REVIEW

EFFECT OF AUTOGENOUS BONE GRAFT SITE ON DENTAL IMPLANT SURVIVAL AND DONOR SITE COMPLICATIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS☆

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ABSTRACT

Objectives

This systematic review and meta-analysis was undertaken to answer the following focus questions:

Is the implant survival in augmented bone utilizing iliac crest bone grafts the same as while using intraoral autologous bone grafts? Is the incidence of post-operative donor site complications the same when using iliac crest bone grafts as opposed to intraoral grafts?

Methods

Systematic searches of electronic databases (PubMed, Embase, CENTRAL) were performed to identify studies which reported on implant survival and postoperative complications for dental implants placed in grafted partially/completely edentulous human jaws. Studies were included if: they reported on 2-piece micro-rough surface root form dental implants placed in bone-augmented completely or partially edentulous human jaws, and the jaws must have been augmented with autologous bone graft materials. Time and nature of postoperative complications must have been reported. Two investigators performed data extraction and a Cohen's unweighted kappa was calculated for inter-investigator reliability. A meta-analysis was performed for the extracted data on implant survival rate in both iliac crest grafts and intra-oral grafts. A qualitative analysis was performed on the information extracted on graft donor site complications. Quality assessment of the included studies were done using the Cochrane collaboration tool and the Newcastle-Ottawa scales.

Results

A total of 23 studies were included in the final analysis. The calculated kappa ranged between 0.77-0.89 for the literature search and identification process. Fourteen studies were included with data on implant survival including five randomized controlled clinical trials. The meta-analysis of included studies revealed that the implant survival rate of dental implants placed in jaws augmented with iliac crest grafts was lower than those placed in jaws augmented with intra-

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KEYWORDS

Dental implant, Autologous bone graft, Intra-oral bone graft, Postoperative complications, Implant survival, Systematic review, Meta-analysis

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oral bone grafts at 6-months [ICG = 95.8% IOG = 98.4%; $P < .001$], 12-months [ICG = 97.0%, IOG = 98.4%; $P < .001$], 24-months [ICG = 85.9%, IOG = 98.2%; $P < .001$], 60-months [ICG = 90.0%, IOG = 91.5%; $P < .001$], and at 120-months [ICG = 88.8%, IOG = 95.2%; $P < .001$] follow-up periods. Iliac crest grafts were also frequently associated with donor site complications including pain / discomfort, gait disturbance, and sensory disturbance.

Conclusions
This systematic review and meta-analysis demonstrates that implant survival is consistently higher in bone harvested from intraoral sites compared to iliac crest grafts. Donor site complications seemed to be a frequent finding with iliac crest grafts and mental grafts.

Funding
None.

Registration
The review protocol was registered with PROSPERO: International prospective register of systematic reviews (CRD42021283738).

INTRODUCTION

Dental implants offer an alternative treatment modality in the management of missing teeth, facilitating both fixed and removable prosthodontic options.[1] Successful dental implant treatment requires a thorough and accurate planning assessment utilizing radiographic examination.[2,3] Three-dimensional imaging using Cone Beam Computed Tomography (CBCT) is often necessary to identify vital anatomical structures and to assess both the quantity and quality of alveolar bone available for placement.[4,5] However, resorption of the edentulous or partially edentulous alveolar ridge can compromise dental implant placement in a prosthetically-driven ideal position. Therefore, augmentation of insufficient bone volume can be required prior to or in conjunction with implant placement to ensure predictable long-term function and an aesthetically pleasing outcome.[6]

Bone augmentation can be achieved in a number of different ways including autogenous grafts, xenografts and alloplastic materials.[7] Currently autogenous bone grafts are regarded as the gold standard in bone regeneration procedures from a biological viewpoint with common donor sites including iliac crest and intraoral sites such as mandibular symphysis and coronoid process.[8] However, donor site morbidity, unpredictable resorption, limited available quantities, and the need to include additional surgical sites are the drawbacks associated with this augmentation technique.[9] Given the associated potential morbidity with autogenous bone grafting it is essential that clinicians and patients understand the success rates of implants placed in grafted bone at the outset of treatment to ensure informed consent.

The aim of this systematic review was to screen and pool the available evidence to establish:

(1) Is there a difference in implant survival in autogenous grafts sourced from iliac crest compared to intraoral bone?
(2) Is there a difference in postoperative donor site complications for iliac crest compared to intraoral bone grafts?

The focused question set for this systematic review was "In patients undergoing dental implant therapy with autogenous bone grafting, what is the effect of the site of bone grafting (iliac crest vs intraoral) on implant survival and biological complications associated with the donor site?"

MATERIALS AND METHODS

Protocol and Registration

This systematic review and meta-analysis were conducted and reported according to the PRISMA guidelines.[10-13] The review protocol was registered with PROSPERO: International prospective register of systematic reviews (CRD42021283738). Ethical approval was not required for this systematic review.

Eligibility Criteria

All prospective human studies reporting on survival and postoperative complications for dental implants placed in autogenous bone which satisfied the listed predefined inclusion criteria (Table 1) were included in the systematic review.

Information Sources

Three electronic databases were searched: MEDLINE (PubMed), EMBASE, and CENTRAL. Hand searches of dental journals were performed for records that were not

Table 1. PICO focused question, criteria for inclusion, sources of information, search terms, search strategy, search filters, and search dates.

Focus questions	Is the Implant survival in augmented bone utilizing iliac crest bone grafts the same as while using intraoral autologous bone grafts? Is the incidence of postoperative donor site complications the same when using iliac crest bone grafts as opposed to intraoral grafts?	
Search terms	Population	# 1 – ((Jaw, edentulous [MeSH]) OR (mouth, edentulous [MeSH]) OR (humans [MeSH]) OR (dental prosthesis, implant supported [MeSH]) OR (edentulous ridge [all fields]) OR (reduced alveolar bone height [all fields]) OR (extraction sockets [all fields]) OR (alveolar ridge deficiency [all fields]) OR (horizontal ridge deficiency [all fields]) OR (insufficient bone volume [all fields]) OR (implant supported fixed dental prostheses [all fields]) OR (implant supported overdentures [all fields]))
	Intervention or exposure	#2 – ((Osseointegration/physiology [MeSH]) OR (alveolar ridge augmentation [MeSH]) OR (alveolar ridge augmentation/methods* [MeSH]) OR (alveolar bone loss/surgery* [MeSH]) OR (bone transplantation/methods* [MeSH]) OR (bone grafting [MeSH]) OR (guided tissue regeneration [MeSH]) OR (maxillary sinus/surgery [MeSH]) OR (maxillary sinus/pathology [MeSH]) OR (maxilla/surgery* [MeSH]) OR (maxilla/pathology [MeSH]) OR (mandible/surgery [MeSH]) OR (mandible/pathology [MeSH]) OR (ilium/surgery [MeSH]) OR (mandibular reconstruction/methods* [MeSH]) OR (maxillary reconstruction/methods* [MeSH]) OR (dental implantation, endosseous [MeSH]) OR (dental implants [MeSH]) OR (chin/surgery* [MeSH]) OR (guided bone regeneration [all fields] OR (alveolar bone grafting [all fields]) OR (maxillary sinus grafting [all fields]) OR (sinus floor elevation* [all fields]) OR (maxillary sinus floor elevation* [all fields]) OR (maxillary sinus lift* [all fields]) OR (maxillary sinus augmentation [all fields]) OR (socket preservation [all fields]) OR (ridge preservation procedures* [all fields]) OR (ridge preservation techniques* [all fields]) OR (socket grafting [all fields]) OR (implantation* [all fields]) OR (implant [all fields]) OR (implants [all fields]))
	Comparison	#3 – ((Bone grafts [MeSH]) OR (transplantation, autologous [MeSH]) OR (autografts/transplantation* [MeSH]) OR (ilium/transplantation* [MeSH]) OR (biocompatible materials [MeSH]) OR (Bone transplantation/methods* [MeSH]) OR Bone transplantation/pathology [MeSH]) (bone transplantation/instrumentation* [MeSH]) OR (osteoblasts/transplantation* [MeSH] OR (osteogenesis/physiology [MeSH]) OR (tissue engineering/methods* [MeSH]) OR (bone regeneration/physiology [MeSH]) OR (Periosteum/transplantation* [MeSH]) OR (tissue scaffolds* [MeSH]) OR (tissue and organ harvesting/methods* [MeSH]))
	Outcome	#4 – ((Graft survival [MeSH]) OR (survival [MeSH]) OR (survival rate [MeSH]) OR (survival analysis [MeSH]) OR (bone regeneration [MeSH]) OR (graft rejection [MeSH]) OR (intraoperative complications [MeSH]) OR (postoperative complications [MeSH]) OR (treatment failure [MeSH]) OR (tissue and organ harvesting/adverse effects [MeSH]) OR (treatment outcome [MeSH]) OR (vertical bone gain [all fields]) OR (horizontal bone gain [all fields]) OR (complication* [all fields]) OR (de novo bone formation [all fields]) OR (graft failure [all fields]) OR (success* [all fields]) OR (failure* [all fields]))
Filters applied	Language	#5 – ((English [lang]) OR (French [Lang]) OR (German [Lang]) OR (Norwegian [Lang]) OR (Swedish [Lang]) OR (Danish [Lang]))
	Species	#6 – (Human [Species])
	Journal categories	#7 - (Dental journals [journal categories])
Search combination	#1 AND #2 AND #3 AND #4 AND #5 AND #6 AND #7	
Search dates	Between January 1, 1980 and June 30, 2021. Last confirmatory search as updated on March 7, 2022.	
Database search	Electronic	PubMed, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL)
	Journals	All peer reviewed dental journals available in PubMed, Embase and CENTRAL. No filters were applied for the journals
Selection criteria	Inclusion criteria	Studies reporting on dental implants placed in bone-augmented completely or partially edentulous human jaws. The jaws must have been augmented with autologous bone graft materials. Studies must specify the study design, number of patients and number of dropouts, type of autologous graft placed, time of graft and implant placement, number of implants placed and failed, number of implants dropped out and time of implant loading. Implant type: 2-piece, micro-rough surface root form implants. Patients must have been clinically examined during recall visits. Time and nature of postoperative complications must have been reported.
	Exclusion criteria	Retrospective studies, Studies not specifying follow-up period or post grafting follow-up period of less than 6 months. Grafting done with synthetic or xenografts. Grafts placed in irradiated bone or in medically compromised patients. Grafts placed in combination with Platelet Rich Plasma (PRP) / Platelet Rich Fibrin (PRF). Case reports with sample size of less than 10 cases.

accessible electronically or for those records without an electronic abstract available. Further searches resulting from reference cross-checks were performed to identify studies that were not discovered online. Further attempts to maximize the pool of relevant studies and avoid any erroneous exclusion involved posting queries on research community websites (https://www.researchgate.net/) and, personal communications sent to selected authors. The final update for all the electronic searches was performed on March 7, 2022.

Search Strategy

The original search strategy was designed and set up by experts (MS, HG, & GMK) in database searches (Table 1). An initial electronic search was performed by a single reviewer (MS). Then the search was repeated and updated by 3 reviewers (NH, JH, CM) to confirm the number of discovered articles by the search strategy. The search terms employed were either medical subject headings (MeSH) terms or keywords classified under general (all fields) category. The search terms were then combined with an "OR," and PICO categories were combined using "AND" to create a final logic search query.

Study Selection

All relevant studies were included in this review, if they fulfilled the inclusion criteria (Table 1). An initial title and abstract screening were performed by one investigator (MS) and updated by 2 investigators independently (NH, JK). A final list of studies was put forth for full-text analysis and data extraction, only after a mutual agreement between the 2 investigators; disagreements, if any, were resolved by means of a consensus discussion lead by a fourth investigator (GMK). In cases of identified studies reporting on the same cohort at different time points, only the most recent publication was included in the review.

Data Collection Process

Two investigators (NH, & JK) extracted data from the included studies independently and were reciprocally blinded. During data extraction, for any uncertainty involving the extracted variable, a consensus was always reached by the investigators before finalizing the extracted data. In cases of significant doubts, corresponding authors were contacted for confirmation of the extracted information. The data items extracted from the included studies are specified in Table 2.

MISSING DATA

Information was requested by email from the corresponding authors of included studies for missing or unclear data. In case of a non-response, email reminders were sent. A non-response from the corresponding author ultimately resulted in the exclusion of the study from the review.

Summary Measures and Synthesis of Results

Implant survival rate was calculated for each study from the data extracted with 95% confidence intervals (95% CI) using the comprehensive meta-analysis software, (CMA, version 3.3, Biostat, Englewood, NJ). A meta-analysis was performed on this calculated survival rate (SR%) based on the recall period of 6-months, 12 months, 24-months, 36-months, 60-months and 120-months. When an implant survival was reported at 100%, then a continuity correction with the SR% was set to 99.9% and a random effects model was applied.[14] Heterogeneity was assessed using I^2 - statistics, and a sensitivity analysis was conducted to check the robustness of the pooled results. A funnel plot was used to graphically explore publication bias,[15] and the trim-and-fill method was applied to investigate the impact of potentially non-published studies.[16,17]

Risk of Bias and Quality Assessment of the Included Studies

The Cochrane collaboration's tool and the Newcastle-Ottawa scales were used for the assessment of the risk of bias and quality assessment of the included RCTs and prospective cohort/case–control studies, respectively.[18,19]

RESULTS

Study Selection

The search queries identified a total of 640 studies from the 3 electronic databases. After an initial sweep to remove duplicates, 593 studies were included in a title / abstract screening ($\kappa = 0.89$). At this stage, 539 articles were excluded ($\kappa = 0.77$), leaving 54 articles for full text screening. After full text screening a further 23 articles were excluded with a further 8 articles unavailable. A final total of 23 articles were included in the review for data extraction.[20-42] A final update of the search was performed on the March 7, 2022 and 9 records were identified but none qualified as they were irrelevant.[43-51] The flow of the entire search, article identification and inclusion process is shown in Figure 1.

Study Characteristics

From the 23 included studies, 14 studies (5 RCTs and 9 nonrandomised clinical studies) reported data with implant survival and were included in the metanalysis (Table 2).[20,24-30,32,33,35,38,41,42] Information on donor site complications was available in 13 of the included studies (Tables 3 and 4).[20-23,26,31,33,34,36-40]

Meta-Analysis of Included Studies: Implant Survival

A meta-analysis was performed for implant survival in both iliac crest grafts and intra-oral grafts, calculated for observation periods up to 10 years. The overall implant survival rate for implants placed in iliac crest bone after 6 months was

Table 2. List of RCTs and prospective non-randomized clinical studies reporting implant success in grafted bone (mos.- months; NR- not reported).

Study (First author)	Publication year	Donor site	Number of patients	Number of implants	Study design	Implant system	Success rate%					
							6 mos.	12 mos.	24 mos.	36 mos.	60 mos.	120 mos.
Lundgren	1997	Iliac Crest (inlay grant)	10	66	Non-randomised clinical study	Branemark MK II	92.43	83.0	NR	NR	NR	NR
Iliac crest (inlay / onlay grant)	10	70	95.72	82.86	NR	NR	NR	NR				
Sjöström	2005	Iliac Crest	29	222	Non-randomised clinical study	Standard Branemark (193) MKII Branemark (29)	NR	92	NR	NR	NR	NR
Thor	2005	Iliac Crest	19	152	Non-randomised clinical study	Asta Tech TiOblast	98.7	98.7	NR	NR	NR	NR
Chiapasco	2007	Ramus	8	19	Non-randomised clinical study	Straumann	100	100	100	100	100	NR
Hassan	2008	Osteotomy	10	10	Non-randomised clinical study	Titanium Plasma Spray	100	100	NR	NR	NR	NR
Felice	2009	Iliac Crest	9	18	RCT	Biomet 3i, Ankylos, Xive	100	100	NR	NR	NR	NR
Johansson	2010	Adjacent to osteotomy	17	20	Non-randomised clinical study	Straumann Standard Plus	100	100	100	100	50	NR
Zygomatic buttress, lateral sinus wall			41	61			100	100	62.2	22.95	0	NR
Merli	2010	Adjacent to osteotomy	22	77	RCT	Xive S PLus	100	100	100	100	NR	NR
Rasmusson	2012	Iliac Crest	21	260	Non-randomised clinical study	Asta Tech TiOblast	98.5	NR	NR	NR	NR	NR
de Freitas	2013	Retromolar	12	30	RCT	Flash	100	NR	NR	NR	NR	NR
Stellingsma	2014	Iliac Crest	20	80	RCT	IMZ Apical Screws	NR	NR	90	90	90	75
Chiapasco	2015	Iliac Crest	7	49	Non-randomised clinical study	Straumann (33) Astra (16)	100	100	100	NR	NR	NR
Meijndert	2017	Mental	31	31	RCT	Straumann Plus	100	100	100	100	100	100
Mental with membrane			31	31	100	100	96.78	96.78	96.78	93.5		
Noelken	2018	Ramus, mandible	19	33	Non-randomised clinical study	Dentsply Sirona	100	100	100	100	96.97	NR

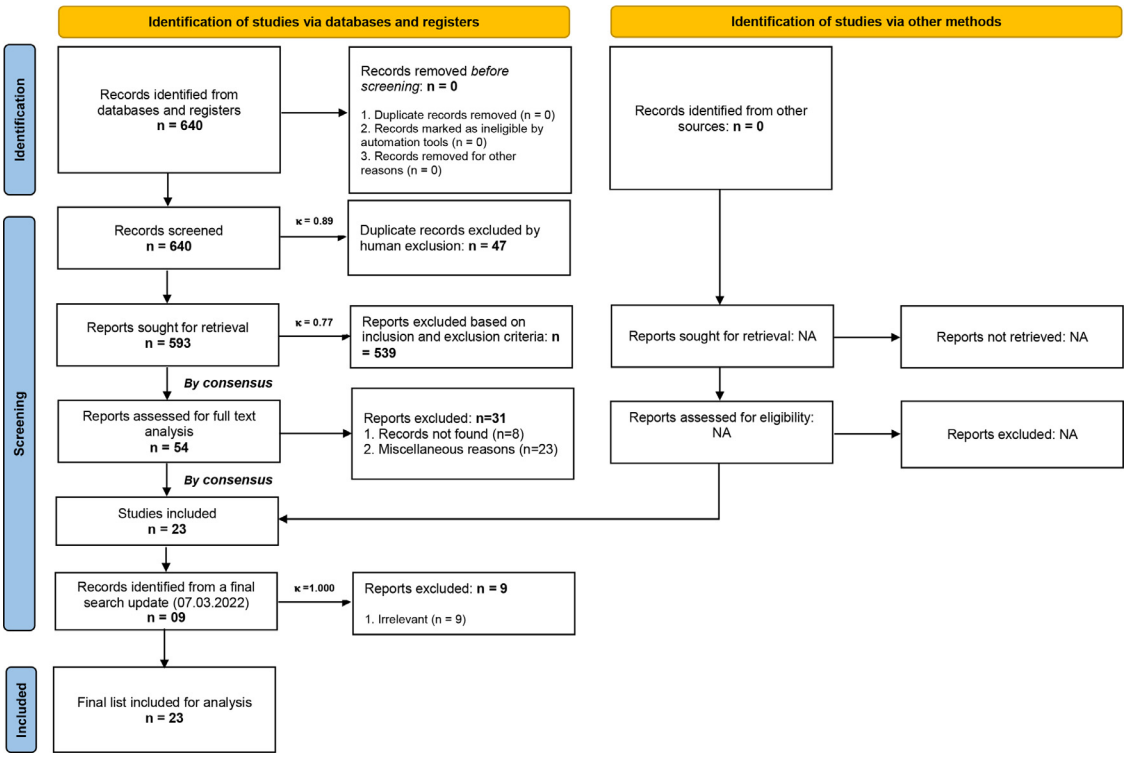
Table 3. List of included studies reporting donor site complications for iliac crest grafts.

Study (First author)	Publication year	Donor site	Number of patients	Study design	Reported donor site complication
Lundgren	1997	Iliac Crest	20	Non-randomised clinical study	Hip pain ($n = 7/20$)
Chiapasco	1999	Iliac Crest	15	Non-randomised clinical study	Gait disturbance ($n = 15/15$)
Hellem	2003	Iliac Crest	3	Non-randomised clinical study	Discomfort ($n = 3/3$)
van der Mark	2011	Iliac Crest	27 ($n = 10$ Le Fort; $n = 17$ Sinus Lift)	Non-randomised clinical study	Post-operative gait disturbance Sensory disturbance ($n = 2/27$) Mild pain ($n = 2/27$) Residual pain ($n = 1/27$)
Chiapasco	2015	Iliac Crest	7	Non-randomised clinical study	Gait disturbance
Fretwurst	2015	Iliac Crest	20	Non-randomised clinical study	Haematoma ($n = 1/20$) Seroma ($n = 2/20$) Sensory disturbance ($n = 1/20$) Hip pain ($n = 14/20$) Gait disturbance ($n = 13/20$)
Kuik	2016	Iliac Crest	27	Non-randomised clinical study	Perforation of the iliac crest ($n = 1/27$) Haematoma ($n = 2/27$) Persistent hip pain ($n = 4/27$) Headache ($n = 9/27$) Tenderness ($n = 3/27$) Sensory disturbance ($n = 3/27$)

Table 4. List of included studies reporting donor site complications for intra-oral grafts.

Study (First author)	Publication year	Donor site	Number of patients	Study design	Reported donor site complications
Chiapasco	1999	Mental	15	Non-randomised clinical study	Paresthesia of lower lip ($n = 8/15$) Paresthesia of anterior mandibular teeth ($n = 10/15$)
Chiapasco	2004	Mental	2	Non-randomised clinical study	Paresthesia of lower lip / paresthesia of anterior mandibular teeth ($n = 2/2$)
Chiapasco	2007	Ramus of mandible	8	Non-randomised clinical study	Paresthesia ($n = 2/8$)
De Freitas	2013	Retromolar	12	RCT	Discomfort / Pain / Sensory Loss / Paresthesia
Schmitt	2013	Angle of mandible	12	RCT	Swelling exposition of inferior alveolar nerve
Stimmelmayr	2014	Retromolar	22	Non-randomised clinical study	None
Streckbein	2014	Retromolar	25	Non-randomised clinical study	Paresthesia ($n = 1/25$)

Figure 1. The search flow diagram, for the systematic literature search and selection process according to the PRISMA guidelines.

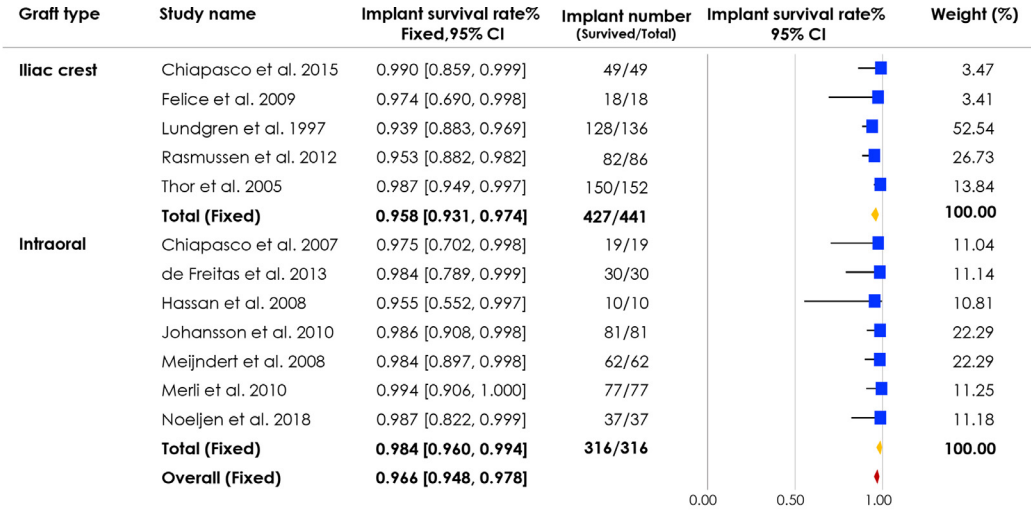


95.8% (95% CI: 93.1-97.4, $I^2 = 0.00\%$, $n = 5$ studies) compared to 98.4% (95% CI: 96.0-99.4, $I^2 = 0.00\%$, $n = 7$ studies) for intraoral bone which was significant (overall effect: $Z = 14.508$, $P < .001$; Figure 2). At 12 months, implant survival in iliac crest bone was 97.0% (95% CI: 90.1-99.2, $I^2 = 0.00\%$, $n = 4$ studies) and 98.4% (95% CI: 95.8-99.4, $I^2 = 0.00\%$, $n = 6$ studies) in intraoral bone, which was significant (overall effect: $Z = 9.716$, $P < .001$; Fig. 3). At 24 months, implant survival in iliac crest bone was 85.9% (95% CI: 80.7-89.9, $I^2 = 0.00\%$, $n = 3$ studies) and 76.3% in intraoral bone (Figure 4A); however, when a sensitivity analysis was performed and one study was excluded (Johansson et al. 2010),[29] the survival rate for the intra-oral bone graft climbed to 98.2% (95% CI: 94.6-99.4, $I^2 = 0.00\%$, $n = 4$ studies; Figure 4B) and was significant (overall effect: $Z = 11.051$, $P < .001$). The study Johansson et al.[29] contributed to 85.5% of the total weight which grossly undermined the effects of the other included studies. Hence a sensitivity analysis, was performed where removing this study revealed a reversal of the overall effect as observed in Figure 4B. At 36 months, implant survival in intraoral bone was 96.4% (95% CI: 75.2-99.6, $I^2 = 0.003\%$, $n = 5$ studies) with no included studies reporting implant survival at 36 months in iliac crest bone (Figure 5). At 60 months (5 years), one study reported implant survival in iliac crest bone of 90.0% (95% CI: 81.3-94.9) compared to 91.5% (95% CI: 31.8-99.6%, $I^2 = 0.138\%$, $n = 4$ studies) for intraoral bone which was significant (overall effect: $Z = 6.078$, $P < .001$; Figure 6). At the 120-month follow up (10 years), one study reported implant survival in iliac crest bone of 88.8% (95% CI: 79.8-94.0) and one study reported implant survival in intraoral bone of 95.2% (95% CI: 84.6-98.6) and this was statistically significant (overall effect: $Z = 7.317$, $P < .001$; Figure 7). A funnel plot analysis was undertaken at each follow up interval to explore potential publication bias, but this was ruled out (Appendices 1-4).

Qualitative Analysis of the Included Studies: Donor Site Complications

Thirteen studies provided information on complications arising from the donor site. Seven studies reported complications arising from bone grafted from the iliac crest, all of these studies were non-randomized clinical studies (Table 3).[20-22,31,38-40] The most commonly reported donor site complications for iliac crest grafts were discomfort / pain in

Figure 2. Forest plot showing implant survival rate for implants placed in iliac crest vs intraoral bone at 6 months (CI, confidence interval).

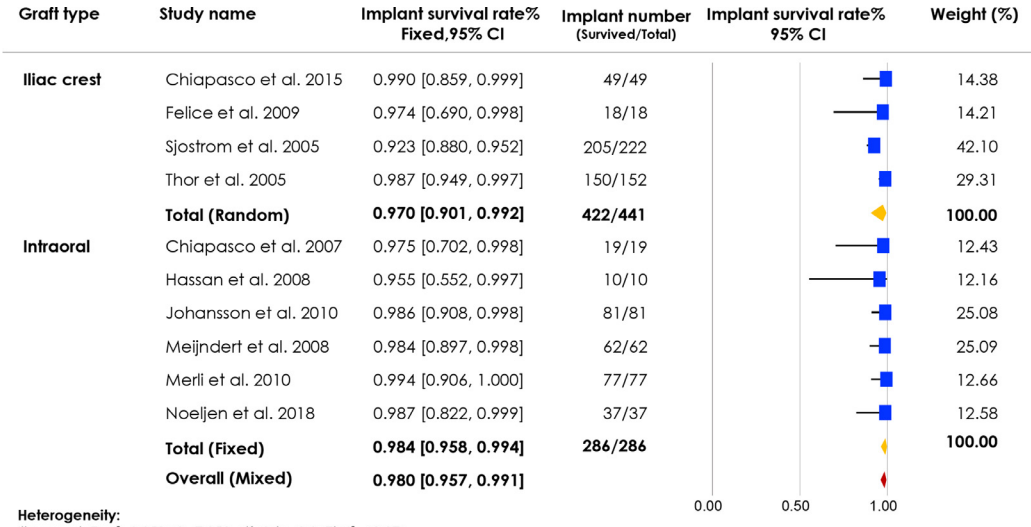


Graft type	Study name	Implant survival rate% Fixed,95% CI	Implant number (Survived/Total)	Implant survival rate% 95% CI	Weight (%)
Iliac crest	Chiapasco et al. 2015	0.990 [0.859, 0.999]	49/49		3.47
	Felice et al. 2009	0.974 [0.690, 0.998]	18/18		3.41
	Lundgren et al. 1997	0.939 [0.883, 0.969]	128/136		52.54
	Rasmussen et al. 2012	0.953 [0.882, 0.982]	82/86		26.73
	Thor et al. 2005	0.987 [0.949, 0.997]	150/152		13.84
	Total (Fixed)	**0.958 [0.931, 0.974]**	**427/441**		**100.00**
Intraoral	Chiapasco et al. 2007	0.975 [0.702, 0.998]	19/19		11.04
	de Freitas et al. 2013	0.984 [0.789, 0.999]	30/30		11.14
	Hassan et al. 2008	0.955 [0.552, 0.997]	10/10		10.81
	Johansson et al. 2010	0.986 [0.908, 0.998]	81/81		22.29
	Meijndert et al. 2008	0.984 [0.897, 0.998]	62/62		22.29
	Merli et al. 2010	0.994 [0.906, 1.000]	77/77		11.25
	Noeljen et al. 2018	0.987 [0.822, 0.999]	37/37		11.18
	Total (Fixed)	**0.984 [0.960, 0.994]**	**316/316**		**100.00**
	Overall (Fixed)	**0.966 [0.948, 0.978]**			

Heterogeneity:
Iliac crest: Tau^2=0.132; Q=5.189, df=4 (p=0.268); I^2=22.914
Intraoral: Tau^2=0.000; Q=1.118, df=6 (p=0.981); I^2=0.0

Test for overall effect: Z=14.508, (p<0.001)

Figure 3. Forest plot showing implant survival rate for implants placed in iliac crest vs intraoral bone at 12 months (CI, confidence interval).

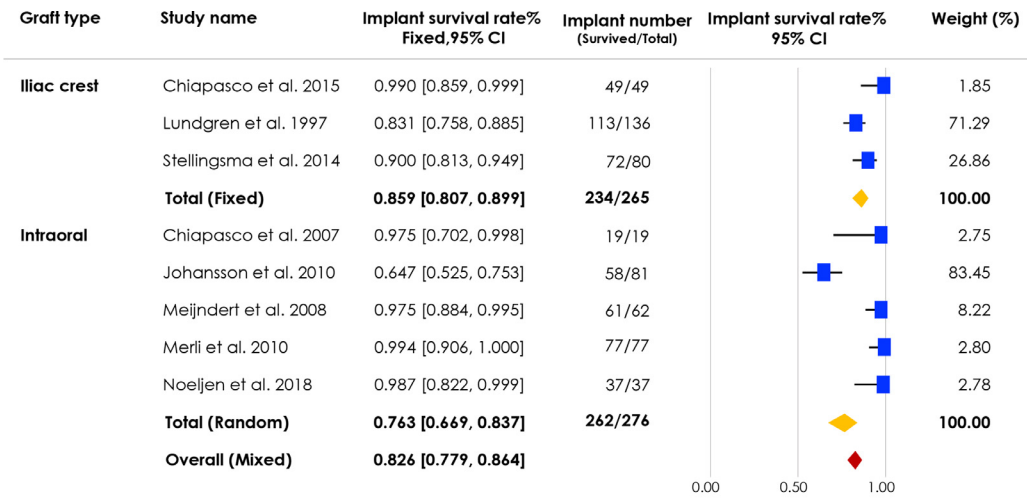


Graft type	Study name	Implant survival rate% Fixed,95% CI	Implant number (Survived/Total)	Implant survival rate% 95% CI	Weight (%)
Iliac crest	Chiapasco et al. 2015	0.990 [0.859, 0.999]	49/49		14.38
	Felice et al. 2009	0.974 [0.690, 0.998]	18/18		14.21
	Sjostrom et al. 2005	0.923 [0.880, 0.952]	205/222		42.10
	Thor et al. 2005	0.987 [0.949, 0.997]	150/152		29.31
	Total (Random)	**0.970 [0.901, 0.992]**	**422/441**		**100.00**
Intraoral	Chiapasco et al. 2007	0.975 [0.702, 0.998]	19/19		12.43
	Hassan et al. 2008	0.955 [0.552, 0.997]	10/10		12.16
	Johansson et al. 2010	0.986 [0.908, 0.998]	81/81		25.08
	Meijndert et al. 2008	0.984 [0.897, 0.998]	62/62		25.09
	Merli et al. 2010	0.994 [0.906, 1.000]	77/77		12.66
	Noeljen et al. 2018	0.987 [0.822, 0.999]	37/37		12.58
	Total (Fixed)	**0.984 [0.958, 0.994]**	**286/286**		**100.00**
	Overall (Mixed)	**0.980 [0.957, 0.991]**			

Heterogeneity:
Iliac crest: Tau^2=0.951; Q=7.952, df=3 (p=0.047); I^2=62.274
Intraoral: Tau^2=0.000; Q=1.118, df=5 (p=0.952); I^2=0.0

Test for overall effect: Z=9.716, (p<0.001)

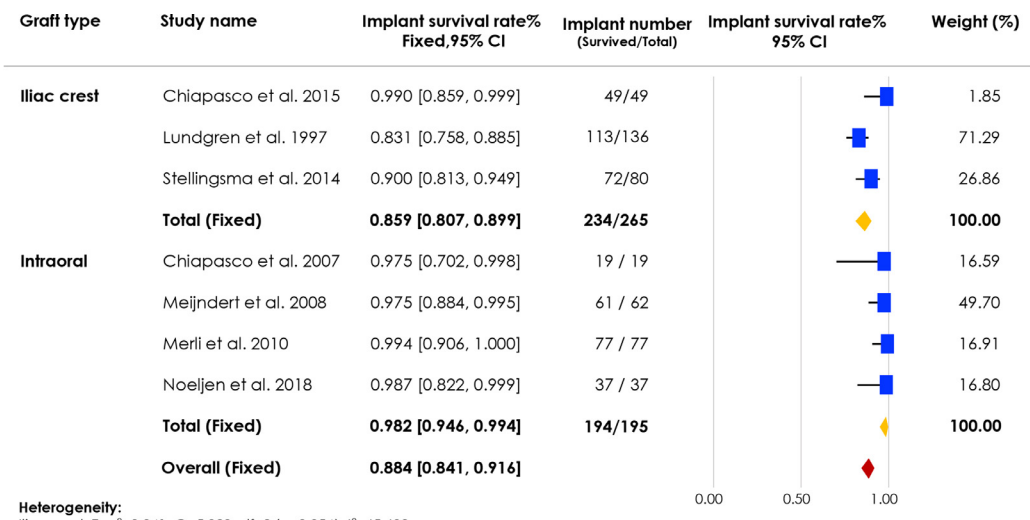
Figure 4A. Forest plot showing implant survival rate for implants placed in iliac crest vs intraoral bone at 24 months (CI, confidence interval).



Heterogeneity:
Iliac crest: Tau^2=0.341; Q=5.829, df=2 (p=0.054); I^2=65.689
Intraoral: Tau^2=4.790; Q=29.043, df=4 (p<0.001); I^2=86.227

Test for overall effect: Z=10.378, (p<0.001)

Figure 4B. Forest plot showing implant survival rate for implants placed in iliac crest vs intraoral bone at 24 months one study removed Johansson et al. 2010 (CI, confidence interval).



Heterogeneity:
Iliac crest: Tau^2=0.341; Q=5.829, df=2 (p=0.054); I^2=65.689
Intraoral: Tau^2=0.000; Q=0.823, df=3 (p=0.844); I^2=0.000

Test for overall effect: Z=11.051, (p<0.001)

Figure 5. Forest plot showing implant survival rate for implants placed in intraoral bone at 36 months; 3-year follow-up data not available for iliac crest grafts (CI, confidence interval).

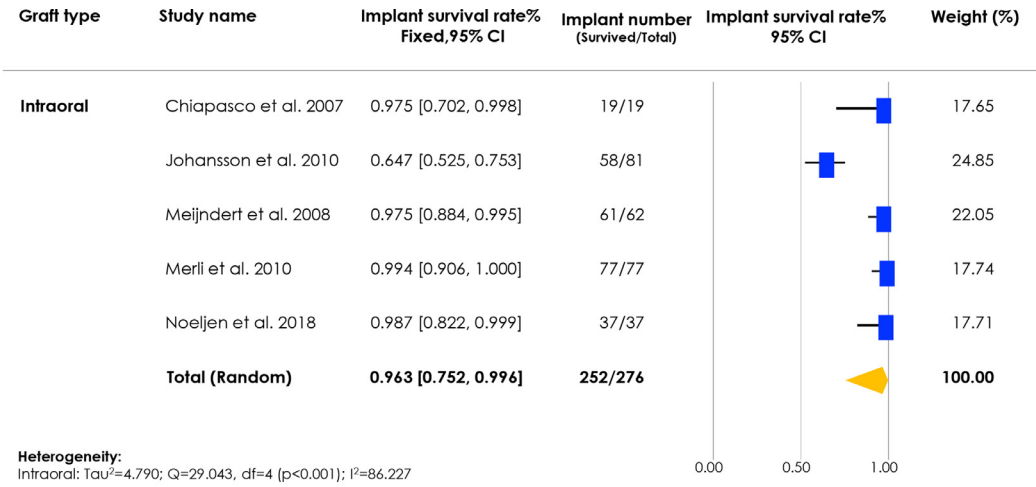


Figure 6. Forest plot showing implant survival rate for implants placed in iliac crest vs intraoral bone at 60 months (CI, confidence interval).

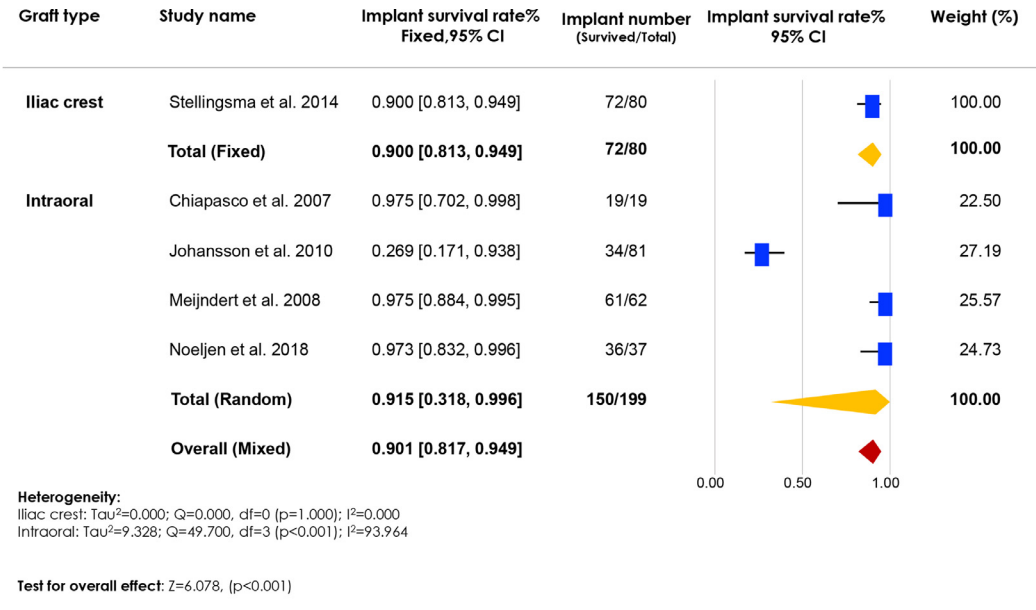
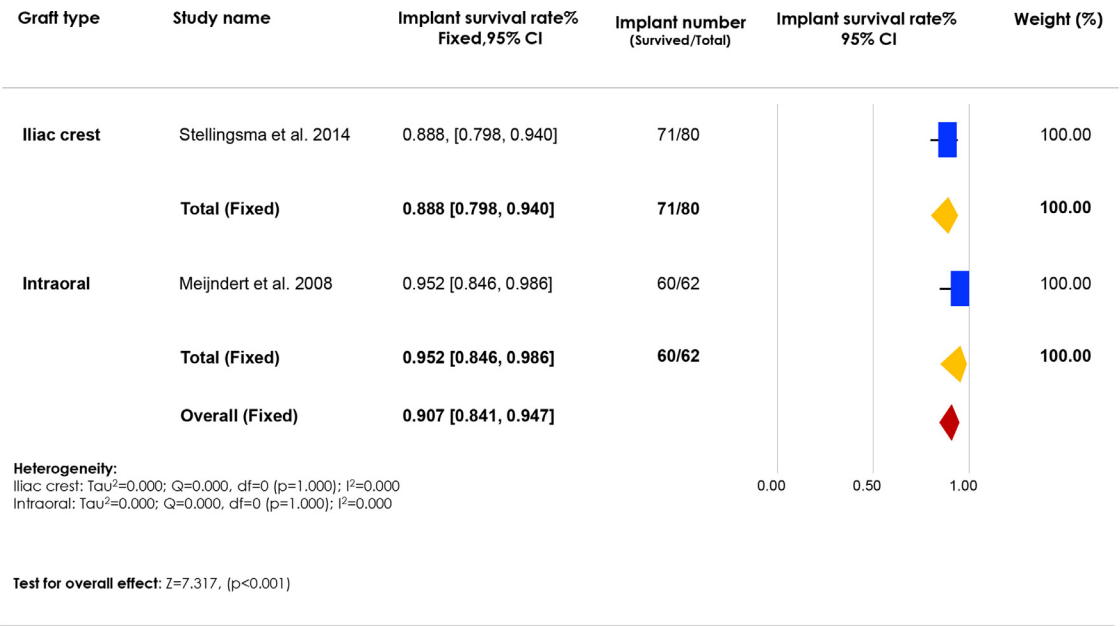


Figure 7. Forest plot showing implant survival rate for implants placed in iliac crest vs intraoral bone at 120 months (CI, confidence interval).



5 studies,[20,22,31,39,40] gait disturbance in 5 studies,[21,25,27,29,30] and sensory disturbances in 4 studies.[22,31,39,40]

For intra-oral complications, 2 of the included studies were randomized controlled trials[33,34] with a further 5 non-randomized clinical studies (Table 4).[21,23,26,36,37] Dividing the intraoral donor sites anatomically it would appear that the mental region is associated with the largest number of complications including paresthesia of the lower lip,[21,23] and mandibular anterior teeth.[21,23] Grafts taken from the mandibular retromolar region and the angle of the mandible were associated with sensory disturbance,[33,34,37] swelling[34] and pain.[33] Those harvested from the mandibular ramus were associated with paresthesia of the inferior alveolar nerve.[26] The data reported on donor site complications was not suitable for meta-analyses. The information available on the complications was heterogenous, and mostly descriptive. Moreover, different studies reported different complications and it was not possible to classify them under a common theme to compute a summary measure for analysis.

Risk of Bias and Quality Assessment of the Included Studies

The results of the risk of bias and quality assessment of the included studies is reported in Tables 5 and 6. The summary of the risk of bias of the included RCTs was considered low.

DISCUSSION

This systematic review and meta-analysis demonstrate that implant survival in intraoral grafts is consistently higher than iliac crest grafts at follow-up intervals up to 10 years. Although the data was not suitable for meta-analysis, iliac crest grafts were frequently associated with donor site complications including pain/discomfort, gait disturbance and sensory disturbance. Whilst intraoral grafts were typically associated with less frequent donor site complications, those taken from the mental region did generate a relatively high proportion of cases with paresthesia of the mandibular anterior teeth or lower lip.

Previous systematic reviews in this area have focused on comparison of dental implant survival rates in autogenous bone compared to bone substitutes and using various different surgical techniques.[8,52,53] Traditionally it has been reported that implant survival in grafts taken from the iliac crest was significantly lower than non-grafted sites or bone harvested intraorally.[54,55] It is well established that the donor site plays a major factor in successful grafting, long-term resorption rates, graft- and implant survival rates. Situations requiring large volumes for larger bone defects are often grafted with iliac crest. Although this has many advantages,[56] the most serious problem associated with this graft is the higher bone resorption during the healing phase.[57,58] It has been

Table 5. Results of the quality assessment of the included RCTs using the Cochrane collaboration tool for the assessment of risk of bias.

Study	Sequence generation	Allocation concealment	Blinding	Incomplete outcome data	Selective reporting	Other bias	Summary
Meijndert et al. 2017	Low	Unclear	Low	Low	Low	Unclear	Low
Stellingsma et al. 2014	Low	Unclear	Unclear	Low	Low	Unclear	Unclear
de Freitas et al. 2013	Low	Low	Low	Low	Low	Unclear	Low
Merli et al. 2010	Low	Low	Low	Low	Low	Unclear	Low
Felice et al. 2009	Low	Low	Unclear	Low	Low	Unclear	Low

evidenced that higher volumetric changes are observed with iliac crest grafts when compared to intraoral jaw grafts.[56,59-61] Furthermore, iliac crest grafts show greater resorption rate and lower mineralization than chin grafts.[62] This may be explained well by the difference in their embryonic origins. The jawbones are formed by membranous formation while the ilium is by endochondral ossification.[63,64] This difference can play a role in the resorption rates, graft- and implant survival. Therefore, the chin graft transplanted into a jaw bone defect has a better potential for long-term success and implant survival because of its similarity in the embryonic origin with the recipient site, when compared to the iliac crest graft transplanted into the jawbone.[61,63,65]

However, clinical case selection is very important when considering these survival rates. As with the studies included in this review, there are very few high-quality studies with adequate follow up time examining this area. Donor site complications from bone grafts are generally well reported in the scientific literature, particularly those taken from the iliac crest.[66] Whilst this data has traditionally been captured using clinical quantitative approaches, recent research has also utilized patient-reported outcome measures to measure the impact of this treatment on oral health-related quality of life (OHRQoL).[67]

Given the reduced success rates and donor site complications associated with implants in grafted bone, alternative treatment modalities have emerged. The relatively recent development and availability of short dental implants has eliminated the need for extensive bone grafting in many cases. Whilst long term follow-ups of short implants is limited, research has demonstrated similar success rates to implants in grafted sites but without donor site complications.[68] As part of the informed consent process, all of these options should be discussed with patients when considering implant treatment.

Comparing the effectiveness of 2 different types of grafts is always interesting because it provides important information for clinicians on the selection of an ideal graft material based on its effectiveness for the site employed, as well as the information on possible adverse effects. Although the results of this study, demonstrate that implants placed in the chin graft showed superior effectiveness, this may not be necessarily true. Evaluating the effectiveness of dental implants in regions grafted with iliac bone or chin bone can generate conflicting results because each of these grafts have different indications and are normally used for different rehabilitations. Iliac bone graft is normally reserved for cases of major rehabilitations in the maxilla, while the chin graft can be used for several types of rehabilitation, including unitary, partial/total, and may/may not be associated with biomaterials. This divergence can generate a biased result, as shown in the results of this study and these findings must be interpreted with caution.

Whilst this systematic review has been conducted according to PRISMA guidelines,[10-13] only a small number of high-quality studies were eligible for inclusion. The data extracted for donor site complications was unfortunately not suitable for meta-analysis due to the significant variation in reporting terms and methods. A number of studies provided no timelines for follow up or development of donor site complications and authors reported outcomes using differing terms. Across implant dentistry to facilitate future research the development and application of a core outcome set would be beneficial.[69]

Table 6. Results of the quality assessment of the included nonrandomized studies using the Newcastle-Ottawa scale.

Study	Selection representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that the outcome of interest was not present at the start of the study	Comparability of the cohorts on the basis of the design or analysis	Outcome assessment	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts
Lundgren et al. 1997	*		*	*	*	*	*	*
Sjöström et al. 2005	*		*	*	*	*	*	*
Thor et al. 2005	*		*	*	*	*	*	*
Chiapasco et al. 2007	*		*	*	*	*	*	*
Hassan et al. 2008	*		*	*	*	*	*	*
Johansson et al. 2010	*		*	*	*	*	*	*
Rasmusson et al. 2012	*		*	*	*	*	*	*
Chiapasco et al. 2015	*		*	*	*	*	*	*
Noelken et al. 2018	*		*	*	*	*	*	*

CONCLUSIONS

This systematic review and meta-analysis has demonstrated that implant survival is consistently higher in autogenous grafts sourced from intraoral bone compared to iliac crest. Donor site complications seemed to be a frequent finding with iliac crest grafts and mental grafts.

CLINICAL IMPORTANCE

- Patients and clinicians should be aware of the different survival rates of dental implants placed in autogenous bone harvested from both iliac crest and intraoral sites.
- Patients and clinicians should be aware of the different rates of postoperative complications of autogenous bone harvested from both iliac crest and intraoral sites.
- These discussions should form an integral part of the consent and treatment planning process.

APPENDICES

Appendix 1. Funnel plot of the included studies at 6-months follow up

Appendix 2. Funnel plot of the included studies at 12-months follow up

Appendix 3. Funnel plot of the included studies at 24-months follow up

Appendix 4. Funnel plot of the included studies at 36-months follow up

Appendix 5. Funnel plot of the included studies at 60-months follow up

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