*. (2020)	Resin-based sealant	Fluoride varnish	**Caries incidence**; no difference (2 pooled trials)	2-3 years	Very low	
						Caries incidence/new carious lesions: slight DFS/DMFS: very high

Sealants – glass-ionomer

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Kashbour *et al*. (2020)	Glass-ionomer sealant	Fluoride varnish	**New carious lesions**; "no overall difference" (3 trials, narrative synthesis)*	3 years	Low	
Ahovuo-Saloranta *et al*. (2017)	Glass-ionomer sealant	No sealant	**DFS**; no difference (1 trial)	2 years	Very low	
	Glass-ionomer sealant	Resin-based sealant	**Caries incidence**; no difference (6 pooled trials)	1 year	Moderate	
	Low-viscosity glass-ionomer sealant	Resin-based sealant	**Caries incidence**; no difference (10 pooled trials)	2 years	Moderate	
	High-viscosity glass-ionomer sealant	Resin-based sealant	**Caries incidence**; no difference (2 pooled trials)	2 years	Moderate	
	Resin-modified glass-ionomer sealant	Resin-based sealant	**Caries incidence**; significant favouring the comparator (2 pooled trials)	2 years	Moderate	
	Glass-ionomer sealant	Resin-based sealant	**Caries incidence**; significant favouring the comparator (5 trials, narrative synthesis)	3-4 years	Moderate	
	Low-viscosity glass-ionomer sealant	Resin-based sealant	**Caries incidence**; no difference (2 trials, narrative synthesis)	3-4 years	Moderate	
	Low-viscosity glass-ionomer sealant	Second-generation resin-based sealant	**Caries incidence**; significantly lower (1 trial)	4 years	Very low	
	ART high-viscosity glass-ionomer sealant	Resin-composite sealant	**Cumulative survival rate**; significantly higher (1 trial)	4 years	Very low	

Sealants – glass-ionomer cont'd

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Wright *et al*. (2016)	Glass-ionomer sealant	Resin-based sealant	**Presence of new caries lesions**; no difference (9 pooled trials)	2-3 years	Very low	
	Glass-ionomer sealant	Resin-modified glass-ionomer sealant	**Presence of new caries lesions**; no difference (1 trial)			
	Glass-ionomer sealant	Polyacid-modified resin sealant	**Presence of new caries lesions**; no difference (1 trial)			
CADTH (2016)	ART glass-ionomer cement	Supervised toothbrushing	**Caries incidence**; no difference (1 trial)	3 years	Very low	
						Caries incidence: moderate DFS: no overlap

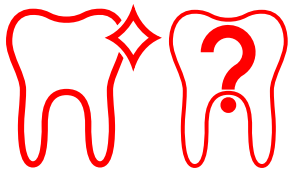
Sealants – combined

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Wright *et al*. (2016)	Sealant	No sealant	**No. new caries lesions**; significantly lower (6 pooled trials)	2-3 years	Very low	
		Fluoride varnish	**No. new caries lesions**; significantly lower (2 pooled trials)			
CADTH (2016)	Sealant	No sealant	**Caries prevention***; no effect (1 trial)	1 year	Very low	
Akera *et al*. (2022)	Sealant	No sealant	**DMFT**; significantly lower (1 trial)	7 years	Very low	
Li *et al*. (2020)	Sealant	Fluoride varnish	**Caries incidence and DMFS**; no difference (6 pooled trials)	2-3 years	Very low	
			DMFS; no difference (3 pooled trials)	2 years		
						No. new caries/caries incidence: slight DMFS: no overlap DMFT: no overlap

Summary

- F supplements
- F mouthrinse
- F gels
- F solution
- Polyols

- F toothpaste
- F varnish
- CHX
- Calcium phosphate
- Resin
- Glass-ionomer
- Sealants (combined)



- Supervised brushing
- Xylitol

Evidence gaps

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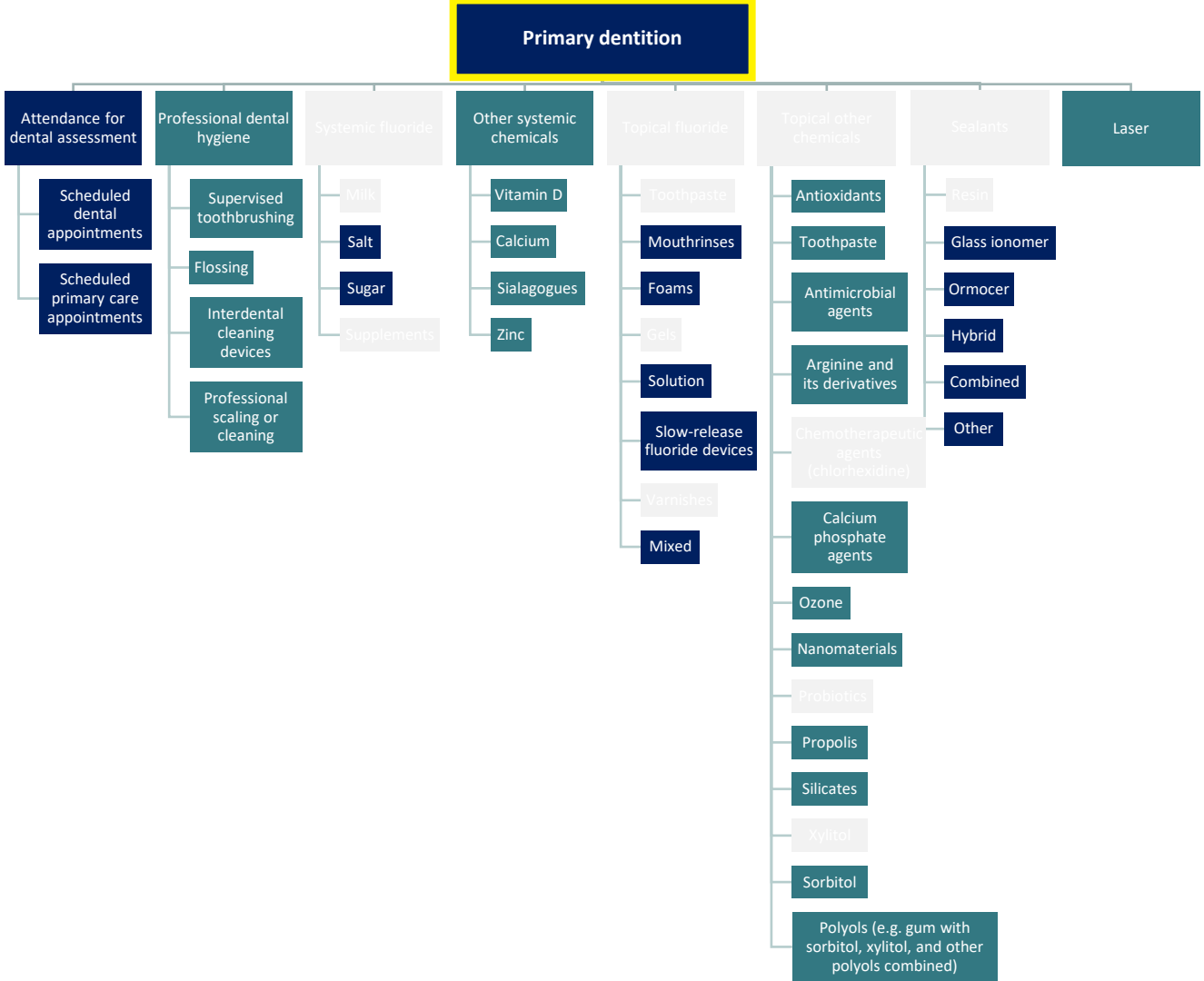
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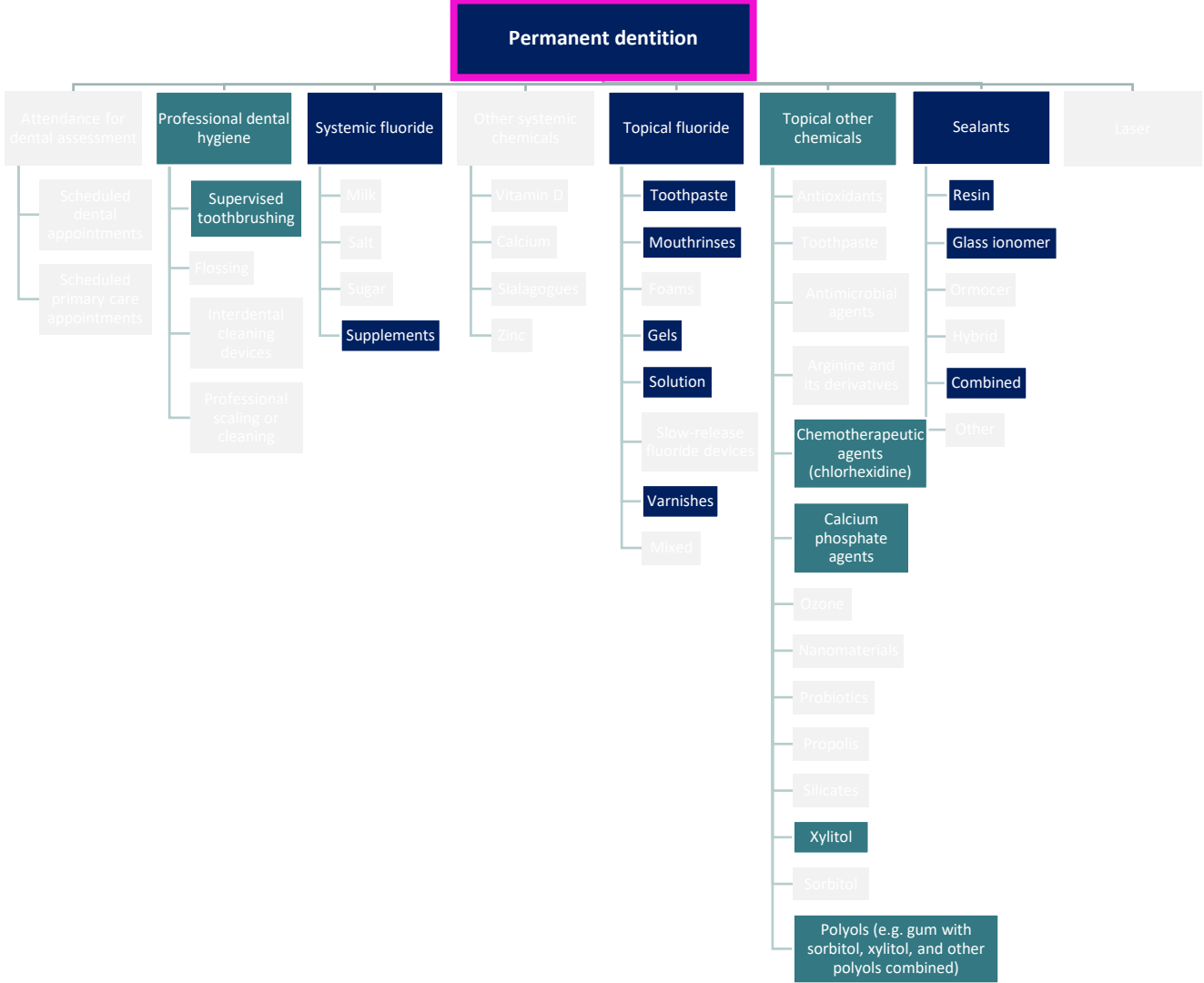
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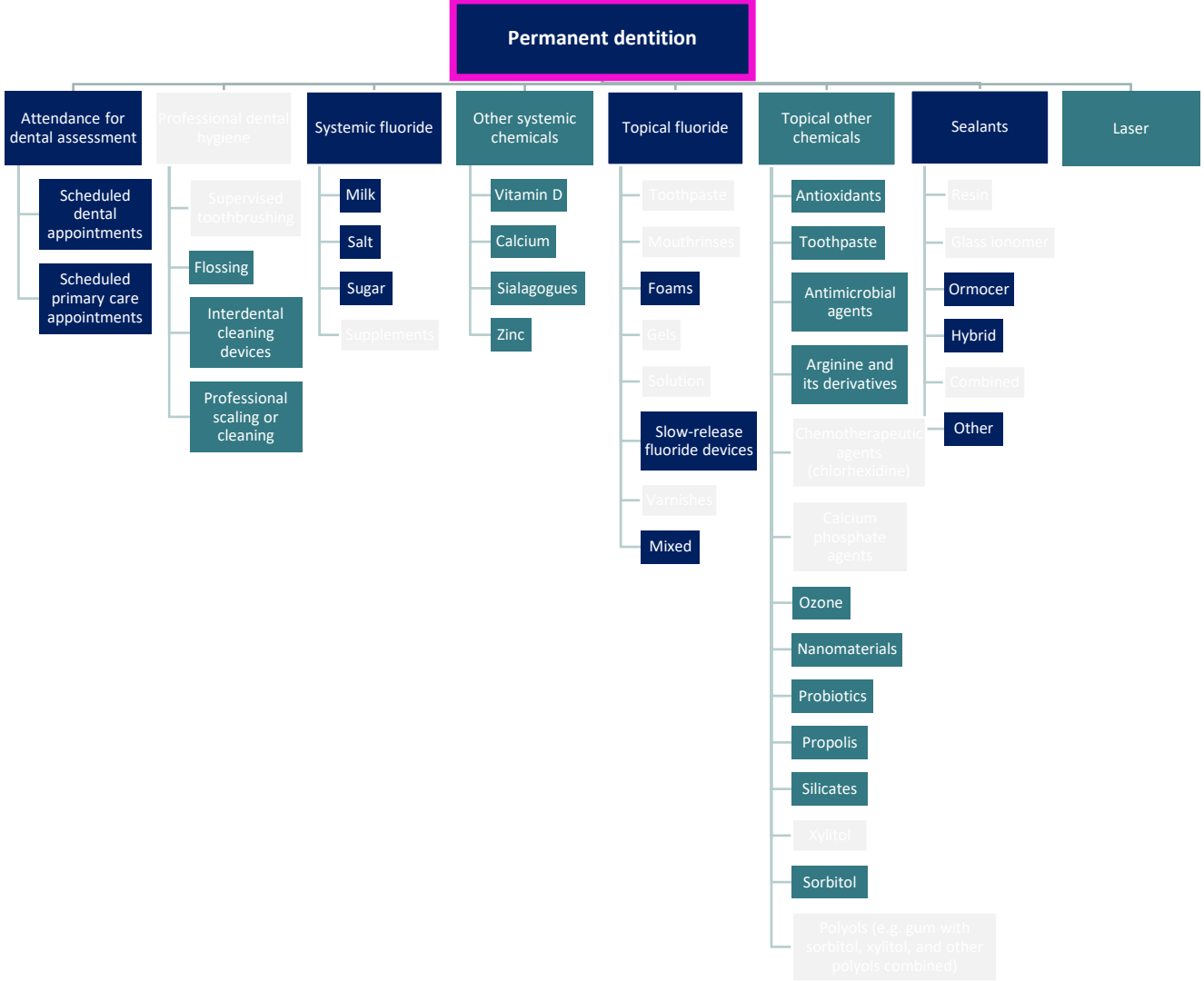
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Things to consider

Quantity of evidence

- 68 systematic reviews
  - 68 single trial outcomes
    - 14 outcomes informed by only 2 trials

- Just in primary and permanent dentition
  - Mixed dentition
  - Combined interventions

Certainty of evidence

GRADE	No. reviews
High	0
Moderate	8
Low	31
Very low*	29

Reporting of reporting

Topical other chemicals – xylitol

Review	Intervention	Comparator	Outcome measure(s)	Follow-up	Certainty of evidence	Overlap of primary studies
Chou *et al*. (2021)	Xylitol tablets (0.5mg/day)	No tablets	**dmfs**; no difference (1 trial)	2 years	Very low	
	Xylitol wipes (4.2g/day)	Placebo wipes	**dmfs & caries incidence**; no difference (1 trial)	1 year		
Wang *et al*. (2017)	Xylitol wipes (4.2g/day)	No wipes	**dmfs**; no difference (1 trial)	2-2.5 years	Very low	
	Xylitol gummies (7.8g/day)	Placebo gummies	**dmfs**; no difference (1 trial)	2-2.5 years		
	Xylitol wipes (4.2g/day)	Placebo wipes	**% new caries**; significantly lower (1 trial)*	1 year		

Conclusions

Conclusions

- More methodologically sound reviews are required
- Reporting standards vary widely and impact the validity of the findings
- Very low certainty evidence → clinical practice
- Best evidence for fluoride-based interventions
- Lots of evidence gaps

Primary prevention of dental caries

An overview of reviews

Lisa Murphy, Louise Farragher, Kayleigh Clements, Annette Burns, Mary Archibald, and Jean Long

Health Research Board

Research. Evidence. Action.