Bijlage 13. GRADE Evidence Profiles

Extraction compared to retention in adolescents or adults with asymptomatic disease-free impacted wisdom teeth

Bibliography: Ghaeminia H, Perry J, Nienhuijs MEL, Toedtling V, Tummers M, Hoppenreijs TJM, Van der Sanden WJM, Mettes TG. Surgical removal versus retention for the management of asymptomatic disease-free impacted wisdom teeth. Cochrane Database of Systematic Reviews 2016, Issue 8. Art. No.: CD003879.

Outcomes	№ of participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with retention	Risk difference with extraction
Periodontis: probing depth (> 4 mm) 'soft tissue' impaction. follow up: range 3 years to 25 years	416 (1 observational study)	⊕◯◯◯ VERY LOW [a,b]	**RR 6.41** (2.92 to 14.10)	-	**-**
Periodontitis: probing depth (> 4 mm) 'bony tissue' impaction follow up: range 3 years to 25 years	416 (1 observational study)	⊕◯◯◯ VERY LOW [a,b,c]	**RR 1.60** (0.96 to 2.67)	-	**-**
Periodontitis: alveolar bone loss 'soft tissue' impaction follow up: range 3 years to 25 years	416 (1 observational study)	⊕◯◯◯ VERY LOW [a,b]	**RR 9.15** (4.63 to 18.10)	-	**-**
Periodontitis: aveolar bone loss 'bony tissue' impaction follow up: range 3 years to 25 years	416 (1 observational study)	⊕◯◯◯ VERY LOW [a,b]	**RR 3.09** (1.83 to 5.22)	-	-
Caries: 'soft tissue' impaction follow up: range 3 years to 25 years	416 (1 observational study)	⊕◯◯◯ VERY LOW [a,b,d]	**RR 0.83** (0.11 to 6.04)	-	**-**
Caries: 'bony' impaction follow up: range 3 years to 25 years	416 (1 observational study)	⊕◯◯◯ VERY LOW [a,d]	**RR 1.44** (0.55 to 3.72)	-	**-**

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

GRADE Working Group grades of evidence

High quality: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate quality: We are moderately confident in the effect estimate: The the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low quality: Our confidence in the effect estimate is limited: The the true effect may be substantially different from the estimate of the effect

Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Confounding (oral hygiene and frequency of dental checkups was not controlled for) and missing data. Downgraded by 1 level.

b. Only males. It is likely that gender does not have a causal effect. Not downgraded.

c. RR 0.75 (appreciable benefit) crosses confidence interval. Downgrade by 1 level.

d. very wide confidence interval.

Extraction compared to retention in adolescents or adults with asymptomatic disease-free impacted wisdom teeth

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Outcomes	№ of participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with retention	Risk difference with extraction
Dimensional changes in the dental arch: Little's irregularity index follow up: mean 66 months	77 (1 RCT)	⊕⊕◯◯ LOW [a,b]	-	The mean dimensional changes in the dental arch: Little's irregularity index was **1.1** mm	MD **0.3 mm lower** (1.3 lower to 0.7 higher)
Dimensional changes in the dental arch: intercanine width follow up: mean 66 months	77 (1 RCT)	⊕⊕◯◯ LOW [a,b]	-	The mean dimensional changes in the dental arch: intercanine width was **0.38** mm	MD **0.01 mm lower** (0.37 lower to 0.7 higher)
Dimensional changes in the dental arch: arch length follow up: mean 66 months	77 (1 RCT)	⊕⊕◯◯ LOW [a,b]	-	The mean dimensional changes in the dental arch: arch length was **2.13** mm	MD **1.03 mm lower** (1.5 lower to 0.56 lower)

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a. Unclear concealment of allocation. High risk of attrition bias. Downgraded by 1 level.

b. Rule of thumb is at least 400 patients in case of continuous outcomes. 77 patients is substantially less. Downgraded by 1 level.

Difference in diagnostic accuracy OPT versus CBCT to assess the relationship third molar and canalis mandibularis.
Range of sensitivities OPT: 0.29 to 1.00 | **Range of specificities OPT**: 0.00 to 0.78
Range of sensitivities CBCT: 0.67 to 0.96 | **Range of specificities CBCT**: 0.23 to 0.95

Test result	Effect per 1.000 patients tested						Number of partici-pants (studies)	Quality of the Evidence (GRADE)
	Prevalence 40%		Prevalence 60%		Prevalence 20%			
	OPT	CBCT	OPT	CBCT	OPT	CBCT		
True positives (TP) (patients with IAN)	116 to 400	268 to 384	174 to 600	402 to 576	58 to 200	134 to 192	402 (4)	⊕◯◯◯ VERY LOW [a,b]
	152 fewer to 16 more TP in OPT		**228 fewer to 24 more TP in OPT**		**76 fewer to 8 more TP in OPT**			
False negatives (FN) (patients incorrectly classified as not having IAN)	0 to 284	16 to 132	0 to 426	24 to 198	0 to 142	8 to 66		
	152 more to 16 fewer FN in OPT		**228 more to 24 fewer FN in OPT**		**76 more to 8 fewer FN in OPT**			
True negatives (TN) (patients without IAN)	1 to 468	138 to 570	0 to 312	92 to 380	1 to 624	184 to 760	402 (4)	⊕◯◯◯ VERY LOW [a,b]
	137 fewer to 102 fewer TN in OPT		**92 fewer to 68 fewer TN in OPT**		**183 fewer to 136 fewer TN in OPT**			
False positives (FP) (patients incorrectly classified as having IAN)	132 to 599	30 to 462	88 to 400	20 to 308	176 to 799	40 to 616		
	137 more to 102 more FP in OPT		**92 more to 68 more FP in OPT**		**183 more to 136 more FP in OPT**			

a. Most criteria indicate unclear risk of bias. Downgraded by 1 level.
b. There is very substantial variation in sensitivity & specificity, and non-overlapping confidence intervals. Downgraded by 2 levels.

CBCT compared to OPT for mandibular third molar removal

Bibliography: Petersen et al, 2016; Ghaeminia et al, 2015; Guerrero et al, 2014;

Outcomes	№ of participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with OPT	Risk difference of CBCT with OPT
Overall incidence of IAN injury 1 week after surgery.	806 (3 RCTs)	⊕⊕◯◯ LOW [a,b]	**RR 1.29** (0.71 to 2.33)	63 per 1.000	**18 more per 1.000** (18 fewer to 84 more)
Permanent IAN-damage follow up: range >6 months to	550 (2 RCTs)	⊕⊕◯◯ LOW [c,d]	**RR ranged from** 1.02 to 2.63	11 per 1.000	**11 fewer per 1.000** (0 fewer to 17 more)
Dry socket 1 week postoperative	256 (1 RCT)	⊕◯◯◯ VERY LOW [b,e]	**RR 0.69** (0.12 to 4.05)	23 per 1.000	**7 fewer per 1.000** (20 fewer to 70 more)
Infection 2 months postoperative	320 (1 RCT)	⊕⊕◯◯ LOW [b]	**RR 0.81** (0.50 to 1.32)	189 per 1.000	**36 fewer per 1.000** (95 fewer to 60 more)
Infection 1 week postoperative	256 (1 RCT)	⊕◯◯◯ VERY LOW [b,e]	**RR 0.86** (0.27 to 2.75)	46 per 1.000	**6 fewer per 1.000** (34 fewer to 81 more)
Swelling 1 week postoperative	256 (1 RCT)	⊕◯◯◯ VERY LOW [b,e]	**RR 0.83** (0.23 to 3.00)	38 per 1.000	**7 fewer per 1.000** (30 fewer to 77 more)
Bleeding 1 week postoperative	256 (1 RCT)	⊕◯◯◯ VERY LOW [b,e]	not estimable	0 per 1.000	**0 fewer per 1.000** (0 fewer to 0 fewer)

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GRADE Working Group grades of evidence

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Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Althought patients and operators were unblinded not downgraded for serious risk of bias. Blinding was not possible. Therefore other aspects of risk of bias were assessed more strict.

b. Substantially less than 300 events. Confidence interval crosses thresholds for appreciable benefit (RR=0.75) AND appreciable harm (RR=1.25). Downgraded by 2 levels

c. One study is not a multicentre trial (limited generalizability) and has unblinded outcome assessors

d. Less than 300 events. Confidence interval crosses threshold for appreciable benefit OR appreciable harm. Downgraded by 1 level.

e. Outcome assessors not blinded, and unclear random sequence generation.

CBCT compared to OPT for mandibular third molar removal

Bibliography: Petersen et al, 2016; Ghaeminia et al, 2015; Guerrero et al, 2014;

Outcomes	№ of participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with OPT	Risk difference of CBCT with OPT
Ecchymosis 1 week postoperative	256 (1 RCT)	⊕◯◯◯ VERY LOW [a,b]	**RR 0.77** (0.18 to 3.39)	31 per 1.000	**7 fewer per 1.000** (25 fewer to 74 more)
Trismus 1 week postoperative	256 (1 RCT)	⊕◯◯◯ VERY LOW [a,b]	**RR 0.26** (0.03 to 2.28)	31 per 1.000	**23 fewer per 1.000** (30 fewer to 39 more)
Emergency visits 1 week postoperative	320 (1 RCT)	⊕⊕⊕◯ MODERATE [c]	**RR 0.73** (0.46 to 1.16)	220 per 1.000	**59 fewer per 1.000** (119 fewer to 35 more)
Duration of surgery	576 (2 RCTs)	⊕⊕⊕◯ MODERATE [d,e]	-	The mean duration of surgery ranged from **11.9 to 17.4** min.	0.8 minutes less in CBCT to 0.5 minutes more in CBCT group
OHIP-14 1 week postoperative. Scale from: 0 to 56	320 (1 RCT)	⊕⊕⊕◯ MODERATE [f]	-	The mean OHIP-14 1 week postoperative was **17**	MD **1 more** (1.68 fewer to 3.68 more)
Pain 1 week postoperative assessed with: VAS scale. Scale from: 0 to 10	320 (1 RCT)	⊕⊕⊕◯ MODERATE [f]	-	The mean pain 1 week postoperative was **4.1** mm	MD **0.1 mm more** (0.38 fewer to 0.58 more)
Days study or work absence	320 (1 RCT)	⊕⊕⊕◯ MODERATE [f]	-	The mean days study or work absence was **2.1** days	MD **0.3 days fewer** (0.83 fewer to 0.23 more)

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Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Outcome assessors not blinded, and unclear random sequence generation.

b. Substantially less than 300 events. Confidence interval crosses thresholds for appreciable benefit (RR=0.75) AND appreciable harm (RR=1.25). Downgraded by 2 levels

c. Less than 300 events. Confidence interval crosses threshold for appreciable benefit OR appreciable harm. Downgraded by 1 level.

d. difference in direction of effects

e. Rule of thumb for continuous outcomes: downgrading by 1 level if number of patients is less than 400. Two studies comprised more than 500 patients.

f. Less than 400 patients (rule of thumb in case of continuous outcome measures).

Preoperative antibiotics compared to placebo for third molar removal

Bibliography: Lodi G, Figini L, Sardella A, Carrassi A, Del Fabbro M, Furness S. Antibiotics to prevent complications following tooth extractions. Cochrane Database of Systematic Reviews 2012, Issue 11. Art.No.:CD003811. Marcussen KB, Laulund AS, Jørgensen HL, Pinholt EM. A Systematic Review on Effect of Single-Dose Preoperative Antibiotics at Surgical Osteotomy Extraction of Lower Third Molars. J Oral Maxillofac Surg. 2016 Apr;74(4):693-703.

Outcomes	№ of participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with placebo	Risk difference antibiotics versus placebo
surgical site infection (preop) (SSI-preop) follow up: mean 7 days	541 (6 RCTs)	⊕⊕◯◯ LOW [a,b]	RR 0.21 (0.09 to 0.49)	109 per 1.000	**86 fewer per 1.000** (100 fewer to 56 fewer)
surigical site infection (preop amoxicillin) (SSI-preop amoxicillin) follow up: mean 7 days	287 (4 RCTs)	⊕⊕◯◯ LOW [a,b]	RR 0.26 (0.10 to 0.64)	151 per 1.000	**112 fewer per 1.000** (136 fewer to 54 fewer)
dry socket (preop) follow up: mean 7 days	849 (7 RCTs)	⊕⊕⊕◯ MODERATE [b,e]	RR 0.42 (0.18 to 0.99)	115 per 1.000	**67 fewer per 1.000** (94 fewer to 1 fewer)
pain at day 7 (preop) (Pain) follow up: mean 7 days	61 (1 RCT)	⊕⊕⊕◯ MODERATE [b]	RR 0.97 (0.53 to 1.76)	471 per 1.000	**14 fewer per 1.000** (221 fewer to 358 more)
swelling at day 7 (preop) follow up: mean 7 days	165 (3 RCTs)	⊕⊕◯◯ LOW [b,c]	RR 1.16 (0.71 to 1.89)	294 per 1.000	**47 more per 1.000** (85 fewer to 262 more)
trismus at day 7 (preop) follow up: mean 7 days	134 (2 RCTs)	⊕⊕◯◯ LOW [b,c]	RR 0.80 (0.34 to 1.87)	163 per 1.000	**33 fewer per 1.000** (107 fewer to 142 more)
adverse events (preop) follow up: mean 7 days	144 (2 RCTs)	⊕⊕◯◯ LOW [c,d]	RR 0.46 (0.03 to 7.05)	22 per 1.000	**12 fewer per 1.000** (22 fewer to 134 more)

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Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. two studies with attrition and report bias; two other studies with indequate or unclear concealement of allocation. Downgraded by 1 level.

b. Number of events needed for 30% RRR is 250. Substantially less events. Downgraded by 1 level.

c. All studies had attrition bias that could have influenced the effect estimate. Downgraded by 1 level..

d. Only 28 events did occur in 590 patients. At least 2000 patients would be needed for precise results.. Downgraded by 1 level.

e. Two studies unclear or inadequate concealment of allocation. Not downgraded.

Postoperative antibiotics compared to placebo for third molar removal

Bibliography: Lodi G, Figini L, Sardella A, Carrassi A, Del Fabbro M, Furness S. Antibiotics to prevent complications following tooth extractions. Cochrane Database of Systematic Reviews 2012, Issue 11. Art.No.:CD003811. Marcussen KB, Laulund AS, Jørgensen HL, Pinholt EM. A Systematic Review on Effect of Single-Dose Preoperative Antibiotics at Surgical Osteotomy Extraction of Lower Third Molars. J Oral Maxillofac Surg. 2016 Apr;74(4):693-703.

Outcomes	№ of participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with placebo	Risk difference with antibiotics
surgical site infection (postop) (SSI-postop) follow up: mean 7 days	727 (4 RCTs)	⊕⊕◯◯ LOW [a,b]	RR 0.15 (0.07 to 0.32)	125 per 1.000	**106 fewer per 1.000** (116 fewer to 85 fewer)
Pain at day 7 (postop) (Pain) follow up: mean 7 days	554 (2 RCTs)	⊕⊕◯◯ LOW [b,c]	RR 0.51 (0.14 to 1.82)	85 per 1.000	**41 fewer per 1.000** (73 fewer to 69 more)
Swelling at day 7 (postop) follow up: mean 7 days	64 (1 RCT)	⊕⊕◯◯ LOW [b,c]	RR 0.50 (0.24 to 1.02)	471 per 1.000	**235 fewer per 1.000** (358 fewer to 9 more)
adverse events (postop) follow up: mean 7 days	590 (2 RCTs)	⊕⊕◯◯ LOW [c,d]	RR 3.98 (1.45 to 10.94)	15 per 1.000	**45 more per 1.000** (7 more to 152 more)
dry socket (postop) follow up: mean 7 days	554 (2 RCTs)	⊕⊕◯◯ LOW [b,c]	RR 0.18 (0.01 to 3.70)	8 per 1.000	**7 fewer per 1.000** (8 fewer to 22 more)

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Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Three of four studies have attrition bias that could bias the effect estimate. Downgraded by 1 level.

b. Number of events needed for 30% RRR is 250. Substantially less events. Downgraded by 1 level.

c. All studies had attrition bias that could have influenced the effect estimate.

d. Only two events did occur in 144 patients. At least 2000 patients would be needed for precise results.

Preoperative and postoperative antibiotics compared to placebo for third molar removal

Bibliography: Lodi G, Figini L, Sardella A, Carrassi A, Del Fabbro M, Furness S. Antibiotics to prevent complications following tooth extractions. Cochrane Database of Systematic Reviews 2012, Issue 11. Art.No.:CD003811. Marcussen KB, Laulund AS, Jørgensen HL, Pinholt EM. A Systematic Review on Effect of Single-Dose Preoperative Antibiotics at Surgical Osteotomy Extraction of Lower Third Molars. J Oral Maxillofac Surg. 2016 Apr;74(4):693-703.

Outcomes	№ of participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with placebo	Risk difference with antibiotics
surgical site infection (preop & postop) (SSI-preop&postop) follow up: mean 7 days	238 (4 RCTs)	⊕⊕◯◯ LOW [a,b]	RR 1.09 (0.40 to 2.94)	51 per 1.000	**5 more per 1.000** (31 fewer to 99 more)
Pain at day 7 (preop&postop) (Pain) follow up: mean 7 days	60 (2 RCTs)	⊕⊕◯◯ LOW [c,d]	RR 0.36 (0.13 to 0.98)	350 per 1.000	**224 fewer per 1.000** (305 fewer to 7 fewer)
Swelling at day 7 (preop&postop) follow up: mean 7 days	105 (1 RCT)	⊕⊕◯◯ LOW [d,e]	RR 1.09 (0.53 to 2.21)	242 per 1.000	**22 more per 1.000** (114 fewer to 293 more)
adverse events (preop&postop) follow up: mean 7 days	196 (2 RCTs)	⊕⊕◯◯ LOW [d,e]	RR 1.67 (0.97 to 2.90)	169 per 1.000	**113 more per 1.000** (5 fewer to 320 more)
dry socket (prep&postop) follow up: mean 7 days	197 (2 RCTs)	⊕⊕◯◯ LOW [d,e]	RR 0.52 (0.27 to 0.98)	250 per 1.000	**120 fewer per 1.000** (183 fewer to 5 fewer)
Trismus at day 7 (preop & postop)	41 (1 RCT)	⊕◯◯◯ VERY LOW [b,e]	RR 0.93 (0.27 to 3.14)	231 per 1.000	**16 fewer per 1.000** (168 fewer to 494 more)
Fever at day 7 (preop & postop)	196 (2 RCTs)	⊕⊕◯◯ LOW [c,d]	RR 0.66 (0.24 to 1.79)	92 per 1.000	**31 fewer per 1.000** (70 fewer to 73 more)

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Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Attrition bias in one study. Not downgraded.

b. Very wide confidence interval: both substantial benefit and substantial harm is possible. Downgraded by 2 levels.

c. unclear randomisation sequence generation as well as unclear concealment of allocation. Downgraded by 1 level.

d. Number of events needed for 30% RRR is 250. Substantially less events. Downgraded by 1 level.

e. All studies had attrition bias that could have influenced the effect estimate