



University of Dundee

Comparator choice in cariology trials limits conclusions on the comparative effectiveness of caries interventions

Schwendicke, Falk; Innes, Nicola; Levey, Colin; Lamont, Thomas; Göstemeyer, Gerd

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Appendix Table 1: Classification of comparators.

Invasiveness (Level 1)	Approach (Level 2)	Technique/Material (Level 3)	Definition	Interventions
NI (Non-Invasive): comparators without any operative (surface- modifying or breaching) component	NI_B (Biofilm)	NI_B_H (Oral Hygiene)	Self-performed mechanical biofilm removal	Oral hygiene education, supervised tooth brushing, sorbitol chewing gum, professional tooth cleaning, oral home care with dental floss, brushing techniques, toothbrushes
		NI_B_A (Antibacterial)	Self- or professionally performed application of antibacterial agents to control or remove biofilms	Chlorhexidine (CHX)- varnish/rinse/swab, Povidone Iodine, Terminalia chebula, chloramine-T dentifrice, CHX-coating, toothpaste with triclosan, essential oils
		NI_B_O (Others)	Other interventions targeting biofilm control or removal	Ozone, amphotericin B, Oil pulling, probiotics (Lactobacillus rhamnosus, Bifidobacter Bb12, Lactobacillus reuteri), herbal mouthrinse
	NI_D (Diet)	NI_D_C (Counselling)	Dietary behavior change intervention by counselling	DVD for mothers about nutrition of children
		NI_D_S (Sugar substitutes)	Substitution of sugars	substitution of sucrose with by invert sugar, sugar alternatives or non-caloric sugar substitutes, fructose diet
	NI_M (Mineralization)	NI_M_F (Fluoride)	Mineral control using fluorides	NaF, amine fluoride, stannous fluoride, silane fluoride, sodium phosphate fluoride, calcium fluoride, ferric aluminum fluoride, titanium tetrafluoride, monofluorophosphate, acidulated phosphate sodium fluoride (APF)
		NI_M_C (CPP)	Mineral control using casein phosphopeptide – amorphous calcium phosphate (CPP-ACP)	CPP-ACP in various formulations
		NI_M_S (SDF)	Mineral control using silver compounds	Silver diamine fluoride, nitrate or silver nanofluoride used as preventive and caries arresting agent
		NI_M_O (Others)	Other means for mineral control	Calcium pyro phosphate dentifrice, NaHCO ₃ and KH ₂ PO ₄ additive to sugar sweetened food, calcium carbonate toothpaste, Sodium trimetaphosphate toothpaste, arginine bicarbonate/calcium carbonate
	NI_C (Combination)		Interventions combining minimum two of the above named intervention groups	Caries prevention programs using different non-invasive approaches (professional tooth cleaning and CHX/fluoride application, regular check-ups and fluoride gel applications, supervised tooth brushing and fluoride application, invert sugar and fluoride application), alternate weekly application of CHX and fluoride, rinsing with fluoride combined with CHX, application of silver diamine fluoride and stannous fluoride, dentifrice containing CHX, application of thymol varnish and fluoride, fluoride and dicalcium phosphate, application of Ozone and remineralizing agents, educational programs containing oral hygiene instructions and CHX/fluoride application, education about nutrition and fluoride application, educational programs containing education in different non-invasive approaches, non-restorative cavity treatment using different non-invasive approaches, all applications of xylitol due to dual mode of action (sugar supplement and biofilm inhibitor)

MI (Micro-Invasive): comparators modifying the surface, but not breaching it	MI_F (Fissure)	MI_F_R (Resin sealant)	Resin sealants placed over surfaces assumed to be sound	Resin sealants (filled, unfilled, autopolymerized, light cured, UV-light cured), adhesives used as a sealant, resin sealants containing fluoride, compomer sealants, ormocer sealants
		MI_F_G (glass-ionomer cement (GIC) sealant)	GIC sealants placed over surfaces assumed to be sound	GIC sealants, resin modified GIC sealants, glass carbomer sealants
		MI_F_A (Amalgam sealant)	Amalgam sealants over surfaces assumed to be sound	Amalgam sealants
		MI_F_C (Sealing over Caries)	Any sealants placed over carious surfaces	Sealing carious fissures (regardless of sealing material)
	MI_A (Proximal)	MI_A_S (Sealing)	Proximal sealing	Proximal sealing (regardless of sealing material)
		MI_A_I (Infiltration)	Proximal resin infiltration	Proximal resin infiltration
	MI_O (Others)			Refurbishing or sealing defective restorations or around brackets, sealant application techniques (tooth preparation, etching, surface conditioning, use of an adhesive, use of a drying agent, tooth isolation, tooth cleaning), assessing the influence of the operator
I (Invasive): comparators breaching the surface of a tooth	I_M (Material)	I_M_R (Resin based)	An invasive intervention testing a resin-based material	Composites (light cured, autopolymerized, different filler sizes or amounts, packable composites, composite restoration with a fibre layer), compomers, ormocers, siloranes
		I_M_A (Amalgam)	An invasive intervention testing an amalgam material	Amalgam restorations
		I_M_C (Cement)	An invasive intervention testing a cement material	GIC, cermet cement, zinc phosphate cement, resin modified GIC, copper phosphate cement, zinc oxide eugenol cement, antibiotic GIC, CHX containing GIC
		I_M_AH (Adhesives)	An invasive intervention testing an adhesive material	Etch and rinse adhesives, self-etch adhesives, CHX containing adhesive
		I_M_IC (Indirect Ceramic)	An invasive intervention testing an indirect ceramic material	indirect ceramic restoration
		I_M_IM (Indirect Metal)	An invasive intervention testing an indirect metal material	indirect metal restoration
		I_M_IR (Indirect Resin-based)	An invasive intervention testing an indirect resin-based material	Indirect resin based restoration
		I_M_CT (Cementation)	An invasive intervention testing a cementation material	Different luting agents (cement or resin based)
	I_T (Techniques)	I_T_C (Caries removal)	An invasive intervention testing a caries removal technique. If additional interventions were tested (materials, sealants), we treated caries removal as the dominant	Rotary bur (steel or polymer), hand instruments, air abrasion, chemomechanical removal, Hall-technique, complete excavation, selective excavation, stepwise excavation, sealed composite restoration placed over lesions, direct/indirect pulp cap

			intervention	
		I_T_P (Preparation)	An invasive intervention testing a preparation technique	rotary bur, laser, cavity design (conventional, tunnel, slot, dovetail, bevelling)
		I_T_L (Liner)	An invasive intervention testing a liner material. If additional interventions were tested (restoration materials, caries removal techniques), we treated liner as the dominant intervention	Zinc oxide eugenol liner, calcium hydroxide liner, dentine adhesive as a liner, copal varnish, GIC, resin modified GIC, triclosan containing compomer, GIC containing antibiotics, calcium silicate cement, polyantibiotic paste, fluoride releasing hydroxyapatite
		I_T_O (Others*)	Any invasive intervention not fitting into the above described categories	Bonded amalgams, pin retained amalgam, provisional cementation or restoration, anesthesia/sedation techniques, cavity conditioning, influence of setting or operator on an intervention, application techniques of filling materials (open sandwich technique, bulk fill technique, use of surface sealer, adhesive placement steps, intermediate layer of a flowable composite), cavity disinfection (e.g. Ozone, SDF, CHX), repair filling, groups were restorative materials had not been reported or different materials were used within one group, curing technique, contamination control
		C (Combination): A combination of comparators with different degree of invasiveness (e.g. invasive and micro-invasive)		ART, early caries treatment (sealants and restorations), proximal sealing with flossing, application of fluoride after caries removal (with no filling), sealing with tooth brushing,
		P (Placebo, routine or no treatment): A comparator with no assumed effect		No treatment or use of placebo (placebo varnish/rinse/dentifrice, routine care/treatment)