SUPPORTING INFORMATION

Efficacy and morbidity of biodegradable versus titanium osteosyntheses in orthognathic surgery: a systematic review with meta-analysis and trial sequential analysis

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Table S1: Electronic databases with the corresponding search details (11 February 2021).

Database	Search terms	Hits
PubMed (http://www.ncbi.nlm.nih.gov/pubmed/)	("Orthognathic Surgery"[Mesh] OR "Orthognathic Surgical Procedures"[Mesh] OR "Osteotomy, Le Fort"[Mesh] OR "Osteotomy, Sagittal Split Ramus"[Mesh] OR "Mandibular Advancement"[Mesh] OR "Facial Bones/surgery"[Mesh] OR "Facial Injuries"[Mesh:NoExp] OR "Maxillofacial Injuries"[Mesh] OR "Maxillofacial Abnormalities"[Mesh] OR "Malocclusion/surgery"[Mesh] OR maxill*[tiab] OR mandib*[tiab] OR jaw[tiab] OR orthognat*[tiab] OR craniofac*[tiab] OR craniomaxil*[tiab] OR retrognat*[tiab] OR orthodont*[tiab] OR zygom*[tiab] OR split ramus[tiab] OR "Facial injuries"[MeSH] OR ((orbit*[tiab] OR facial[tiab] OR face[tiab] OR nose[tiab] OR nasal[tiab]) AND (fract*[tiab] OR injur*[tiab] OR reconstruct*[tiab]))) AND ("Absorbable Implants"[Mesh] OR "Internal Fixators"[Mesh] OR "Fracture Fixation, Internal"[Mesh] OR plate*[tiab] OR screw*[tiab] OR miniscrew*[tiab] OR miniplate*[tiab] OR implant*[tiab] OR osteosynth*[tiab] OR osseointegrat*[tiab] OR osteofixat*[tiab] OR osteotom*[tiab] OR fixat*[tiab]) AND ("Absorbable Implants"[Mesh] OR bioresorb*[tiab] OR biodegrad*[tiab] OR bioabsorb*[tiab] OR bioadsorb*[tiab] OR absorb*[tiab] OR resorb*[tiab] OR adsorb*[tiab] OR "Lactic acid"[MeSH] OR lactic acid[tiab] OR "Polyglycolic acid"[MeSH] OR polyglycolic acid[tiab] OR "Hydroxyapatites"[MeSH] OR hydroxyapatite[tiab] OR biologically inert[tiab]) NOT ("Case Reports" [Publication Type] OR "Review" [Publication Type]) NOT ("Animals"[Mesh] NOT "Humans"[Mesh])	2535
EMBASE (http://www.embase.com/home)	('craniofacial surgery'/de OR 'cranioplasty'/exp OR 'face surgery'/de OR 'maxillofacial surgery'/exp OR 'nose surgery'/exp OR 'orthognathic surgery'/exp OR 'orbit reconstruction'/exp OR 'maxillofacial injury'/de OR 'skull injury'/exp OR 'skull'/exp OR 'face fracture'/exp OR 'skull malformation'/exp/dm_su OR 'craniofacial malformation'/exp OR 'face malformation'/dm_su OR 'malocclusion'/exp/dm_su OR (maxill* OR mandib* OR jaw OR orthognat* OR craniofac* OR craniomaxil* OR retrognat* OR orthodont* OR zygom* OR 'split ramus' OR ((orbit* OR facial OR face OR nose OR nasal) AND (fract* OR injur* OR reconstruct*))):ab,ti) AND ('bone plate'/exp OR 'bone screw'/exp OR 'internal fixator'/exp OR 'fracture fixation'/exp OR 'bioabsorbable screw'/exp OR 'biodegradable screw'/exp OR 'biodegradable implant'/exp OR 'orthopedic fixation device'/de OR (plate* OR screw* OR miniscrew* OR miniplate* OR implant* OR osteosynth* OR osseointegrat* OR osteofixat* OR osteotom* OR fixat*):ab,ti) AND ('biodegradable implant'/exp OR 'bioabsorbable screw'/exp OR 'biodegradable screw'/exp OR 'lactic acid'/exp/mj OR 'polyglycolic acid'/exp/mj OR 'hydroxyapatite'/exp/mj OR 'biosorbent'/exp OR (bioresorb* OR biodegrad* OR bioabsorb* OR bioadsorb* OR absorb* OR resorb* OR adsorb* OR 'lactic acid' OR 'polyglycolic acid' OR hydroxyapatite OR 'biologically inert'):ab,ti) NOT (('animal'/exp OR 'nonhuman'/exp) NOT 'human'/exp) NOT ('review'/exp OR 'case report'/exp OR 'conference abstract'/it)	2656
Cochrane Central Register of Controlled Trials (www.thecochranelibrary.com)	(maxill* OR mandib* OR jaw OR orthognat* OR craniofac* OR craniomaxil* OR retrognat* OR orthodont* OR osteotom* OR zygom* OR "split ramus" OR (malocclus* AND surg*) OR ((orbit* OR facial OR face OR nose OR nasal) AND (fract* OR injur* OR reconstruct* OR surg*))) AND (plate* OR screw* OR miniscrew* OR miniplate* OR implant* OR osteosynth* OR osseointegrat* OR osteofixat* OR osteotom* OR fixat*) AND (bioresorb* OR biodegrad* OR bioabsorb* OR bioadsorb* OR absorb* OR resorb* OR adsorb* OR "Lactic acid" OR "Polyglycolic acid" OR Hydroxyapatite* OR "biologically inert")	663
Web of Science (www.webofknowledge.com)	TS=(maxill* OR mandib* OR jaw OR orthognat* OR craniofac* OR craniomaxil* OR retrognat* OR orthodont* OR osteotom* OR zygom* OR "split ramus" OR (malocclus* AND surg*) OR ((orbit* OR facial OR face OR nose OR nasal) AND (fract* OR injur* OR reconstruct* OR surg*))) AND TS=(plate* OR screw* OR miniscrew* OR miniplate* OR implant* OR osteosynth* OR osseointegrat* OR osteofixat* OR osteotom* OR fixat*) AND TS=(bioresorb* OR biodegrad* OR bioabsorb* OR bioadsorb* OR absorb* OR resorb* OR adsorb* OR "Lactic acid" OR "Polyglycolic acid" OR Hydroxyapatite* OR "biologically inert") NOT DT=(review OR "meeting abstract")	7820
EBSCOhost (search.ebscohost.com) Databases:	((maxill* OR mandib* OR jaw OR orthognat* OR craniofac* OR craniomaxil* OR retrognat* OR orthodont* OR osteotom* OR zygom* OR "split ramus" OR (malocclus* AND surg*) OR ((orbit* OR facial OR face OR nose OR nasal) AND (fract* OR injur* OR reconstruct* OR surg*))) AND	2608

Academic search Premier, Business Source Premier, Military & Government Collection, and CINAHL	(plate* OR screw* OR miniscrew* OR miniplate* OR implant* OR osteosynth* OR osseointegrat* OR osteofixat* OR osteotom* OR fixat*) AND (bioresorb* OR biodegrad* OR bioabsorb* OR bioadsorb* OR absorb* OR resorb* OR adsorb* OR "Lactic acid" OR "Polyglycolic acid" OR Hydroxyapatite* OR “biologically inert”))	
Scopus (www.scopus.com/)	TITLE-ABS-KEY(maxill* OR mandib* OR jaw OR orthognat* OR craniofac* OR craniomaxil* OR retrognat* OR orthodont* OR osteotom* OR zygom* OR “split ramus” OR (malocclus* AND surg*) OR ((orbit* OR facial OR face OR nose OR nasal) AND (fract* OR injur* OR reconstruct* OR surg*))) AND TITLE-ABS-KEY(plate* OR screw* OR miniscrew* OR miniplate* OR implant* OR osteosynth* OR osseointegrat* OR osteofixat* OR osteotom* OR fixat*) AND TITLE-ABS-KEY(bioresorb* OR biodegrad* OR bioabsorb* OR bioadsorb* OR absorb* OR resorb* OR adsorb* OR "Lactic acid" OR "Polyglycolic acid" OR Hydroxyapatite* OR “biologically inert”)	7981
African Journals Online (www.ajol.info/)	(maxillary OR mandibular OR orthognathic OR craniofacial OR craniomaxillofacial) AND (bioresorbable OR biodegradable)	41
OpenGrey (www.opengrey.eu)	((maxill* OR mandib* OR jaw OR orthognat* OR craniofac* OR craniomaxil* OR retrognat* OR orthodont* OR osteotom* OR zygom* OR “split ramus” OR (malocclus* AND surg*) OR ((orbit* OR facial OR face OR nose OR nasal) AND (fract* OR injur* OR reconstruct* OR surg*))) AND (bioresorb* OR biodegrad* OR bioabsorb* OR bioadsorb* OR absorb* OR resorb* OR adsorb* OR "Lactic acid" OR "Polyglycolic acid" OR Hydroxyapatite* OR “biologically inert”))	40
ClinicalTrials.gov	Condition: (maxillary OR mandibular OR orthognathic OR craniofacial OR craniomaxillofacial) Other terms: (bioresorbable OR biodegradable)	5

Table S2: Endpoints divided into five time units.

Time unit	Endpoints
Perioperative	Plate and/or screw breakage, operation time, and handling by surgeon
Short-term (0-4 weeks; soft tissue healing)	Infection, dehiscence, malocclusion, pain, swelling, plate exposure, MMO, abscess, and analgesics used
Intermediate follow-up (6 – 12 weeks; bone healing)	Malunion, mobility of bone segments, malocclusion, MMO, TMJ-dysfunction, and pain
Long-term follow-up (>12 weeks; degradation effects)	Palpability of plate and screws, malocclusion, pain, swelling, satisfaction, TMJ-dysfunction, MMO, abscess, and MFIQ
Overall	Skeletal stability (i.e., skeletal relapse), symptomatic device removal, additional surgery (not device removal), and total costs

MMO: maximal mouth opening; TMJ-dysfunction: temporomandibular joint dysfunction; MFIQ: Mandibular Function Impairment Questionnaire.

Table S3: List with contacted authors of original articles.

Study	Dates of contact	Reasons for contact	Responses
Matthews et al. (2003)[1]	19 May 2018, 29 May 2018, and 22 August 2018.	1. Details regarding study design 2. Details regarding the distribution of data of the outcomes 'operative displacement' and 'relapse' 3. Details regarding the allocation of two patients with TMJ-dysfunction.	1. "It was a randomised study using odd/even registration numbers that are linked to concealed envelops." 2. "Unfortunately, I don't have access to the original data, it has been more than 15 years since we conducted this study." 3. "Apology, I can't remember."
Cheung et al. (2008)[2]	29 May 2018, 1 August 2018, 22 August 2018, 19 October 2018	1. All reported data are presented in figures only. No numbers are available to include in the meta-analyses.	No response
Stockmann et al. (2010)[3]	29 May 2018, 1 August 2018, 10 August 2018	1. Data not reported per treatment group 2. Definition of relapse (i.e., it currently is a binary variable).	No response
Tuovinen et al. (2010)[4]	23 August 2018, 24 August 2018, and 19 October 2018	1. Only P-values of difference between relapse of both treatment groups are reported, not the amount of relapse itself.	1. "Thank you for your interest concerning my report. I have not found my raw data yet. I'll keep on digging in my old cd-copies. My computer has been changed several times and we have been moving to three different location since that report and in the archive where the data should be I could not find it. I'll continue to look for the data." 2. "I have not found SPSS files but all handmade (written) measurements can be find, but it would be quite a job to copy and explain my notes and put them again in

			SPSS. Attached one example of measurements." 3. No response after asking for all the data.
Landes et al. (2006)[5]	29 May 2018, 22 August 2018, 19 October 2018	1. Details regarding the absolute number of screw and plate breakage per treatment group.	No response
Paeng et al. (2012)[6]	29 May 2018, 22 August 2018, and 19 October 2018	1. Details regarding the single patient that demonstrated infection after 7 days follow-up: which treatment group?	No response

Table S4: Excluded articles with reasons for exclusion after full-text screening.

Author (year)	Reason for exclusion	Reference
Ahmed et al. (2013)	Surgical procedure not relevant for this review	[7]
Arshad et al. (2019)	Surgical procedure not relevant for this review	[8]
Arya et al. (2020)	Surgical procedure not relevant for this review	[9]
Bekal et al. (2017)	Surgical procedure not relevant for this review	[10]
Bell et al. (2006)	Surgical procedure not relevant for this review	[11]
Bhatt et al. (2010)	Surgical procedure not relevant for this review	[12]
Bhatt et al. (2015)	Surgical procedure not relevant for this review	[13]
Bohm et al. (1998)	Surgical procedure not relevant for this review	[14]
Bouletreau et al. (2005)	Both groups consist of biodegradable and titanium osteosynthesis	[15]
Burlini et al. (2015)	Surgical procedure not relevant for this review	[16]
Champy et al. (1992)	No control group	[17]
Wang et al. (2013)	Surgical procedure not relevant for this review	[18]
Fakourand et al. (2012	Surgical procedure not relevant for this review	[19]
Filinte et al. (2015)	Surgical procedure not relevant for this review	[20]
Fuente del Campo et al. (1996)	No control group; Biodegradable plates with titanium screws used	[21]
Hashiba et al. (2007)	No relevant endpoints for this review	[22]
Ho et al. (2011)	No pure biodegradable group, only titanium or mixed groups	[23]
Hwang et al. (2017)	No pure biodegradable group, only titanium or mixed groups	[24]
Iatrou et al. (2010)	Surgical procedure not relevant for this review	[25]
Illi et al. (1989)	Children with syndromic disorders included	[26]
Imola et al. (2002)	Review paper	[27]
Janickova et al. (2018)	Surgical procedure not relevant for this review	[28]
Kallela et al. (1999)	Review paper	[29]
Kang et al. (2014)	Surgical procedure not relevant for this review	[30]
Kim et al. (2018)	Surgical procedure not relevant for this review	[31]
Kobayashi et al. (2004)	No control group	[32]
Kretschmer et al. (2011)	Surgical procedure not relevant for this review	[33]
Landes et al. (2014)	Patients with cleft lip and palate included	[34]
Landes et al. (2015)	No control group	[35]
Lee et al. (2010)	Surgical procedure not relevant for this review	[36]
Lee et al. (2014)	Surgical procedure not relevant for this review	[37]
Lee et al. (2014)	Endpoint not relevant for this review	[38]
Leno et al. (2017)	Surgical procedure not relevant for this review	[39]

Leonhardt et al. (2008)	Surgical procedure not relevant for this review	[40]
Lim et al. (2014)	Surgical procedure not relevant for this review	[41]
Liu et al. (2016)	Surgical procedure not relevant for this review	[42]
Mahmoud et al. (2016)	Surgical procedure not relevant for this review	[43]
Menon et al. (2007)	Surgical procedure not relevant for this review	[44]
Menon et al. (2012)	Surgical procedure not relevant for this review	[45]
Netto et al. (2013)	Surgical procedure not relevant for this review	[46]
Obwegeser et al. (1994)	No biodegradable osteosynthesis used, only biodegradable sutures	[47]
Park et al. (2005)	Surgical procedure not relevant for this review	[48]
Park et al. (2011)	Surgical procedure not relevant for this review	[49]
Pistner et al. (1991)	Review paper	[50]
Qiu et al. (2015)	Surgical procedure not relevant for this review	[51]
Stuck et al. (2011)	Review paper	[52]
Sukegawa et al. (2016)	Surgical procedure not relevant for this review	[53]
Tan et al. (2011)	Surgical procedure not relevant for this review	[54]
Tripathi et al. (2013)	Surgical procedure not relevant for this review	[55]
Ueki et al. (2011b)	Does not fulfill inclusion criteria	[56]
Ueki et al. (2015b)	Does not fulfill inclusion criteria	[57]
Ueki et al. (2017)	Does not fulfill inclusion criteria	[58]
Wittwer et al. (2006)	Surgical procedure not relevant for this review	[59]
Wu et al. (2017)	Surgical procedure not relevant for this review	[60]
Zheng et al. (2001)	No control group	[61]

Table S5: All assessed endpoints of the included studies, except skeletal stability.

Study name (year)	Osteosynthesis system	Plate breakage (%)	Screw breakage (%)	Operation time (mean±SD, in minutes)[a]	Handling by surgeon (0: worst; 10: excellent)	Infection (%)	Swelling (%)	Abscess (%)	Pain (%)	MMO (%)	Dehiscence (%)	Plate exposure (%)	Malunion (%)	Mobility segments (%)	Malocclusion (%)	Pain (%)	MMO (mean±SD)	TMJ-dysfunction (%)	Malocclusion (%)	Pain (%)	MMO (mean±SD)	TMJ-dysfunction (%)	MFIQ (median, IQR)	Abscess (%)	Swelling (%)	Palpability screw/plate (%)	Satisfaction (%)	Symptomatic plate/screw removal (%)	Costs (direct and indirect; mean±SD)[a]	Revision surgery (not device removal; %)	Skeletal stability assessed (yes)
		Perioperative endpoints				Short-term follow-up								Intermediate follow-up					Long-term follow-up										Overall follow-up		
Randomised controlled trials																															
Matthews (2003)[1]	B	0	0			0						9.1						0								9.1				0	x
	T	0	0			0						0						0								0				0	x
Norholt (2004)[62]	B				82.1[b]	0	42.9		25		3.6	0		22.2		18.5				20					4	12		0		8.3	x
	T				100[b]	3.7	40.7		29.6		0	0		10.7		21.4				28.6					0	61.9		14.3		0	x
Cheung (2004)[63]	B	4.2[*]	10.9[#]			3.3			3.63± 2.27[a†]		6.7			6.7		1.2± 1.35[a†]				0.46± 1.10[a†]							8.63± 1.44[a†]	20			
	T	0[*]	0[#]			0			4.40± 2.29[a†]		10			10		1.47± 1.50[a†]				0.67± 1.13[a†]							8.50± 1.84[a†]	10			
Ueki (2005)[64]	B					0					0	0[c]	0	0					0 (O)	0.8± 1.8[a]	-3.40± 2.26[f]	15									x
	T					0					0	0[c]	0	0					0 (O)	1.0± 2.1[a]	-5.60± 1.86[f]	25									x
Cheung (2008)[2]	B								NNA					NNA		NNA				NNA						NNA					x
	T								NNA					NNA		NNA				NNA						NNA					x

Study name (year)	Osteosynthesis system	Plate breakage (%)	Screw breakage (%)	Operation time (mean±SD, in minutes)[a]	Handling by surgeon (0: worst; 10: excellent)	Infection (%)	Swelling (%)	Abscess (%)	Pain (%)	MMO (%)	Dehiscence (%)	Plate exposure (%)	Malunion (%)	Mobility segments (%)	Malocclusion (%)	Pain (%)	MMO (mean±SD)	TMJ-dysfunction (%)	Malocclusion (%)	Pain (%)	MMO (mean±SD)	TMJ-dysfunction (%)	MFIQ (median, IQR)	Abscess (%)	Swelling (%)	Palpability screw/plate (%)	Satisfaction (%)	Symptomatic plate/screw removal (%)	Costs (direct and indirect; mean±SD)[a]	Revision surgery (not device removal; %)	Skeletal stability assessed (yes)
		Perioperative endpoints				Short-term follow-up								Intermediate follow-up					Long-term follow-up									Overall follow-up			
Park (2010)[65]	B																														x
	T																														x
Stockmann (2010)[3]	B		9.1	+36[d]		3				NNA	3	NNA					NNA		5.9 (O)		NNA						62	0			
	T		3	NNA[d]		3				NNA	0	0[c]					NNA		5.9 (O)		NNA							3			
Tuovinen (2010)[4]	B					0																						2		2	x
	T					0																						4		4	x
Buijs (2012)[66]	B	0	0	137±59	7.6±0.7[a]		17.1	11.8			3.9		2.6		9.2 (O)	5.15±8.9[a]												1.3		0	
	T	0	0	116±64	8.5±1.2[a]		7.3	4.8			1.6		0		12.9 (O)	4.7±10.6[a]												1.6		0.8	
Yoshioka (2012)[67]	B	2.7				0																				1.8		5.5		0	
	T	0				1.1																				0		3.3		0	
Bakelen (2013)[68],[e]	B																		7.5 & 11.3 (O)	2±9 & 2±6			17 (17-23) & 17 (17-19)	3 & 1.9	9 & 5.7	50.7 & 47.2		24		2.5	

Study name (year)	Osteosynthesis system	Plate breakage (%)	Screw breakage (%)	Operation time (mean±SD, in minutes)[a]	Handling by surgeon (0: worst; 10: excellent)	Infection (%)	Swelling (%)	Abscess (%)	Pain (%)	MMO (%)	Dehiscence (%)	Plate exposure (%)	Malunion (%)	Mobility segments (%)	Malocclusion (%)	Pain (%)	MMO (mean±SD)	TMJ-dysfunction (%)	Malocclusion (%)	Pain (%)	MMO (mean±SD)	TMJ-dysfunction (%)	MFIQ (median, IQR)	Abscess (%)	Swelling (%)	Palpability screw/plate (%)	Satisfaction (%)	Symptomatic plate/screw removal (%)	Costs (direct and indirect; mean±SD)[a]	Revision surgery (not device removal; %)	Skeletal stability assessed (yes)
		Perioperative endpoints				Short-term follow-up								Intermediate follow-up					Long-term follow-up									Overall follow-up			
	T																		12.1 & 12.2 (O)	1±7 & 2±9			21 (17-27) & 19 (17-23)	2.6 & 0	3.4 & 0	34.5 & 47.8		8		1.6	
Yu et al. (2014)[69]	B					16															-0.31±6.80[f]							0			
	T					13.7															-1.86±7.51[f]							3.9			
Bakelen (2015)[70]	B																												6589±3492		
	T																												6787±5014		
Gareb (2017)[71]	B																		11.8 (S)	7.0±18.7[a]			18 (17-21)		5.9	7.8		29.1			
	T																		14.8 (S)	5.7±17.6[a]			18 (17-21)		2.5	42		15.3			

Study name (year)	Osteosynthesis system	Plate breakage (%)	Screw breakage (%)	Operation time (mean±SD, in minutes)[a]	Handling by surgeon (0: worst; 10: excellent)	Infection (%)	Swelling (%)	Abscess (%)	Pain (%)	MMO (%)	Dehiscence (%)	Plate exposure (%)	Malunion (%)	Mobility segments (%)	Malocclusion (%)	Pain (%)	MMO (mean±SD)	TMJ-dysfunction (%)	Malocclusion (%)	Pain (%)	MMO (mean±SD)	TMJ-dysfunction (%)	MFIQ (median, IQR)	Abscess (%)	Swelling (%)	Palpability screw/plate (%)	Satisfaction (%)	Symptomatic plate/screw removal (%)	Costs (direct and indirect; mean±SD)[a]	Revision surgery (not device removal; %)	Skeletal stability assessed (yes)
		Perioperative endpoints				Short-term follow-up								Intermediate follow-up						Long-term follow-up								Overall follow-up			
Prospective cohort studies																															
Ferretti (2002)[72]	B					0																									x
	T					0																									x
Dhol (2008)[73]	B					0	0		0							0				0				0							x
	T					0	0		0							0				0				0							x
Bakelen (2014)[74]	B																														x
	T																														x
Retrospective cohort studies																															
Harada (1997)[75]	B																	0				0									x
	T																	0				0									x
Costa (2006)[76]	B					0					0	0[c]	0	0						20					20					20	x
	T					0					0	0[c]	0	0						0					0					0	x
Landes (2006)[5]	B		5[#]											0																	x
	T		0[#]											0																	x
Turvey (2006)[77]	B																														x
	T																														x

Study name (year)	Osteosynthesis system	Plate breakage (%)	Screw breakage (%)	Operation time (mean±SD, in minutes)[a]	Handling by surgeon (0: worst; 10: excellent)	Infection (%)	Swelling (%)	Abscess (%)	Pain (%)	MMO (%)	Dehiscence (%)	Plate exposure (%)	Malunion (%)	Mobility segments (%)	Malocclusion (%)	Pain (%)	MMO (mean±SD)	TMJ-dysfunction (%)	Malocclusion (%)	Pain (%)	MMO (mean±SD)	TMJ-dysfunction (%)	MFIQ (median, IQR)	Abscess (%)	Swelling (%)	Palpability screw/plate (%)	Satisfaction (%)	Symptomatic plate/screw removal (%)	Costs (direct and indirect; mean±SD)[a]	Revision surgery (not device removal; %)	Skeletal stability assessed (yes)
		Perioperative endpoints				Short-term follow-up								Intermediate follow-up							Long-term follow-up							Overall follow-up			
Ueki (2006a and b)[78]	B					a & b: 0					a & b: 0	a & b: 0[c]							a & b: 0												x
	T					a & b: 0					a & b: 0	a & b: 0[c]							a & b: 0												x
Landes (2007)[79]	B		12[#]											0																x
	T		0[#]											0																x
Ueki (2009)[80]	B					0					0	0[c]	0	0					0											
	T					0					0	0[c]	0	0					0											
Ahn (2010)[81]	B					4.2															5.8								2.5	
	T					0															6.6								0	
Choi (2010)[82]	B																													x
	T																													x
Ueki (2011)[83]	B					0												0												x
	T					0												0												x
Ballon (2012)[84]	B																													x
	T																													x

Study name (year)	Osteosynthesis system	Plate breakage (%)	Screw breakage (%)	Operation time (mean±SD, in minutes)[a]	Handling by surgeon (0: worst; 10: excellent)	Infection (%)	Swelling (%)	Abscess (%)	Pain (%)	MMO (%)	Dehiscence (%)	Plate exposure (%)	Malunion (%)	Mobility segments (%)	Malocclusion (%)	Pain (%)	MMO (mean±SD)	TMJ-dysfunction (%)	Malocclusion (%)	Pain (%)	MMO (mean±SD)	TMJ-dysfunction (%)	MFIQ (median, IQR)	Abscess (%)	Swelling (%)	Palpability screw/plate (%)	Satisfaction (%)	Symptomatic plate/screw removal (%)	Costs (direct and indirect; mean±SD)[a]	Revision surgery (not device removal; %)	Skeletal stability assessed (yes)
		Perioperative endpoints				Short-term follow-up								Intermediate follow-up								Long-term follow-up						Overall follow-up		
Paeng (2012)[6]	B		1.6[#]			NNA																							NNA	x
	T		0[#]			NNA																							NNA	x
Ueki (2012)[85]	B					0					0			0					0											x
	T					0					0			0					0											x
Blakey (2014)[86]	B																												0	x
	T																												0	x
Lee (2014)[87]	B					0																								x
	T					0																								x
Ueki (2015)[88]	B					0					0	0[c]	0	0					0											
	T					0					0	0[c]	0	0					0											

All data are given in percentages, unless stated otherwise. All unit of analysis was number of patients, unless stated otherwise. [*]Unit of analysis was plates. [#]Unit of analysis was screws.[†]Data of the follow-up moment 6-12 months given. The follow-up moment 12-24 months had high proportion of participants lost to follow-up. [a]Data given in mean±standard deviation. [b]Percentage of surgeons 'satisfied' or higher with the osteosynthesis system. [c]If no wound dehiscence was present, plate exposure was also assessed as not present. [d]Only the difference in mean operative time of biodegradable compared to titanium osteosyntheses was reported. [e]Two follow-up moments: 1- and 2-year follow-up, respectively. [f]Postoperative minus preoperative MMO. B, biodegradable; T, titanium; O, objectively assessed; S, subjectively assessed; NNA, numbers not available. MMO, maximal mouth opening; TMJ-dysfunction, temporomandibular joint dysfunction; MFIQ, Mandibular Function Impairment Questionnaire; x, assessed (see Table S6). Empty cells: not reported. Note that (i) malocclusion and (ii)

analgesic usage after short-term follow-up are not mentioned in this table as these endpoints were not assessed in any of the included studies, and (iii) that certain continuous variables are shown without standard deviations because these were not reported in the original manuscripts.

Table S6: Operative displacement and relapse.

Study (first author, year)	Type of displacement	Operative displacement (mean±SD or median (IQR), in mm or ° angle)		Relapse (mean±SD or median (IQR), in mm or ° angle)		Follow-up	Lateral cephalometric reference marks
		B	T	B	T		
Randomised controlled trials							
Matthews et al. (2003)[1]	Mandibular horizontal	4.0 (0.0-5.0)	4.0 (3.0-8.0)	NNA		1 yr	Go
	Mandibular vertical	4.5 (2.0-6.0)	4.5 (1.5-5.0)				Go
	Mandibular angle	4.2 (2.2-8.8)	1.5 (1.0-8.0)				Ar-Go-Gn
Norholt et al. (2004)[62]	Maxillary horizontal	2.3±2.8	2.4±2.2	0.03±0.82	0.24±1.4	6 wks	AI
	Maxillary vertical	2.1±1.6	2.2±2.2	0.58±0.60	0.56±1.9		AI
	Maxillary angle	NR	NR	3.6±2.2	0.67±2.6		OP
Ueki et al. (2005)[64]	Mandibular horizontal	2.0±3.6[a]	3.5±5.3[a]	2.4±2.89	0.7±4.99	1 yr	Pg
	Mandibular vertical	2.9±2.6[a]	4.3±3.3[a]	0.1±2.61	2.5±2.94		Pg
	Mandibular angle	8.8±2.0[a]	3.4±2.4[a]	6.7±2.53	2.6±2.33		Ar-Go-Gn
Cheung et al. (2008)[2]	Maxillary horizontal (adv)	3.43±2.03	4.0±2.45		NNA	1 yr	Point-A
	Maxillary horizontal (setb)	1.12±1.12	1.59±0.84		NNA		
	Maxillary vertical (imp)	2.65±2.05	3.27±1.84		NNA		
	Maxillary vertical (elong)	2.87±1.94	1.45±1.1		NNA		
Park et al. (2010)[65]	Maxillary horizontal	1.88±1.19	3.20±2.19	0.08±0.23	0.0±0.0	6 mos	ANS
	Maxillary vertical	1.32±1.66	2.25±1.98	0.07±0.41	0.0±0.24		ANS
	Maxillary angle	2.45±1.12	3.45±1.80	0.12±0.41	0.15±0.24		SNA
	Mandibular horizontal	8.18±5.24	8.70±8.43	0.60±1.96	1.45±2.95		Pg
	Mandibular vertical	1.05±2.89	2.00±2.16	1.26±1.52	1.85±1.73		Pg
	Mandibular angle	0.55±4.20	0.75±6.79	5.01±4.61	2.30±4.10		Ar-Go-Gn
Tuovinen et al. (2010)[4]	All	NNA	NNA	NNA	NNA		
Prospective cohort studies							

Study (first author, year)	Type of displacement	Operative displacement (mean±SD or median (IQR), in mm or ° angle)		Relapse (mean±SD or median (IQR), in mm or ° angle)		Follow-up	Lateral cephalometric reference marks
		B	T	B	T		
Ferretti et al. (2002)[72]	Mandibular horizontal	5.67±1.70[b]	4.80±1.33[b]	0.83±1.25	0.25±1.38	6 mos	Point-B
Dhol et al. (2008)[73]	Maxillary horizontal	2.02±0.39[c]	2.45±0.57[c]	0.20±0.43[c]	0.80±0.43[c]	≥8 mos	Point-A
	Maxillary vertical	2.46±0.71[c]	2.14±0.65[c]	0.12±0.57[c]	0.64±0.57[c]		Point-A
	Maxillary angle	0.99±0.84[c]	2.36±0.74[c]	0.04±0.69[c]	0.00±0.69[c]		Palatal plane
Bakelen et al. (2014)[74]	Mandibular horizontal	3.2±1.6	4.2±2.2	0.03±1.7	0.3±2.3	2 yrs	Point-B
	Mandibular vertical	4.8±1.8	3.2±2.4	1.1±1.5	0.9±1.6		
Retrospective cohort studies							
Harada et al. (1997)[75]	Mandibular horizontal	NNA		1.62±1.28	1.05±1.00	1 yr	Pg
	Mandibular vertical			0.37±1.33	0.00±0.77		
Costa et al. (2006)[76]	Maxillary horizontal	3.50±1.65	3.54±1.54	0.90±1.37	0.16±0.72	1 yr	Point-A
	Maxillary vertical	0.95±1.79	2.33±1.83	1.55±1.36	0.042±1.31		Point-A
	Maxillary angle	3.00±1.28	3.32±1.62	0.57±1.20	0.02±0.64		SNA
Landes et al. (2006)[5],[d]	Maxillary horizontal (adv)	3.5±4.1	5.4±3.5	2.3±1.8	2.4±2.0	1 yr	Point-A
	Maxillary horizontal (setb)	2.8±3.7	1.9±1.8	2.3±1.9	2.5±1.7		Point-A
	Maxillary vertical (imp)	1.9±1.7	3.3±2.7	2.1±1.9	2.2±1.5		ANS
	Maxillary vertical (elong)	4.2±3.6	3.7±5.2	3.8±3.1	3.1±3.6		ANS
	Mandibular horizontal (adv)	4.6±3.6	6.3±8.8	4.9±4.3	5.1±8.2		Point-B
	Mandibular horizontal (setb)	7.5±8.3	7.2±3.2	3.0±2.0	1.7±2.0		Point-B
	Mandibular angle (CW)	11.8±9.9	7.9±6.6	6.7±8.9	8.2±9.6		Ar-Go-Gn
	Mandibular angle (CCW)	4.5±3.2	6.3±6.6	6.8±5.2	4.2±5.9		Ar-Go-Gn

Study (first author, year)	Type of displacement	Operative displacement (mean±SD or median (IQR), in mm or ° angle)		Relapse (mean±SD or median (IQR), in mm or ° angle)		Follow-up	Lateral cephalometric reference marks
		B	T	B	T		
Turvey et al. (2006)[77]	Mandibular horizontal	5.20±2.37	4.96±2.60	0.54±3.25	0.33±2.2	1 yr	Point-B
	Mandibular vertical	4.34±1.68	4.01±2.30	1.36±2.59	1.15±1.80		
Ueki et al. (2006a and b)[78]	Maxillary horizontal (a)	2.9±2.3[a]	3.1±2.9[a]	1.30±2.14	0.90±2.86	1 yr	Point-A
	Maxillary vertical (a)	0.8±2.0[a]	0.4±1.8[a]	2.30±2.10	0.40±1.90		Point-A
	Maxillary angle (a)	2.7±1.4[a]	3.1±1.6[a]	0.20±1.31	0.80±1.43		SNA
	Maxillary horizontal (b)	1.7±2.7[a]	2.8±1.7[a]	2.00±2.27	1.10±2.04		Point-A
	Maxillary vertical (b)	3.7±2.0[a]	0.0±1.2[a]	3.30±2.15	2.00±1.39		Point-A
	Maxillary angle (b)	2.5±2.3[a]	2.6±1.5[a]	0.40±1.92	1.10±1.61		SNA
Landes et al. (2007)[79],[d]	Maxillary horizontal (adv)	2.5±1.0	5.4±3.5	1.2±0.8	2.4±2.0	1yr	Point-A
	Maxillary horizontal (setb)	2.2±2.4	1.9±1.8	1.8±1.9	2.5±1.7		Point-A
	Maxillary vertical (imp)	1.0±0.7	3.3±2.7	1.1±1.1	2.2±1.5		ANS
	Maxillary vertical (elong)	6.5±3.4	3.7±5.2	2.0±1.4	3.1±3.6		ANS
	Mandibular horizontal (adv)	5.5±3.7	6.3±8.8	2.6±2.7	5.1±8.2		Point-B
	Mandibular horizontal (setb)	11.2±7.7	7.2±3.2	2.7±2.6	1.7±2.0		Point-B
	Mandibular angle (CW)	7.9±2.4	7.9±6.6	2.4±2.7	8.2±9.6		Ar-Go-Gn
	Mandibular angle (CCW)	6.9±2.6	6.3±6.6	7.0±5.4	4.2±5.9		Ar-Go-Gn
Choi et al. (2010)[82]	Mandibular horizontal (setb)	7.11±2.7	5.69±1.10	1.94±0.93	1.60±0.58	14.5 mos	Point-B
	Mandibular vertical (setb)	1.58±2.73	1.81±1.44	0.08±1.38	0.10±1.10		Point-B
Ueki et al. (2011)[83]	Mandibular horizontal	5.0±7.2[e]	5.1±6.9	NNA		1 yr	Pg

Study (first author, year)	Type of displacement	Operative displacement (mean±SD or median (IQR), in mm or ° angle)		Relapse (mean±SD or median (IQR), in mm or ° angle)		Follow-up	Lateral cephalometric reference marks
		B	T	B	T		
	Mandibular vertical	1.5±4.0[e]	3.7±5.5				Pg
	Mandibular angle	3.2±5.4[e]	2.4±3.2				Ar-Go-Gn
Ballon et al. (2012)[84]	Maxillary horizontal (adv)	2.70±1.94	4.28±2.37	1.84±1.69	1.59±1.48	≥6 mos	Point-A
	Maxillary horizontal (setb)	3.46±2.63	3.70±2.10	2.02±1.89	1.70±1.64		Point-A
	Maxillary vertical (imp)	3.13±2.25	3.25±1.55	2.67±2.08	1.40±1.42		ANS
	Maxillary vertical (elong)	5.22±4.05	2.92±2.64	2.68±2.65	1.39±1.55		ANS
	Mandibular horizontal (adv)	4.89±3.67	4.09±2.84	3.65±3.39	2.09±1.43		Point-B
	Mandibular horizontal (setb)	9.31±5.46	8.55±4.85	4.86±2.87	1.05±1.31		Point-B
	Mandibular angle (CW)	7.75±6.18	9.57±7.13	4.55±3.52	10.63±9.47		Ar-Go-Gn
	Mandibular angle (CCW)	4.79±3.09	6.50±6.06	6.36±4.86	5.00±6.53		Ar-Go-Gn
Paeng et al. (2012)[6]	Mandibular horizontal	6.7±2.2	7.0±3.2	0.51±1.23	0.75±1.85	6 mos	Point-B
	Mandibular vertical	NNA		0.71±1.35	1.5±1.39		Me
Ueki et al. (2012)[85]	Maxillary horizontal	2.4±2.1[e]	2.7±2.6	0.30±1.25	0.50±1.99	1 yr	Point-A
	Maxillary vertical	1.0±4.3[e]	0.8±2.9	1.00±1.36	1.20±1.45		Point-A
	Maxillary angle	1.2±3.6[e]	2.2±2.9	0.95±0.76	0.60±1.22		SNA
Blakey et al. (2014)[86]	Maxillary horizontal	5.61±1.30	7.07±2.30	2.06±1.91	1.34±1.34	1 yr	Point-A
Lee et al. (2014)[87]	Mandibular horizontal	13.97±1.39	9.59±1.51	1.89±1.33	3.02±1.05	6 mos	Pg
	Mandibular vertical	1.7±1.68	0.65±1.6	0.83±0.53	1.51±1.56		Pg
	Mandibular angle	3.57±1.06	2.81±0.65	0.33±0.85	1.39±0.48		Ar-Pg to FH

Perioperative displacement and relapse are given in absolute values. The direction of operative displacement (e.g., setback or advancement) are only stated in this table whenever this was explicitly stated in the original manuscript. [a]Time interval values of cephalometric data (e.g., 1-year postoperative minus immediate postoperative data) were calculated based on the cephalometric data of specific time points (e.g., 1 year and immediate postoperative data), assuming normal distribution of data. [b]Discrepancy

exists between data in the text and tables of the original manuscript. The authors did not respond to contact attempts. Data presented in the text of the original manuscript were used. [c]*Data presented as mean ± standard error of the mean (SEM).* [d]*Landes et al. (2006) and Landes et al. (2007) have included the identical control groups. The means and standard deviations of both the intervention groups were pooled and analyzed as a single pair-wise comparison with that specific control group, assuming normal distribution of data.* [e]*The two subgroups of biodegradable osteosyntheses (i.e., uHA/PLLA and PLLA subgroups) were pooled and analyzed as a single pair-wise comparison between biodegradable and titanium osteosyntheses. a: subgroup Le Fort advancement + BSSO setback. b: subgroup Le Fort I advancement + IVRO without fixation. IQR, interquartile range; NNA, numbers not available; Go, gonion; Ar-Go-Gn, articular-gonion-gnathion angle (gonial angle); AI, anterior implant; NS, nasion-sella line; NSP, nasion-sella perpendicular line; OP, occlusal plane; Pg, pogonion; SNA, sella-nasion-A point angle; adv, advancement; setb, setback; imp, impaction; elong, elongation; ANS, anterior nasal spine; CW, clockwise rotation; CCW, counter-clockwise rotation; Me, menton; Ar-Pg, articular-pogonion; FH, Frankfurt horizontal plane; wks, weeks; mos, months; yrs, years.*

Table S7: Results of univariable meta-regression analyses to analyze the effect of risk of bias items on the log risk ratio of symptomatic device removal using a random effects model.

Risk of bias item	Regression coefficient	95% CI (lower to upper border)	P-value
Domain 1 (ref. = low RoB)	0.64	-0.15 to 1.43	0.11
Some concerns	-0.56	-1.74 to 0.61	0.35
High RoB	-2.23	-5.40 to 0.94	0.35
Domain 2 (ref. = low RoB)	-0.06	-0.91 to 0.79	0.89
High RoB	0.70	-0.50 to 1.90	0.25
Domain 3 (ref. = low RoB)	-0.31	-1.68 to 1.06	0.65
Some concerns	0.34	-2.00 to 2.69	0.78
High RoB	0.80	-1.87 to 3.48	0.56
Domain 4 (ref. = low RoB)	-0.46	-1.71 to 0.79	0.47
Some concerns	1.15	-1.40 to 3.70	0.38
High RoB	0.95	-1.63 to 3.54	0.47
Domain 5 (ref. = low RoB)	0.42	-0.11 to 0.96	0.12
Some concerns	-2.01	-5.10 to 1.07	0.20
Overall RoB (ref. = some concerns)	-0.18	-1.29 to 0.93	0.75
High RoB	0.64	-0.71 to 2.00	0.35

RoB, Risk of Bias. Ref., reference item. 95% CI, 95% confidence interval. The meta-regression analysis shows none of the individual risk of bias items have a significant effect on the symptomatic device removal rate.

Table S8: Input and results of the trial sequential analyses using the random-effects (DerSimonian-Laird) model with the corresponding interpretations.

Endpoint	Control event proportion (titanium)[a]	Relative risk (95% CI)[a]	Diversity (D^2) [a]	Total N/RIS	Crossed conventional test boundary	Crossed O'Brien-Fleming boundary	Crossed futility boundary	Interpretation
Short-term follow-up								
Infection	4.3%	1.03 (0.46; 2.28)	0.0	645/780586[b]	Not estimable due to <5% of RIS achieved			Inconclusive, potentially false neutral
Swelling	13.2%	1.51 (0.68; 3.38)	0.62	255/2536	No	No	No	Inconclusive, potentially false neutral
Dehiscence	2.3%	1.53 (0.52; 4.50)	0.0	421/5865	No	No	No	Inconclusive, potentially false neutral
Intermediate follow-up								
Mobility bone segments	10.3%	1.37 (0.47; 3.99)	0.0	155/2302	No	No	No	Inconclusive, potentially false neutral
Long-term follow-up								
Malocclusion	11.2%	0.93 (0.39; 2.26)	0.0	217/49794[b]	Not estimable due to <5% of RIS achieved			Inconclusive, potentially false neutral
Swelling	2.0%	2.42 (0.52; 11.19)	0.0	178/1316	No	No	No	Inconclusive, potentially false neutral
Palpability of screws/plates	23.2%	0.38 (0.11; 1.28)	0.67	400/619	No	No	No	Inconclusive, potentially false neutral

Overall follow-up								
Symptomatic device removal	8.3%	1.29 (0.68; 2.44)	0.52	777/9717	No	No	No	Inconclusive, potentially false neutral
Revision surgery (not device removal)	2.0%	1.40 (0.37; 5.34)	0.0	377/11445	No	No	No	Inconclusive, potentially false neutral

RIS, required information size. [a]According to the observed relative risk and diversity of the present meta-analysis including randomised controlled trials only. [b]RIS is very high due to a very small relative risk reduction. Outcomes that are not mentioned were assessed in no or a single randomised controlled trials, or were only assessed in total zero-event trials.

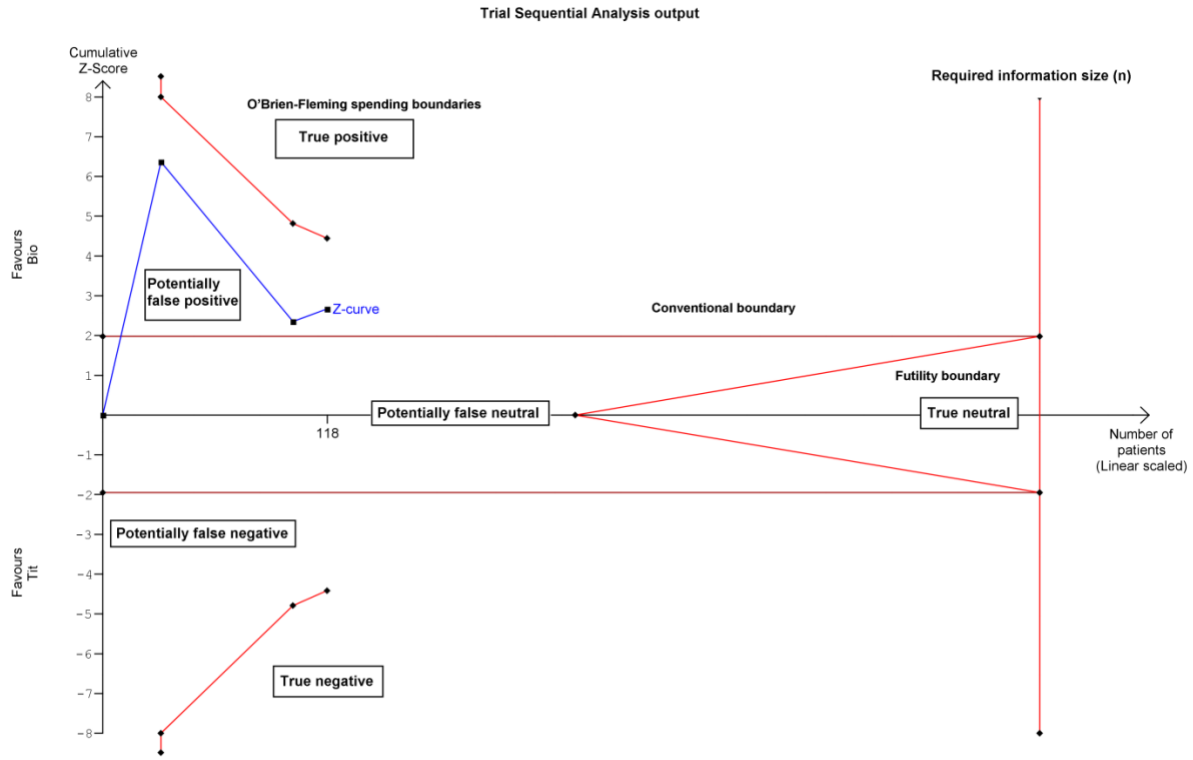

Figure S1: Example graph with explanation of the trial sequential analysis. The y-axis represents the cumulative Z-score and the x-axis the number of patients of included trials. A Z-score of ±1.96 corresponds to α = 0.05 (conventional boundaries). The required information size is the number of patients needed to draw a definite conclusion and this number is comparable to a sample size calculation in randomised controlled trials. The O'Brien-Fleming spending boundaries are trial sequential adjusted boundaries; the fewer patients are randomised, the wider these borders are due to increased chance of random errors. Crossing the futility boundary indicates that the intervention is unlikely to have the anticipated effect. The interpretation of each area is presented as textboxes in the graph. Thus, TSA provides three borders: conventional test boundaries (α = 0.05; Z = +/- 1.96; i.e., crossing boundary means potentially false positive or negative), O'Brien-Fleming spending boundaries (i.e., crossing boundary means true positive or negative effect), and futility boundaries (crossing boundary means true neutral effect). If no boundaries are crossed, the evidence remain inconclusive (i.e., potentially false neutral).

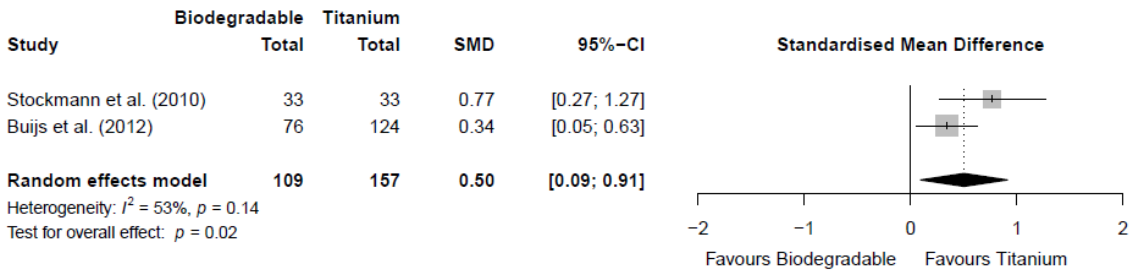

Figure S2: Forest plot of the endpoint operative time in minutes. *SMD, standardised mean difference; 95%-CI, 95% confidence interval.*

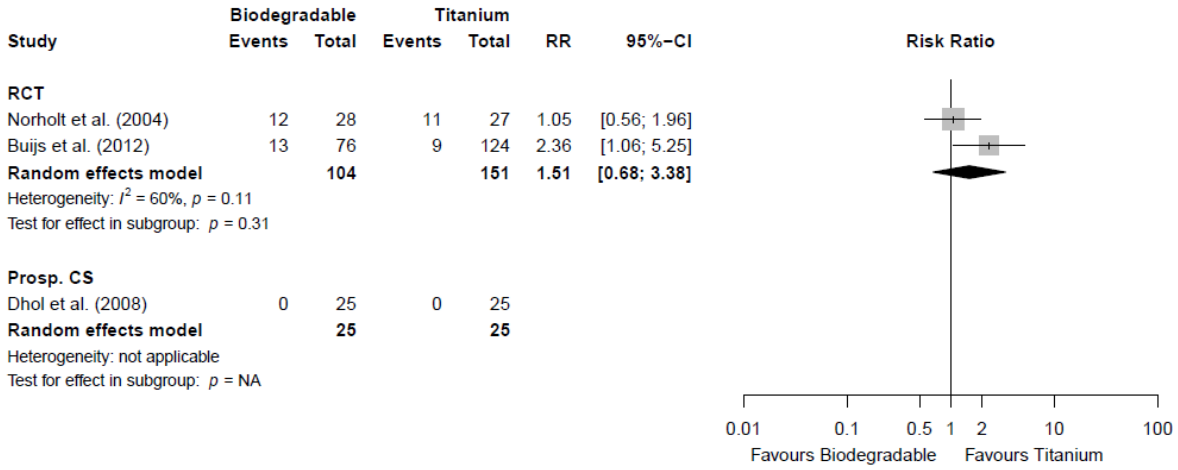

Figure S3: Forest plot of the endpoint swelling (<4 weeks follow-up) stratified by study design. *RCT, randomised controlled trials; Prosp. CS, prospective cohort studies; RR, risk ratio; 95%-CI, 95% confidence interval.*

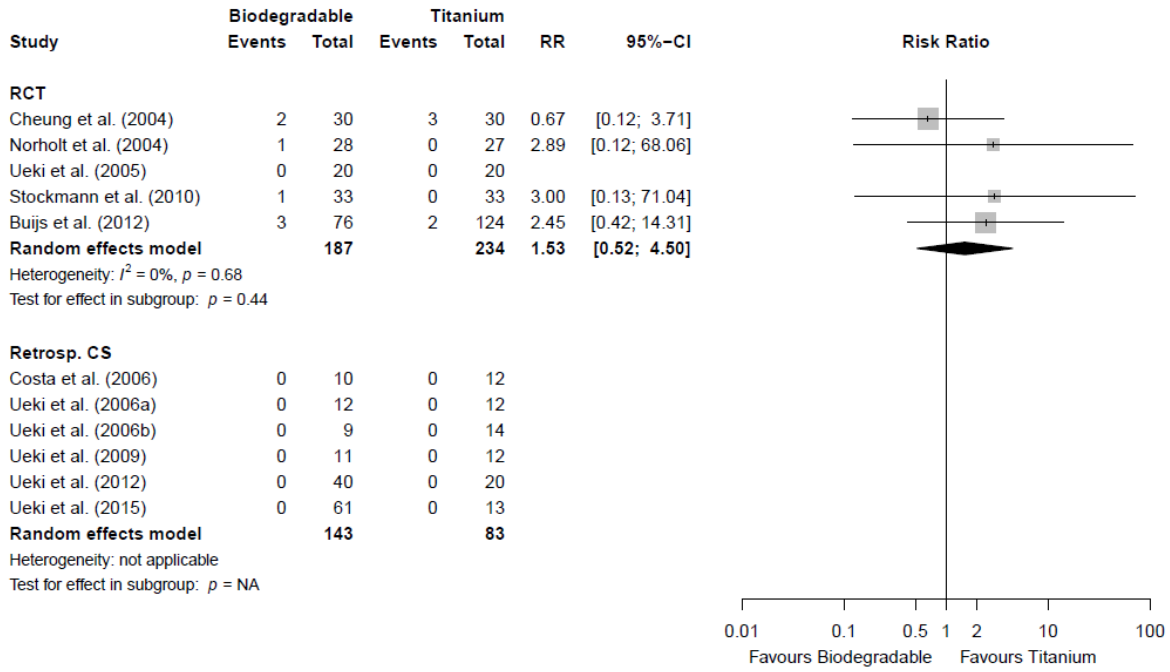

Figure S4: Forest plot of the endpoint dehiscence (<4 weeks follow-up) stratified by study design. *RCT, randomised controlled trials; Retrosp. CS, retrospective cohort studies; RR, risk ratio; 95%-CI, 95% confidence interval.*

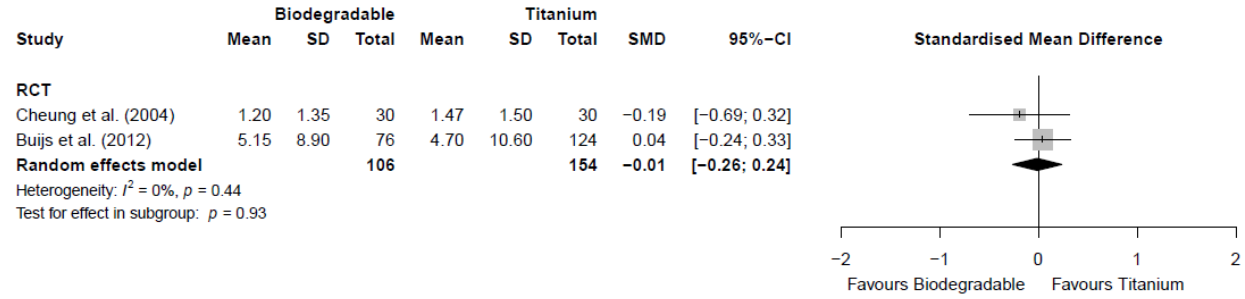

Figure S5: Forest plot of the endpoint pain (6-12 weeks follow-up) stratified by study design. *RCT, randomised controlled trials; SMD, standardised mean difference; 95%-CI, 95% confidence interval.*

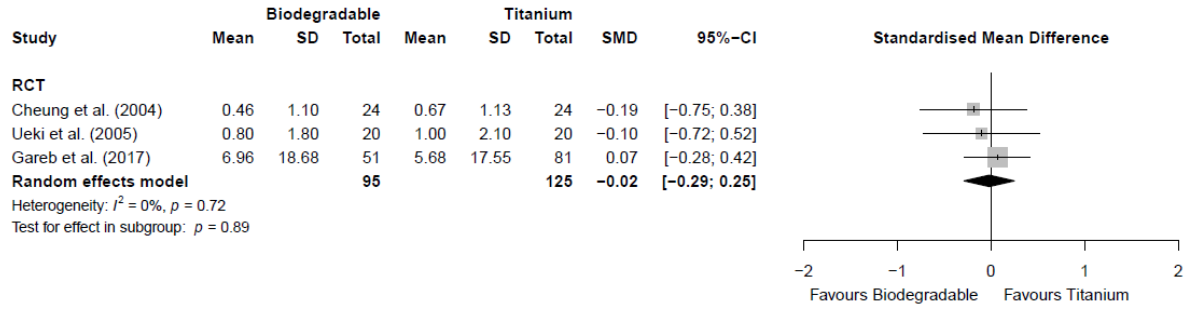

Figure S6: Forest plot of the endpoint pain (>12 weeks follow-up) stratified by study design. *RCT, randomised controlled trials; SMD, standardised mean difference; 95%-CI, 95% confidence interval.*

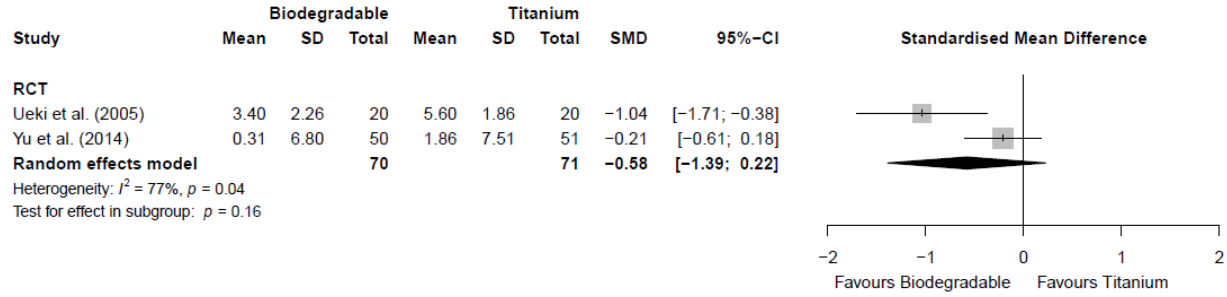

Figure S7: Forest plot of the endpoint maximum mouth opening (>12 weeks follow-up) stratified by study design. *RCT, randomised controlled trials; SMD, standardised mean difference; 95%-CI, 95% confidence interval.*

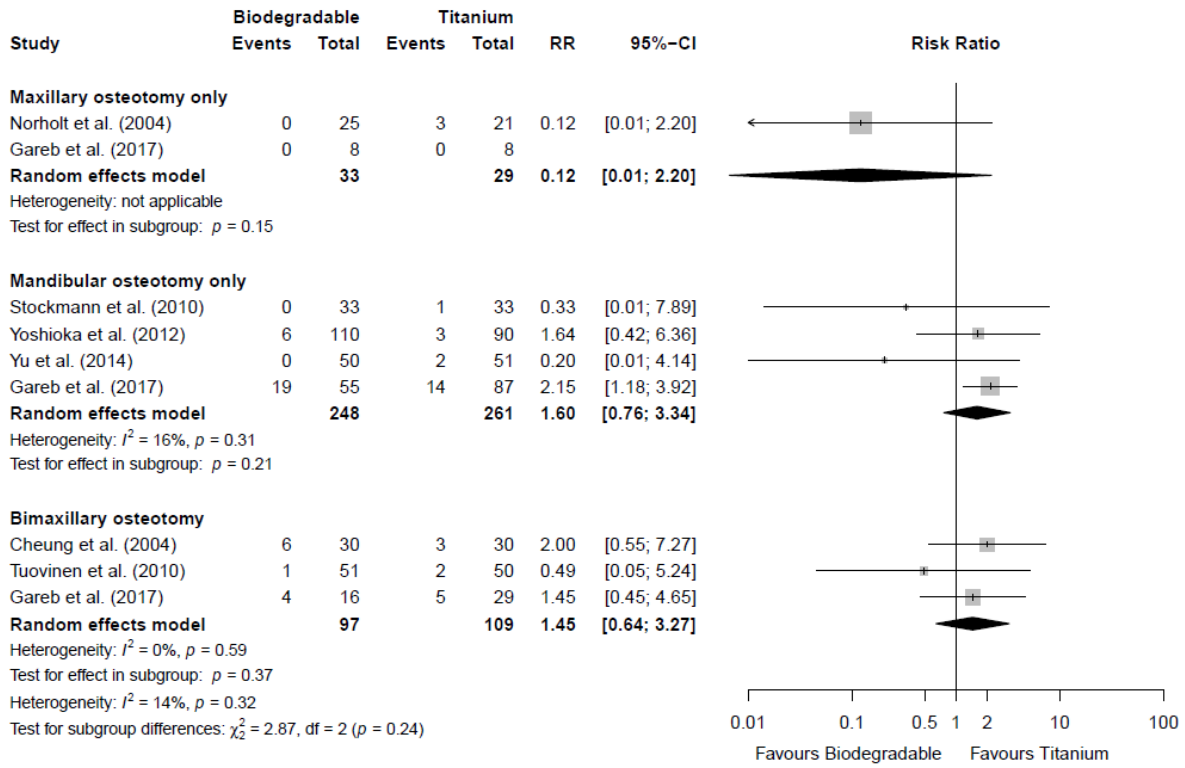

Figure S8: Forest plot of the endpoint symptomatic device removal (overall follow-up) of studies stratified maxillary, mandibular, and bimaxillary osteotomies. *RR, risk ratio; 95%-CI, 95% confidence interval.*

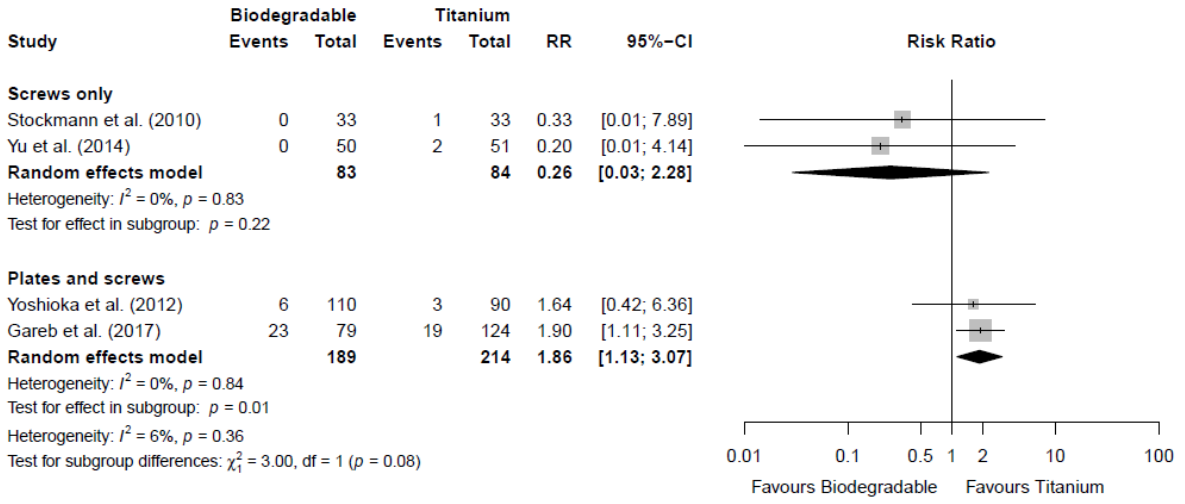

Figure S9: Forest plot of the endpoint symptomatic device removal (overall follow-up) of studies including osteosynthesis by plates and screws versus only screws. *RR, risk ratio; 95%-CI, 95% confidence interval.*

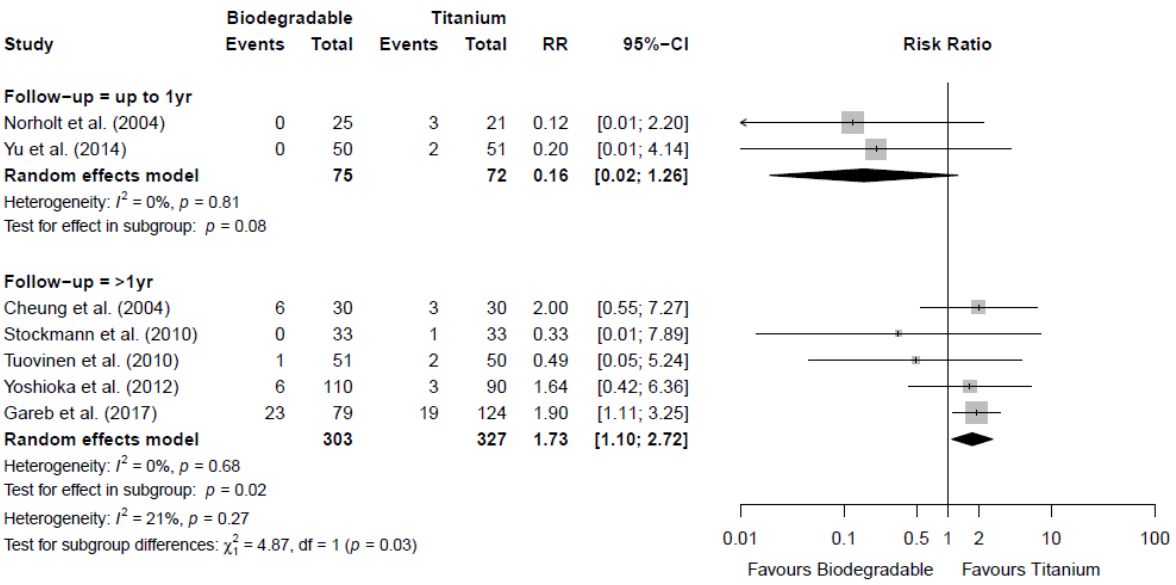

Figure S10: Forest plot of the endpoint symptomatic device removal (overall follow-up) stratified by ≤1-year and >1-year follow-up. *RR, risk ratio; 95%-CI, 95% confidence interval.*

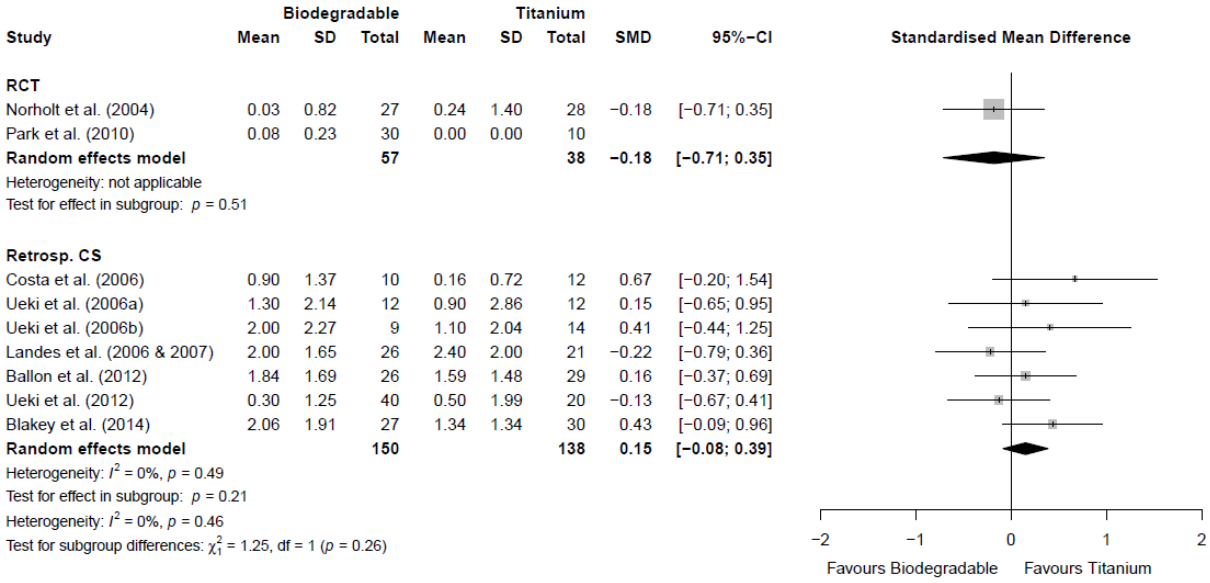

Figure S11: Forest plot of the endpoint maxillary horizontal relapse after maxillary advancement stratified by study design (overall follow-up). *RCT, randomised controlled trials; Retrosp. CS, retrospective cohort studies; SMD, standardised mean difference; 95%-CI, 95% confidence interval.*

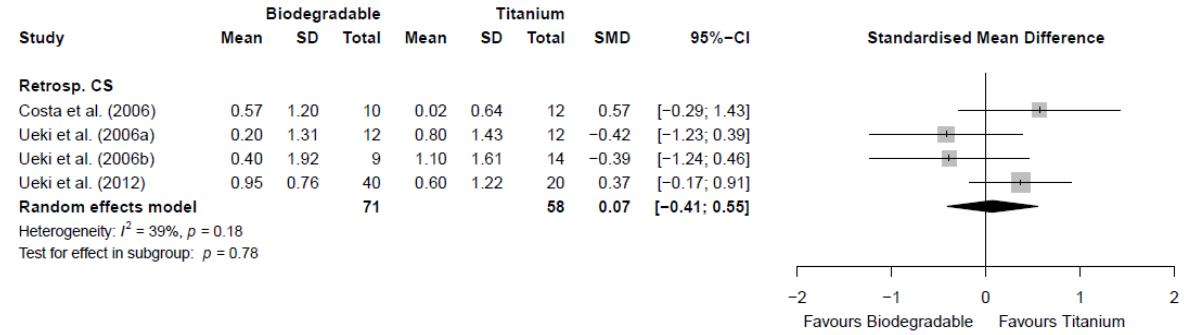

Figure S12: Forest plot of the endpoint maxillary angular relapse after maxillary advancement stratified by study design (overall follow-up). *Retrosp. CS, retrospective cohort studies; SMD, standardised mean difference; 95%-CI, 95% confidence interval.*

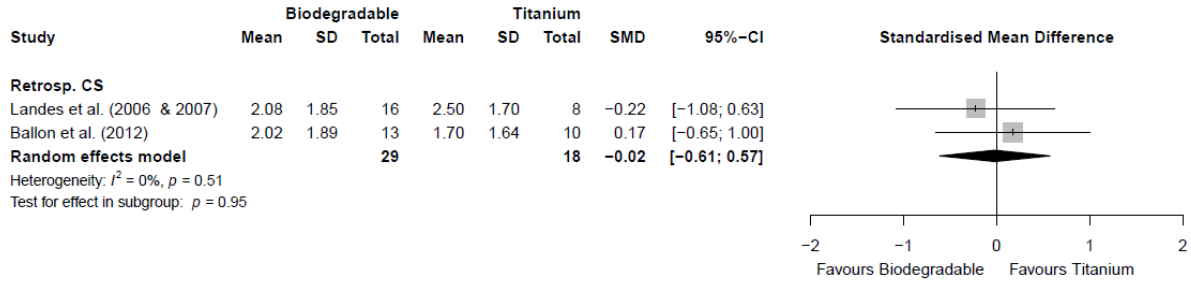

Figure S13: Forest plot of the endpoint maxillary horizontal relapse after maxillary setback stratified by study design (overall follow-up). *Retrosp. CS, retrospective cohort studies; SMD, standardised mean difference; 95%-CI, 95% confidence interval.*

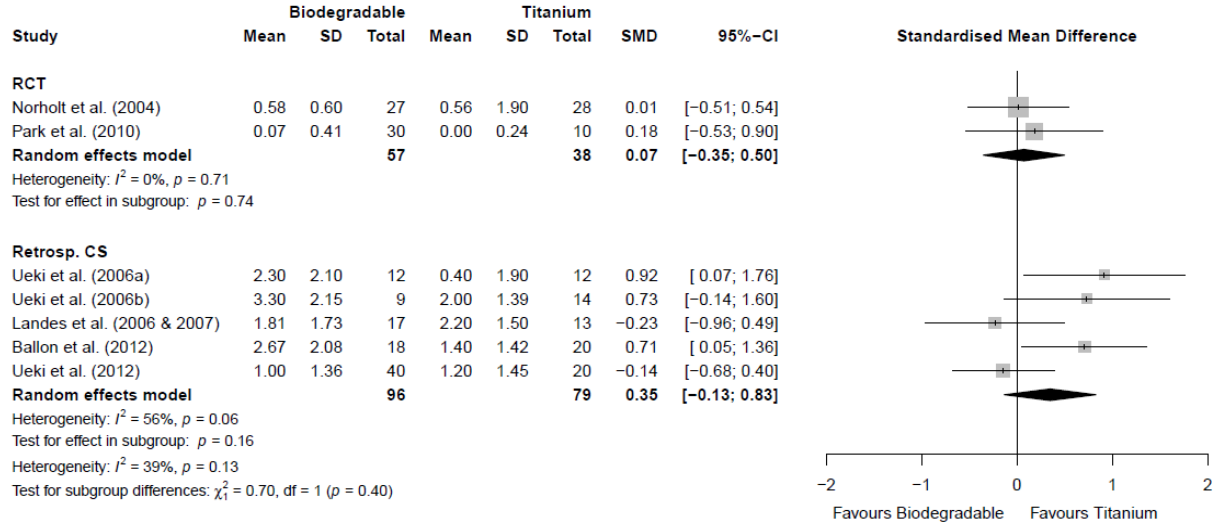

Figure S14: Forest plot of the endpoint maxillary vertical relapse after maxillary impaction stratified by study design (overall follow-up). *RCT, randomised controlled trials; Retrosp. CS, retrospective cohort studies; SMD, standardised mean difference; 95%-CI, 95% confidence interval.*

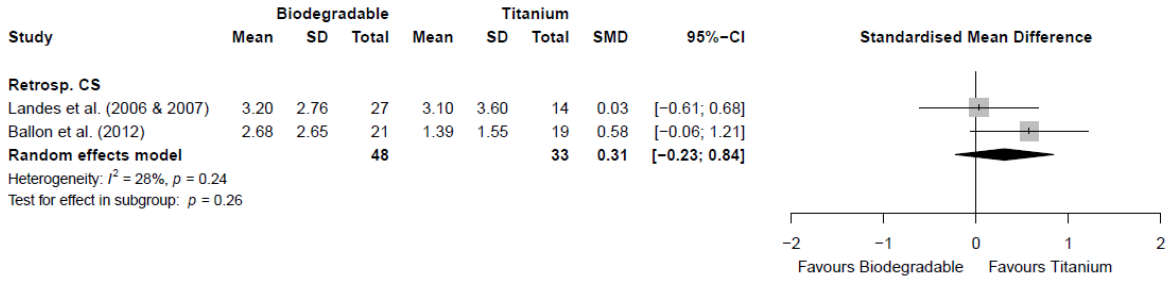

Figure S15: Forest plot of the endpoint maxillary vertical relapse after maxillary elongation stratified by study design (overall follow-up). *Retrosp. CS, retrospective cohort studies; SMD, standardised mean difference; 95%-CI, 95% confidence interval.*

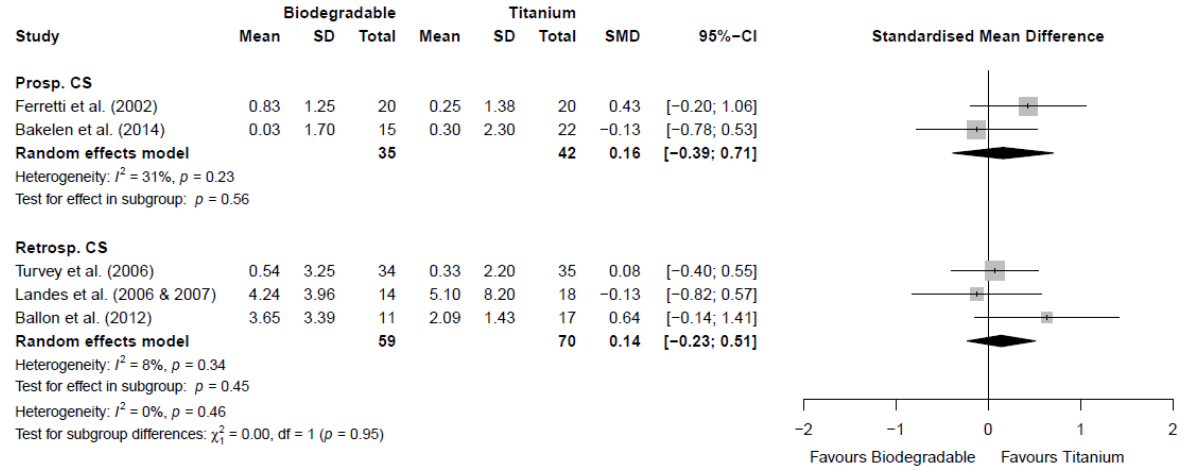

Figure S16: Forest plot of the endpoint mandibular horizontal relapse after mandibular advancement stratified by study design (overall follow-up). *Prosp. CS, prospective cohort studies; Retrosp. CS, retrospective cohort studies; SMD, standardised mean difference; 95%-CI, 95% confidence interval.*

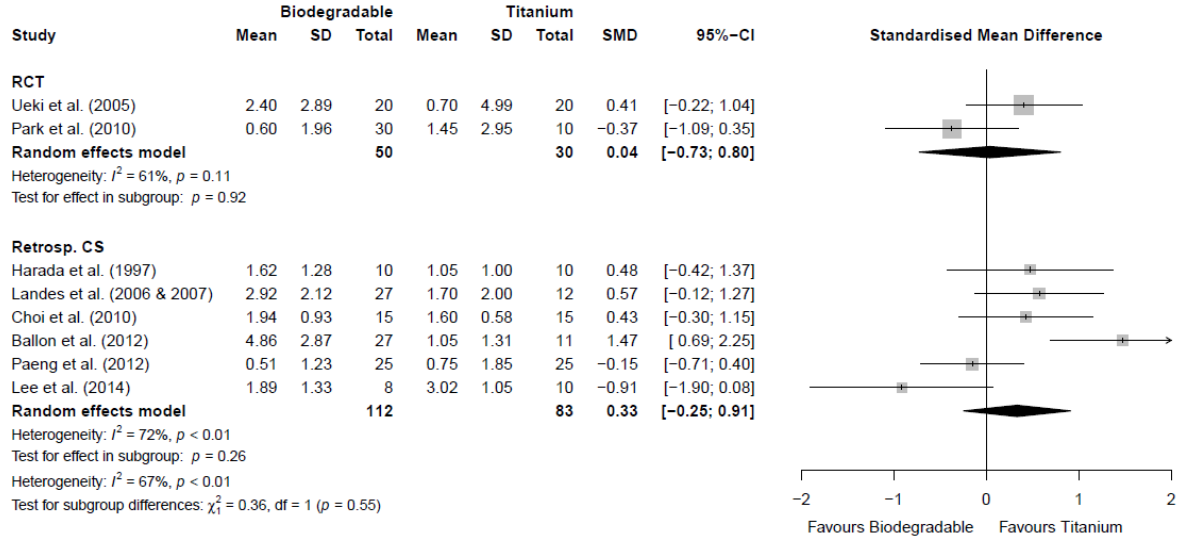

Figure S17: Forest plot of the endpoint mandibular horizontal relapse after mandibular setback stratified by study design (overall follow-up). *RCT, randomised controlled trials; Retrosp. CS, retrospective cohort studies; SMD, standardised mean difference; 95%-CI, 95% confidence interval.*

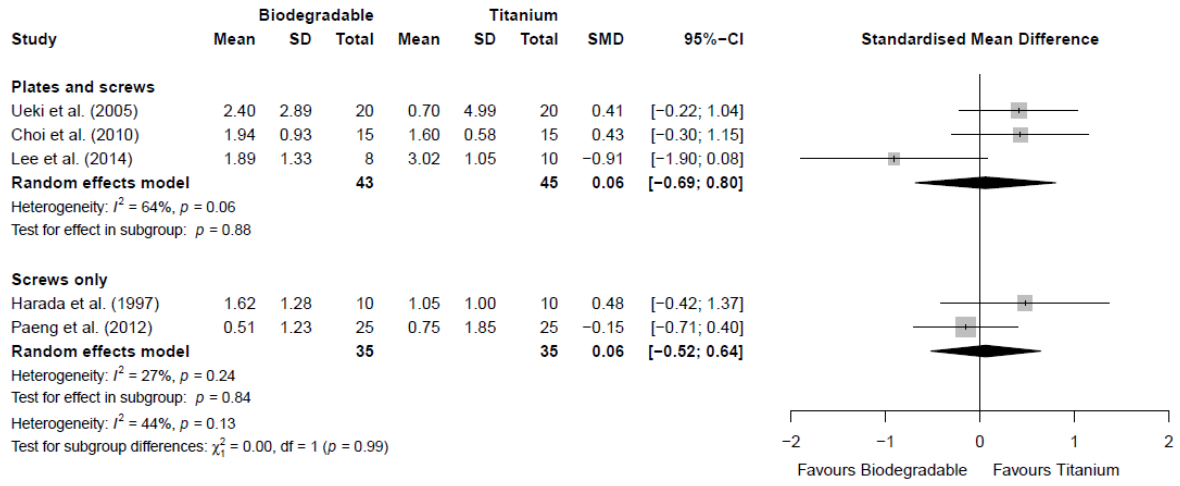

Figure S18: Forest plot of the endpoint mandibular horizontal relapse after mandibular setback of studies including osteosynthesis by plates and screws versus only screws (overall follow-up). *SMD, standardised mean difference; 95%-CI, 95% confidence interval.*

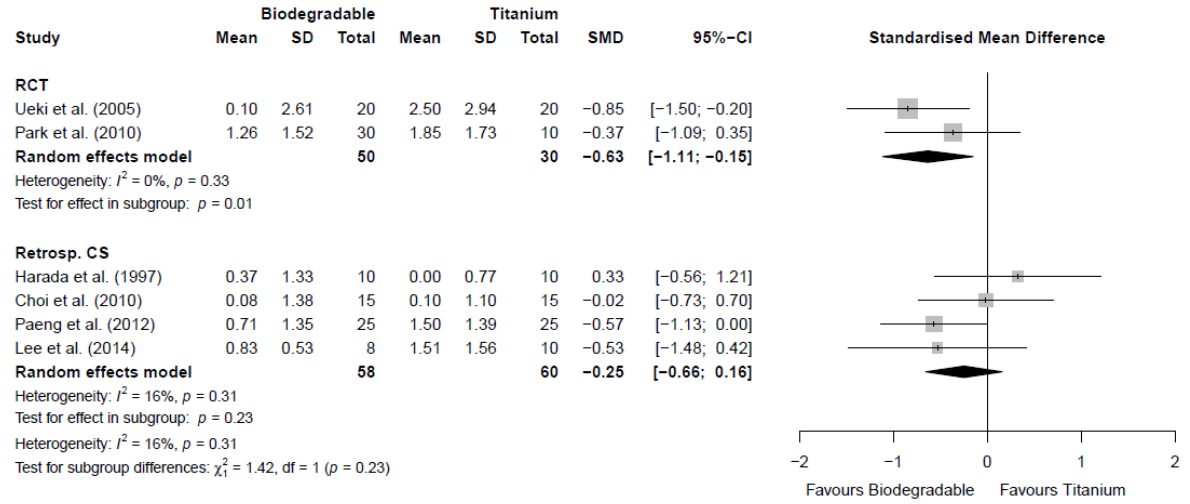

Figure S19: Forest plot of the endpoint mandibular vertical relapse after mandibular setback stratified by study design (overall follow-up). *RCT, randomised controlled trials; Retrosp. CS, retrospective cohort studies; SMD, standardised mean difference; 95%-CI, 95% confidence interval.*

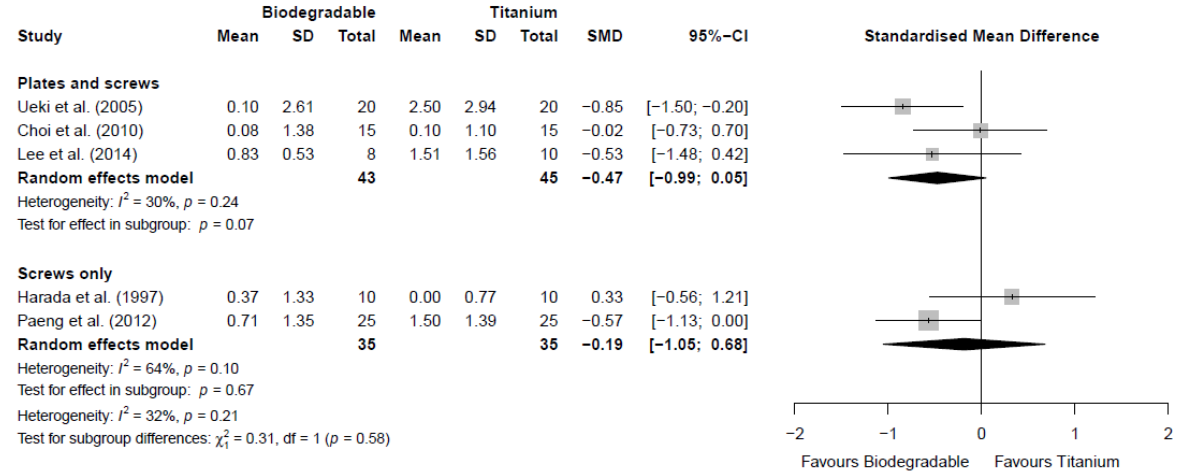

Figure S20: Forest plot of the endpoint mandibular vertical relapse after mandibular setback of studies including osteosynthesis by plates and screws versus only screws (overall follow-up). *SMD, standardised mean difference; 95%-CI, 95% confidence interval.*

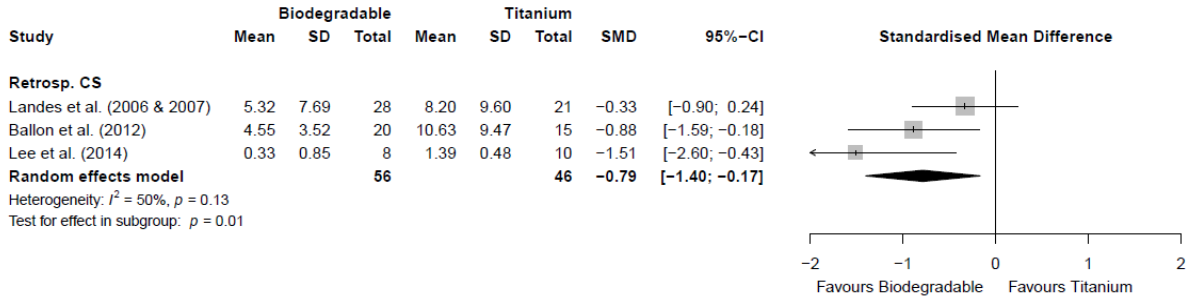

Figure S21: Forest plot of the endpoint mandibular angular relapse after mandibular clockwise rotation stratified by study design (overall follow-up). *Retrosp. CS, retrospective cohort studies; SMD, standardised mean difference; 95%-CI, 95% confidence interval.*

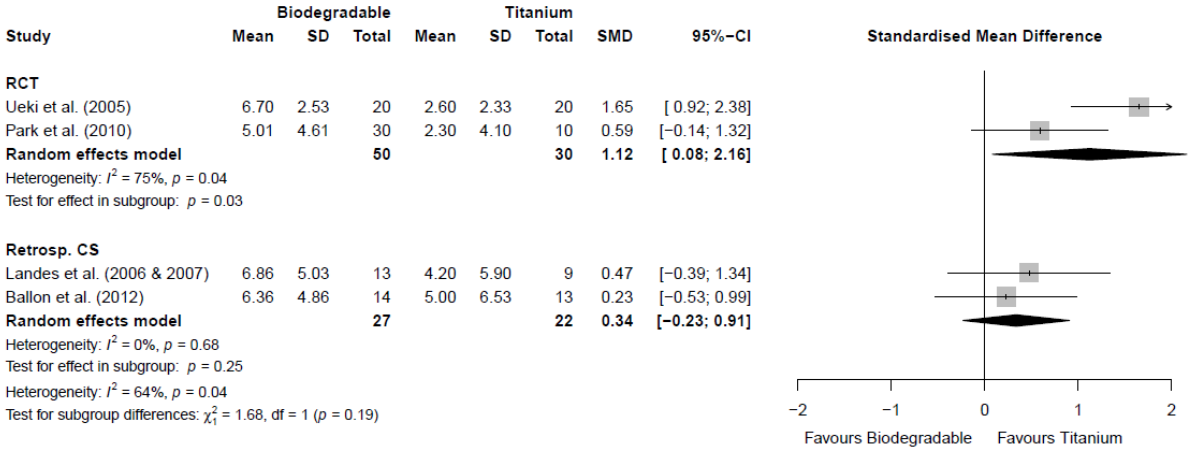

Figure S22: Forest plot of the endpoint mandibular angular relapse after mandibular counter clockwise rotation stratified by study design (overall follow-up). *RCT, randomised controlled trials; Retrosp. CS, retrospective cohort studies; SMD, standardised mean difference; 95%-CI, 95% confidence interval.*

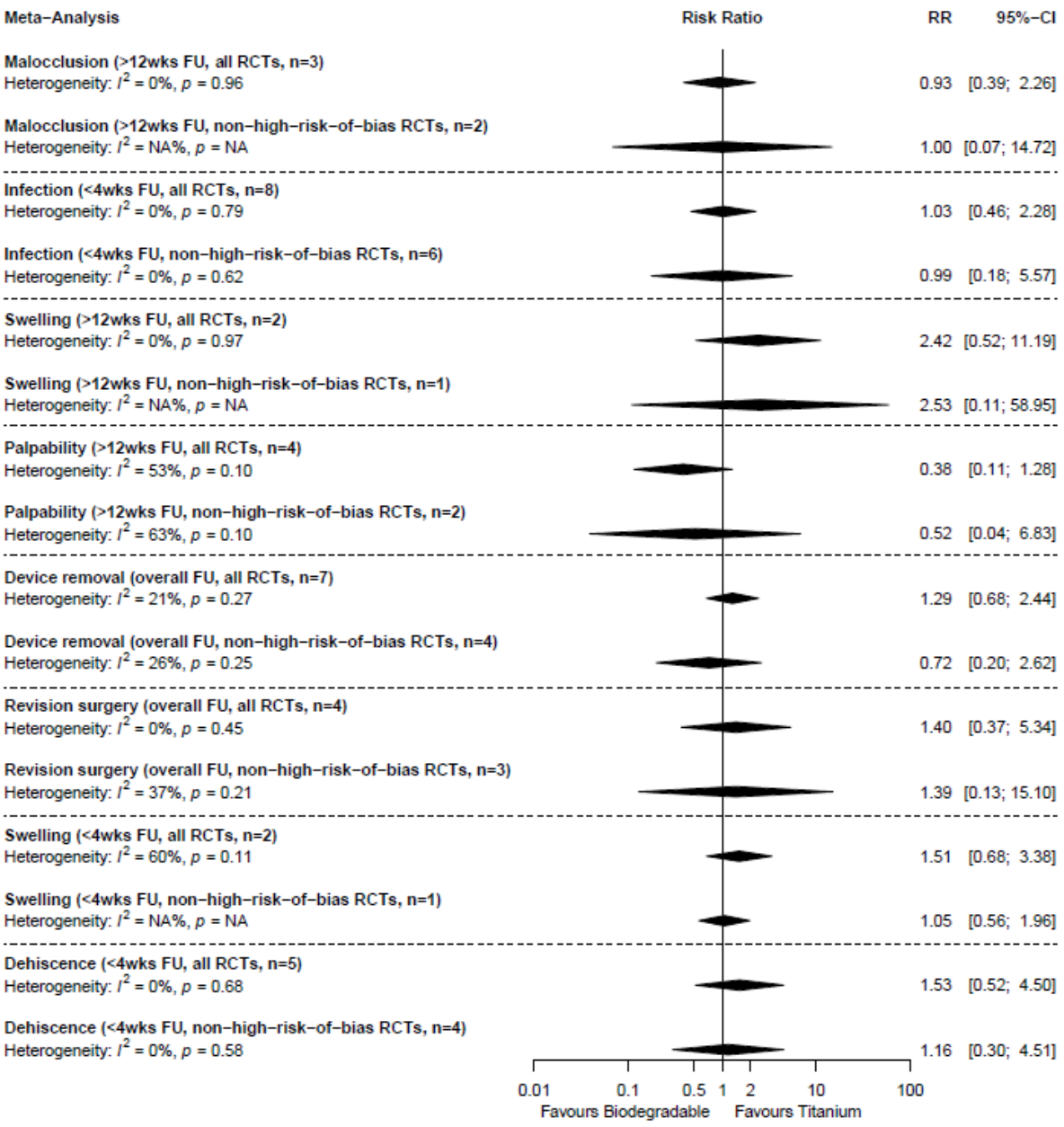

Figure S23: Sensitivity analysis with summary risk ratios for all pooled outcomes according to the inclusion of all randomized controlled trials and non-high-risk-of-bias RCTs only. *RCT, randomised controlled trials; RR, risk ratio; 95%-CI, 95% confidence interval.*

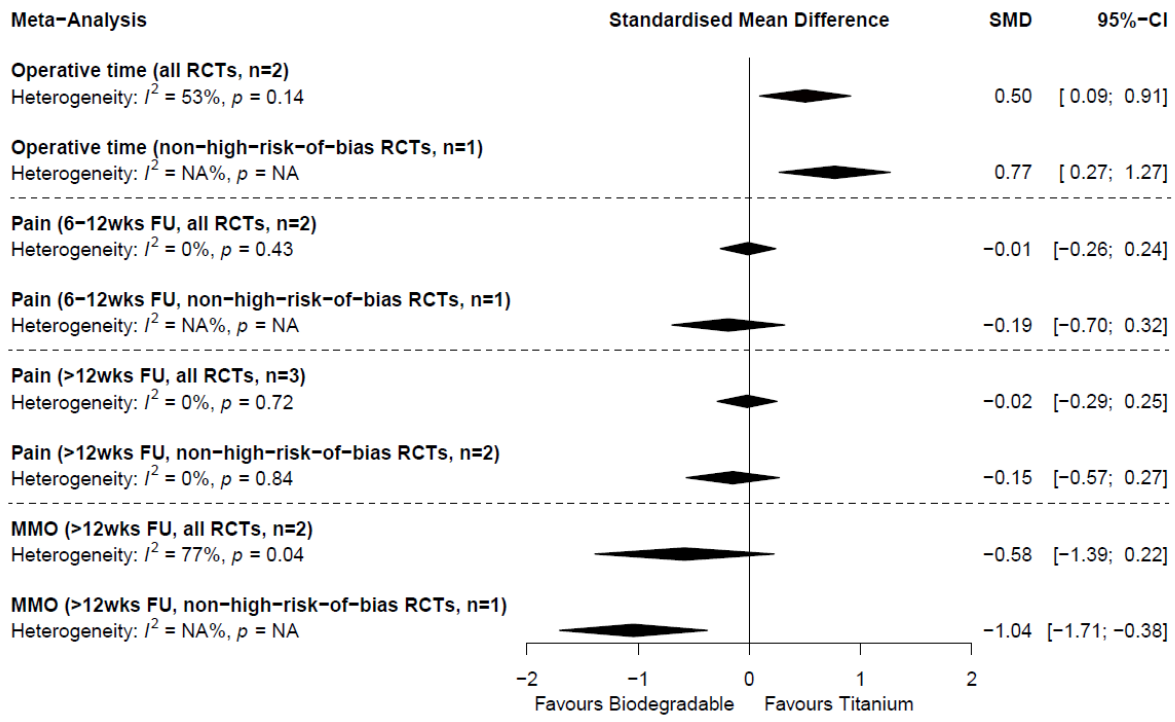

Figure S24: Sensitivity analysis with summary standardized mean differences for all pooled outcomes according to the inclusion of all randomized controlled trials and non-high-risk-of-bias RCTs only. *RCT, randomised controlled trials; SMD, standardised mean difference; 95%-CI, 95% confidence interval.*

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