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DETERMINANTS OF EARLY FAILURE OF DENTAL IMPLANTS

BY

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ABSTRACT

In modern dentistry, the use of osseointegrated dental implants is widely accepted as a valid treatment that can provide reliable rehabilitation for fully or partially edentulous patients. Efforts are continuously being made in the field of implant dentistry to further improve treatment outcomes and reduce failures.

There is a growing interest in improving treatment planning for dental implants, starting with tooth extraction techniques, as every dental implant procedure essentially begins with tooth extraction. In this context, minimally invasive vertical tooth extraction systems have been developed to reduce bone loss after tooth extraction and facilitate subsequent implant restoration.

This PhD project started with investigating the Benex vertical tooth extraction system. We developed an in vitro animal model system to replicate the clinical procedure of vertical tooth extraction using the Benex system. Using this model, we measured the axial forces associated with the tooth removal process. Furthermore, we examined potential modifications in the Benex vertical extraction technique that may increase the success rate of tooth extraction and reduce maximal extraction force and associated untoward sequelae. However, due to the impact of the COVID-19 pandemic and the subsequent closure of the laboratories, we could not pursue lab work further as planned. Furthermore, these unforeseen circumstances have disrupted the original plans for conducting clinical trials to determine the effectiveness of vertical tooth extraction using the Benex system in reducing the need for flap surgery and post-extraction alveolar bone loss. Therefore, we have made necessary adjustments to the work plan and have developed an alternative PhD plan to investigate risk factors for early implant failure.

The main aim of this thesis was to assess risk factors associated with early implant failure. Identifying and assessing the potential risk factors for early implant failure can be of great importance in predicting treatment outcomes. Furthermore, surgeons can make informed decisions to improve implant therapy outcomes by recognising high-risk conditions and adjusting treatment plans accordingly.

To achieve our aim, we first conducted a systematic review and meta-analysis to identify risk factors for early implant failure reported in the literature. We also investigated the statistical methods used to adjust for confounders in these studies. We found that studies frequently reported univariate analyses only, or, where adjustments for covariates were made, the selection of these variables was typically not based on a robust causal structure, which prevents a causal interpretation of the results. Therefore, we constructed a causal model using Directed Acyclic Graphs (DAGs), incorporating variables potentially related to early implant failure and defining their causal relationship based on available literature, expert knowledge, and plausible assumptions. This was done to make the underlying assumptions regarding the causal structure explicit and to guide covariate selection for the statistical models.

To assess potential risk factors for early implant failure, we conducted a retrospective cohort study using data from the European Centres for Dental Implantology (ECDI) database. This study included 150,896 implants placed in 63,414 patients between 2010 and 2022. First, we performed a descriptive analysis of all variables to gain an overview of the dataset and identify its strengths and limitations. Then, we analysed the data by creating multilevel mixed-effects logistic regression models for each potential risk factor for early implant failure. The covariate adjustment sets used in these models were selected based on our previously proposed causal model. We found that certain factors have a causal association with early implant failure. These factors are male sex, cigarette smoking, immediate implant placement, low primary stability, using narrow and short implants, placing implants in upper molar and lower anterior sites, poor bone quality, insufficient alveolar bone height, bone augmentation, and transmucosal healing mode. We did not find an association of age and diabetes mellitus with early implant failure.

DEDICATION

I dedicate this thesis

To my wife, love, and friend

Galya

For her love, sacrifice, patience, and support.

I couldn’t have done this without you, my sweetheart.

As the proverb goes: “Behind every successful man there stands a woman”.

You, my Galya, are that woman for me.

To my children

Moad, Leen, Eyad, and Lama

Who have brought happiness and joy to my life and made me smile even in the most difficult times.

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LIST OF ABBREVIATIONS

BMPs	Bone Morphogenic Proteins
BSM	Bone Substitute Material
CBCT	Cone Beam Computed Tomography
CI	Confidence interval
COVID	Coronavirus disease 2019
CT	Computed Tomography
DAGs	Directed Acyclic Graphs
D	Density
ECDI	European Centres for Dental Implantology
ePTFE	Expanded Polytetrafluoroethylene
EThOS	Electronic theses Online Service
F-max	Maximum extraction forces
GEE	Generalized Estimating Equations
HIF-1	hypoxia-inducible factor 1
ICC	Intraclass Correlation Coefficient
ISQ	Implant Stability Quotient
L C	Left Canine
L CI	Left Central Incisor
L LI	Left Lateral Incisor
L M1	Left 1st Molar
L M2	Left 2nd Molar
L PM1	Left 1st Premolar
L PM2	Left 2nd Premolar
Max	Maximum
MBF	Maximal Bite Force

Micro-CT	Microcomputed tomography
min	Minute
Min	Minimum
mm	millimeter
MOOSE	Meta-analysis of Observational Studies in Epidemiology
N	Newton
NOS	Newcastle-Ottawa Scale
OMFS	Oral & Maxillofacial Surgeon
OR	Odds Ratio
OS	Oral Surgeon
PCo	Prospective Cohort
PDL	Periodontal Ligament
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	Prospective Register of Systematic Reviews
PTV	Periotest value
R C	Righr Canine
R CI	Right Central Incisor
R LI	Right Lateral Incisor
R M1	Right 1st Molar
R M2	Right 2nd Molar
R PM1	Right 1st Premolar
R PM2	Right 2nd Premolar
RCo	Retrospective Cohort
RD	Risk Difference
REDCap	Research Electronic Data Capture

RFA	Resonance Frequency Analysis
RR	Risk Ratio
SD	Standard Deviation
SPT	Supportive Periodontal Therapy
St. Error	Standard error
VEGF	Vascular Endothelial Growth Factor

CHAPTER 1: INVESTIGATION INTO THE EFFICACY OF A VERTICAL TOOTH EXTRACTION SYSTEM (BENEX®) FOR THE EXTRACTION AND SURGICAL EXTRUSION OF NON-RESTORABLE TEETH

1.1. Introduction

Alveolar bone is a tooth-dependent tissue that forms and develops in association with the eruption of the developing teeth. The form of the teeth, the direction of their eruption, and their inclination determine the shape as well as the volume of the alveolar process (Marks and Schroeder, 1996).

Tooth extraction is considered one of the most commonly performed procedures in dentistry. In general, both hard and soft tissue heal uneventfully following tooth extraction. However, removing a tooth from its bony socket is associated with varying degrees of alveolar bone loss and soft tissue contour changes (Schropp et al., 2003).

Several studies and systematic reviews have previously demonstrated alveolar bone dimensional changes following tooth extraction. In a systematic review including 20 studies reporting on post-extraction dimensional changes of the alveolar bone relative to a particular reference point, the mean horizontal dimensional reduction of the post-extraction socket was 3.79mm, which was more than the mean reduction in buccal vertical height of 1.24 at six months after extraction (Tan et al., 2012). These results were close to findings in another systematic review which reported a mean reduction of 3.87 mm in width of the alveolar ridges and a mean mid-buccal height loss of 1.67 mm during observation periods of up to 12 months following extraction (Van der Weijden et al., 2009).

Several factors have been addressed in the literature for their presumed influence on the extent of alveolar bone loss after tooth extraction. These include the general health of the patient (Chen et al., 2004), habits such as smoking (Saldanha et al., 2006), the type and location of the tooth (Schropp et al., 2003), the number and proximity of teeth in case of multiple extractions (Chen et al., 2004), and post-extraction treatment

protocols (Brägger et al., 1994). Furthermore, the extraction technique has also been suggested as a risk factor for alveolar bone resorption (Quayle, 1990, Oghli and Steveling, 2010).

Forceps extraction, also called simple tooth extraction, involves the expansion of the tooth's bony socket and, subsequently, the separation of the tooth from its ligaments to a point where the tooth becomes loose and free to come out. Other extraction techniques using elevators, luxators, or periotomes are considered less invasive than forceps extraction; however, they also cause some bone expansion (Saund and Dietrich, 2013); therefore, it is inevitable to traumatize the alveolar bone to some degree when using these conventional techniques to extract teeth. In cases where teeth cannot be extracted using conventional techniques, surgical tooth extraction would be indicated, which involves the reflection of a mucoperiosteal flap and, often, removing part of the bone surrounding the tooth to facilitate its removal from the socket. This bone removal, no matter how small or large the removed amount, is considered an additional cause of alveolar bone loss that occurs even before any physiological bone remodeling takes place. Furthermore, it has been argued that the reflection of the mucoperiosteal flap itself could increase the rate of alveolar bone resorption (Blanco et al., 2008, Fickl et al., 2008). Therefore, it would be desirable for any novel extraction technique to reduce the need for flap surgery.

It is well established that the post-extraction loss of the alveolar process's width and height can jeopardize the functional and esthetic outcomes of many possible restorative treatments, including dental implant therapy (Quayle, 1990, Mecall and Rosenfeld, 1991, Van der Weijden et al., 2009). This has stimulated efforts to develop extraction techniques that aim to minimise the amount of trauma sustained by alveolar bone during tooth extraction. The development of vertical extraction systems is

perhaps the most innovative improvement in this area. The basic principle of these systems is to pull the tooth in an axial direction from its socket so that no direct trauma can occur to socket walls (Muska et al., 2013); this can be achieved by anchoring a screw in the tooth root and the application of a vertical pulling force to remove the root in the vertical direction (Babbush, 2007, Saund and Dietrich, 2013). This extraction mode is considered minimally invasive because it avoids any manipulation of alveolar bone, which may reduce bone resorption. However, no randomized controlled clinical trial has been conducted to investigate the assumption that reduction of trauma to the bone during tooth extraction, while maintaining adequate efficacy, could reduce the post-extraction dimensional changes of the alveolar ridge.

1.2. Benex vertical tooth extraction system

One currently available and widely used vertical tooth extraction system is the Benex system (Benex, Helmut Zepf Medizintechnik and Hager & Meisinger). This system is specifically designed to remove grossly destructed teeth without expansion of the alveolar sockets by applying a tensile force directed along the long axis of the tooth being extracted.

1.2.1. Components

The Benex system consists of

- The extractor device (Figure 1.1-A)
- Pull rope (Figure 1.1-B)
- Diamond burs with diameters of 1.6 and 1.8mm (Figure 1.1-B)
- Self-tapping screws (Figure 1.1-B)
- Sectional impression tray (Figure 1.1-B)



Figure 1.1 Benex system components. (A) The extractor device. (B) Diamond burs, extraction screws, pull rope, sectional impression tray and screw driver. (Saund and Dietrich, 2013), used with permission.

1.2.2. The Benex tooth extraction technique

The procedure of Benex extraction basically involves the preparation of a hole in the centre of the tooth to be extracted using a diamond bur to enable subsequent insertion of a corresponding self-tapping screw and minimise wedging forces during the insertion process to avoid root fracture (Figures 1.2-A, B). The provided screwdriver is used to insert the self-tapping screw until it becomes firmly secured in the desired position (Figure 1.2-C). The pull rope is then attached to the head of the screw from one side and to and to the extractor device from the other side (Figure 1.2-D). To establish optimal axial alignment of the pull rope and to stabilise the Benex extractor during the procedure, a sectional impression tray with silicone putty impression material can be utilised (Figures 1.2-C, D). Once the vertical alignment is achieved, the pull rope is gradually tightened by manual clockwise turning of a knob at the end of the extractor device. The applied vertical traction force serves the periodontal ligaments in a controlled way and leads to tooth removal without straining the alveolar bone (Figures 1.2-E, F) (Muska et al., 2013).



Figure 1.2 Clinical procedure. (A) Carious tooth to be extracted. (B) Preparation of screw hole. (C) Self-tapping screw and impression tray in place. (D) Benex® extractor assembled Benex device is applied, the pull rope is attached to the screw. (E) extraction of the root. (F) post-extraction socket. (Dietrich et al., 2020b), used with permission.

1.3. Literature review

The purpose of this section is to summarise previous research work relevant to this project. Section 1.3.1 presents previous clinical work that was carried out to evaluate the Benex system in relation to vertical tooth extraction. Section 1.3.2 discusses the use of the Benex system for surgical tooth extrusion. Finally, Section 1.3.3 provides a brief overview of the mechanical and viscoelastic properties of the periodontal ligament; this is particularly important since vertical tooth extraction techniques aim mainly to overcome the tensile strength of the periodontal ligament.

1.3.1. Vertical tooth extraction with the Benex system

In 2013, Muska et al. conducted the first proof of principle clinical study in which they evaluated the technical applicability, success rates, and limitations of the Benex tooth extraction system. This study documented the results of using the Benex system to extract 111 grossly carious teeth or remaining roots from 72 patients in routine clinical practice. This study showed a high overall success rate of (83%) for Benex extractions. However, the reported success rate was much higher for single-rooted teeth (89%) than for multi-rooted teeth, which was as low as 43%. These findings suggest that the Benex system is of limited benefit in extracting molars.

Failure to extract teeth with the Benex system has been reported to be mainly associated with inadequate retention of the self-tapping extraction screw and/or root fractures (Muska et al., 2013); these could be caused by the presence of a carious lesion or failure to place the extraction screw in an optimal position into the center of the root. Another suggested cause of failure was the root morphology which renders it unsuitable for vertical extraction, such as severe root curvature, root bulbosity, and root divergence in cases of multirooted teeth that could not be identified

preoperatively. In this regard, first upper premolars pose a unique challenge since conventional preoperative assessments frequently fail to determine whether the tooth is actually multirooted and, if so, whether the roots are diverging; Therefore, Muska et al. (2013) suggested treating the maxillary first premolar as if it has a single root by inserting the self-tapping screw into its center; doing so will likely result in successful extraction in cases where the tooth was truly single-rooted or if it was multirooted with non-divergent roots.

In their pioneering study, Muska et al. (2013) showed that the Benex system works well in the incisor, canine, and premolar regions, where it would be desirable to preserve the alveolar ridge, while it was of limited use for the extraction of molars. However, this cannot be considered evidence that the minimally invasive vertical tooth extraction with the Benex system is associated with less postoperative morbidity, particularly regarding post-extraction dimensional changes in the alveolar ridge. Ideally, this question should be addressed by randomized controlled clinical trials comparing the Benex system with alternative techniques.

In a prospective observational clinical study on the performance of the Benex vertical extraction system, Hong et al. (2018) extended the work by Muska et al. and documented 323 extractions of anterior teeth and premolars using the Benex system in 223 patients in routine clinical practice. The reported success was 85.4%, comparable to that reported earlier for the smaller subset of patients (Muska et al., 2013). Furthermore, in this study, the need for flap surgery after using the Benex system to extract anterior teeth and premolars was compared to conventional tooth extraction techniques. In this study's context, flap surgery refers to the elevation of a mucoperiosteal flap with or without bone removal. Only 6% of the 323 performed extractions were reported to require flap surgery, which was considerably lower than

the incidence of 22% following conventional extraction techniques. These findings suggest that the use of the Benex extraction system might be associated with a marked reduction in the need for flap surgery; this would be highly desirable because, as explained earlier in the background section, flap surgery is more likely to be associated with bone removal and increased postoperative morbidity. However, randomized controlled clinical trials are required to give more robust evidence for the effectiveness of the Benex vertical extraction system to reduce the need for flap surgery.

A more recent study by Dietrich et al. (2020a) investigated the force required for vertical tooth extraction with the Benex system. The authors stated that their study was the first in vivo human study in the literature devoted to directly measuring the forces required for tooth extraction. To achieve their objective, the investigators coupled the Benex device with a precision load cell and recorded the maximum vertical force required for successful tooth root extraction. The reported extraction forces with the Benex system were largely variable, ranging from 41N to 629N, with an average of 104N. In addition, Dietrich et al. (2020a) also evaluated the determinants of extraction forces and found that teeth that were in functional occlusion at the time of their extraction required higher extraction forces than those that were not. Furthermore, the increase in root surface attachment area was significantly associated with higher extraction forces. This association between the amount of the vertical extraction force and the root surface area could be explained in light of the main principle upon which the vertical extraction systems are based. As previously discussed, unlike conventional extraction techniques, vertical tooth extraction does not involve the expansion of the tooth's bony socket. Instead, it relies on applying a vertical traction force to sever the periodontal ligament fibres. Therefore, it can be assumed

that in teeth with conical roots with no undercuts, the vertical tooth extraction process can be achieved mainly by overcoming the mechanical strength of the periodontal ligaments (Dietrich et al., 2020a).

1.3.2. Surgical tooth extrusion with the Benex system

Although the Benex system was originally designed for teeth extraction in a minimally invasive way (Muska et al., 2013), it has also been used for the surgical extrusion of non-molar teeth with deep subgingival caries or crown fractures with a subgingival extension that would usually be considered to be non-restorable by conventional restorative and endodontic treatments (Dietrich et al., 2019).

Surgical tooth extrusion is usually considered unpredictable and might be associated with several adverse events, such as tooth root resorption (Tegsjö et al., 1987, Kahnberg, 1988, Hermann et al., 2012), marginal bone loss (Khayat and Fatehi, 2006), and tooth mobility above physiological limits that ultimately leads to tooth loss (Kahnberg, 1988, Kelly et al., 2016). In a systematic review of studies that evaluated the potential adverse events that could accompany surgical tooth extrusion, non-progressive root resorption was reported as the most common adverse event with an incidence rate of 30%, followed by a low incidence rate of tooth loss (5%), marginal bone loss (3.7%) and progressive root resorption (3.3%) (Elkhadem et al., 2014).

Extrusive techniques that reduce bone socket deformation, periodontal ligament disruption, and root surface damage have been proposed as they may provide predictable biological outcomes (Kelly et al., 2016, Krug et al., 2018). Interestingly, an animal study by Oikarinen et al. (1996) involved histological analysis to compare

cementoblast loss between teeth extracted by the conventional forceps technique and teeth extracted by an extrusion instrument that applies vertical axial traction forces. This study showed that teeth extracted with forceps had significantly more cementoblast loss than extruded teeth; this implies that minimising trauma during tooth extrusion may reduce the chance of developing root resorption by preserving cemental tissue and increasing the chance of periodontal healing. In this context, using the Benex system for the surgical extrusion of teeth appears to have an advantage over surgical extrusion using conventional extraction techniques in that it minimises the amount of trauma to the surrounding periodontium (Muska et al., 2013, Dietrich et al., 2019).

Krug et al. (2018) conducted a clinical trial investigating the success rate and incidence of biological adverse events after tooth extrusion with the Benex system. The study involved 51 patients who underwent surgical extrusion of 51 non-restorable teeth with the Benex system, followed by root canal treatment and coronal restoration. Participants were followed up for a mean period of 3.1 years. The results of this study showed that the success rate for the recalled teeth was 92.2%, and all treated teeth were asymptomatic and had no clinical signs of inflammation. Only 5 of 51 treated teeth were reported to have developed transient root resorption with a slight alteration in root contour. The findings of this study indicate that the Benex vertical tooth extraction system may be successfully used for surgical extrusion to save non-restorable teeth. However, further studies with large-scale samples and more extended observation periods are required to validate these findings, particularly with regard to long-term tooth preservation.

1.3.3. Mechanical strength and viscoelasticity of periodontal ligament

From a physiological point of view, the mechanical strength of periodontal ligaments can be described as the load required to cause breaks in covalent cross-links between collagen fibrils and slippages between the molecular chains (Komatsu, 2010). The safety margin of the periodontal ligaments, defined as the ratio of the stress that can cause the breaks to the stress normally experienced during function (Alexander, 1981), ranged between 2 and 5 (Komatsu et al., 1998). This range is comparable to that observed for tendons and bones (between 1 and 6) (Currey, 2002). Tissues with such a range of safety margins are believed to be strong enough to perform their specific supportive function (Komatsu, 2010).

The mechanical strength of the periodontal ligament was first evaluated by Yoshimatsu et al. (1956); they used human cadaver specimens to measure the vertical forces required to extract teeth. The investigators used a material testing machine to achieve vertical tooth extraction. The crown of the tooth to be extracted was grasped by a special clamp connected to a load cell, and the rest of the specimen was firmly secured to a holding device that moved downwards to extract the tooth. This study reported that the mechanical strength of human periodontal ligaments ranges from 1.2 and 1.7 N/mm. However, one major drawback of Yoshimatsu et al.'s approach to measuring the periodontal ligament's mechanical strength is that the periodontal ligament fibres would tend to rupture unevenly due to the root curvature and the different alignment of PDL fibres along the root. Hence, the rupture begins in the apical area where the vertical apical fibres are located, followed by horizontal fibres (Atkinson and Ralph, 1977). Ralph (1982) used a transverse section of a tooth with its surrounding PDL and bone to overcome this issue. He developed a technique for

loading the PDL in shear, so it becomes possible to get a standardised stress-strain curve of the PDL in shear or tension, which also permits the comparison between different teeth sizes (Komatsu, 2010).

Several experimental studies have investigated factors that influence the mechanical strength of the periodontal ligament. Kawada and Komatsu (2000) examined the role of collagen fibres in the mechanical strength of the periodontal ligament by exposing them to different concentrations of collagenase enzyme. They found that treatment with 8, 16, and 24 units of collagenase enzyme caused concentration-dependent degradation of collagen fibres and reduced the mechanical strength of periodontal ligament by 55%, 88%, and 96%, respectively. Similarly, Ujiie et al. (2008) reported that treatment of the oxytalan fibres with elastase enzyme reduced the mechanical strength of the PDL in a concentration-dependent manner. In addition, the interfibrillar ground substances were also found to play a role in the strength of the PDL, and a concentration-dependent reduction of the PDL strength was noted when the PDL was treated with α-amylase enzyme which can digest and remove interfibrillar elements from the periodontal ligament, such as neutral polysaccharides and acid glycosaminoglycans (Watanabe and Komatsu, 1997).

Periodontal ligament was found to exhibit time-dependent viscoelastic responses to the applied forces (Komatsu, 2010). One sort of these responses is the stress-relaxation response which has been demonstrated in several studies (Toms et al., 2002, Komatsu et al., 2004a, Komatsu et al., 2004b, Sanctuary et al., 2005). The findings from these studies suggest that PDL exhibits a distinctive stress-relaxation property. Komatsu et al. (2004a) reported that the initially applied stress to the PDL can decrease by 50% in only 10 minutes. This phenomenon indicates that during the application of excessive force, the PDL can absorb and dissipate the stress energy

stored in the tissue, which is considered a protective property that could reduce PDL injury (Komatsu, 2010). The Quantity and the organisation of collagen fibres play an essential role in the stress-relaxation process of the PDL (Komatsu, 2010); this was evidenced by the decrease in the relaxation time when the PDL was treated with collagenase enzyme (Komatsu et al., 2007). furthermore, other factors, such as water content, can also affect the stress-relaxation behaviour of PDL (Provenzano et al., 2001). Chimich et al. (1992) reported that the ligaments with higher water content showed greater relaxation than those with low water content.

Another viscoelastic property of the PDL is that the shear mechanical strength of PDL varies according to the applied strain rate. In vitro studies investigating the stress-strain properties of the PDL have shown that the shear mechanical strength of PDL increases with increasing loading velocity (Chiba and Komatsu, 1993, Komatsu et al., 1993); this was explained to be the result of decreased time available for stress-relaxation of the tissue at higher loading velocities (Chiba and Komatsu, 1993).

1.4. Aims of the research

-To develop an in vitro model system that replicates the clinical procedure of tooth extraction using the Benex system in order to better understand the Benex vertical extraction dynamics and identify determinants of success or failure of this technique.

-To accurately measure the axial forces associated with tooth extraction using the Benex system.

-To examine potential modifications in the Benex extraction technique that may increase the success rate of tooth extraction using this system and reduce maximal extraction force and associated untoward sequelae.

1.5. Design and Methods

This project involves:

- Developing an animal model system that replicates the clinical procedure of vertical tooth extraction using the Benex system and evaluating this model in a preliminary experiment.

- Conducting an experimental study to investigate the effect of different strain rates during vertical tooth extraction using the Benex system on the extraction force and the success rate of tooth extraction.

1.6. Laboratory experiments

1.6.1 Preliminary experiment to establish and evaluate an animal model system for the Benex vertical tooth extraction

1.6.1.1. Aims

-To develop an animal model system that replicates the vertical tooth extraction using the Benex system

-To evaluate the model in terms of the following:

- The maximum force required for tooth extraction and its comparability to that of humans.
- Variations between the extracted teeth in terms of length and the maximum force required for their extraction

1.6.1.2. Setting up the model system

The domestic pig (Swine) aged 9-12 months was chosen as the animal model because pigs' jaws have relatively similar sizes to those of humans and are anatomically and physiologically similar to humans (Bassols et al., 2014). Moreover, they are widely available, cost-effective, and easily obtainable.

Only fresh pigs' jaws were used to minimize the effect of freezing on the behaviour of the periodontal ligament. The lower jaw was preferred over the upper jaw because it is smaller and more easily manipulated. The Benex system was attached to an Instron testing machine to extract 120 teeth from 60 pigs' jaws at a 1 mm/min strain rate. Central incisors (right and left) of the lower jaws were the target teeth because they have single long conical roots without significant curvatures or undercuts (Tonge and

McCance, 1973, Swindle, 2007). This morphology was desirable because it would allow examining the stress-strain behaviour of the periodontal ligament in response to the vertically applied forces.

Failure load (maximum applied force), successful or failed extraction, the reason for failure, and tooth length were recorded as appropriate.

1.6.1.3. Experiment setup

- A diamond bur in a 1:1 straight handpiece was used to prepare an access cavity in the tooth; then, a conventional dental explorer was used to locate the root canal, and a screw pilot hole was prepared with the diamond bur in the centre of the tooth following the root canal's path when possible.

- A self-tapping screw that matches the size of the used drill was inserted and secured in the prepared hole using the Benex screwdriver.

- The Benex extractor was attached to the load frame of an Instron machine with a 2kN load cell, while the Pig jaw was fixed in an adjustable grip and mounted to the lower table of the Instron machine. The Benex pull-rope was connected to the Benex extractor on one side and the self-tapping screw on the other (Figure 1.3).

- Once axial alignment of the pull-rope with the screw was achieved (Figure 1.4-A), an Axial pull-out force was applied by the Instron machine at a constant strain rate of 1mm/min until failure of the specimen occurs either by successful extraction (Figure 1.4-B, C, D) or by other causes such as tooth fracture or loss of screw retention.

- Maximum extraction force and extraction duration were recorded. In cases of successful tooth extractions, the root length of the extracted tooth was measured from the mid-buccal cementoenamel junction to the root apex using a digital caliper.

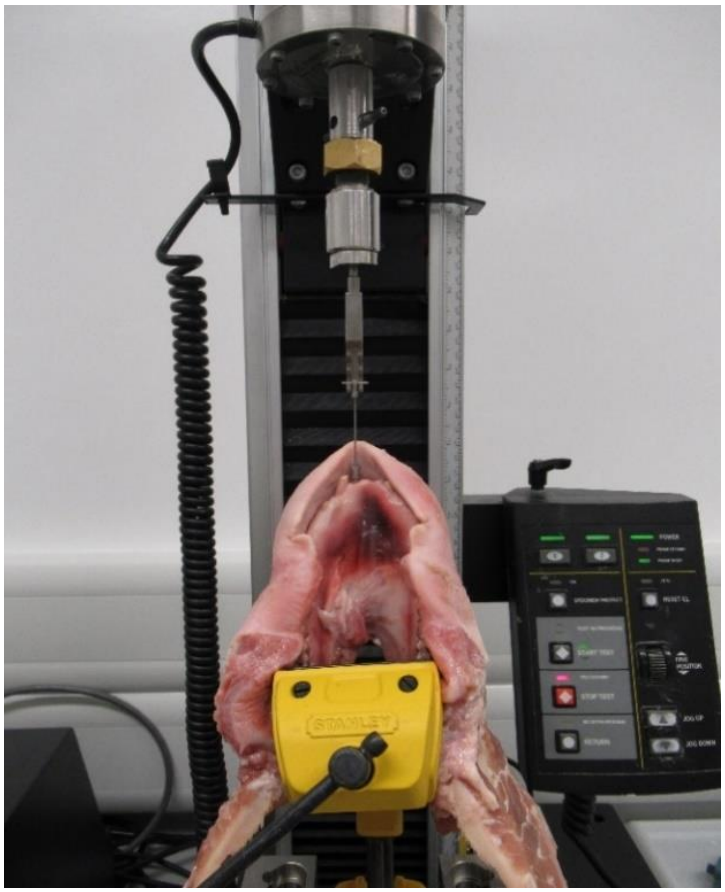


Figure 1.3 Laboratory procedure. The Benex system attached to Instron machine to extract pig's central incisor.

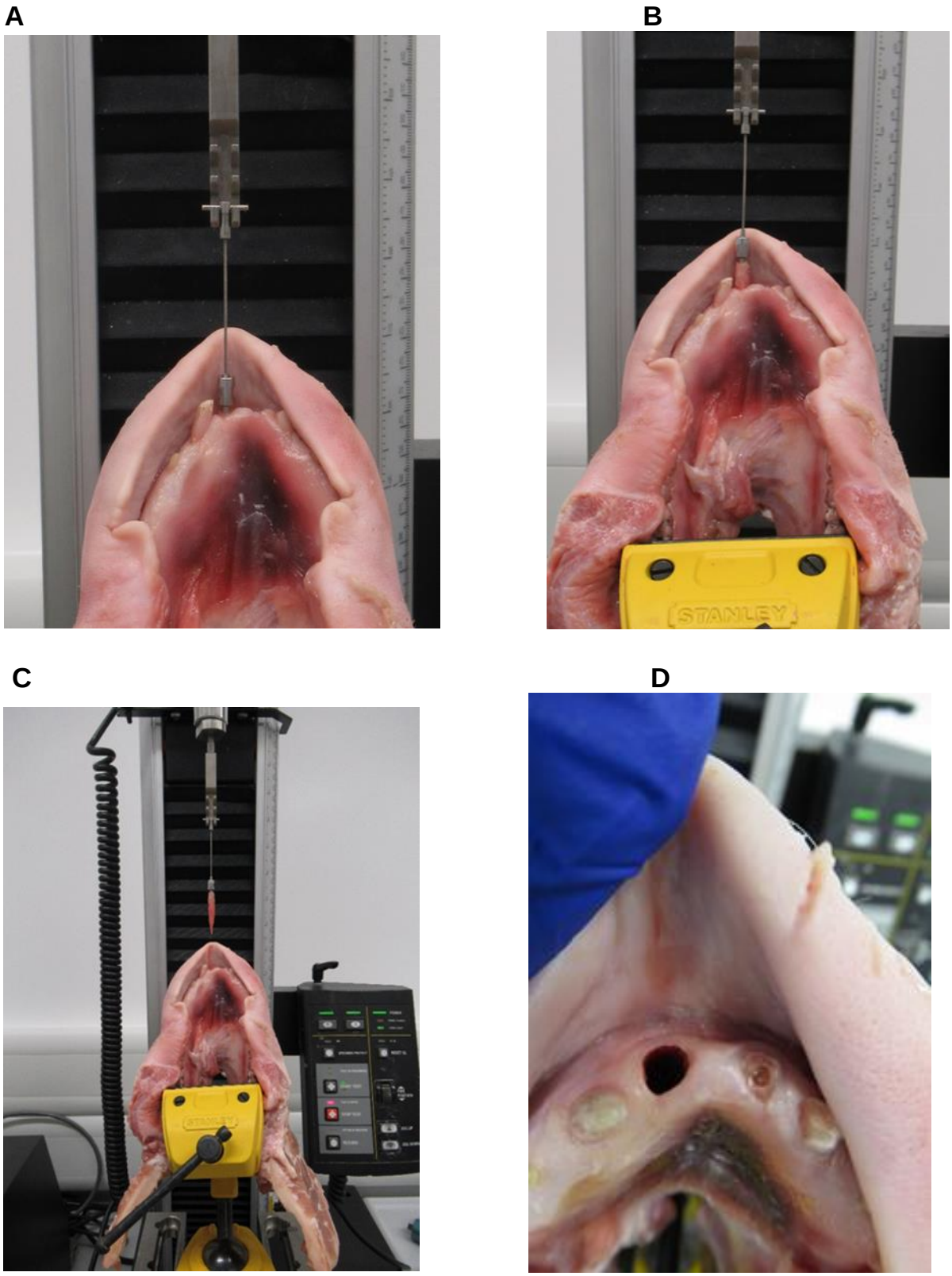


Figure 1.4 Laboratory procedure. (A) Optimal axial alignment of the pull-rope. (B) Progressive root extrusion in a vertical direction. (C) Successful extraction of tooth. (D) The socket after extraction.

1.6.1.4. Results

Altogether, 87 out of 120 teeth (72.5%) were successfully extracted using the Benex system at a 1mm/min strain rate. Root fracture was the most common cause of failed extractions, representing 82% of all failures, followed by the detachment of the screw from the tooth (15%) and, to less extent, screw fracture (3%).

The maximum failure load for successful extractions, which represents the maximum extraction force (F-max), varied from 186 N to 385 N, with an average of 293 N (SD=41), and these forces were normally distributed (Figure 1.5). On the other hand, the failure load associated with the failed extractions ranged from 262 N to 375 N, with a mean of 304 N (SD=32). Figure 1.6 shows box plots illustrating the distribution of maximum force between the success and failure groups.

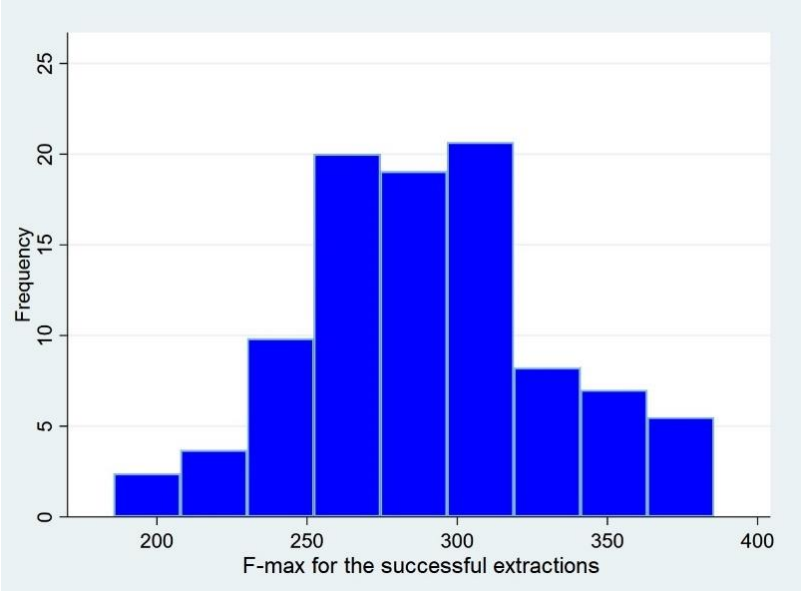


Figure 1.5 Histogram of the maximum failure load for successful extractions

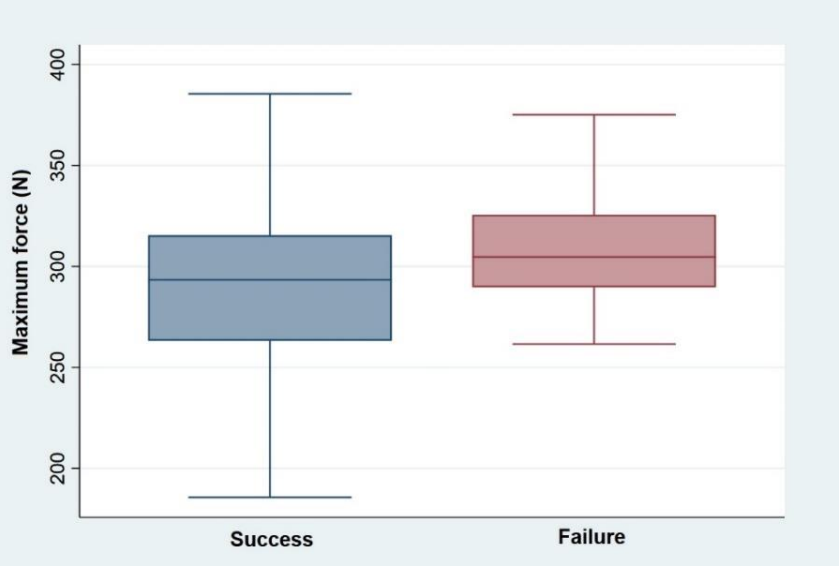


Figure 1. 6 Box plots of maximum forces for successful and failed extractions

When comparing the maximum forces required to extract the right and left central incisors, we found that the average maximum force required to extract the right incisors was 290.7 N (95% CI: 276.8, 305.6 N), and for the left incisors was 291 N (95% CI: 275.7, 306.4 N).

A paired t-test was used to calculate the mean difference of the extraction force between the right and left incisors, and there was no statistically significant difference between them (Mean difference= -0.3; 95% CI: -12.2, 11.5).

Rooth length was measured for the successfully extracted 87 teeth; the mean length was 30.7 mm (SD=1.66) and ranged from 27 to 34 mm. The histogram of the measured teeth lengths shows an approximately normal distribution (Figure 1.7).

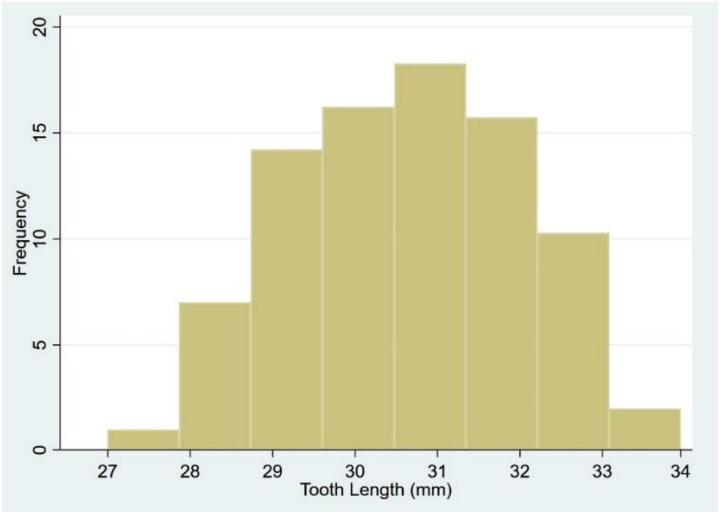


Figure 1. 7 Root length distribution of the extracted central incisors of pigs

Looking at the root lengths of the right and left central incisors, the mean root length of the right incisors was 30.5 mm (95% CI: 30.0, 31.1 mm), while the left incisors had approximately similar mean root lengths of 30.4 mm (95% CI: 29.8, 31.1 mm). Taking into account the clustering of the right and left central incisors within the pigs' jaws, paired t-tests showed no statistically significant difference in the mean length of the right and left extracted roots. (Mean difference=0.06; 95% CI: -0.46, 0.58; P=0.4076). We investigated the relationship between root length and maximum extraction force. As illustrated in Figure 1.8, there was a linear relation between root length and extraction force. A linear mixed effects model was used to account for clustering within pigs' jaws because observations from the right and left incisors within the same jaw may not be independent (Table 1.1). An increase in the root length of one standard deviation was associated with a significant increase in F-max by approximately 16N (95% CI: 12, 20; P < 0.001). The side, wether right or left, had no significant effect on F-max.

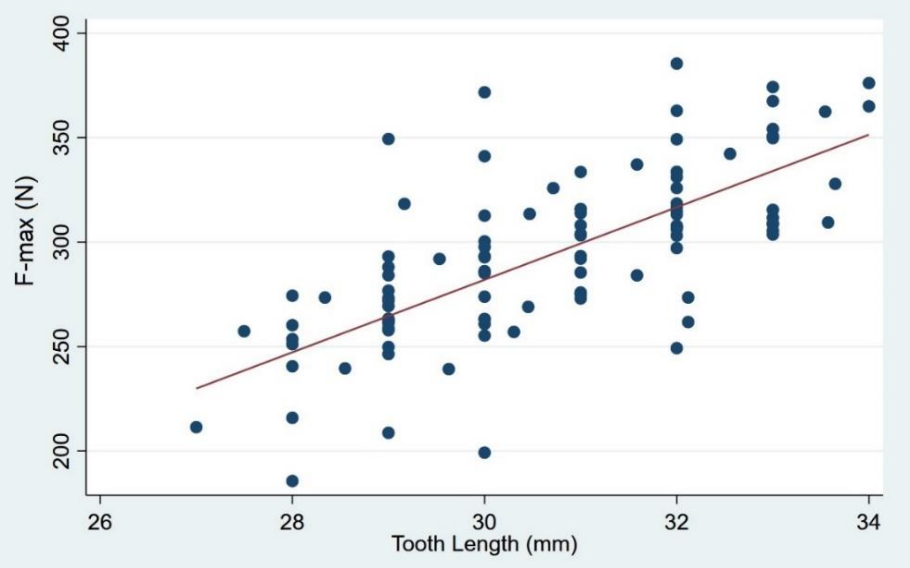


Figure 1. 8 Linear association between root length and F-max

	Dependent variable (F-max)			
Explanatory variables	**β - coefficient**	**St. Error**	**95% CI**	**p-value**
Length	16	2	12, 20	<0.001
Side	4	5	-6, 14	0.429
Constant	-101.6	62.21	-223.6, 20.3	0.102

Table 1.1 Association of tooth length and side with maximum extraction force (Mixed-effects model for linear regression; grouping variable: pig jaw)

The intraclass correlation coefficient (ICC) was also calculated to indicate the correlation of the right and left incisors' extraction forces within the same pig jaw. It was found to be 0.4, indicating a high similarity between them; this could also be interpreted as 40% of the variability is explained by two teeth in the same pig, i.e., the maximum extraction forces are highly correlated within pigs.

1.6.1.5. Conclusion

The developed pig jaw model can be considered suitable for simulating the Benex vertical tooth extraction and for further evaluation of the Benex system. The extraction system can be easily assembled in a controlled and reproducible way; the maximum extraction forces recorded for the pigs' central incisors are comparable to and within the force range reported for extracting human teeth using the Benex system. There was a substantial similarity between left and right incisors within the same jaw with regard to root lengths and the force required to extract them; therefore, future studies should take clustering into account during study planning.

1.6.2. Determination of a clinically meaningful range of strain rates

Before starting any further experiments on the potential effects of applied strain rates on Benex tooth extractions, it was necessary to relate the strain rates that will be used to extract the teeth in the animal model system with that in the clinical situation. In order to do that, the previously reported preliminary experiment was repeated using different strain rates ranging from 0.1 to 10 mm/min and the average time required for successful tooth extraction was measured for each strain rate. This investigation considered what constitutes clinically reasonable time required to extract single-rooted teeth using the Benex system. We considered clinically acceptable ranges between 3 and 15 minutes. Putting this into the context of the laboratory experiment on the pigs' jaw model, we found that extracting pig's teeth at strain rates ranging from 0.1 to 7.5 mm/min have average extraction times consistent with what has been considered clinically meaningful time.

1.6.3. The influences of the applied strain rate on vertical tooth extraction using the Benex System: An experimental study

1.6.3.1. Aims

To examine the effects of different strain rates on vertical tooth extraction using the Benex system in terms of success rate and maximum force required for tooth extraction.

1.6.3.2. Methods

We selected strain rates of 0.1, 2.5, 5, and 7.5mm/min, based on what we believed to include clinically meaningful range of strain rates (0.1-7.5). Eighty-eight pigs' central incisors were randomised to the four groups of strain rate (22 teeth for each group). The randomisation process was conducted using REDCap (Research Electronic Data Capture) software, and block randomisation (blocks of 8) was chosen to allow equal numbers in each group, provided that the same strain rates do not follow one another.

Full details of the setting up of the pig jaw model system for the vertical tooth extraction using the Benex extractor have been previously described in detail in the preliminary experiment (see section 1.6.1.3). Briefly, a self-tapping screw was anchored in a hole prepared in the centre of the root to be extracted. The pig jaw was mounted to the lower table of the Instron machine, and a pull rope was attached to the head of the screw; then, a vertical extraction force was applied with the Instron machine through the attached Benex extractor according to the desired strain rate until failure of the specimen occurs, whether by successful extraction or not. Maximum extraction force (F-max) and the successfully extracted roots' lengths were recorded. All steps of the experiment were performed by a single individual.

1.6.3.3. Statistical methods

Descriptive statistics (mean, standard deviation (SD), range, frequency and per cent) were calculated to characterize the distribution of values for study parameters. Mixed-effects logistic regression models were used to compare the outcome of tooth extraction between the different strain rate groups. Odds ratios and associated 95% confidence intervals were computed for each strain rate group relative to the reference group of 0.1 mm/min strain rate.

Possible non-linear relationships were investigated using fractional polynomials. Linear mixed models were used to evaluate the association between applied strain rate and the odds of extraction failure, as well as between strain rate and maximum extraction force (F-max). All models were adjusted for the clustering of teeth (right and left incisors) within pigs' jaws.

1.6.3.4. Results

The success rate of tooth extraction varied among the different stress rates applied. It was higher for lower strain rate groups and decreased as the strain rate increased (Table 1.2, Figure1.9). Root fracture was the most common cause of failure across the four strain rate groups, accounting for about 90 % of all failures.

Strain rate	Successful extractions	Failed extractions	Total
0.1	20 (90.9%)	2 (9.1%)	22 (100%)
2.5	14 (63.6%)	8 (36.4%)	22 (100%)
5	13 (59.1%)	9 (40.9%)	22 (100%)
7.5	11(50%)	11 (50%)	22 (100%)
Total	58 (65.9%)	30 (34.1%)	88 (100%)

Table 1.2 Success and failure rates of tooth extraction for the different applied strain rates

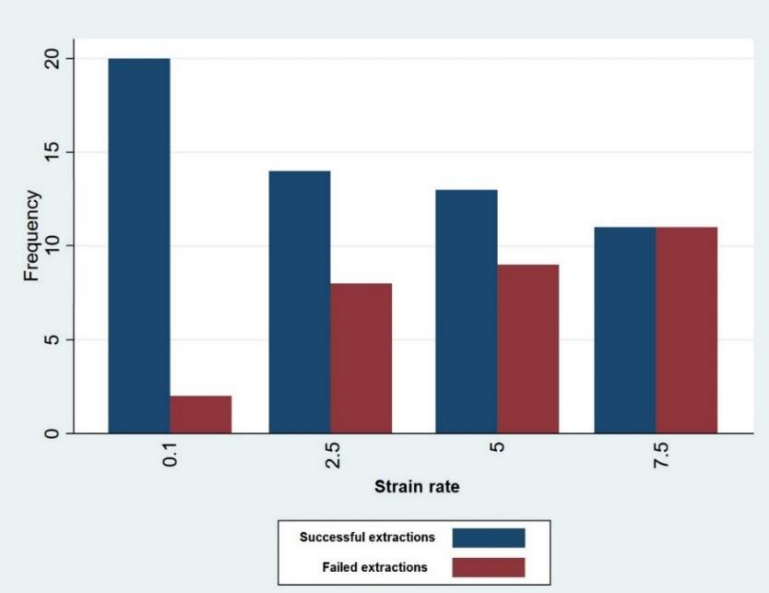


Figure 1.9 Successful and failed tooth extractions for the four applied strain rates

When selecting the 0.1 mm/min strain rate as the reference category in the logistic regression analysis of failure versus strain rate, the 2.5, 5, and 7.5 mm/min strain rate groups showed statistically significantly higher odds ratios of failure (Table 1.3). The predicted probabilities and the 95% CI tooth extraction failure were estimated from the logistic model for each applied strain rate and displayed in Figure 1.10. Assuming linearity between the effects of strain rate on the logarithm odds of failure in tooth extraction (no statistical evidence for non-linearity), the odds of failure increase significantly by 27% with each unit increase in the applied strain rate within the examined strain rates range (OR =1.27, 95%CI: 1.07-1.52, P= 0.007).

Strain rate	Failed	Success	Odd Ratio	95% CI	p-value
0.1 mm/min	2	20	1 (reference)		
2.5 mm/min	8	14	5.7	(1 - 31)	0.034
5 mm/min	9	13	6.8	(1.4 - 37)	0.024
7.5 mm/min	11	11	10	(1.8 - 53.5)	0.007

Table 1.3 Results of Mixed-effects logistic regression model evaluating associations between strain rate (independent variable) and extraction failure (dependent variable)

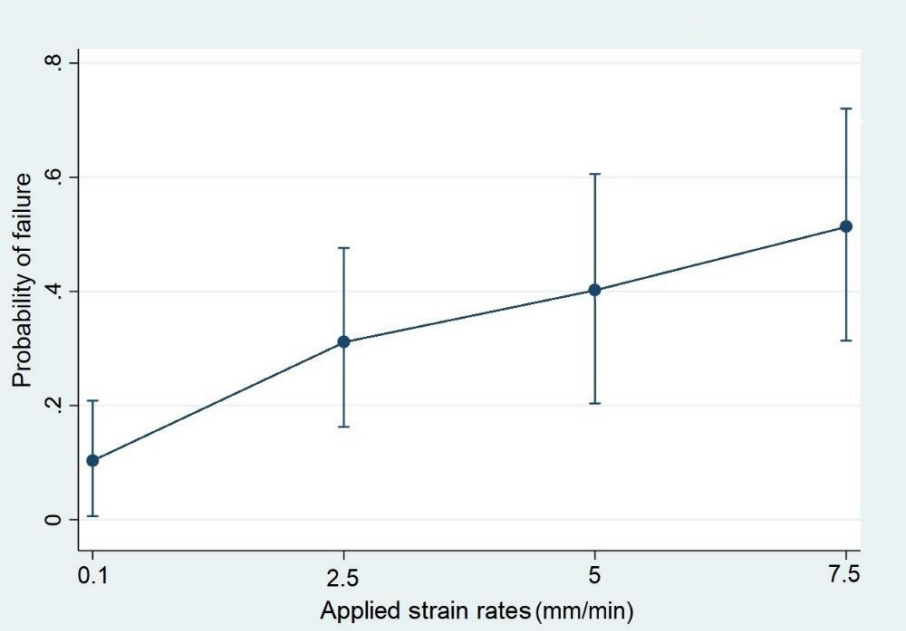


Figure 1.10 Predicted probability of tooth extraction failure for each applied strain rate

The maximum force required for a successful tooth extraction (F-max) was recorded for each strain rate group (Table 1.4). F-max varied widely across strain rate groups, with a larger mean for higher strain rates. Figure 1.11 shows box diagrams showing the distribution of ultimate force for each strain rate group. When using fractional polynomials, there was no statistical evidence of non-linearity in the relationship between strain rate and F-max.

Strain rate	Observations	Mean F-max	Std, dev	Min	Max
0.1 mm/min	20	234	74.4	78	351
2.5 mm/min	14	318	101	112	462
5 mm/min	13	365	96.8	148	489
7.5 mm/min	11	397	56.8	332	510

Table 1.4 F-max measurements for each strain rate group

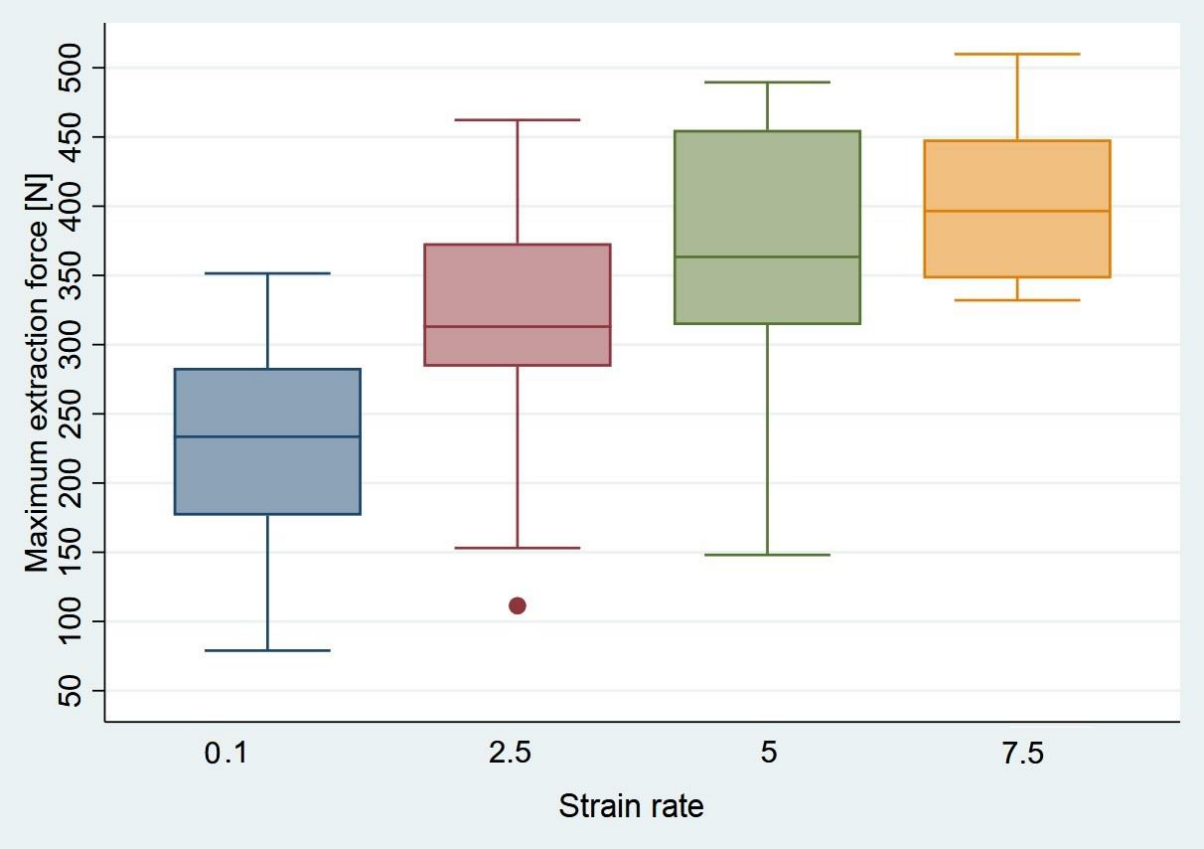


Figure 1.11 Box plots of maximum forces for each strain rate group

On average, the maximum tooth extraction force for the investigated strain rates was 314N (95% CI: 287N, 342N). In a linear mixed model that accounts for differences in tooth lengths and the clustering of teeth within pigs' jaws, an increase in the applied strain rate by 1mm/min was associated with a significant increase in F-max by 22N (Table 1.5, Figure 1.12). No significant differences between extractions forces were observed according to tooth length.

	Dependent variable (F-max)			
Explanatory variables	**β - coefficient**	**St. Error**	**95% CI**	**p-value**
Strain rate	22	3.8	15 - 30	<0.001
Tooth length	3.7	2.3	-0.84 - 8.33	0.109
Constant	112	83	-50 - 274	0.177

Table 1.5 Association of strain rate and tooth length with maximum extraction force (Linear mixed effects model; grouping variable: pig jaw)

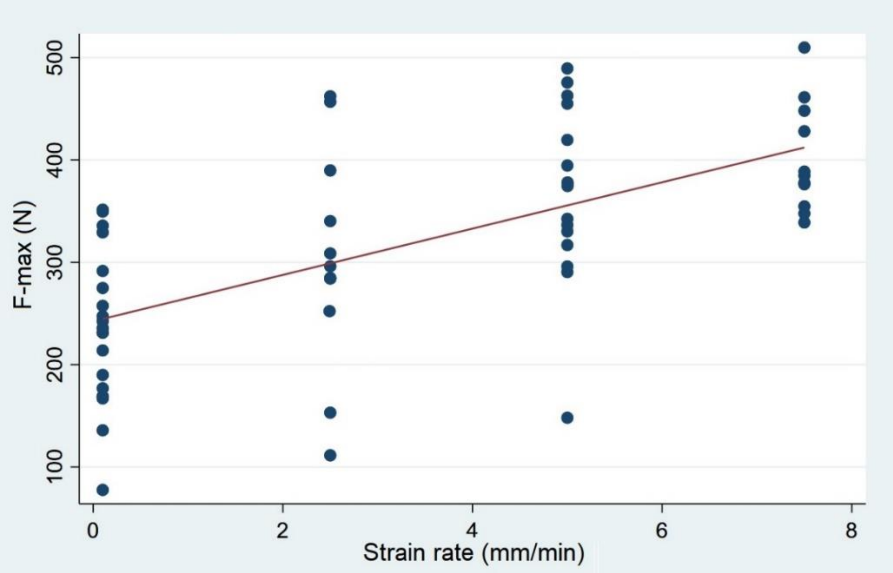


Figure 1. 12 Linear association between strain rate and F-max

1.6.3.5. Discussion

In the present study, we found that applying higher strain rates during the vertical extraction of central incisors from a pig jaw model was associated with an increased risk of tooth extraction failure. Furthermore, the maximum force required for a successful tooth extraction (F-max) varied widely between the applied strain rates. There was a significant increase in the F-max as the strain rate increased. This finding is consistent with the viscoelastic properties of periodontal ligaments that the mechanical strength of PDL increases in response to rapidly applied loads (Komatsu, 2010). This is due to the reduced time available for stress-relaxation of the periodontal tissue at higher loading velocities (Komatsu et al., 1993, Komatsu, 2010).

The maximum extraction forces measured in this animal model system ranged from 78N to 510N, falling within the observed clinical range of forces required to extract human teeth (41N - 629N) (Dietrich et al., 2020a). However, some differences exist between extracting teeth from the pig jaw model and extracting human teeth in a clinical setting using the vertical extraction system.

The current animal model system only involves the vertical extraction of single-rooted teeth. In a clinical setting, multirooted teeth are also extracted using the vertical extraction system, and if necessary, they may be sectioned and the roots extracted separately (Saund and Dietrich, 2013). Furthermore, the central incisors of pigs are longer than those of humans. This means that they have a larger root surface attachment area, which may increase the maximum extraction force. Moreover, the mechanical properties of pigs' teeth might also be different from human teeth in terms of brittleness and resistance fracture.

In the present animal model system, the extraction force was applied continuously without pausing until failure of the specimen occurs either by successful extraction or by other causes such as tooth fracture or loss of screw retention. In contrast, the clinical application of the Benex system usually involves intermittent application of vertical force. The operator pauses when encountering significant resistance and applies a constant force for a short time (30-40 seconds) before increasing the pull force again (Muska et al., 2013). This technique allows for stress-relaxation of the periodontal ligament and reduces the maximum extraction force (Dietrich et al., 2020a). However, the decision of when and how long to pause is subjective and depends on the surgeon's experience. Therefore, it would be helpful if the extraction system had a sensing mechanism to provide feedback on when the surgeon should pause before increasing the traction force further.

Future work could improve the representation of the clinical Benex vertical tooth extraction by adjusting the Instron testing machine to apply intermittent forces with predetermined hold periods. Furthermore, it would be interesting to investigate the relationship between the duration of the hold periods and the maximum extraction force.

It is worth mentioning here that due to the impact of the COVID-19 pandemic and the subsequent closure of the laboratories, we could not pursue lab work further as planned. Furthermore, these unforeseen circumstances have disrupted the original plans for conducting the clinical trials related to minimally invasive extraction as initially intended. We were unable to undertake record reviews and collection of other preliminary clinical data required for clinical trial protocol development; therefore, these plans had to be abandoned. In light of these challenges, we have made necessary adjustments to the work plan and have developed an alternative PhD plan to investigate risk factors for early implant failure by conducting secondary data analyses using existing implant databases.

1.6.3.6. Conclusion

Within the strain rate range from 0.1 to 7.5 mm/min, there is a significant association between the applied strain rate and the maximum extraction force. The slower the strain rate, the lower the extraction force and the greater the chance of successful tooth extraction in this model. Taking into account the differences between teeth in the animal model and humans, the speed at which the tooth is pulled using the Benex vertical extraction system in clinical situations may have an effect on the risk of complications such as root fracture, screw detachment from the tooth, and screw fracture.

CHAPTER 2: GENERAL INTRODUCTION

2.1. Introduction

In contemporary dental practice, the use of osseointegrated dental implants is widely accepted as a reliable and predictable treatment modality for replacing missing teeth in partially or fully edentulous patients. An increasing number of studies have evaluated the long-term prognosis of different dental implant types and reported high survival rates of approximately 85-95% over 5-10 years of follow-up (Lindquist et al., 1996, Lekholm et al., 1999, Al-Nawas et al., 2012, Howe et al., 2019). However, dental implant failure can still occur. Hence, there is increasing interest in improving dental implant treatment planning and evaluating factors that potentially increase the risk of dental implant failure.

Implant failure occurs when an implant's condition or performance, as measured in some quantitative way, falls below an acceptable level in terms of establishment and maintenance of osseointegration, function, tissue physiology, absence of pain and other pathological processes, and patient satisfaction (Misch et al., 2008, Papaspyridakos et al., 2012). This definition of implant failure covers a wide range of biological and clinical situations which can be categorised into biological failures (related to the osseointegration process), mechanical failures of the components (including fracture of implants, connecting screws, etc.), iatrogenic failure (including misaligned implants, violation of anatomical structures such as the inferior alveolar nerve, etc.), and failures due to aesthetic and phonetic issues (Esposito et al., 1998).

Implant failure resulting from failure in the osseointegration (biological failure) can be divided according to the chronological order of events into early failure, which is the failure to achieve osseointegration, and late failure, which is the failure to maintain previously achieved osseointegration (Esposito et al., 1998). Several cut-off points

have been proposed to distinguish between early and late failures, such as abutment connection, final prosthesis delivery, and six months or one year after implant placement (Jemt, 2017, Troiano et al., 2018, Carr et al., 2019). This categorisation suggests that implant failures occurring in these two distinct periods may be associated with different risk factors.

Several studies have demonstrated the impact of both local and systemic factors on the long-term results of dental implants (Moy et al., 2005, Alsaadi et al., 2008a, Levin et al., 2011, Neves et al., 2018). However, the factors that may affect the osseointegration process and, thus, early implant failure still need to be better understood.

Losing the implant early after it has been placed can be frustrating for patients, and it may require additional surgical intervention to remove the implant. Therefore, identifying and assessing the potential risk factors for early implant failure can be of great importance in predicting treatment outcomes. Furthermore, surgeons can make informed decisions to improve outcomes of implant therapy by recognising high-risk conditions for early failure and adjusting the treatment plan accordingly.

2.2. The concept of osseointegration

The principle of osseointegration, introduced by Per-Ingvar Branemark in the 1960s, forms the scientific basis for dental implants. Branemark was researching the microcirculation of rabbit bones. During the course of his research, he noticed that some chambers composed of titanium metal became so fused with the rabbit bone to the point where they could not be separated without fracture (Brånemark, 1983). Based on this, Branemark introduced the term ‘’osseointegration’’ to describe this state of incorporation observed between bone and titanium. Since this finding, osseointegration has gained significant importance, not only in dentistry but also in medical fields such as orthopaedics (Brånemark et al., 2001, Walter et al., 2022).

Osseointegration was first defined as a ‘’direct structural and functional connection between living bone and the surface of a load-carrying implant’’ (Branemark, 1977). Although the term osseointegration was originally used to refer to titanium implants, it now includes other biomaterials, such as ceramics, that can also osseointegrate into the bone (Borba et al., 2017, Guglielmotti et al., 2019).

The definition of osseointegration has changed slightly over the years. Zarb and Albrektsson (1991) included the clinical aspect as part of the definition of osseointegration. They required asymptomatic rigid fixation during functional loading in order for the implant to be considered osseointegrated, as a movement of the implant might indicate the presence of connective tissue at the implant-osseous interface, which is contrary to the principle of osseointegration. More recently, the histological profile of the bone-implant interface was involved in the definition of osseointegration in terms of the formation of highly mineralised collagen fibrils and the

number of osteocytes capable of establishing and maintaining a rigid connection with the implant surface (Shah et al., 2019).

2.3. Definitions of Success and Failure of dental implants

In general terms, success can be defined as achieving what is aimed for. In the field of dental implantology, to be considered successful, dental implants should meet specific success criteria regarding tissue physiology (achieving and maintaining osseointegration), function, and patient satisfaction (Papaspyridakos et al., 2012). However, if the implant is still functioning despite not meeting all the success criteria, it can still be considered a surviving implant rather than a failed one (ten Bruggenkate et al., 1990, Misch et al., 2008). In contrast, implant failure refers to a large variety of clinical situations in which the condition and performance of the implant are below a specified acceptable level, which therefore mandates the removal of the implant (Esposito et al., 1998, Misch et al., 2008).

Failures of dental implants can be categorised into biological failures, mechanical failures and iatrogenic failures (Esposito et al., 1998). Biological failure is primarily related to the inability of the host bone tissue to initiate the osseointegration process (early failure) or to maintain the already achieved osseointegration (late failure). Mechanical failure, on the other hand, refers to the failure of the implant components, such as a fracture of the implant body, screw, or abutment. An iatrogenic failure includes mispositioned implants or implants that must be removed due to the violation of the nearby anatomical structures, such as the inferior alveolar nerve. Another group of failures can be related to patient dissatisfaction due to aesthetical, functional, or

phonetical problems (Esposito et al., 1998, Papaspyridakos et al., 2012). Our main focus in this thesis will be on the early biological failure of dental implants.

2.4. Success criteria for dental implants

For a dental implant to be considered successful, it must meet specific criteria regarding tissue physiology, function, and patient satisfaction.

Several authors have previously proposed success criteria to evaluate dental implants (Albrektsson et al., 1986, Smith and Zarb, 1989, Buser et al., 1990, Misch et al., 2008). However, the criteria established by Albrektsson et al. (1986) have long been one of the most widely used standards for determining the success of dental implant treatment. The primary basis for these criteria was the identification of clinical indicators of successful osseointegration of dental implants.

Although the definition of success criteria has expanded in scope over the years with new parameters such as patient satisfaction, peri-implant soft tissue status, prosthetic function, and aesthetics (Papaspyridakos et al., 2012), clinical evidence of successful osseointegration remains the primary standard for evaluating the success of dental implants.

2.4.1. Clinical parameters to identify implant success or failure

2.4.1.1. Pain

Pain or discomfort should not be present after a dental implant has achieved initial healing and during function. When pain or discomfort is experienced, it is usually caused by a poorly fitting prosthetic component or compression of soft tissue by the prosthesis. The body of the implant does not often induce pain unless the implant is mobile and surrounded by inflammatory tissue or if the body of the implant is immobile but encroaches on nearby anatomical structures, such as the inferior alveolar nerve (Misch et al., 2008).

When assessing dental implants for pain or tenderness in clinical settings, a percussion test is typically used as the method of investigation. Once the initial healing process of the implant is complete and osseointegration has been achieved, there should be no pain in response to vertical or horizontal pressure. Pain emanating from an implant body, either when the implant is being tapped (percussion) or while it is functioning, is a subjective criterion that signals that the implant has failed (Misch et al., 2008, Misch, 2014).

2.4.1.2. Mobility

The absence of clinical mobility of the implant when subjected to horizontal and vertical forces is a critical criterion for determining implant success and a clinical indicator for achieving osseointegration.

The lack of implant movement almost always indicates direct contact between the implant and the bone. However, clinical immobility of the implant does not necessarily

mean the actual absence of movement because a healthy dental implant may move up to 75 μm. Nevertheless, this movement appears as zero clinical mobility because the human eye cannot perceive it (Misch et al., 2008). On the other hand, clinically detectable implant mobility implies the existence of connective tissue mediating between the implant and the bone, indicating implant failure (Smith and Zarb, 1989). The connective tissue that may form around dental implants has a different embryonic origin than the periodontal ligament and cannot handle movements as the periodontal ligament does with natural teeth (Ten Cate, 1985). Therefore, the movement continues to increase, the implant becomes tender to pressure, and its removal becomes necessary.

Dental implant movement can be assessed using a variety of methods. The simplest method involves applying light pressure (less than 500 grams) to the implant with a rigid instrument in both vertical and horizontal directions while simultaneously detecting any movement visually or manually with a different rigid instrument (Misch et al., 2008). More precisely, implant movement can be assessed using electronic devices, such as Periotest and resonance frequency analysis devices, which provide objective methods for measuring implant mobility.

Periotest device provides a reliable method for assessing implant movement by quantifying the damping properties of the tissues surrounding the implant (Teerlinck et al., 1991). It applies a constant force of 12-18N to the implant using an electronically controlled tapping instrument. When the tapping instrument strikes the implant, it slows down or stops. The greater the implant's mobility, the lower the damping impact of the tissues surrounding it, resulting in less recoil and delayed rod retraction (Olivé and Aparicio, 1990, Teerlinck et al., 1991). The device has a built-in accelerometer to measure the duration of contact between the tapping rod and the implant, which is

then converted into Periotest value (PTV) to indicate implant movement (Atsumi et al., 2007). The absence of clinical implant mobility corresponds to PTV values ranging between -8 and +9 (Andreotti et al., 2017).

Resonance frequency analysis (RFA) is a non-invasive technique that uses vibration to assess the stability and osseointegration of dental implants. In order to measure the resonant frequency of the implant-bone complex, the RFA device uses a small transducer that attaches directly to the implant and sends electromagnetic pulses over a predetermined range of frequencies. The perceived resonance frequency values are translated into units of implant stability quotient (ISQ) ranging from 1 to 100. A low ISQ value indicates low implant stability, whereas a high ISQ value suggests good stability (Al-Jetaily and Al-Dosari, 2011, Sennerby, 2015).

2.4.1.3. Marginal bone loss

The marginal bone (crestal bone) surrounding the upper part of the implant body is a crucial indicator for evaluating dental implant success as it reflects the level of the bone supporting the implant. A low level of this bone means that the implant loses its anchorage, which can threaten the success of the implant.

In general, a vertical marginal bone loss of 1.5–2 mm within the first year of placement is considered normal and within the range of successful outcomes (Lekholm et al., 1986, Misch et al., 2008, Cecchinato et al., 2013). However, the bone supporting the implant is expected to stabilise after the first year. Several studies have reported that the acceptable rate of marginal bone loss after the first year of implantation is less than 0.2 mm per year (Albrektsson et al., 1986, Cox and Zarb, 1987, Smith and Zarb, 1989, Wennström et al., 2004, Misch et al., 2008).

Marginal bone loss can be assessed using conventional radiographs. In order to measure the amount of marginal bone loss around the implant, the crestal bone level should be measured relative to a reference point on the implant and compared to the bone level recorded immediately after implant placement (Berberi et al., 2014). Even though cone beam computed tomography (CBCT) and conventional computed tomography (CT) are capable of producing highly accurate 3D images of peri-implant bone, it is not always feasible or suitable to use them routinely in the evaluation of marginal bone loss around dental implants due to the higher radiation dose delivered to the patient and the increased cost when compared to conventional radiography for the purpose mentioned above.

2.4.1.4. Peri-implant diseases

Diseases affecting the tissues surrounding the implant can be classified into peri-implant mucositis and peri-implantitis (Lindhe and Meyle, 2008). Peri-implant mucositis is an inflammation confined to the soft tissues surrounding the implant, while the term peri-implantitis refers to the pathological inflammatory changes involving the bone that supports the implant, usually resulting in bone loss (Mombelli and Lang, 1998, Lindhe and Meyle, 2008). Bacteria are likely the main factor responsible for bone loss around dental implants. A growing number of studies show that anaerobic plaque bacteria may have detrimental effects on the health of the tissues surrounding the implant, resulting in peri-implantitis (Lang et al., 2000, Tallarico et al., 2017). Bone loss can also occur around implants without bacteria being the primary factor. Implant overloading, for example, can result in stress-induced peri-implant bone loss (Oh et al., 2002, Misch et al., 2005). However, as the peri-implant sulcus becomes deep and the oxygen tension becomes low, the environment becomes suitable for the anaerobic

bacteria to colonise and continue bone loss. Peri-implant diseases may cause pain, suppuration, accelerated peri-implant bone loss, mobility, and implant failure (Lindhe and Meyle, 2008). Clinical and radiographic examinations are usually used to assess peri-implant diseases.

2.5. Aims and objectives

2.5.1. Aims

The main aim of this thesis was to assess risk factors associated with early implant failure.

2.5.2. Objectives

- To determine the risk factors for early implant failure.
- To examine the methods used to adjust for covariates in studies investigating risk factors for early implant failure.
- To propose a causal model to be used for investigating causal risk factors for early implant failure.
- To perform secondary data analyses using the European Centres for Dental Implantology (ECDI) database:
    - To analyse the ECDI implant dataset descriptively and assess the incidence of early implant failure.
    - To assess potential risk factors for early implant failure in the ECDI implant dataset using our proposed causal model.

CHAPTER 3: RISK FACTORS FOR EARLY IMPLANT FAILURE: A SYSTEMATIC REVIEW AND META-ANALYSIS

3.1. Aims

-To assess risk factors for early implant failure.

-To examine the methods used in previous studies to adjust for covariates when investigating risk factors for early implant failure.

3.2. Methods

This systematic review and meta-analysis was registered in PROSPERO (registration number: CRD42023493789)

3.2.1. Criteria for considering studies for this review

3.2.1.1. Inclusion criteria

- Human studies.
- Controlled trials, cohort studies (prospective or retrospective) and case-control studies.
- Studies that reported on early implant failures as an outcome.
- Studies that looked at the determinants of early implant failure.
- Studies involving adult patients over 18 years old with no restriction on the number of patients.
- English language articles.
- No restrictions on publication date.

3.2.1.2. Exclusion criteria

- Animal studies
- Case reports, case series, and review articles.
- Studies on the late failure of dental implants.
- Studies that did not clearly specify early implant failure.
- Studies evaluating zygomatic implants, mini-implants or subperiosteal implants
- Studies published in languages other than English.

3.2.2. Search methods for identification of studies

3.2.2.1. Electronic searches

A comprehensive systematic search of various electronic databases was performed to identify relevant studies for inclusion or consideration in this review.

These databases were:

- PubMed.
- MEDLINE via OVID (1946 to most recent).
- EMBASE via OVID (1974 to most recent).
- The Cochrane Library.

A detailed search strategy was developed for each database searched to identify relevant studies for inclusion in this review. These are primarily based on the search strategy developed for the MEDLINE database but revised as appropriate for each database. The search strategy combined a set of controlled vocabularies (MeSH titles) with free text terms. Synonyms, proximity operators and truncation were used as appropriate to make the search more comprehensive. Boolean operators “AND’’ and “OR’’ were also used to narrow and broaden the search.

The last search was conducted on the 25th of May 2022. Details of the search strategy on PubMed, MEDLINE, EMBASE and The Cochrane Library are listed in Appendices 1, 2, 3 and 4, respectively.

3.2.2.2. Searching other sources

3.2.2.2.1. Reference lists

Reference lists of identified studies and relevant review articles were screened for potential additional studies.

3.2.2.2.2. Unpublished studies

Unpublished and ongoing studies were searched for in conferences' proceedings and in the following registries:

- Open Grey
- Web of Science Conference Proceedings
- ClinicalTrials.gov database
- WorldCat Dissertations and Theses
- E-Theses Online Service (EThOS) by the British Library
- Google Scholar

3.2.3. Data collection and analysis

3.2.3.1. Selection of studies

Individual search results were merged together, and duplicate publications were excluded. The titles and abstracts of all identified reports were examined independently by two reviewers to identify potentially relevant studies. For studies that appeared to meet pre-specified inclusion criteria or whose title and abstract did not provide enough information to make a clear decision, full-text reports were obtained and evaluated in duplicate by two reviewers to determine whether the studies met the inclusion criteria. Any disagreements were resolved by discussion.

3.2.3.2. Quality Assessment of included studies

The quality of the included studies was assessed according to the Newcastle-Ottawa Scale (NOS), which is a widely used tool for assessing the quality of observational studies included in systematic reviews (Wells et al., 2000).

NOS calculates study quality based on three main components: selection of study groups, comparability between groups, and outcome confirmation. It assigns a maximum of four points for selection, two for comparability, and three for outcome. Studies with a rating of seven to nine points were considered to be of high quality, four to six points of medium quality, while studies with a score of three or less were considered to be low quality.

Two reviewers independently assessed the quality of the included studies, and any disagreements were resolved by consensus.

3.2.3.3. Data extraction and analysis

3.2.3.3.1. Data Extraction

Where possible, the following data were extracted from each eligible study included in the final analysis:

1. Study characteristics:
    - Authors' names
    - Year of publication
    - Country of origin
    - Study setting
    - Number of centres
    - Main aims
    - Definition of early implant failure
    - Study design
    - Criteria for inclusion and exclusion
    - Total study duration
    - Adjustment for covariates
    - Accounting for clustering of implants within patients

2. Details of the participants:
    - Total number of patients
    - Age
    - Sex distribution
    - Total number of implants inserted

3. Details of exposure (risk factor)
    - Type of exposure
    - Number of implants placed in the exposed group

4. Details of comparison
    - Type of comparator
    - Number of implants placed in the unexposed group

5. Outcomes:
    - Method of assessment.
    - Number failed implants in each group
    - Duration of follow-up

6. Results:
    - Summary statistics for each group (Frequencies and proportions).
    - Estimate of effect with confidence interval and P value.
    - Missing participants (withdrawals and drop-outs).

3.2.3.3.2. Measures of risk factor effect

Various effect measures can be used to estimate the relative effect of a risk factor on early implant failure, including risk ratio, odds ratio, and hazard ratios. Since early implant failure (outcome of interest) is a rare event, these measures are assumed to be similar. Therefore, for this systematic review, an estimate of the relative effect of a risk factor on the dichotomous outcome of early implant failure was expressed as an odds ratio (OR) along with associated 95% confidence intervals (CIs), with the implant being the statistical unit of analysis. Using the odds ratio will be a robust approximation of the risk ratio. This is also consistent with the secondary data analysis conducted in Chapter 5.

We took a pragmatic approach to facilitate comparisons by dichotomising certain exposure variables using cut-off points (thresholds). We defined implants with a diameter of less than 3.75 mm as narrow implants and compared them with wider implants, and implants with a length of less than 10 mm as short implants and compared them with longer implants. For patient age, we compared early implant failure in patients aged 60 years and older with younger patients.

3.2.3.3.3. Meta-analysis

A meta-analysis was performed where possible for each risk factor identified, and this was only attempted if there were studies with similar comparisons that reported the outcome of interest. The implant was considered the statistical unit in these analyses, and early implant failure (yes/no) was the dichotomous outcome measure to be evaluated.

Estimates for early implant failure (dichotomous outcome) from individual studies were expressed as odds ratio with 95% confidence intervals (CIs). Meta-analyses were conducted using crude estimates as they were consistent across studies in terms of covariate adjustment. We investigated how studies adjusted for potential confounders. We ignored estimates obtained from the "single model" approach, where all risk factors are included in one model and the resulting estimates are reported, as they do not have a causal interpretation (see Discussion section).

For studies that did not account for grouping (clustering) of implants within patients, we performed an approximate analysis to get cluster-adjusted estimates of standard errors and confidence intervals, as an individual patient may have received multiple implants and failure to account for this could result in an underestimation of standard errors and confidence interval. First, we calculated the design effect (design effect = 1 + (M – 1) ICC) using the average cluster size of the study (M) and an estimate of the intraclass correlation coefficient (ICC) obtained from a large dataset of 150,896 implants placed in 63,414 patents (ICC = 0.5) (see Chapters 4 and 5), then multiplied the standard error of the effect estimate (obtained from the analysis that ignores clustering) by the square root of the design effect (Higgins et al., 2021).

We used the random effects model based on the DerSimonian and Laird method to estimate the final pooled effect. This robust method was chosen because it takes into account the variability within and between studies, as we expected a variation across the studies due to different patient populations, settings, clinicians, etc.

Statistical heterogeneity between studies was assessed using both a chi-square hypothesis test and the (I^2) statistic. The chi-square test was used to investigate whether the variation in the estimates from different studies is solely due to chance

(P<0.1), while the I^2 statistic was used to estimate the total variation across studies due to heterogeneity (Higgins et al., 2021).

A leave-one-out sensitivity analysis was conducted to assess the robustness of our results by evaluating the influence of individual studies on the pooled estimate; this was achieved by deleting each of the studies in turn and computing the overall effect with a 95% confidence interval from a meta-analysis of the remaining studies. An influence plot was then generated, which is similar to a forest plot but with pooled estimates corresponding to each omitted study and a vertical line representing the overall estimate of the complete set of studies (without deletion) to help identify influential studies. Any estimate that appears to differ substantially from others on visual inspection or is associated with a different statistical significance compared to the original estimate (changes from non-significant to significant or vice versa) may result in the omitted study being considered influential (Petrie, 2020).

A funnel plot, which is a scatter diagram of effect estimates against their standard errors, was drawn to assess publication bias in the meta-analyses that included ten or more studies to allow for appropriate regression analysis of funnel plot asymmetry (Higgins et al., 2021). Each point in the plot represents one study in the meta-analysis. In the absence of publication bias, the funnel plot would be approximately symmetrical with a large scattering of points at the bottom where study sizes are small and narrowing upwards where studies' sizes are large. On the other hand, an asymmetric funnel plot with a gap towards the lower left corner, where study sizes and effect sizes are small, indicates the possibility of publication bias (Petrie, 2020). The asymmetry of each funnel plot was assessed visually and tested for statistical significance using Harbord's regression test (p<0.1) (Harbord et al., 2006).

The reporting of these meta-analyses adhered to the MOOSE (Meta-analysis Of Observational Studies in Epidemiology) guidelines (Stroup et al., 2000), and data were analysed using Stata 17.0 statistical software (Stata Corporation, College Station, TX, USA).

3.2.3.4. Dealing with incomplete or missing data

If there was unclear, incomplete, or missing data from a study, the study authors were contacted for clarification, and additional information was requested. If the original authors could not be contacted to obtain the information requested, missing data were assumed to be missing at random, and the analysis was based solely on available data according to the recommendations for handling missing data described in the Cochrane Handbook for Systematic Reviews (Higgins et al., 2021).

3.3. Results

3.3.1. Literature search

The search strategy identified a total of 2846 potentially relevant studies; 775 references were obtained from PubMed, 455 from Medline (via Ovid), 935 from Embase (via Ovid), 655 from the Cochrane Library and 26 from reference lists of relevant papers and reviews identified. No relevant unpublished studies were obtained. All identified citations were then imported into EndNote reference management software (V.20), and duplicate publications were removed.

Five hundred seventy-eight articles remained for the title and abstract screening after elimination of duplicates. If the title and abstract provided insufficient information, the full texts of the articles were retrieved and evaluated to confirm eligibility. Five hundred forty-nine articles were clearly irrelevant to this review, so they were removed.

The full texts of the remaining 29 studies were retrieved for a detailed review to assess whether they met the inclusion criteria for this review. Nine studies were excluded, and 20 studies were included in this review. Studies excluded after full-text review and the reason for exclusion were recorded in Table 3.1.

The study selection process is summarised in a flow chart (Figure 3.1) as recommended in the PRISMA statement (Moher et al., 2009)

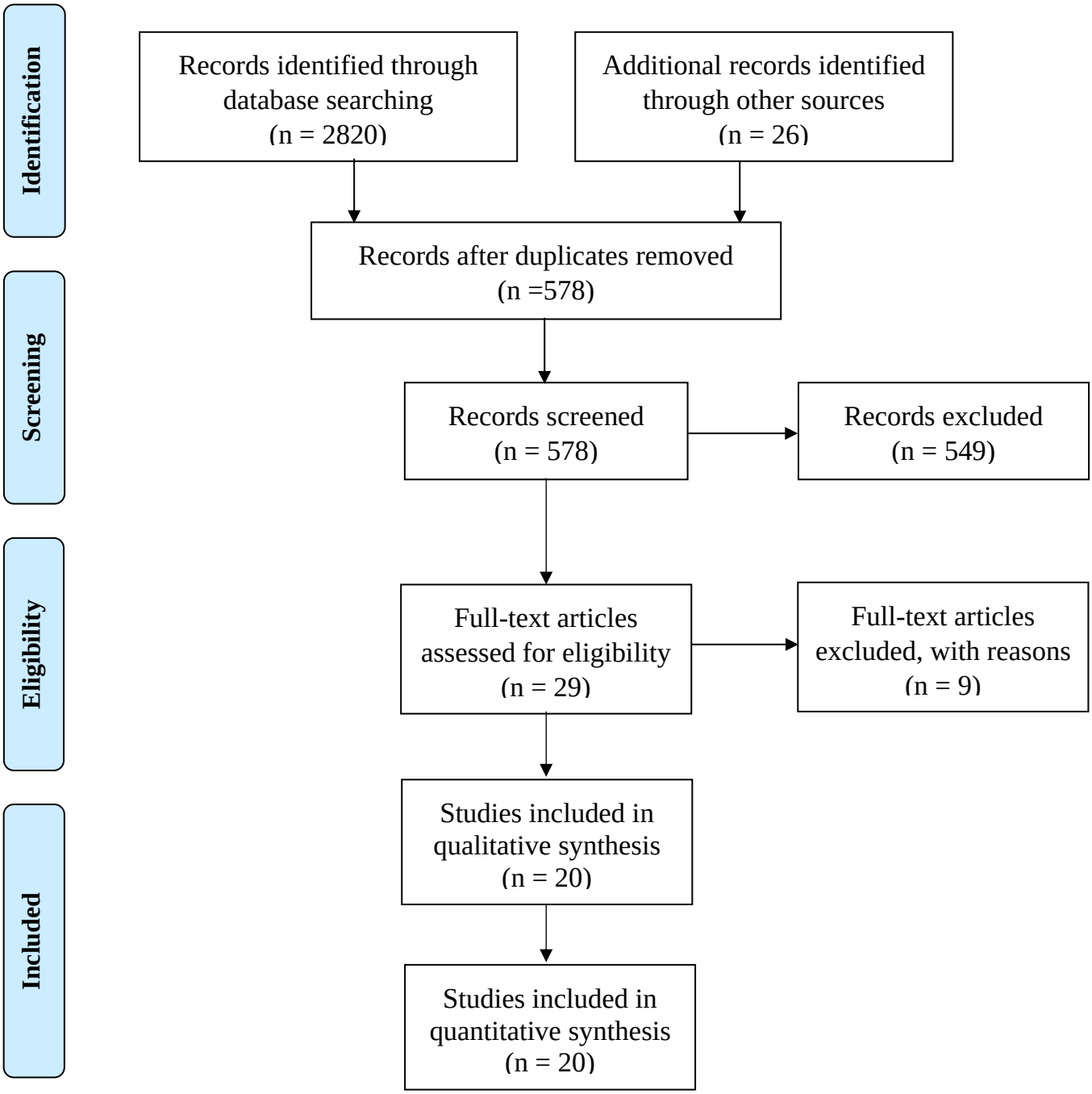


Figure 3.1 PRISMA flow chart for the screening and selection of studies

Table 3.1 Studies excluded after full text review

Study	Reason for exclusion
Vehemente et al. (2002)	There is no distinction between early and late Failures.
McDermott et al. (2003)	There is no distinction between early and late Failures.
Anitua et al. (2008)	There is no distinction between early and late Failures.
Huynh-Ba et al. (2008)	There is no distinction between early and late Failures.
Koldsland et al. (2009)	Cross-sectional study
Gianserra et al. (2010)	Insufficient data: Patient-level data only, no implant-level data.
Han et al. (2014)	Insufficient data: The number of early implant failures was not reported for study variables (risk factors)
Jemt (2017)	Insufficient data: The number of early implant failures was not reported for study variables (risk factors)
Kim et al. (2018)	Insufficient data: The number of early implant failures was not reported for study variables (risk factors)

3.3.2. Description of the studies

Detailed characteristics of the 20 included studies are listed in Tables 3.2 and 3.3. These studies were published between 2006 and 2021, with study durations ranging from 1-34 years (median: 5 years), and their main aim was to assess the effect of single or multiple risk factors on early failure of dental implants. All studies included in this review were observational studies, with three being prospective observational studies and 17 being retrospective observational studies. In terms of study setting and population, most of the studies (19 out of 20 studies) were single-centre studies, 16 of which reported universities (clinics/hospitals) as the institutions where the studies were conducted, while three studies were conducted in private dental clinics. The only multicenter study was based on data collected from several private and public practices through the Swedish National Data Register (Derks et al., 2015). In terms of the countries where the studies were conducted, three studies each were in Belgium, Brazil and Sweden; two studies each in Spain, Switzerland, Japan and China; and one study each in Jordan, Germany and South Korea.

All included studies defined early implant failure as implant loss before functional loading. Regarding the risk factors for early implant failure reported and assessed by these studies, patient age was analysed as a risk factor in eight studies, sex in eight studies, smoking in 11 studies, implant length in 14 studies, implant diameter in 12 studies, the jaw in which the implant was placed (maxilla/mandible) in 15 studies, implant location (anterior=canine to canine / posterior=premolars and molars, in each jaw) in 14 studies, implant healing mode (submerged/non-submerged) in three studies, bone augmentation in 11 studies, previous history of periodontitis in four studies, and diabetes (type I and II) in four studies. Individual studies' relative effect measures of these risk factors on early implant failure are presented in Table 3.3.

Five of the 20 included studies did not adjust for confounders, while the other 15 made multiple adjustments to the effect estimates of exposures using a single model. Furthermore, only ten studies used a statistical approach that accounted for implant clustering within patients (e.g. GEE, Multilevel model) (Table 3.2).

Table 3.2 Characteristics of the included studies

Author (Year)	Study design*	Country /setting	Sample size	Study period	Definition of early failure	Risk factor/s assessed	Adjustment for covariates	Statistics (accounting for clustering)
Noguerol et al. (2006)	RCo (Single centre)	Spain / Private practice	1,084 implants 316 patients.	10 yrs	Implant loss before functional loading	Age Smoking Jaw (max/mand) Location (ant/post) Prev. Periodontitis	Single model adjustment	Multiple logistic regression (not accounted for clustering)
Roos-Jansåker et al. (2006)	PCo (Single centre)	Sweden / Public Service	1057 implants 218 patients	5 yrs	Implant loss before functional loading	Jaw (max/mand) Location (ant/post)	No adjustment	Cox's regression , (accounted for clustering)
Alsaadi et al. (2007)	RCo (Single centre)	Belgium / University hospital	6,946 implants 2004 patients.	22 yrs	Implant loss before functional loading	Smoking Implant length Implant diameter Jaw(max/mand) Location (ant/post)	Single model adjustment	GEE logistic regression (accounted for clustering)
Alsaadi et al. (2008b)	PCo (Single centre)	Belgium / University hospital	720 implants 283 patients.	2 yrs	Implant loss before functional loading	Smoking Implant length Implant diameter Jaw(max/mand) Location (ant/post) Diabetes	Single model adjustment	GEE logistic regression (accounted for clustering)
Bornstein et al. (2008)	RCo (Single centre)	Switzerland / University clinic	1,817 implants 1,206 patients	3 yrs	Implant loss before functional loading	Smoking Jaw (max/mand) Location (ant/post) Bone Augmentation	No adjustment	Simple logistic regression (not accounted for clustering)
Sverzut et al. (2008)	RCo (Single centre)	Brazil / University clinic	1,628 implants 650 patients	8 yrs	Implant loss before functional loading	Smoking	No adjustment	Simple logistic regression (not accounted for clustering)

Table 3.2 (Continued)

Author (Year)	Study design*	Country /setting	Sample size	Study period	Definition of early failure	Risk factor/s assessed	Adjustment for covariates	Statistics (accounting for clustering)
Olate et al. (2010)	RCo (Single centre)	Brazil / University clinic	1,649 implants 650 patients	8 yrs	Implant loss before functional loading	Implant length Implant diameter Jaw (max/mand) Location (ant/post)	Single model adjustment	Multiple logistic regression (not accounted for clustering)
Baqain et al. (2012)	PCo (Single centre)	Jordan / University hospital	399 implants 169 patients	4 yrs	Implant loss before functional loading	Sex (male/female) Smoking Implant length Implant diameter Jaw (max/mand) Location (ant/post) Healing mode Bone Augmentation	Single model adjustment	Multiple logistic regression (not accounted for clustering)
Shibuya et al. (2012)	RCo (Single centre)	Japan / University hospital	619 implants 151 patients	7 yrs	Implant loss before functional loading	Sex (male/female) Smoking Implant length Implant diameter Diabetes	Single model adjustment	Multiple logistic regression (not accounted for clustering)
Brügger et al. (2015)	RCo (Single centre)	Switzerland / University clinic	2,279 implants 1,568 patients	3 yrs	Implant loss before functional loading	Age Implant length Implant diameter Jaw (max/mand) Location (ant/post) Bone Augmentation	No adjustment	Simple logistic regression (not accounted for clustering)
Derks et al. (2015)	RCo (Multicentre)	Sweden/ Public + Private Practices	11,311 implants 2,765 patients	1 yr	Implant loss before functional loading	Smoking Implant length Prev. Periodontitis	Single model adjustment	Multilevel logistic regression (accounted for clustering)

Table 3.2 (Continued)

Author (Year)	Study design*	Country /setting	Sample size	Study period	Definition of early failure	Risk factor/s assessed	Adjustment for covariates	Statistics (accounting for clustering)
Chrcanovic et al. (2016)	RCo (Single centre)	Sweden / Specialist clinic	10,096 implants 2670 patients	34 yrs	Implant loss before functional loading	Smoking Jaw (max/mand) location (ant/post) Bone Augmentation Prev. Periodontitis Diabetes	Single model adjustment	GEE logistic regression (accounted for clustering)
Olmedo-Gaya et al. (2016)	RCo (Single centre)	Spain / Private practice	276 implants 142 patients	5 yrs	Implant loss before functional loading	Age Sex Smoking Implant length Implant diameter Jaw (max/mand) Location (ant/post) Bone Augmentation Prev. Periodontitis	Single model adjustment	Multilevel logistic regression (accounted for clustering)
Grisar et al. (2017)	RCo (Single centre)	Belgium / University hospital	1,139 implants 509 patients	3 yrs	Implant loss before functional loading	Age Sex Smoking Implant length Jaw (max/mand) Location (ant/post) Bone Augmentation	Single model adjustment	Multiple logistic regression (not accounted for clustering)
Borba et al. (2017)	RCo (Single centre)	Brazil / University clinic	774 implants 202 patients	12 yrs	Implant loss before functional loading	Age sex Implant length Implant diameter Jaw (max/mand) Location (ant/post Bone Augmentation	Single model adjustment	GEE logistic regression (accounted for clustering)

Table 3.2 (Continued)

Author (Year)	Study design*	Country /setting	Sample size	Study period	Definition of early failure	Risk factor/s assessed	Adjustment for covariates	Statistics (accounting for clustering)
Lin et al. (2018)	RCo (Single centre)	China / University hospital	30,959 implants 18,199 patients	5 yrs	Implant loss before functional loading	Age Sex Implant length Implant diameter Jaw (max/mand) Location (ant/post Bone Augmentation	Single model adjustment	GEE logistic regression (accounted for clustering)
Hirota et al. (2018)	RCo (Single centre)	Japan / University hospital	563 implants 219 patients	13 yrs	Implant loss before functional loading	Implant length Implant diameter Jaw (max/mand) Location (ant/post) Healing mode Bone Augmentation	Single model adjustment	Multiple logistic regression (not accounted for clustering)
Krisam et al. (2019)	RCo (Single centre)	Gemany / Private practice	186 implants 106 patients	6 yrs	Implant loss before functional loading	Age Sex Smoking Implant length Implant diameter Bone Augmentation Prev. Periodontitis Diabetes	No adjustment	Univariate mixed effects logistic regression (accounted for clustering)
Kang et al. (2019)	RCo (Single centre)	South Korea / University hospital	1,031 implants 409 patients	3 yrs	Implant loss before functional loading	Age Implant length Implant diameter Sex Healing mode	Single model adjustment	Multiple logistic regression (not accounted for clustering)
Wu et al. (2021)	RCo (Single centre)	China / University hospital	6,113 implants 3,785 patients	5 yrs	Implant loss before functional loading	Jaw (max/mand) Bone Augmentation	Single model adjustment	GEE logistic regression (accounted for clustering)

*PCo = Prospective cohort, RCo = Retrospective cohort

Table 3.3 Crude effect estimates from individual studies for each identified early failure risk factor

Reported risk factor	No. of studies	Failed / Placed implants (n)	Measures of relative effect
Age (≥60yrs)	Noguerol et al. (2006)	3/263 (≥60yrs); 52/821 (<60yrs)	Implants in patients aged ≥60yrs vs <60yrs (OR: 0.17; 95%CI: 0.03, 0.98; P=0.047)
	Brügger et al. (2015)	3/949 (≥60yrs); 10/1330 (<60yrs)	Implants in patients aged ≥60yrs vs <60yrs (OR: 0.42; 95%CI: 0.10, 1.75; P=0.233)
	Olmedo-Gaya et al. (2016)	3/67 (≥60yrs); 13/182 (<60yrs)	Implants in patients aged ≥60yrs vs <60yrs (OR: 0.71; 95%CI: 0.15, 3.37; P=0.662)
	Grisar et al. (2017)	38/828 (≥60yrs); 14/311 (<60yrs)	Implants in patients aged ≥60yrs vs <60yrs (OR: 1.00; 95%CI: 0.46, 2.27; P=0.960)
	Borba et al. (2017)	3/116 (≥60yrs); 19/658 (<60yrs)	Implants in patients aged ≥60yrs vs <60yrs (OR: 0.89; 95%CI: 0.13, 6.08; P=0.907)
	Lin et al. (2018)	49/5787 (≥60yrs); 145/24127 (<60yrs)	Implants in patients aged ≥60yrs vs <60yrs (OR: 1.41; 95%CI: 0.97; 2.06; P=0.073)
	Kang et al. (2019)	13/320 (≥60yrs); 22/711 (<60yrs)	Implants in patients aged ≥60yrs vs <60yrs (OR: 1.33; 95%CI: 0.52, 3.35; P=0.550)
	Krisam et al. (2019)	3/94 (≥60yrs); 6/92 (<60yrs)	Implants in patients aged ≥60yrs vs <60yrs (OR: 0.47; 95%CI: 0.09, 2.49; P=0.376)
Sex (Males)	Baqain et al. (2012)	5/53 (males); 9/116 (females)	Implants in males vs females (OR: 1.24; 95%CI: 0.28, 5.46, P=0.7777)
	Shibuya et al. (2012)	5/373 (males); 3/246 (females)	Implants in males vs females (OR: 1.1; 95%CI: 0.16, 7.40, P=0.9349)
	Olmedo, Gaya et al. (2016)	8/103 (males); 8/173 (females)	Implants in males vs females (OR:1.74; 95%CI: 0.51, 5.93, P=0.3781)
	Grisar et al. (2017)	36/550 (males); 16/589 (females)	Implants in males vs females (OR: 2.51; 95%CI: 1.17, 5.39, P=0.0183)

Table 3.3 (Continued)

Reported risk factor	No. of studies	Failed / Placed implants (n)	Measures of relative effect
Sex (Males) (Continued)	Borba et al. (2017)	7/316 (males); 15/458 (females)	Implants in males vs females (OR: 0.67; 95%CI: 0.16, 2.75, P=0.5771)
	Lin et al. (2018)	130/15254 (males); 64/14660 (females)	Implants in males vs females (OR: 1.96; 95%CI: 1.38, 2.78; P<0.001)
	Kang et al. (2019)	23/624 (males); 12/407 (females)	Implants in males vs females (OR: 1.26; 95%CI: 0.49, 3.23, P=0.6307)
	Krisam et al. (2019)	5/79 (males); 4/107 (females)	Implants in males vs females (OR: 1.74; 95%CI: 0.36, 8.47, P=0.4927)
Smoking status (Smokers)	Noguerol et al. (2006)	65/592(smokers); 22/521(non-smokers)	Implants in smokers vs non-smokers (OR: 2.8; 95%CI:1.33, 5.88, P=0.0065)
	Alsaadi et al. (2007)	54/916 (smokers); 198/6030 (non-smokers)	Implants in smokers vs non-smokers (OR: 1.85; 95%CI: 1.16, 2.93, P=0.0093)
	Alsaadi et al. (2008)	5/95 (smokers); 7/623 (non-smokers)	Implants in smokers vs non-smokers (OR: 4.89; 95%CI: 1.32, 18.06, P=0.0172)
	Bornstein et al. (2008)	3/241 (smokers); 7/965 (non-smokers)	Implants in smokers vs non-smokers (OR: 1.73; 95%CI: 0.38, 7.91, P=0.4827)
	Sverzut et al. (2008)	7/197 (smokers); 43/1431 (non-smokers)	Implants in smokers vs non-smokers (OR: 1.19; 95%CI: 0.41, 3.49, P=0.7523)
	Baqain et al. (2012)	4/29 (smokers); 10/140 (non-smokers)	Implants in smokers vs non-smokers (OR: 2.08; 95%CI: 0.42, 10.33, P=0.3703)
	Shibuya et al. (2012)	5/276 (smokers); 3/343 (non-smokers)	Implants in smokers vs non-smokers (OR: 2.09; 95%CI: 0.31, 14.05, P=0.4479)
	Olmedo-Gaya et al. (2016)	9/80 (smokers); 7/196 (non-smokers)	Implants in smokers vs non-smokers (OR: 3.42; 95%CI: 0.98, 11.86, P=0.0524)
	Chrcanovic et al. (2016)	180/2018 (smokers); 232/4357 (non-smokers)	Implants in smokers vs non-smokers (OR: 1.74; 95%CI: 1.27, 2.38, P=0.0005)
	Grisar et al. (2017)	24/255 (smokers); 28/884 (non-smokers)	Implants in smokers vs non-smokers (OR: 3.18; 95%CI: 1.55, 6.51, P=0.0016)
	Krisam et al. (2019)	3/44 (smokers); 6/142 (non-smokers)	Implants in smokers vs non-smokers (OR: 1.66, 95%CI: 0.31, 8.88, P=0.5544)

Table 3.3 (Continued)

Reported risk factor	No. of studies	Failed / Placed implants (n)	Measures of relative effect
Implant length (<10mm)	Alsaadi et al. (2007)	29/456 (<10mm); 223/6490 (≥10mm)	Short implants (<10mm) vs longer implants (OR: 1.91; 95%CI: 1.05, 3.47, P=0.0336)
	Alsaadi et al. (2008)	5/248 (<10mm); 9/472 (≥10mm)	Short implants (<10mm) vs longer implants (OR: 1.06; 95%CI: 0.24, 4.6, P=0.9395)
	Olate et al. (2010)	13/131 (<10mm); 49/1518 (≥10mm)	Short implants (<10mm) vs longer implants (OR: 3.3; 95%CI: 1.41, 7.73, P=0.0059)
	Baqain et al. (2012)	4/80 (<10mm); 11/319 (≥10mm)	Short implants (<10mm) vs longer implants (OR: 1.47; 95%CI: 0.32, 6.73, P=0.6167)
	Shibuya et al. (2012)	1/104 (<10mm); 7/515 (≥10mm)	Short implants (<10mm) vs longer implants (OR: 0.70; 95%CI: 0.04, 11.43, P=0.8054)
	Brügger et al. (2015)	5/256 (<10mm); 8/2022 (≥10mm)	Short implants (<10mm) vs longer implants (OR: 5.01; 95%CI: 1.44, 17.44, P=0.0112)
	Derks et al. (2015)	31/1018 (<10mm); 124/10293 (≥10mm)	Short implants (<10mm) vs longer implants (OR: 2.58; 95%CI: 1.36, 4.87, P=0035)
	Olmedo, Gaya et al. (2016)	5/16 (<10mm); 11/260 (≥10mm)	Short implants (<10mm) vs longer implants (OR: 10.29; 95%CI: 2.35, 45.07, P=0.0019)
	Borba et al. (2017)	1/53 (<10mm); 21/721 (≥10mm)	Short implants (<10mm) vs longer implants (OR: 0.64; 95%CI: 0.04, 9.35, P=0.7450)
	Grisar et al. (2017)	13/287 (<10mm); 39/852 (≥10mm)	Short implants (<10mm) vs longer implants (OR: 0.98; 95%CI: 0.44, 2.24, P=0.9790)
	Lin et al. (2018)	34/4938 (<10mm); 160/24976 (≥10mm)	Short implants (<10mm) vs longer implants (OR: 1.08; 95%CI: 0.7, 1.66, P=0.7416)
	Hirota et al. (2018)	3/42 (<10mm); 12/521 (≥10mm)	Short implants (<10mm) vs longer implants (OR: 3.26; 95%CI: 0.57, 18.69, P=0.1842)
	Kang et al. (2019)	25/802 (<10mm); 10/194 (≥10mm)	Short implants (<10mm) vs longer implants (OR: 0.6, 95%CI: 0.22, 1.64, P=0.3221)
	Krisam et al. (2019)	3/17 (<10mm); 6/169 (≥10mm)	Short implants (<10mm) vs longer implants (OR: 5.82, 95%CI: 1.01, 33.44, P=0.0482)

Table 3.3 (Continued)

Reported risk factor	No. of studies	Failed / Placed implants (n)	Measures of relative effect
Implant diameter (<3.75mm)	Alsaadi et al. (2007)	4/73 (<3.75mm); 248/6863 (≥3.75mm)	Narrow implants (<3.75) vs wider implants (OR: 1.55; 95%CI 0.34, 7.06, P=0.5736)
	Alsaadi et al. (2008)	10/499 (<3.75mm); 4/221 (≥3.75mm)	Narrow implants (<3.75) vs wider implants (OR: 1.11; 95%CI: 0.23, 5.27, P=0.8961)
	Olate et al. (2010)	7/137 (<3.75mm); 54/1512 (≥3.75mm)	Narrow implants (<3.75) vs wider implants (OR: 1.45; 95%CI:0.5, 4.26, P=0.4946)
	Baqain et al. (2012)	7/85 (<3.75mm); 8/314 (≥3.75mm)	Narrow implants (<3.75) vs wider implants (OR: 3.43; 95%CI: 0.9, 13.29, P=0.0741)
	Shibuya et al. (2012)	1/99 (<3.75mm); 7/520 (≥3.75mm)	Narrow implants (<3.75) vs wider implants (OR: 0.75; 95%CI: 0.05, 12.13, P=0.8380)
	Brügger et al. (2015)	1/290 (<3.75mm); 12/1988 (≥3.75mm)	Narrow implants (<3.75) vs wider implants (OR: 0.57; 95%CI 0.06, 5.48, P=0.6262)
	Olmedo-Gaya et al. (2016)	4/44 (<3.75mm); 12/232 (≥3.75mm)	Narrow implants (<3.75) vs wider implants (OR: 1.83; 95%CI: 0.44, 7.68, P=0.4069)
	Borba et al. (2017)	7/104 (<3.75mm); 15/670 (≥3.75mm)	Narrow implants (<3.75) vs wider implants (OR: 3.15; 95%CI: 0.75, 13.21, P=0.1165)
	Lin et al. (2018)	55/5728 (<3.75mm); 139/24186 (≥3.75mm)	Narrow implants (<3.75) vs wider implants (OR: 1.68; 95%CI: 1.17, 2.41, P=0.0054)
	Hirota et al. (2018)	1/22 (<3.75mm); 14/541 (≥3.75mm)	Narrow implants (<3.75) vs wider implants (OR: 1.79; 95%CI: 0.18, 18.24, P=0.6220)
	Kang et al. (2019)	3/42 (<3.75mm); 32/954 (≥3.75mm)	Narrow implants (<3.75) vs wider implants (OR: 2.13; 95%CI: 0.42, 10.79, P=0.3613)
	Krisam et al. (2019)	2/42 (<4mm); 7/144 (≥4mm)	Implants (<4) vs wider implants (OR: 0.98; 95%CI: 0.15, 6.48, P=0.9824)

Table 3.3 (Continued)

Reported risk factor	No. of studies	Failed / Placed implants (n)	Measures of relative effect
Jaw (Maxilla)	Noguerol et al. (2006)	40/651 (maxilla); 15/433 (mandible)	Maxilla vs mandible (OR: 1.82; 95%CI: 0.74, 4.50, P=0.1916)
	Roos-Jansåker et al. (2006)	17/524 (maxilla); 12/533 (mandible)	Maxilla vs mandible (OR: 1.46; 95%CI: 0.40, 5.24, P=0.5655)
	Alsaadi et al. (2007)	143/3625 (maxilla); 109/3306 (mandible)	Maxilla vs mandible (OR: 1.20; 95%CI: 0.82, 1.76, P=0.3362)
	Alsaadi et al. (2008)	8/388 (maxilla); 6/332 (mandible)	Maxilla vs mandible (OR: 1.14; 95%CI: 0.28, 4.75, P=0.8531)
	Bornstein et al. (2008)	6/1077 (maxilla); 7/740 (mandible)	Maxilla vs mandible (OR: 0.59; 95%CI: 0.17, 2, P=0.3936)
	Olate et al. (2010)	28/807 (maxilla); 22/821 (mandible)	Maxilla vs mandible (OR: 1.31; 95%CI: 0.61, 2.77, P=0.4884)
	Baqain et al. (2012)	9/200 (maxilla); 6/199 (mandible)	Maxilla vs mandible (OR: 1.52; 95%CI: 0.39, 5.93, P=0.5501)
	Brügger et al. (2015)	8/1468 (maxilla); 5/811 (mandible)	Maxilla vs mandible (OR: 0.88; 95%CI: 0.26, 3.06, P=0.8446)
	Chrcanovic et al. (2016)	473/5776 (maxilla); 169/4320 (mandible)	Maxilla vs mandible (OR: 2.19; 95%CI: 1.66, 2.90, P < 0.001)
	Olmedo-Gaya et al. (2016)	12/156 (maxilla); 4/120 (mandible)	Maxilla vs mandible (OR: 2.42; 95%CI: 0.59, 9.84, P=0.2182)
	Grisar et al. (2017)	35/626 (maxilla); 17/513 (mandible)	Maxilla vs mandible (OR: 1.73; 95%CI: 0.81, 3.67, P=0.1544)
	Borba et al. (2017)	17/392 (maxilla); 5/382 (mandible)	Maxilla vs mandible (OR: 3.42; 95%CI: 0.71, 16.36, P=0.1239)
	Lin et al. (2018)	80/13647 (maxilla); 114/16267 (mandible)	Maxilla vs mandible (OR: 0.84; 95%CI: 0.60, 1.17, P=0.2906)
	Hirota et al. (2018)	9/262 (maxilla); 6/301 (mandible)	Maxilla vs mandible (OR: 1.75; 95%CI: 0.43, 7.08, P=0.4333)
	Wu et al. (2021)	51/2917 (maxilla); 21/3196 (mandible)	Maxilla vs mandible (OR: 2.69; 95%CI: 1.50, 4.82, P < 0.001)

Table 3.3 (Continued)

Reported risk factor	No. of studies	Failed / Placed implants (n)	Measures of relative effect
Posterior Locations (premolars, molars)	Noguerol et al. (2006)	35/577 (posterior); 20/507 (anterior)	Posterior vs anterior sites (OR: 1.57, 95%CI, 0.68, 3.63, P=0.2896)
	Roos-Jansåker et al. (2006)	14/396 (posterior); 15/661 (anterior)	Posterior vs anterior sites (OR: 1.58, 95%CI, 0.45, 5.59, P=0.4792)
	Alsaadi et al. (2007)	137/2943 (posterior); 115/3988 (anterior)	Posterior vs anterior sites (OR: 1.64, 95%CI, 1.13, 2.40, P=0.0098)
	Alsaadi et al. (2008)	9/380 (posterior); 5/340 (anterior)	Posterior vs anterior sites (OR: 1.63, 95%CI, 0.37, 7.06, P=0.5168)
	Bornstein et al. (2008)	9/1167 (posterior); 4/663 (anterior)	Posterior vs anterior sites (OR: 1.28, 95%CI, 0.34, 4.81, P=0.7142)
	Olate et al. (2010)	19/900 (posterior); 31/728 (anterior)	Posterior vs anterior sites (OR: 0.48, 95%CI, 0.22, 1.05, P=0.0657)
	Baqain et al. (2012)	11/298 (posterior); 4/101 (anterior)	Posterior vs anterior sites (OR: 0.93, 95%CI, 0.20, 4.22, P=0.9245)
	Brügger et al. (2015)	9/879 (posterior); 4/620 (anterior)	Posterior vs anterior sites (OR: 1.59, 95%CI, 0.43, 5.90, P=0.4858)
	Chrcanovic et al. (2016)	252/4004 (posterior); 390/6092 (anterior)	Posterior vs anterior sites (OR: 0.98, 95%CI, 0.76, 1.26, P=0.8880)
	Olmedo-Gaya et al. (2016)	11/217 (posterior); 5/59 (anterior)	Posterior vs anterior sites (OR: 0.58, 95%CI, 0.15, 2.19, P=0.4183)
	Borba et al. (2017)	19/577 (posterior); 3/197 (anterior)	Posterior vs anterior sites (OR: 2.20, 95%CI, 0.33, 14.86, P=0.4178)
	Grisar et al. (2017)	31/698 (posterior); 21/441 (anterior)	Posterior vs anterior sites (OR: 0.93, 95%CI, 0.45, 1.91, P=0.8427)
	Lin et al. (2018)	165/23625 (posterior); 44/6381 (anterior)	Posterior vs anterior sites (OR: 1.01, 95%CI, 0.69, 1.49, P=0.9481)
	Hirota et al. (2018)	10/398 (posterior); 5/165 (anterior)	Posterior vs anterior sites (OR: 0.82, 95%CI ,0.19, 3.53, P=0.7953)

Table 3.3 (Continued)

Reported risk factor	No. of studies	Failed / Placed implants (n)	Measures of relative effect
Healing mode (non-submerged)	Baqain et al. (2012))	3/44 (non-submerged); 12/355 (submerged)	non-submerged vs submerged implants (OR: 2.09; 95%CI: 0.52, 8.36, P=0.2964)
	Hirota et al. (2018)	2/25 (non-submerged); 13/538 (submerged)	non-submerged vs submerged implants (OR: 3.51; 95%CI: 0.68, 18.10, P=0.1333)
	Kang et al. (2019)	14/319 (non-submerged); 21/712 (submerged)	non-submerged vs submerged implants (OR: 1.51, 95%CI: 0.73, 3.14, P=0.2691)
Bone augmentation	Bornstein et al. (2008)	5/939 (augmentation); 8/878(no augmentation)	Implants with augmentation vs without augmentation (OR: 0.58: 95%CI: 0.17, 2.04, P=0.3982)
	Baqain et al. (2012)	4/113 (augmentation); 11/286 (no augmentation)	Implants with augmentation vs without augmentation (OR: 0.92, 95%CI: 0.20, 4.16, P=0.9110)
	Brügger et al. (2015)	10/1368 (augmentation); 3/911 (no augmentation)	Implants with augmentation vs without augmentation (OR: 2.23; 95%CI: 0.53, 9.33, P=0.2726)
	Chrcanovic et al. (2016)	91/564 (augmentation); 550/9530 (no augmentation)	Implants with augmentation vs without augmentation (OR: 3.14; 95%CI: 2.17, 4.55, P < 0.001)
	Olmedo-Gaya et al. (2016)	3/22 (augmentation); 13/254 (no augmentation)	Implants with augmentation vs without augmentation (OR: 2.93, 95%CI: 0.58, 14.87, P=0.1951)
	Borba et al. (2017)	10/178 (augmentation); 12/596 (no augmentation)	Implants with augmentation vs without augmentation (OR: 2.90; 95%CI: 0.77, 10.97, P=0.1174)
	Grisar et al. (2017)	14/166 (augmentation); 38/973 (no augmentation)	Implants with augmentation vs without augmentation (OR: 2.27; 95%CI: 1.01, 5.09 P=0.0476)
	Lin et al. (2018)	48/6116 (augmentation); 146/23798 (no augmentation)	Implants with augmentation vs without augmentation (OR: 1.28; 95%CI: 0.88, 1.87, P=0.2013)
	Hirota et al. (2018)	1/139 (augmentation); 14/424 (no augmentation)	Implants with augmentation vs without augmentation (OR: 0.21; 95%CI: 0.01, 3.23, P=0.2645)
	Krisam et al. (2019)	5/38 (augmentation); 4/148 (no augmentation)	Implants with augmentation vs without augmentation (OR: 4.87; 95%CI: 1.27, 18.64, P=0.0208)
	Wu et al. (2021)	31/1524 (augmentation); 41/4589 (no augmentation)	Implants with augmentation vs without augmentation (OR: 2.30; 95%CI: 1.35, 3.94, P=0.0023)

Table 3.3 (Continued)

Reported risk factor	No. of studies	Failed / Placed implants (n)	Measures of relative effect
Previous history of periodontitis	Noguerol et al. (2006)	45/763 (h/o periodontitis); 10/321(no h/o periodontitis)	Implants in patients with a previous h/o periodontitis vs implants placed in patients without h/o periodontitis (OR: 1.95; 95%CI: 0.69, 5.51, P=0.2079)
	Chrcanovic et al. (2016)	52/944 (h/o periodontitis); 67/1851(no h/o periodontitis)	Implants in patients with a previous h/o periodontitis vs implants placed in patients without h/o periodontitis (OR: 1.55; 95%CI: 1.03, 2.35, P=0.0377)
	Olmedo-Gaya et al. (2016)	12/119 (h/o periodontitis); 4/157 (no h/o periodontitis)	Implants in patients with a previous h/o periodontitis vs implants placed in patients without h/o periodontitis (OR: 4.29; 95%CI: 1.17, 15.66, P=0.0275)
	Krisam et al. (2019)	3/59 (h/o periodontitis); 6/127 (no h/o periodontitis)	Implants in patients with a previous h/o periodontitis vs implants placed in patients without h/o periodontitis (OR: 1.08; 95%CI: 0.20, 5.73, P=0.9277)
Diabetes (type I or II)	Alsaadi et al. (2008)	2/26 (diabetics); 26/1414 (non- diabetics)	Implants in diabetic vs non-diabetic patients (OR: 4.45; 95%CI: 0.84, 23.63, P=0.0798)
	Shibuya et al. (2012)	1/13 (diabetics); 16/606 (non- diabetics)	Implants in diabetic vs non-diabetic patients (OR: 3.07; 95%CI: 0.33, 28.49, P=0.3231)
	Chrcanovic et al. (2016)	40/627 (diabetics); 404/6441 (non- diabetics)	Implants in diabetic vs non-diabetic patients (OR: 1.01; 95%CI: 0.61, 1.71, P=0.9455)
	Krisam et al. (2019)	1/19 (diabetics); 8/167 (non- diabetics)	Implants in diabetic vs non-diabetic patients (OR: 1.1; 95%CI: 0.09, 13.53, P = 0.9382)

3.3.3. Quality assessment

The quality assessment of the included studies is summarized in Table 3.4.

15 studies were considered to be of high quality according to the Newcastle-Ottawa scale (NOS), while five studies were of medium quality. The mean NOS score for all 22 included studies was 7, indicating a satisfactory methodological quality of the included studies.

Table 3.4 Quality assessment of the included studies using the Newcastle-Ottawa Scale

Study	Selection				Comparability		Outcome			Overall score
	Representativene of the exposed group	Selection of the non-exposed group	Ascertainment of exposure	Outcome of Interest not present at start	Main factors	Additional factors	Assessment of outcome	Follow-up long enough	Adequacy of follow-up	
Noguerol et al. (2006)	0	*	0	*	0	*	*	*	*	6/9
Roos-Jansåker et al. (2006)	*	*	*	*	0	0	*	*	*	7/9
Alsaadi et al. (2007)	*	*	*	*	0	*	*	*	*	8/9
Alsaadi et al. (2008)	*	*	*	*	0	0	*	*	*	7/9
Bornstein et al. (2008)	*	*	0	*	0	0	*	*	*	6/9
Sverzut et al. (2008)	*	*	*	*	0	0	*	*	*	7/9
Olate et al. (2010)	*	*	*	*	0	*	*	*	*	8/9
Baqain et al. (2012)	*	*	*	*	0	*	*	*	*	8/9
Shibuya et al. (2012)	*	*	0	*	0	0	*	*	*	6/8
Brügger et al. (2015)	*	*	*	*	0	0	*	*	*	7/9
Derks et al. (2015)	*	*	*	*	0	*	*	*	*	8/9
Chrcanovic et al. (2016)	0	*	*	*	0	*	*	*	*	7/9
Olmedo-Gaya et al. (2016)	0	*	0	*	0	*	*	*	*	6/9
Grisar et al. (2017)	*	*	*	*	0	*	*	*	*	8/9
Borba et al. (2017)	*	*	*	*	0	*	*	*	*	8/9
Lin et al. (2018)	*	*	*	*	*	*	*	*	*	9/9
Hirota et al. (2018)	*	*	*	*	0	*	*	*	*	8/9
Krisam et al. (2019)	0	*	*	*	0	0	*	*	*	6/9
Kang et al. (2019)	*	*	0	*	0	*	*	*	*	7/9
Wu et al. (2021)	*	*	*	*	*	*	*	*	*	9/9

*The study meets the specified criterion

3.3.4. Meta-analyses

3.3.4.1. Age

When assessing age as a risk factor for early implant failure, the pooled estimates for the eight selected studies comparing early implant failure in patients aged 60 years and over with younger patients were obtained using a random effects model. There was evidence of significant heterogeneity across these studies (I^2=60.4%, p=0.017). This meta-analysis showed a non-significantly lower odds of early failure for implants placed in patients aged ≥60 years (OR: 0.88; 95% CI: 0.62, 1.44; p = 0.780) (Figure 3.2).

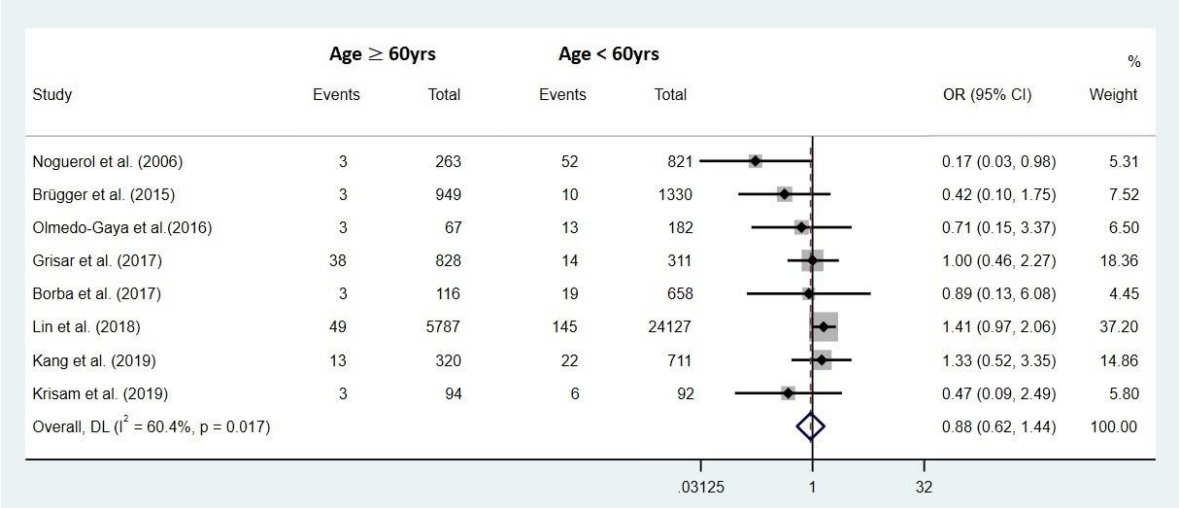


Figure 3.2 Forest plot for comparison of patients ≥60 yrs of age with patients <60 yrs of age for the "early implant failure" event

In a leave-one-out sensitivity analysis, the omission of the Noguerol et al. (2006) study seems to have a relatively larger influence, when compared with other studies, on the overall estimate of odds ratio (OR:1.18; 95%CI: 0,88, 1.59) (Figure 3.3); however, the result remained not statistically significant (p=0.477).

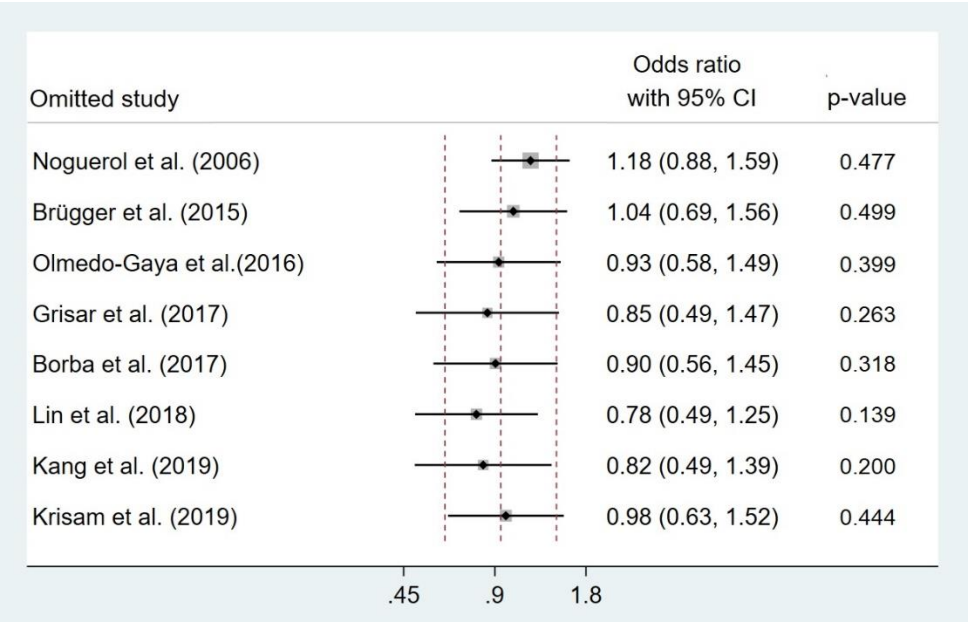


Figure 3.3 Influence plot for the sensitivity analysis (Age ≥60 as a risk factor for early implant failure)

3.3.4.2. Sex

A random effects model was used to obtain the pooled odds ratio (OR) and associated 95% confidence interval for studies assessing the risk of early implant failure in males versus females. There was no significant statistical heterogeneity between studies (I^2=0%, p=0.796) (Figure 3.4), and the estimated overall odds ratio was 1.80 (95% CI: 1.37, 2.37; P<0.001). This result was statistically significant and indicated that inserting implants in male patients increased the risk of early implant failure by 80%.

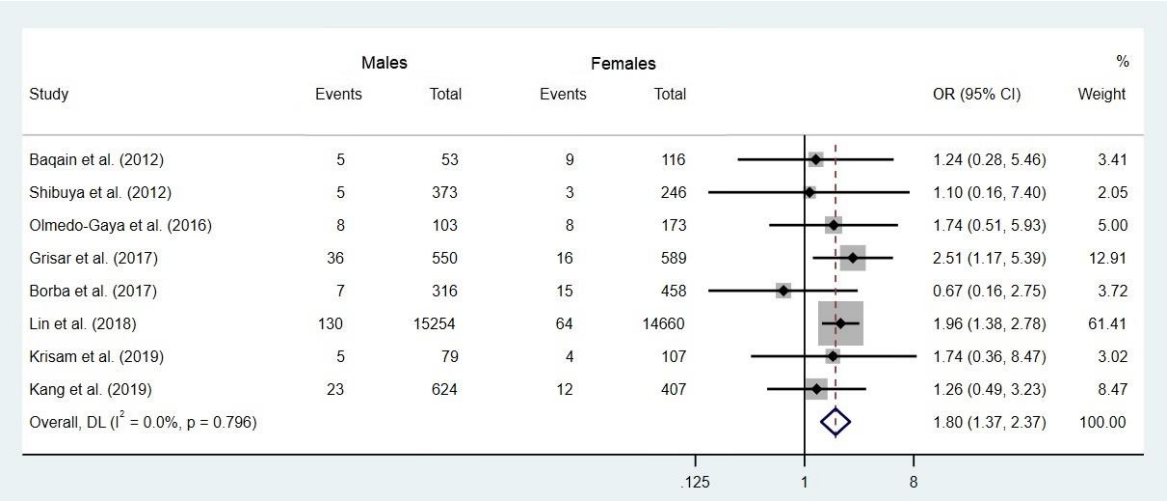


Figure 3.4 Forest plot of comparison between implants placed in males and females for the "early implant failure" event.

The leave-one-out sensitivity analysis showed the greatest decrease in the pooled estimate of odds ratio (OR: 1.58; 95%CI: 1.02, 2.46) after the removal of the study by Lin et al. (2018) (Figure 3.5); however, the overall estimate of the risk of early failure remained significantly higher for implants placed in males relative to females.

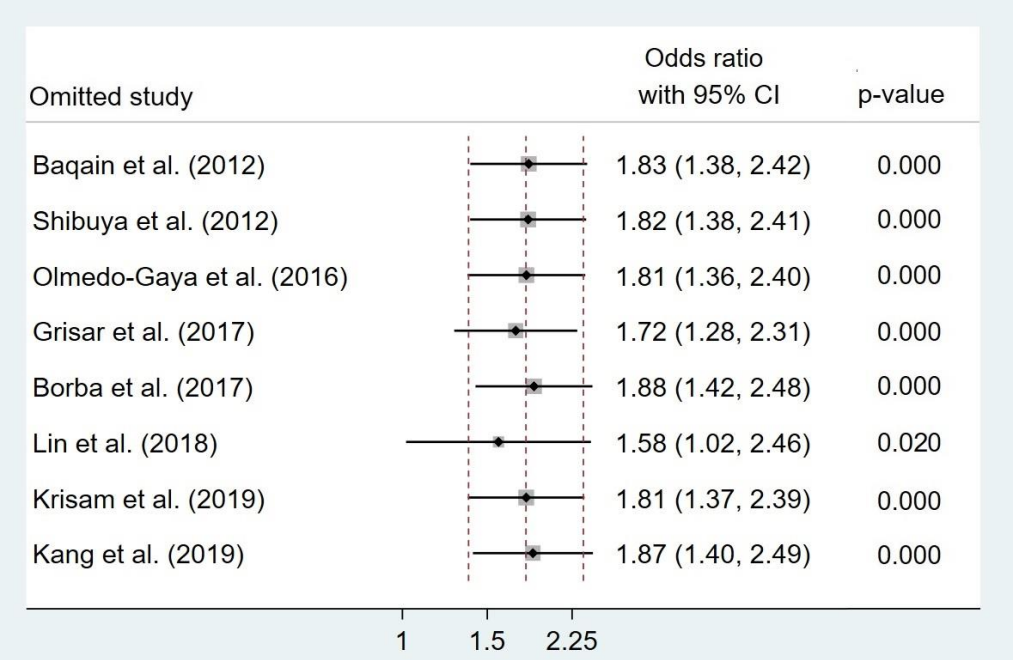


Figure 3.5 Influence plot for the sensitivity analysis (Male sex as a risk factor for early implant failure)

3.3.4.3. Smoking

The estimates from the 11 selected studies comparing early implant failure for smokers versus non-smokers were pooled using a random effects model. The heterogeneity among these studies was low and non-significant (I^2 = 11.5%, p = 0.334) (Figure 3.6). An odds ratio of 1.98 resulted from this meta-analysis (95% CI: 1.62, 2.48; p < 0.001). That is a 98% increased risk of early dental implant failure in smokers.

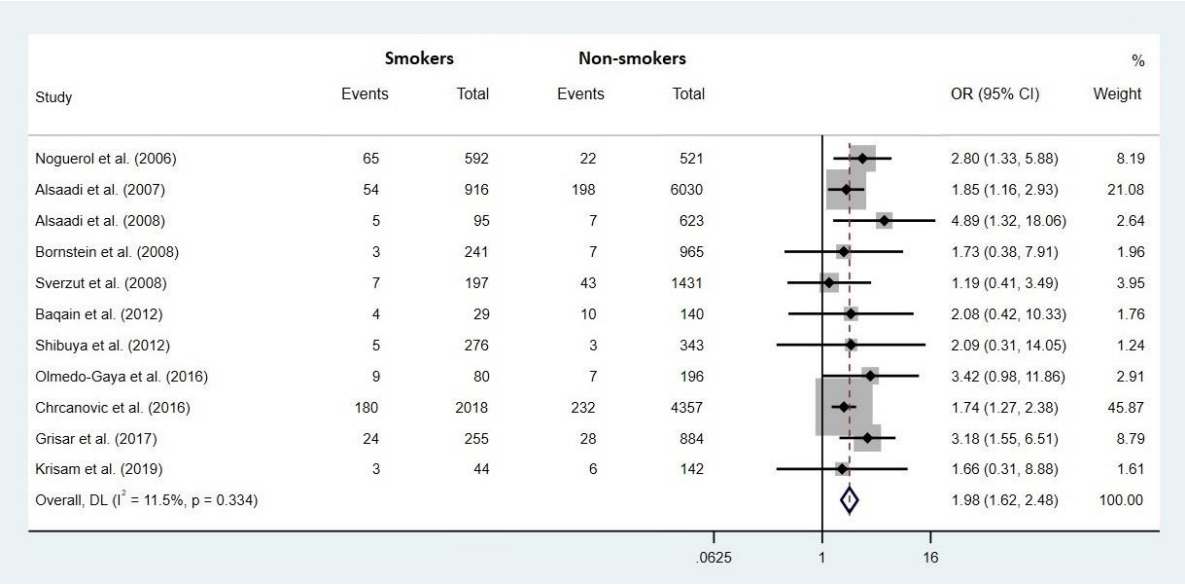


Figure 3.6 Forest plot for comparison of implants placed in smokers and non-smokers for the "early implant failure" event.

The leave-one-out sensitivity analysis showed the greatest increase in the overall estimate of the odds ratio of early implant failure after the removal of the study by Chrcanovic et al. (2016) (OR: 2.26; 95% CI: 1.69, 3.02) and the greatest decrease after the removal of the study by Grisar et al. (2017) (OR: 1.92; 95% CI: 1.53, 2.40) (Figure 3.7). The overall statistical significance did not change when any single study was omitted.

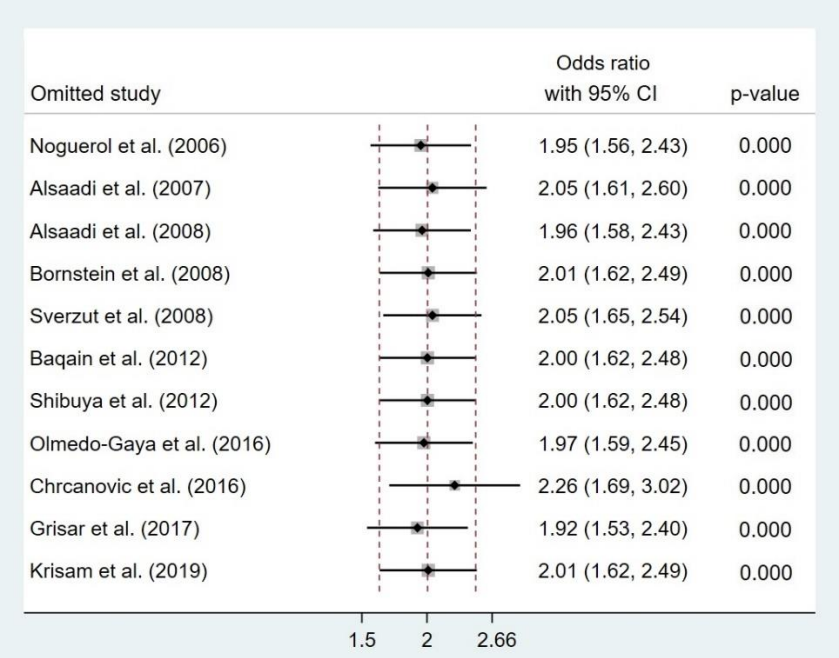


Figure 3.7 Influence plot for the sensitivity analysis (smoking as a risk factor for early implant failure)

Visual inspection of the funnel plot for this meta-analysis showed some asymmetry (Figure 3.8), and the result of Harbord's test was statistically significant (p = 0.078), indicating the existence of publication bias.

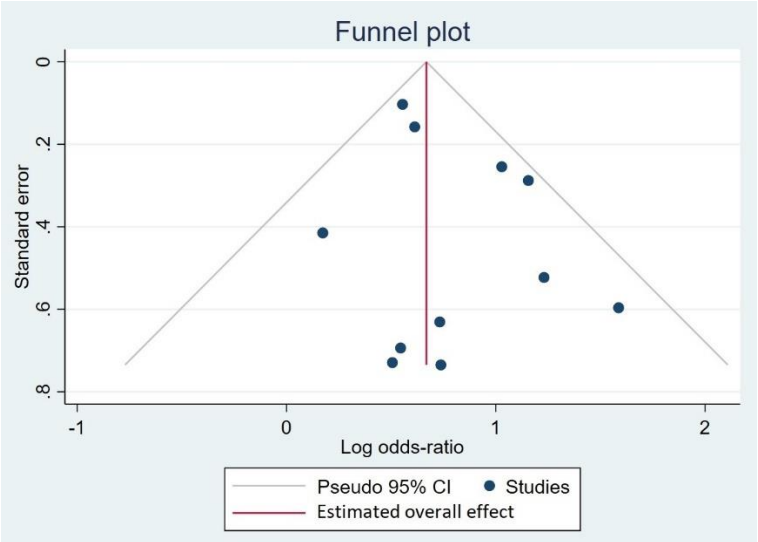


Figure 3.8 Funnel plot for the included studies reporting the outcome event “early implant failure” comparing implants placed in smokers vs non-smokers

3.3.4.4. Implant length

The risk of early implant failure based on implant length was evaluated in 14 studies. Individual estimates from these studies were combined using a random effects meta-analysis. There was significant statistical heterogeneity among the included studies (I^2=51%, p=0.014) (Figure 3.9). Short implants (<10mm) showed a significantly higher overall failure rate compared to longer implants (≥10mm), with an odds ratio of 1.87 (95% CI: 1.25, 2.78; P<0.001). This odds ratio implies that using short implants (<10mm) may increase the odds of early failure by 87% compared to longer implants.

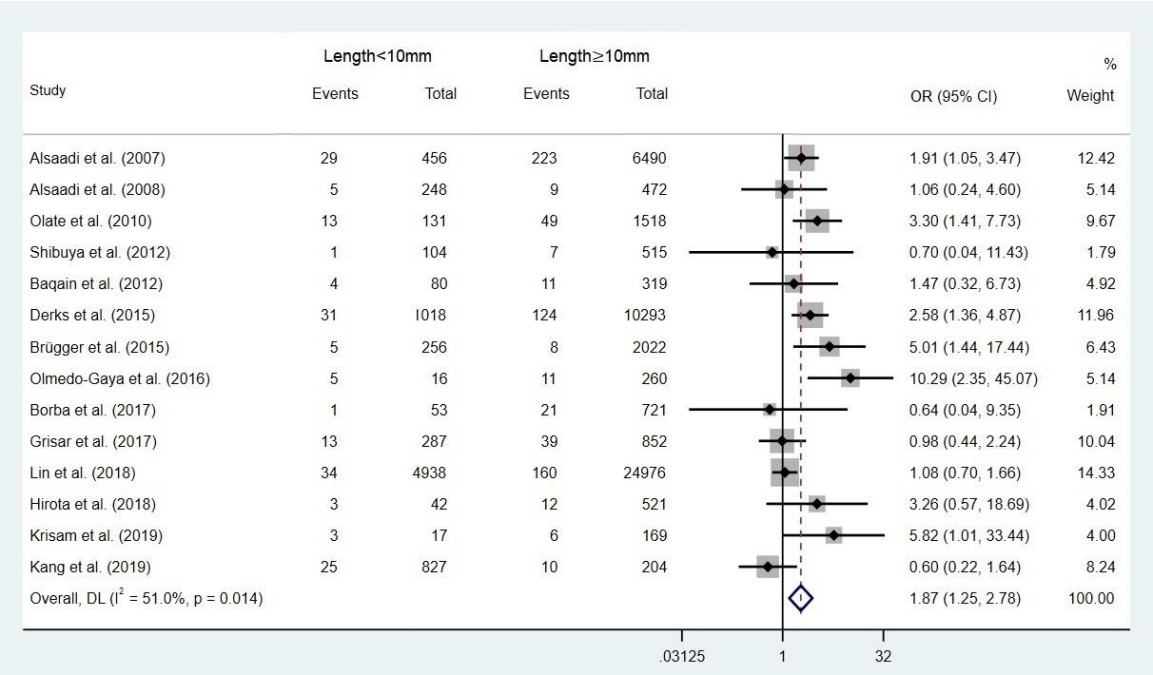


Figure 3.9 Forest plot for comparison of short implants (<10 mm) and longer implants (≥10mm) for the "early implant failure" event.

Although there was significant heterogeneity across studies, our sensitivity analysis revealed that the overall odds ratio estimate in this meta-analysis was not significantly influenced by any individual study (Figure 3.10).

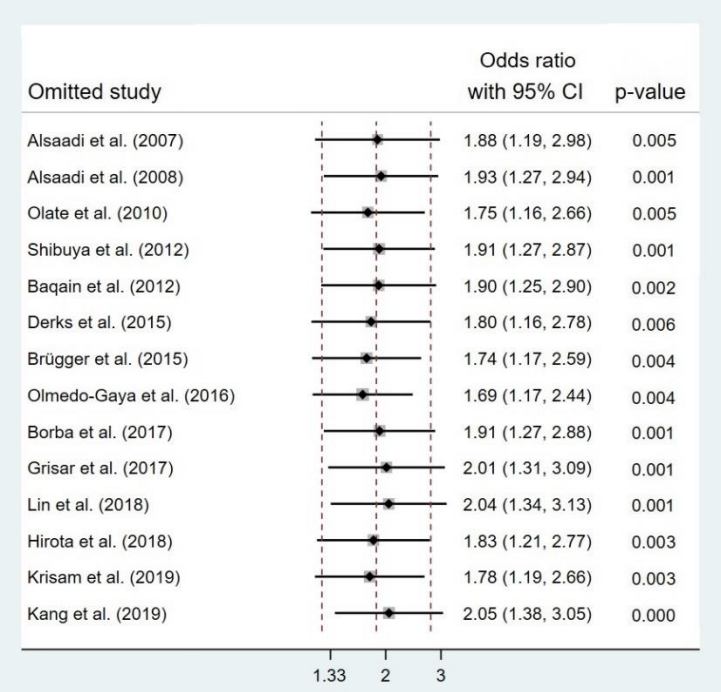


Figure 3.10 Influence plot for the sensitivity analysis (implangth length <10mm as a risk factor for early implant failure)

The shape of the funnel plot for this meta-analysis was symmetrical (Figure 3.11), suggesting no publication bias, and Harbord's test result was not significant (p=0.287), providing statistical evidence for the funnel plot symmetry.

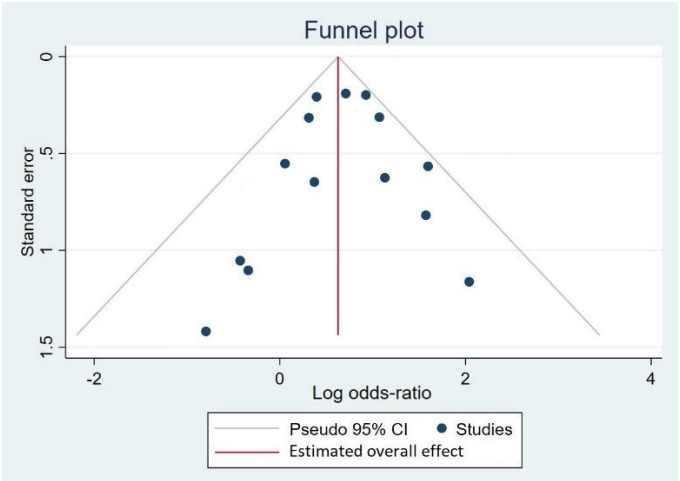


Figure 3.11 Funnel plot for the included studies reporting the outcome event “early implant failure” comparing short (<10 mm) to longer (10 mm) implants

3.3.4.5. Implant diameter

For early failure of narrow-diameter implants (<3.75mm) compared to wider-diameter implants (≥3.75mm), a pooled estimate of the odds ratio with the 95% confidence interval was computed from 11 studies using a random effects model. There was no evidence of significant heterogeneity across studies (I^2 = 0%, p = 0.968) (Figure 3.12). This meta-analysis showed that using narrow implants with a diameter of less than 3.75mm significantly increased the odds of early implant failure compared to wider diameter implants (OR: 1.71; 95% CI: 1.28, 2.28; p < 0.001).

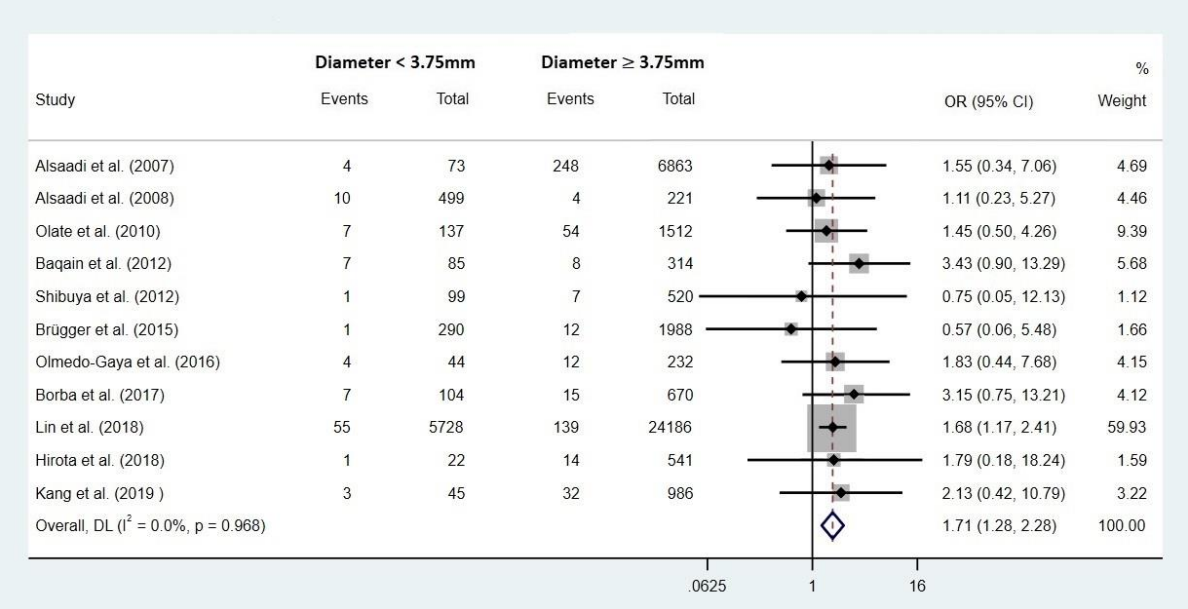


Figure 3.12 Forest plot for comparison of narrow implants (<3.75 mm) and wider implants (≥3.75mm) for the "early implant failure" event.

We excluded the study by Krisam et al. (2019) from this meta-analysis because it used a different implant diameter cut-off point, comparing implants with a diameter of less than 4mm to wider implants, and we could not obtain data for our specified 3.75 mm diameter cut-off point from this study. However, we calculated the crude estimate of OR for this study based on the 4mm diameter cut-off point. There was no significant

difference in odds of early failure between implants with a diameter of less than 4mm and wider implants (OR: 0.98; 95% CI: 0.15, 6.48; P=0.982).

Based on the leave-one-out sensitivity analysis (Figure 3.13), it was clear that none of the individual studies significantly influenced the overall pooled odds ratio of early failure in this meta-analysis.

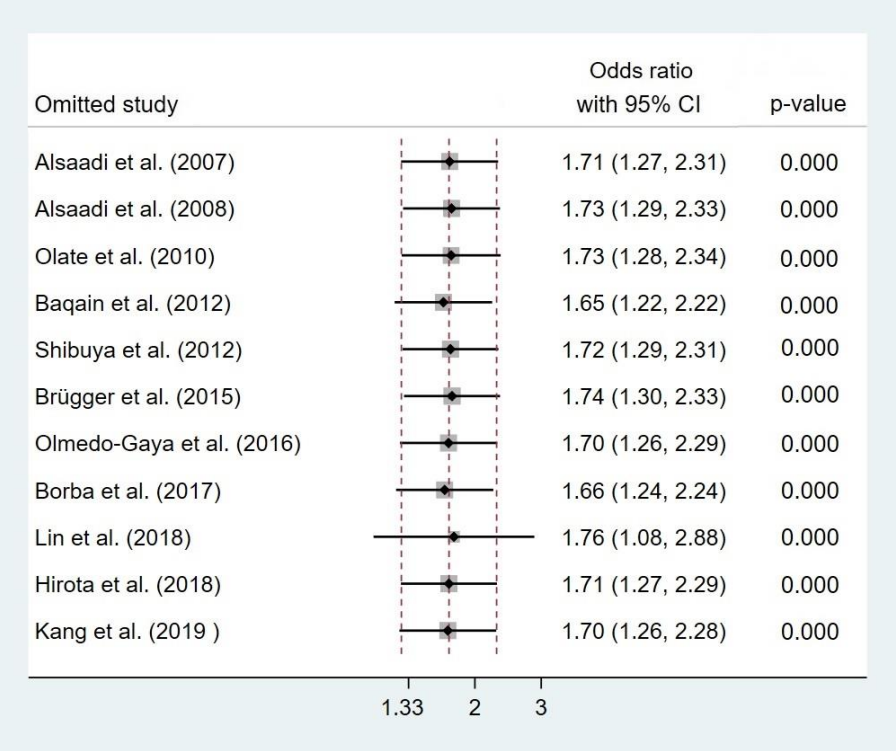


Figure 3.13 Influence plot for the sensitivity analysis (implant diameter <3.75mm as a risk factor for early implant failure)

The shape of the funnel plot for this meta-analysis did not show an obvious asymmetry (Figure 3.14), and the result of Harbord's test was not significant (p=0.6), indicating that publication bias was not evident.

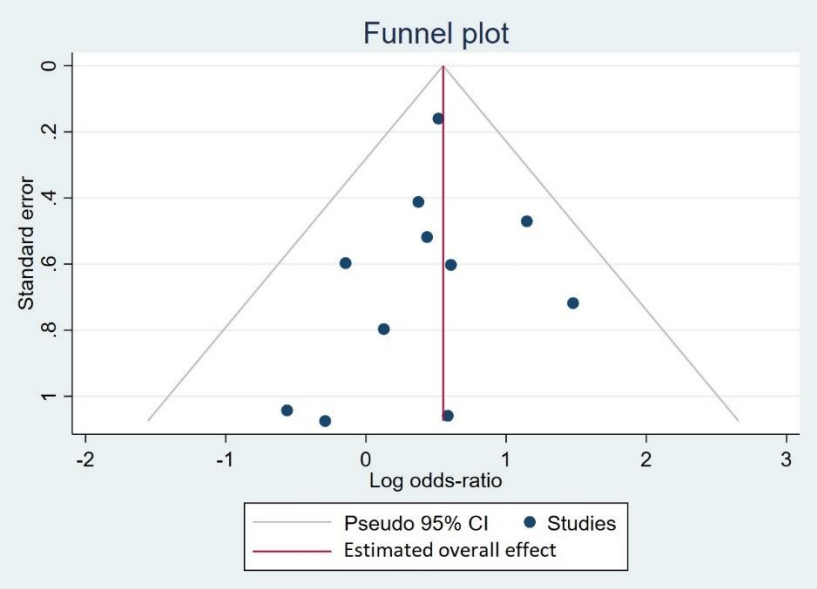


Figure 3.14 Funnel plot for the included studies reporting the outcome event “early implant failure” comparing narrow(<3.75 mm) to wider implants (≥3.75mm)

3.3.4.6. Jaw (maxilla or mandible)

A random effects model was used to estimate the pooled overall odds ratio with the corresponding 95% confidence interval for the 15 selected studies comparing maxillary and mandibular implants in terms of early failure (Figure 3.15). There was significant heterogeneity among these studies (I^2 = 51.5%, p = 0.011). The pooled estimate of odds ratio showed that implant insertion in the upper jaw was associated with a statistically significant increase in the odds of early failure compared to the lower jaw (OR: 1.49; 95% CI: 1.13, 1.96; p = 0.005).

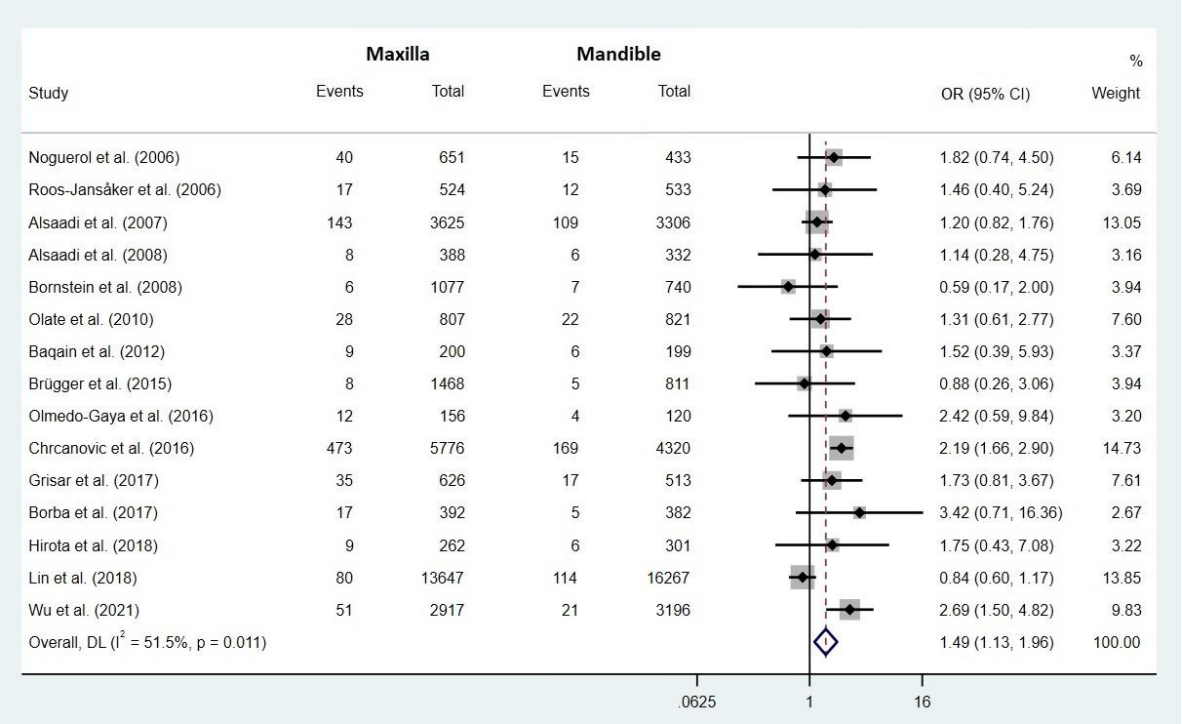


Figure 3.15 Forest plot for comparison of maxillary and mandibular implants for the "early implant failure" event.

In the sensitivity analysis (Figure 3.16), the omission of the Lin et al. (2018) study had a relatively larger effect on the overall estimate of odds ratio (OR: 1.70, 95% CI: 1.38, 2.09) than other studies. However, the pooled estimate remained significant when any individual study was removed.

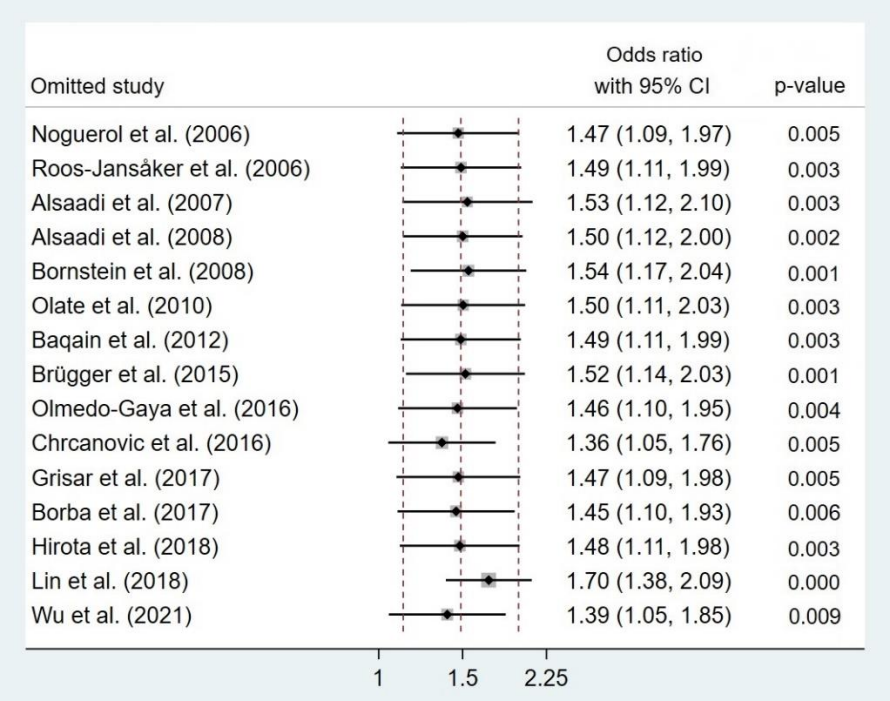


Figure 3.16 Influence plot for the sensitivity analysis (maxillary sites as a risk factor for early implant failure)

The funnel plot for this meta-analysis was approximately symmetrical on visual inspection (Figure 3.17), and Harbord's test provided no statistically significant evidence for publication bias (p = 0.914).

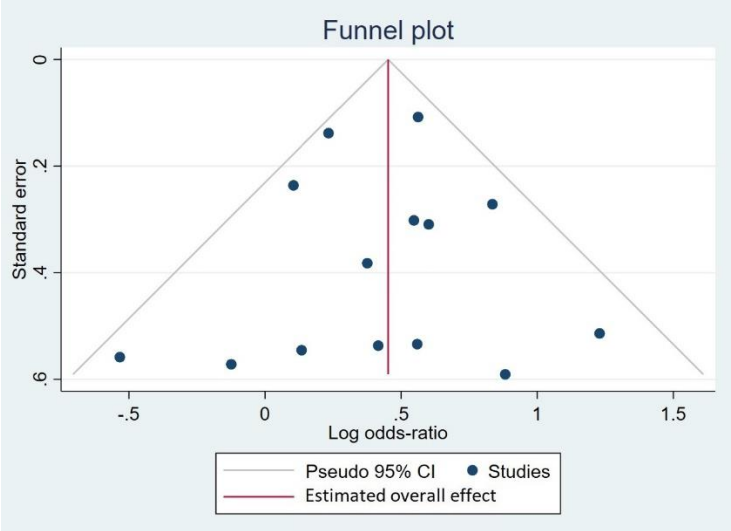


Figure 3.17 Funnel plot for the included studies reporting the outcome event “early implant failure” comparing implants placed in maxilla vs mandible

3.3.4.7. Implant location (anterior or posterior)

The estimates for the 14 included studies comparing early failure between implants placed in posterior and anterior regions of both jaws were pooled together using a random effects model. There was significant heterogeneity across the studies (I^2=0.4%, p=0.444) (Figure 3.18). This meta-analysis showed a non-significantly higher odds of early failure for posterior implants when compared to anterior ones (OR: 1.09; 95% CI: 0.93, 1.28; p = 0.304).

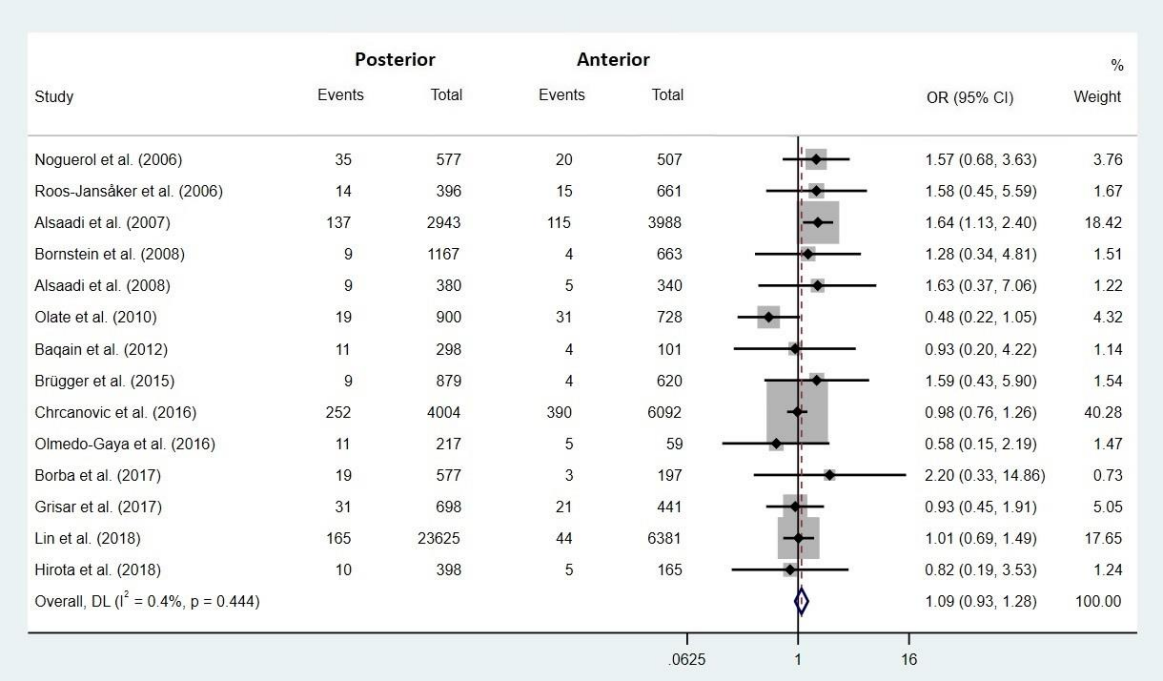


Figure 3.18 Forest plot for comparison of posterior and anterior implants for the "early implant failure" event

Based on the sensitivity analysis (Figure 3.19), it was found that removing the study conducted by Alsaadi et al. (2007) resulted in the highest decrease in the overall estimate of the odds ratio of early implant failure (OR: 0.99; 95% CI: 0.83, 1.19). On the other hand, omitting the study by Chrcanovic et al. (2016) resulted in the greatest increase in the overall estimate (OR: 1.17; 95% CI: 0.95, 1.44) compared to other studies. However, the pooled estimate of odds ratio remained non-significant when any individual study was omitted.

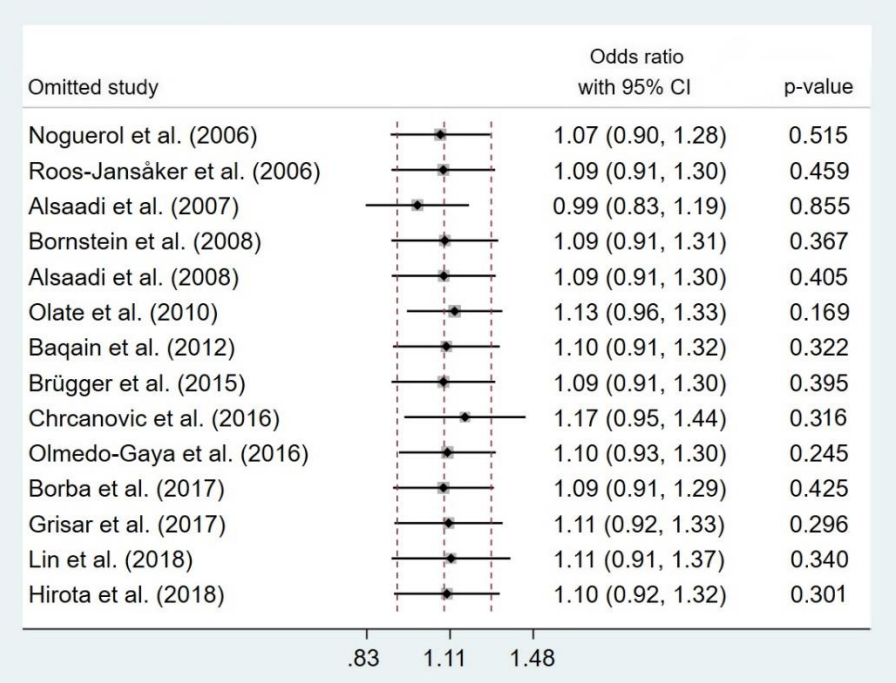


Figure 3.19 Influence plot for the sensitivity analysis (posterior sites as a risk factor for early implant failure)

The shape of the funnel plot for this meta-analysis seemed symmetrical (Figure 3.20), and there was no significant evidence of publication bias based on Harbord's test (p=0.957).

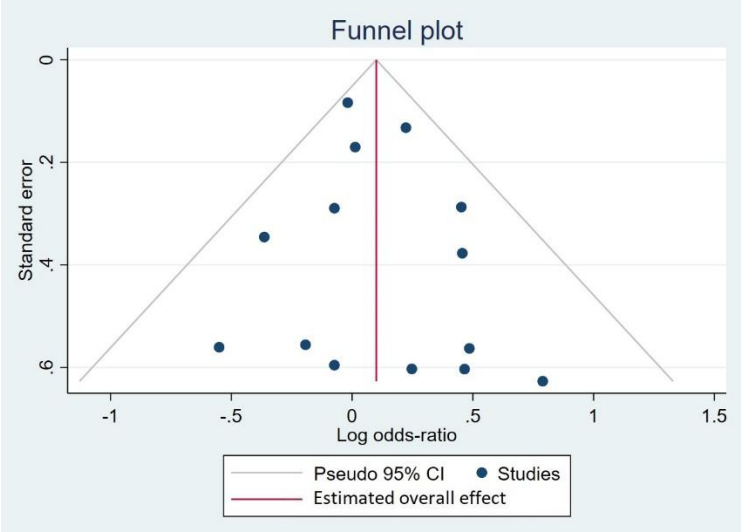


Figure 3.20 Funnel plot for the included studies reporting the outcome event “early implant failure” comparing posterior vs anterior implants

Subgroup analysis was performed for the posterior and anterior sites in each jaw. Posterior maxillary implants were compared with anterior maxillary implants in 9 studies (Figure 3.21). The Pooled estimate from these studies showed a non-significant increase in the odds of early failure when implants were placed in the posterior region of the maxilla (OR:1.24; 95% CI: 0.92, 1.67; p = 0.164).

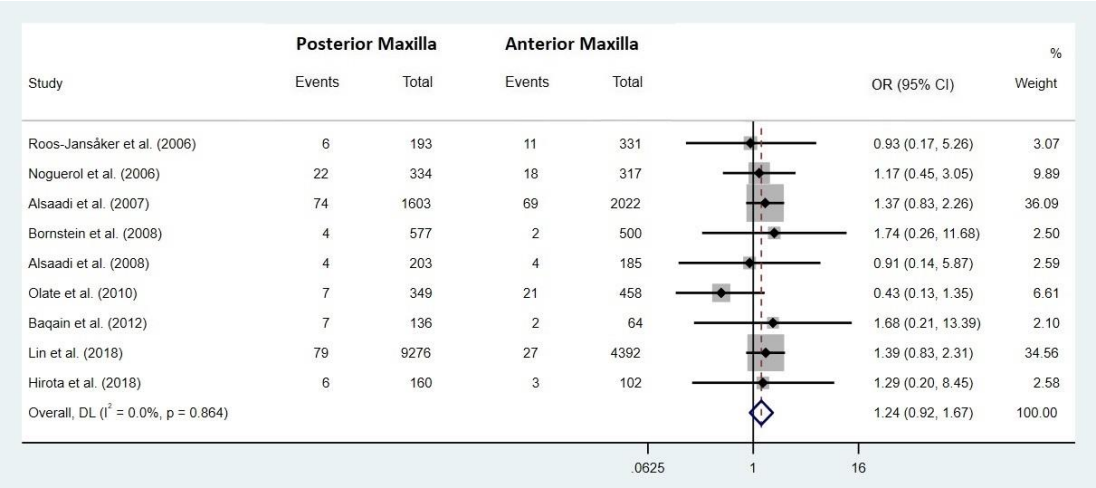


Figure 3.21 Forest plot for comparison of posterior and anterior maxillary implants for the "early implant failure" event

With regard to mandibular sites, the pooled estimates from 9 studies comparing posterior versus anterior mandibular implants revealed a non-significantly higher odds of early failure for implants placed in the posterior region of the mandible (OR: 1.24; 95% CI: 0.68, 2.27; p = 0.485) (Figure 3.22).

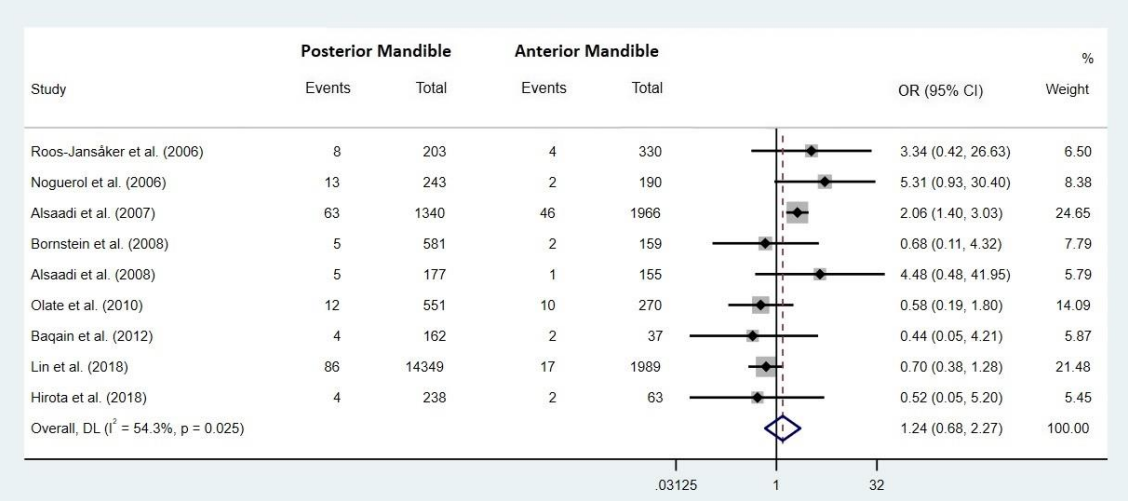


Figure 3. 22 Forest plot for comparison of posterior and anterior mandibular implants for the "early implant failure" event

3.3.4.8. Healing mode

The estimates for the three included studies comparing the risk of early failure between non-submerged (transmucosal) and submerged implants were pooled together using a random effects model. There was no evidence of significant heterogeneity between the studies (I^2 = 0%, p = 0.636) (Figure 3.23). This meta-analysis showed a significantly higher odds of early failure for non-submerged implants when compared to submerged implants (OR: 1.80; 95% CI: 1.14, 3.28; p = 0. 0.029).

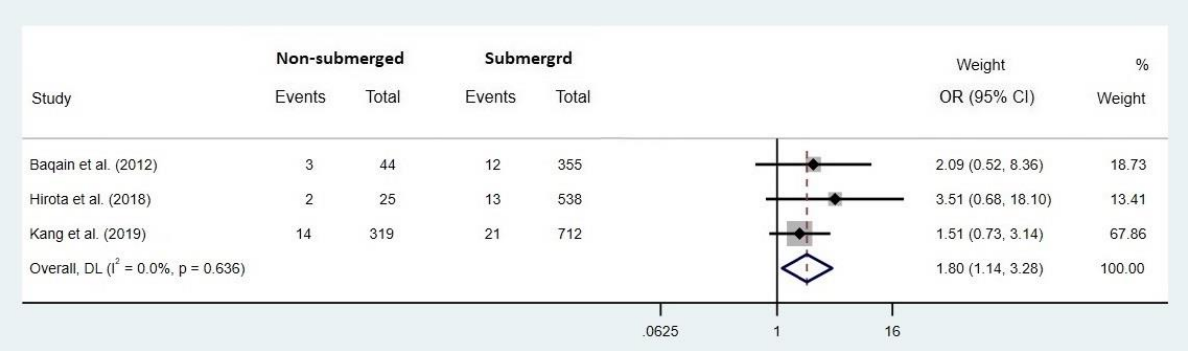


Figure 3.23 Forest plot of comparison between implants non-submerged and submerged implants for the "early implant failure" event.

The leave-one-out sensitivity analysis showed the greatest increase in the pooled estimate of odds ratio (OR: 2.59, 95% CI: 0.90, 7.49) after the removal of the study by Kang et al. (2019). Furthermore, the significance level changed to non-significant when any of the included studies were omitted (Figure 3.24). However, all estimates were consistent with a higher risk of early implant failure with non-submerged healing.

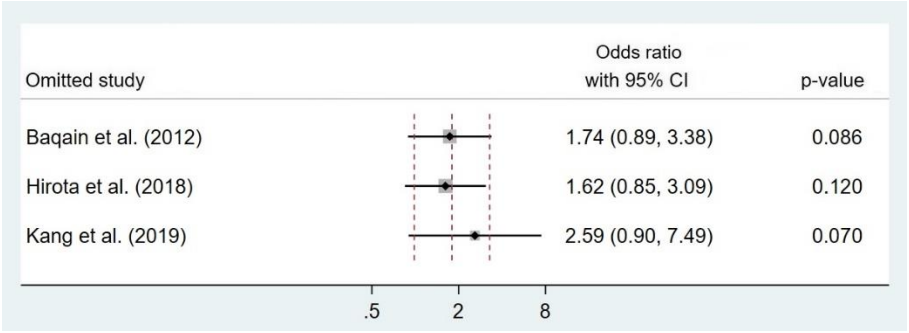


Figure 3.24 Influence plot for the sensitivity analysis (implant healing mode as a risk factor for early implant failure)

3.3.4.9. Bone augmentation

A meta-analysis was conducted on the 11 identified studies that compared the early failure rates of implants inserted with bone augmentation (prior or concurrent) to those inserted without augmentation. A random effects model was used to calculate the pooled odds ratio with 95% CI. There was significant heterogeneity detected across the included studies (I^2=51.9%, p=0.022) (Figure 3.25). This meta-analysis showed that bone augmentation significantly increased the odds of early implant failure by 96% (OR: 1.96; 95% CI: 1.34, 2.86; p < 0.001) compared to not having bone augmentation.

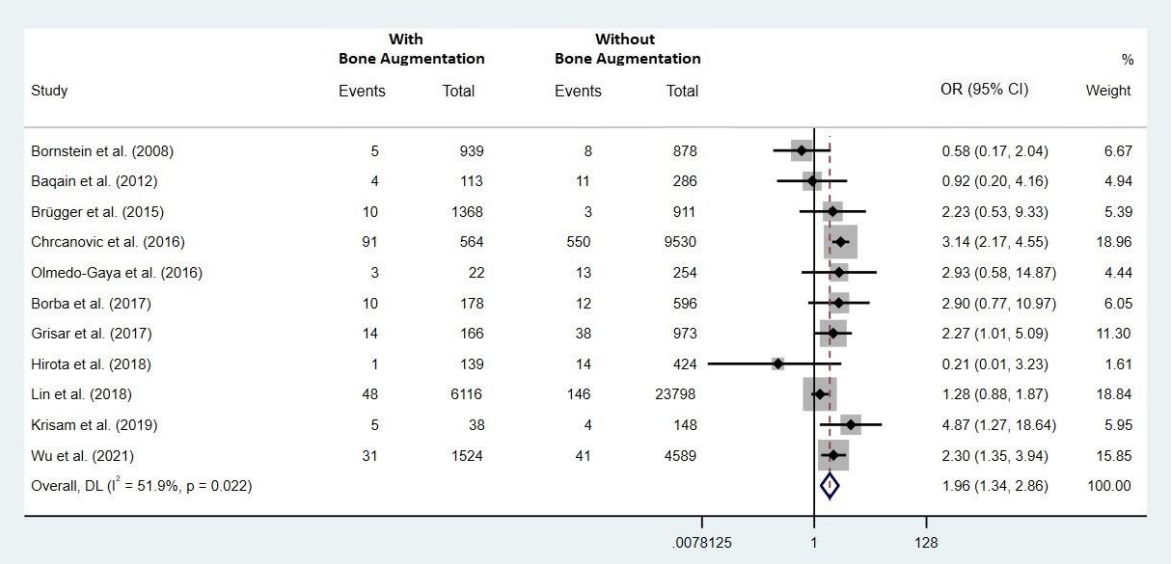


Figure 3.25 Forest plot to compare implants with and without bone augmentation for the "early implant failure" event

According to the sensitivity analysis (Figure 3.26), the estimates for the odds ratio of early implant failure ranged from 1.74 (95% CI: 1.20, 2.53) when the Chrcanovic et al. (2016) study was omitted to 2.25 (95% CI: 1.57, 3.23) after removing the Lin et al. (2018) study. The overall statistical significance did not change when any single study was omitted.

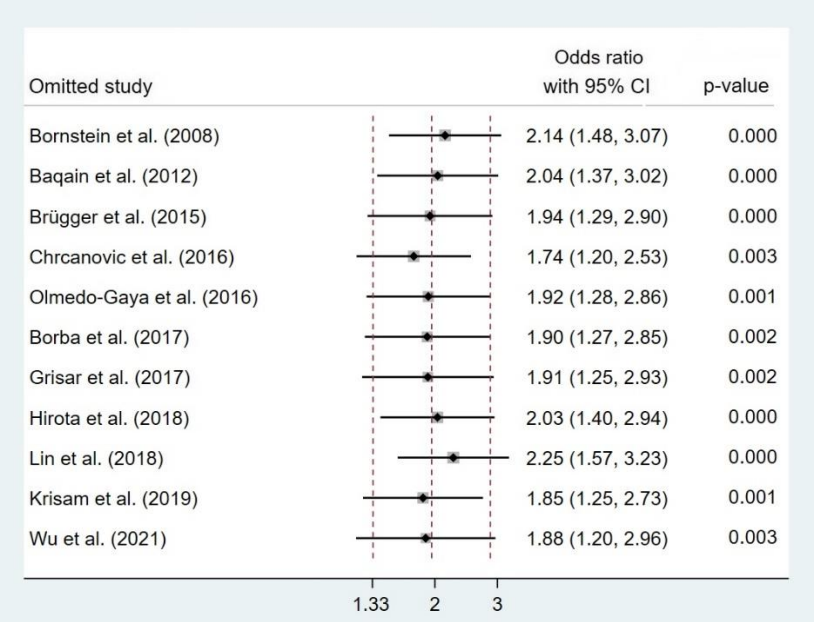


Figure 3.26 Influence plot for the sensitivity analysis (Bone augmentation as a risk factor for early implant failure)

The funnel plot for this meta-analysis did not show a clear asymmetry (Figure 3.27). However, one study by Hirota et al. (2018) fell outside the plot's 95% triangular confidence area as it showed a large odds ratio reduction together with a wide CI (OR: 0.21; 95% CI: 0.01, 3.23). Harbord's test result was non-significant (p = 0.843), providing statistical evidence for the symmetry of the funnel plot and the absence of publication bias.

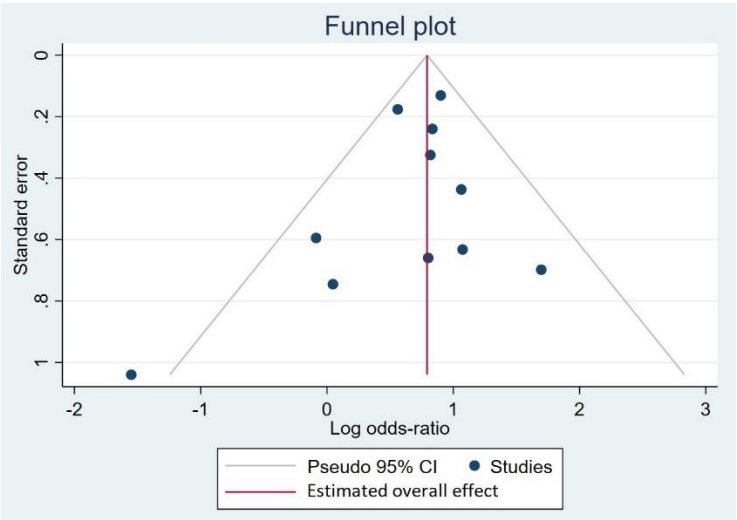


Figure 3.27 Funnel plot for the included studies reporting the outcome event “early implant failure” comparing implants inserted with vs without bone augmentation

3.3.4.10. History of periodontitis

A random effects model was used to obtain a pooled odds ratio and 95% confidence interval from the four selected studies evaluating the risk of early failure of implants placed in patients with a previous history of periodontitis compared to implants placed in patients without a history of periodontitis (Figure 3.28). There was no evidence of significant heterogeneity between the included studies (I^2 = 0%, p = 0.476). The result of this meta-analysis showed a significantly higher odds of early failure for implants inserted in patients with a previous history of periodontitis (OR: 1.69; 95% CI: 1.18, 2.43; p = 0.004).

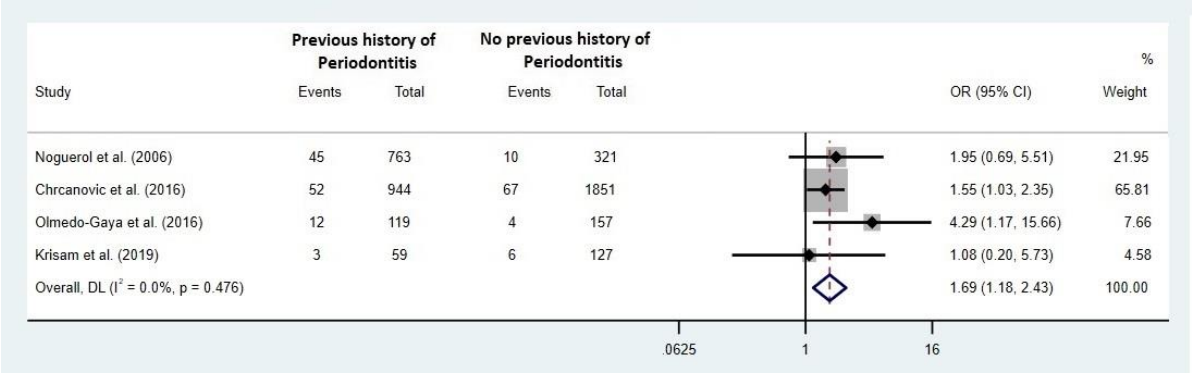


Figure 3.28 Forest plot for the event “early implant failure” in the comparison between implants placed in patients with vs without previous history of periodontitis

According to sensitivity analysis, the removal of the Chrcanovic et al. (2016) study had a greater impact on the overall estimate of odds ratio (OR: 2.24, 95% CI: 1.14, 4.64) (Figure 3.29) than other studies. However, the Pooled estimates remained significant when any one study was omitted.

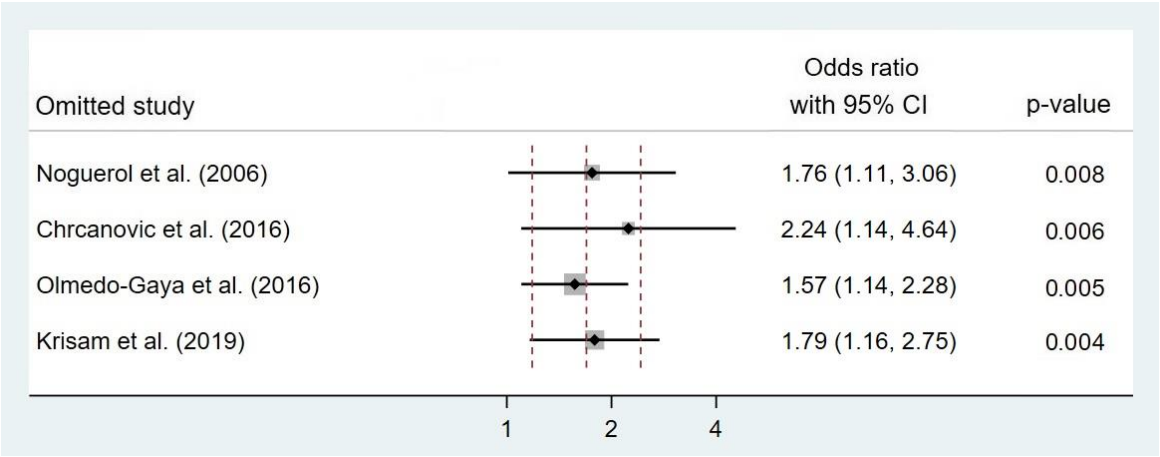


Figure 3.29 Influence plot for the sensitivity analysis (Previous history of periodontitis as a risk factor for early implant failure)

3.3.4.11. Diabetes mellitus

The estimates for the four selected studies comparing the risk of early failure between implants placed in diabetic (type I or II) and non-diabetic patients were pooled together using a random effects model. There was non-significant heterogeneity across the studies (I^2 = 14%, p = 0.322) (Figure 3.30). This meta-analysis showed a non-statistically significant higher odds of early failure for implants inserted in patients with diabetes compared to those without diabetes (OR: 1.38; 95% CI: 0.70, 2.71; p=0.347).

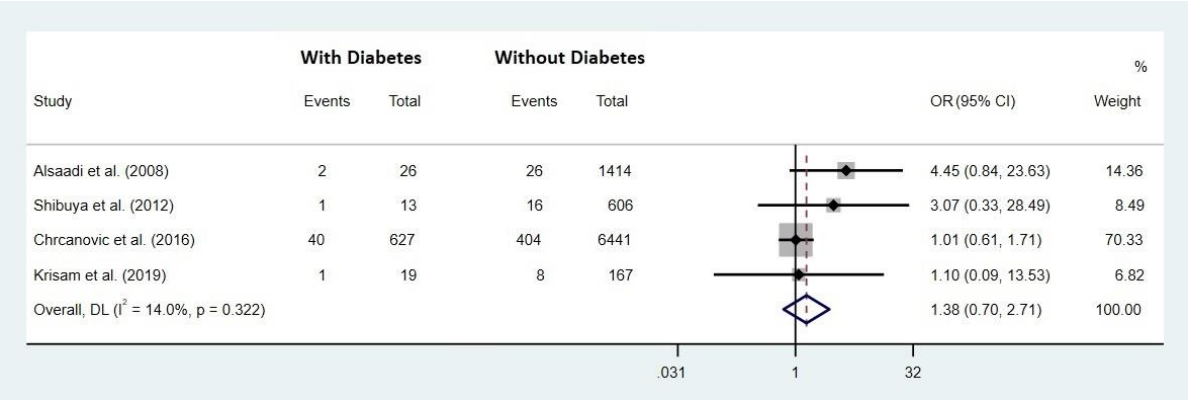


Figure 3.30 Forest plot for the event "early implant failure" in the comparison between implants placed in patients with vs without diabetes

The removal of the Chrcanovic et al. (2016) study in the Leave-one-out sensitivity analysis (Figure 3.31) resulted in a statistically significantly higher overall estimate of the odds of early failure for implants placed in diabetic patients compared to implants inserted in non-diabetic patients (OR: 2.94; 95% CI: 1.08, 9.57, p = 0.03). On the other hand, omitting Alsaadi et al. (2008b) study resulted in the greatest decrease in the overall estimate of the odds ratio (OR: 1.07; 95% CI: 0.65, 1.75) but did not show statistical significance.

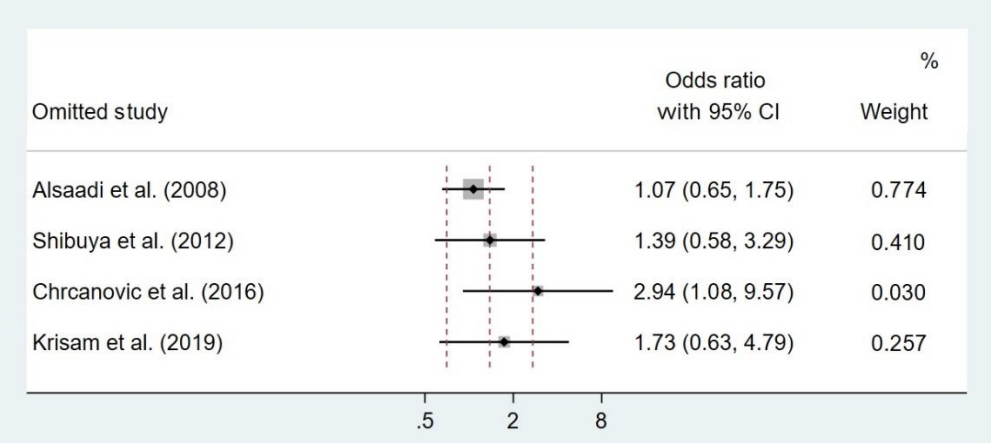


Figure 3.31 Influence plot for the sensitivity analysis (Diabetes as a risk factor for early implant failure)

3.4. Discussion

One of the primary goals of health research is to estimate the causal effects of exposures on outcomes (Hernán, 2004). This could be achieved by conducting randomised controlled trials; however, this approach has ethical and practical limitations (Deaton and Cartwright, 2018) and is only possible if interventions can be designed to address risk factors. For example, factors such as age and sex cannot be randomised as they are not interventions. Other factors, such as smoking, cannot be randomised due to ethical considerations. Therefore, observational studies are commonly used to estimate causal effects (Stroup et al., 2000). When estimating a specific causal effect in observational studies, it is often necessary to adjust for one or more covariates in order to eliminate or reduce confounding bias. Selection of these variables should be based on causal assumptions about their role in relation to the exposure and outcome (Blakely et al., 2021). However, adjustments for other covariates may introduce bias rather than eliminate it. This may occur as a result of adjustment for variables that are in the causal pathway between exposure and outcome, or by adjustment for colliders (selection bias) (Hernán et al., 2002).

In the present systematic review and meta-analysis, 5 included studies did not adjust for any potential confounders (Table 3.2). The remaining 15 studies made multiple adjustments to the effect estimates of exposures using a single model, which was presented in a single table where all exposures were mutually adjusted. Incorporating both direct and total effect estimates for several risk factors in the same model may not provide meaningful causal effect estimates for these risk factors (Westreich and Greenland, 2013). For example, the total effect of age can only be estimated from a crude model because age cannot be influenced by any other factor; therefore, if other

factors are included in the same model with age, the coefficient for age from that model will have no causal interpretation.

Furthermore, there was no clear rationale for why some variables were included in the analyses while others were not, as there was no causal assumption guiding the selection process. Therefore, the adjusted estimates from these studies do not have a causal interpretation as they do not consider potential causal structures. For that reason, we used crude (unadjusted) association in this systematic review and meta-analysis to ensure consistency across studies and provide approximate estimates of risks of early implant failure for each exposure investigated.

3.4.1. Age

Several ageing-related factors may compromise the osseointegration of dental implants. The potential for impaired soft and hard tissue healing is one of the most important biological issues to consider when treating aged patients with dental implants (Bartold et al., 2016). It is widely accepted that wounds heal more slowly in the aged population. Studies in human and animal models have demonstrated that ageing is associated with decreased cell proliferation (Cáceres et al., 2014), impaired angiogenesis (Shimoda et al., 2014), and imbalance in bone remodelling (Kloss and Gassner, 2006). Furthermore, older patients generally show higher rates of systemic disease compared to younger patients. Some medical conditions that may affect the outcome of dental implant treatment become more common with advancing age. Osteoporosis, for example, whose prevalence increases with age, especially in postmenopausal women due to low levels of oestrogen (Bonnick, 2006), causes a reduction in bone mass and density and was shown to impede the osseointegration

process in experimental models (Duarte et al., 2005, Du et al., 2009). Furthermore, a systematic review conducted by de Medeiros et al. (2018) showed that patients with osteoporosis had significantly higher marginal bone loss around implants compared to patients without osteoporosis.

However, our meta-analysis of studies examining ageing as a risk factor for early implant failure indicates that patients older than 60 years do not have a higher risk of early implant failure compared to younger patients. This finding supports previous systematic reviews and meta-analyses showing that advanced age is not a limiting factor for dental implant treatment (Sendyk et al., 2017, Srinivasan et al., 2017).

3.4.2. Sex

According to the results of the present study, male patients may have a 80% higher risk of early implant failure compared to female patients. In accordance with the present results, a previous systematic review by Chrcanovic et al. (2015a) has demonstrated that the patient's sex significantly affects the implant failure rates, and implants placed in males have a 1.21 times higher risk of failure than those placed in females. Chrcanovic et al. (2015a) hypothesized that the increased risk of implant failure in men compared to women might be related to the higher prevalence of smoking among men. This was based on the available evidence that smoking increases the risk of implant failure (Strietzel et al., 2007, Abt, 2009, Chrcanovic et al., 2015b).

Furthermore, several epidemiological studies have shown that men are more likely to develop severe periodontal disease than women (Shiau and Reynolds, 2010b).

Moreover, a gene-sex interaction analysis in relation to aggressive periodontitis has shown a strong association between the risk of aggressive periodontitis and the patient's sex, with the risk increasing in males and decreasing in females (Freitag-Wolf et al., 2014). There is some evidence to suggest that increased susceptibility to periodontitis, as might be the case for male patients, may also be associated with an increased marginal bone loss and a higher risk of implant failure (Chrcanovic et al., 2014b). Furthermore, the present study showed a significantly higher risk of early failure for implants placed in patients with a previous history of periodontitis compared to implants placed in patients with no prior history of periodontitis (RR: 1.65; 95% CI: 1.17, 2.33).

3.4.3. Implant length

The results of the current study suggest that short implants, with a length of less than 10mm, have a higher risk of early failure compared to longer implants. This finding is consistent with a previous meta-analysis of observational studies by Manzano et al. (2016), which also showed that implants less than 10 mm in length had a significantly higher risk of early failure compared to longer implants (OR: 1.60; 95% CI: 1.15, 2.24). Another systematic review and meta-analysis showed that implants shorter than 7 mm in the maxilla and shorter than 5.5 mm in the mandible had significantly higher failure rates compared to longer implants (Pommer et al., 2018).

One probable explanation is that shorter implants are usually used in posterior regions of the jaws that have limited bone height or insufficient bone volume due to advanced bone resorption and anatomical limitations (e.g., inferior alveolar canal, maxillary sinus), and that usually is for patients who are unwilling or unable to be submitted to

bone augmentation procedures. In such cases, the planned implant sites with a reduced bone volume and potentially poorer bone quality to support the implant, as is usually the case in the posterior maxilla, may predispose to an increased risk of early failure of short implants (Chrcanovic et al., 2017). Furthermore, when short implants are used, there is less contact between the bone and the implant because shorter implants have less surface area than longer ones. Assuming that implants of varying lengths experience the same amount of marginal bone loss over time, in this case, it is reasonable to expect that shorter implants will experience a greater loss of supporting bone relative to their lengths than longer implants in the same time period. Furthermore, it has been shown that longer implants may have higher primary stability, indicated by higher insertion torque values (Farronato et al., 2020).

In addition, patients with a history of periodontitis are often treated with shorter implants because they usually have a reduced alveolar bone height due to the resorption process associated with periodontitis. It has been shown that patients previously treated for periodontitis may have increased marginal bone loss and a higher risk of implant failure (Chrcanovic et al., 2014b). The results of the current study also showed that the placement of implants in patients with a previous history of periodontitis was associated with an increased risk of early implant failure (see section 3.3.4.10).

3.4.4. Implant diameter

In this study, we found that implants with a diameter less than 3.75mm had a 71% higher odds of early implant failure compared to wider implants (≥3.75mm). In accordance with the present findings, although there were some differences in the threshold definition of narrow implants, A previous systematic review and meta-

analysis Ortega-Oller et al. (2014) found that implants with a diameter of less than 3.3mm had significantly higher failure rates than wider implants (1.55% vs. 0.40%, respectively). Similarly, a systematic review and meta-analysis by Pommer et al. (2018) showed that implants narrower than 3.3 mm had significantly higher early failure rates (5.5%) compared to wider implants (2.2%).

A possible explanation for the observed findings regarding implant diameter is that narrower implants have less surface area, leading to reduced contact with the bone and potentially less osseointegration compared to wider implants. Furthermore, it has been shown that wider implants may have higher primary stability, indicated by higher insertion torque values (Gómez-Polo et al., 2016).

3.4.5. Smoking

When it comes to smoking as a risk factor for early implant failure, our meta-analysis of the studies comparing the risk of early implant failure between smokers and non-smokers showed a 98% higher odds of early implant failure in smokers; this is in agreement with a previous systematic review and meta-analysis that showed smoking may increase the risk of early implant failure by 2.8 folds (Strietzel et al., 2007), and another systematic review and meta-analysis that showed that smokers are 2.2 times more likely to experience implant failures than non-smokers (Chrcanovic et al., 2015b).

Increased implant failure rates in smokers could be attributed mainly to the effect of tobacco smoking toxic components on the physiological processes of osteogenesis and angiogenesis. Nicotine, one of the most important constituents of tobacco, has been shown to inhibit the gene expression of several enzymes that play a crucial role in regulating osteoblast proliferation, differentiation, and apoptosis (Deng et al., 2008, Ma et al., 2011). It also decreases the expression of some critical angiogenic markers

necessary for the formation of new blood vessels in the early bone healing phase, with consequential effects on bone formation and remodelling. Furthermore, exposure to nicotine has also been shown to have effects on blood vessels, resulting in both local and systemic vasoconstriction (Ma et al., 2010), which reduces blood perfusion and leads to tissue hypoxia and ischemia (Wang et al., 2007).

In addition, smokers have been reported to have an increased incidence of peri-implantitis compared to non-smokers (Heitz-Mayfield and Huynh-Ba, 2009, Dreyer et al., 2018); furthermore, they have more impaired peri-implant biological parameters, such as higher plaque and bleeding indices, peri-implant soft tissue inflammation and marginal bone loss (Al Amri et al., 2017, Mumcu and Dayan, 2019).

In all studies included in the present meta-analysis on smoking, smoking status was determined based on patient self-report methods. Several studies have shown relatively high reliability of self-reporting when documenting smoking status (Fox et al., 1989, Patrick et al., 1994, Dolcini et al., 1996, O'Loughlin et al., 2002). Most of the studies that were included in the present study considered the patient who smokes to be a smoker regardless of the number of cigarettes smoked per day (Sverzut et al., 2008, Baqain et al., 2012, Shibuya et al., 2012, Olmedo-Gaya et al., 2016, Chrcanovic et al., 2016, Grisar et al., 2017, Krisam et al., 2019). However, some of the included studies quantified the number of cigarettes smoked per day but in different ways (Noguerol et al., 2006, Alsaadi et al., 2007, Alsaadi et al., 2008b, Bornstein et al., 2008); for instance, Alsaadi et al. (2007) categorised smoking more than 20 cigarettes per day as heavy smoking, while Bornstein et al. (2008) considered smoking 11 or more cigarettes per day to be heavy smoking. The findings of these studies indicated that smoking may have a dose-related effect on the risk of early implant failure. As the

quantification of tobacco smoking was inconsistent across the included studies, the smoking status was categorised into smokers and non-smokers in this meta-analysis.

3.4.6. Implant site

Our meta-analysis of studies comparing the risk of early implant failure between the maxilla and mandible indicates that implants placed in the upper jaw are more likely to experience early failure than implants placed in the lower jaw, with an odds ratio of 1.49 (95% CI: 1.13, 1.96). This finding is in accordance with a previous systematic review and meta-analysis by Manzano et al. (2016), which showed that implants placed in the upper jaw had a higher risk of early implant failure compared to those placed in the lower jaw (OR: 1.27; 95%CI: 1.02, 1.57).

The higher failure rate of the maxillary implants compared to mandibular implants could be explained by differences in bone quality between the jaws. Based on Lekholm and Zarb classification of bone qualities (Lekholm and Zarb, 1985), it was found that type 3 bone quality was more prevalent in the maxilla, while type 2 was the predominant bone quality in the mandible (Truhlar et al., 1997). The relatively thinner cortical plate and the lower trabecular bone density of the maxilla compared to the mandible may result in lower primary stability of the placed implants (Park et al., 2010). Furthermore, the post-extraction alveolar resorption is generally higher in the maxilla compared to the mandible (Couso-Queiruga et al., 2021), resulting in less bone quantity available for implant placement. In addition, posterior maxillary regions may exhibit limited vertical bone height due to maxillary sinus pneumatization (Cha et al., 2019). Therefore, maxillary sites are more likely to require bone augmentation procedures to allow for implant placement. Some evidence suggests that bone augmentation procedures were associated with an increased risk of early implant

failure (Clauser et al., 2022), which may also explain the reported higher rate of early implant failure in the upper jaw than in the lower jaw.

On the other hand, our meta-analysis comparing the risks of early implant failure between the posterior and anterior locations of both jaws and the sub-group analyses that considered each jaw independently showed slightly higher risks of early implant failure in the posterior regions, although with no statistical significance.

3.4.7. Healing mode

It is widely accepted that even small movements of dental implants may negatively impact the initial stages of osseointegration (Frost, 2004, Troiano et al., 2018). Therefore, the idea of submerged implant healing involves placing the implant in one procedure and then connecting the abutment in another to prevent implant movement during the early stages of osseointegration, allowing for proper new bone formation and remodelling, and reducing the risk of fibrous connective tissue formation between the bone and the implant. On the other hand, non-submerged (transmucosal) implant healing has become increasingly popular as a minimally invasive treatment option for patients. This method involves a one-step surgical procedure in which implant placement and abutment is performed in the same procedure, thereby shortening the time between implant placement and the delivery of the final prosthesis and obviating the need for a second surgery. Several studies have indicated that implant placement using a single-stage surgery (non-submerged implant) is just as reliable as a two-stage surgery (submerged implant), with a high success rate (Cecchinato et al., 2008, Eliasson et al., 2010, Hämmerle et al., 2012). However, in a systematic review and meta-analysis conducted by Troiano et al. (2018), non-submerged implants had a significantly higher risk of early failure compared to submerged implants (RR:2.34;

95% CI:1.25, 4.39). Furthermore, our meta-analysis of studies comparing early implant failure risk between non-submerged and submerged implants found that implants placed with a single-stage surgical approach (non-submerged) had a significantly higher odds of early failure compared to those placed with a two-stage surgical approach, with an odds ratio of 1.80 (95% CI: 1.14, 3.28).

3.4.8. Bone augmentation

Bone augmentation is widely used in implant dentistry to compensate for alveolar ridge deficiencies so that the implant can be placed in an optimal position. Several augmentation techniques have been developed in addition to using different grafting materials. Due to the potential adverse events associated with bone augmentation procedures, such as infection, wound dehiscence, or membrane exposure (Lim et al., 2018, Urban et al., 2019), they may pose an additional risk for implant failure. It has been reported that when such complications arise, the outcomes of bone augmentation are expected to be significantly impacted (Garcia et al., 2018), which might consequently increase the likelihood of implant failure in the grafted sites. It has also been shown that implant insertion in augmented sites was associated with lower insertion torque values and, therefore, lower primary stability compared to non-augmented sites (Huang et al., 2017). At the histological level, grafted sites have been reported to have a lower proportion of vital bone than non-grafted sites (Chan et al., 2013); however, it remains unclear whether the histological changes in bone quality at the grafted sites might affect the outcome of dental implant treatment.

According to the results of the present meta-analysis on bone augmentation as a risk factor for early implant failure, implants placed in augmented sites had a significantly higher odds of early failure compared to those placed in non-augmented sites

(OR:1.96; 95% CI: 1.34, 2.86). This finding is in agreement with a recent systematic review and meta-analysis by Clauser et al. (2022), who found a significant association between bone augmentation procedure and increased risk of early implant failure, suggesting that implant therapy planning should take this into account. However, it is worth noting that the influence of the augmentation technique and the used augmentation material on early implant failure was investigated neither in the present study nor in the previously mentioned review by Clauser et al. (2022); instead, bone augmentation as a risk factor for early implant failure was generally considered in terms of its presence or absence, which might be a limitation of our study. Therefore, the variations in the bone augmentation techniques, grafting materials used, and the timing of bone augmentation relative to implant placement could explain the significant heterogeneity observed among the pooled studies (I^2=51.9%, p=0.022).

3.4.9. History of periodontitis

With regard to the history of periodontitis as a risk factor for implant failure, there is evidence to suggest that patients who have had periodontitis may be at greater risk of experiencing more peri-implant bone loss and implant failure than patients without a history of periodontitis (Ong et al., 2008, Safii et al., 2010, Chrcanovic et al., 2014b). Our meta-analysis in this respect also showed that the insertion of implants in patients with a prior history of periodontitis significantly increased the odds of early failure by 69% (OR:1.69; 95% CI: 1.18, 2.43) compared to implants inserted in patients with no prior history of periodontitis.

There are some possible explanations for this finding. It has been hypothesised that patients with a history of periodontal disease may present a more intense local inflammatory response which could be responsible for the reported higher implant

failure rates among those patients (Rosenberg et al., 2004). Furthermore, patients who have had periodontitis or tooth extractions for periodontal reasons may have a reduced quantity of alveolar bone available for dental implantation after tooth loss; therefore, alveolar ridge augmentation or the placement of short implants is frequently considered in such cases. It has been shown that there might be an increased risk of implant failure associated with bone augmentation (Clauser et al., 2022) or when short implants are used (Abdel-Halim et al., 2021); therefore, these factors may have contributed to the increased risk of implant failure in patients with a history of periodontitis.

3.4.10. Diabetes mellitus

Diabetes can have negative effects on osseointegration due to some adverse events associated with this disease, including delayed healing (Dubey et al., 2022), impaired bone metabolism (Moreira et al., 2015), microvascular complications (Khalil, 2017), and impaired immunological response to infection (Berbudi et al., 2020). Previous systematic reviews and meta-analyses have shown that diabetes presents a risk for increased peri-implant marginal bone loss and implant failure (Chrcanovic et al., 2014a, Al Ansari et al., 2022).

The results of the present meta-analysis of studies looking into diabetes as a risk factor for early implant failure suggest that implants placed in diabetic patients may have a 38% increased odds of early failure compared to those placed in nondiabetic patients; however, with no statistical significance, possibly due to the small number of included studies and small overall sample size. Only one of the four included studies conducted by Alsaadi et al. (2008b) investigated the risk of early implant failure according to the

type of diabetes. This study showed that early implant failure was more likely to occur in patients with type 1 diabetes than in patients with type 2 diabetes.

3.4.11. A causal model of potential risk factors for early implant failure

We constructed a causal model using Directed Acyclic Graphs (DAGs) (Figure 3.32), incorporating variables potentially related to early implant failure and defining their causal relationship based on available literature, expert knowledge, and plausible assumptions. This model may help in reducing bias in selecting confounding variables by indicating which ones should be included in multivariable models when examining the relationship between a risk factor and early implant failure. Furthermore, it may aid in planning future studies by specifying which variables need to be measured in addition to the exposure variable so that they can be adjusted for in the analysis.

Variables are represented by nodes that are connected by arrows pointing in one direction, which indicate the hypothesized relationships between the variables. An arrow connecting two nodes shows the direction of a causal relationship, but it doesn't indicate whether it's positive or negative or its strength. A causal path flows in one direction from one node to another without any circular paths (acyclic) between nodes, as variables cannot affect themselves. For any given exposure, the confounding variable is the one that has a causal relationship with both the exposure and the outcome. An open path between exposure and outcome that passes through one or more confounders is a confounding path that requires adjustments.

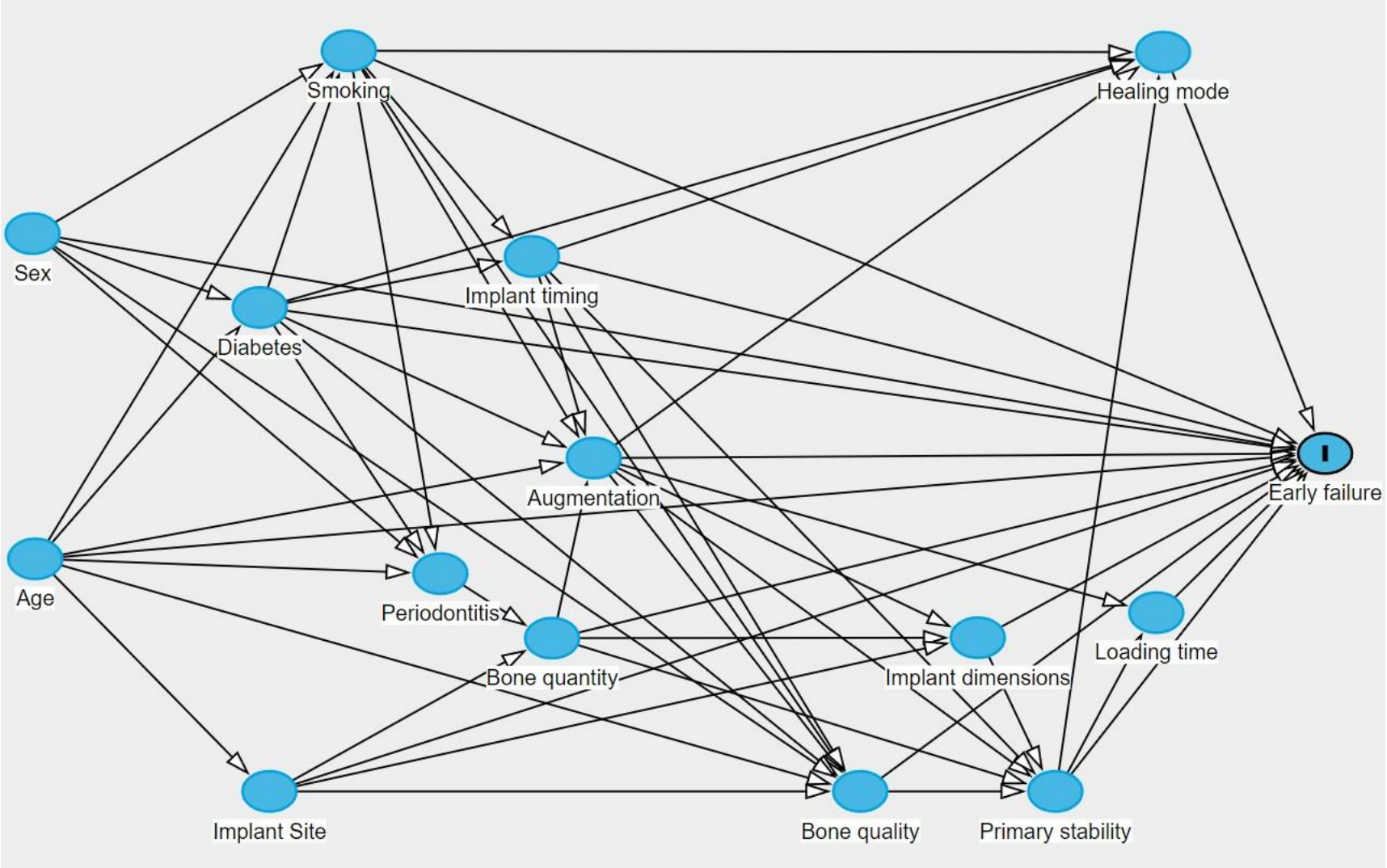


Figure 3.32 Proposed causal model of potential risk factors for early implant failure

The causal model outlines the hypothesized relationships between the variables, which can be summarized as follows:

Sex

Sex → Smoking

In general, the prevalence of cigarette smoking is higher among men compared to women (Dai et al., 2022).

Sex → Diabetes

Men generally have a higher prevalence of type 2 diabetes compared to women (Mauvais-Jarvis, 2018), which is linked to their higher levels of visceral fat in men (Nordström* et al., 2016).

Sex → Bone quality

On average, men have higher bone density compared to women (Alswat, 2017). Furthermore, Oestrogen deficiency in postmenopausal women leads to increased osteoclast formation resulting in increased cancellous bone resorption, cortical porosity, and decreased bone mass (Kalervo and Härkönen, 1996).

Sex → Periodontitis

Men generally have a higher prevalence of periodontitis compared to women (Shiau and Reynolds, 2010a).

Age

Age → Smoking

People generally start smoking and smoke more intensively in early adulthood (approximately age 14–25 yrs) (Reitsma et al., 2021) and often tend to cut down or quit smoking as they age due to increased risk for medical conditions.

Age → Diabetes

Type 2 diabetes is more common in middle-aged and older individuals, while Type 1 diabetes usually affects children and young adults.

Age → Augmentation

As people age, their bones tend to experience more resorption and less formation (Demontiero et al., 2012); therefore, it is more likely for older people to require bone augmentation for implant placement. On the other hand, bone augmentation procedures, particularly the more invasive ones, may be avoided for older patients, especially those with medical conditions.

Age → Periodontitis

Periodontitis is generally more prevalent among older adults compared to younger adults (Burt, 2005).

Age → Bone quality

As individuals get older, the bones experience an increase in bone resorption and cortical porosity, and a decrease in bone mineral density (Riggs et al., 2004).

Age → Site

Posterior teeth, particularly the first permanent molars, are more likely to be extracted at a younger age due to caries. Furthermore, young adults are more prone to lose their anterior teeth due to trauma.

Implant Site

Site → Bone quantity → Augmentation

Post-extraction alveolar resorption is generally higher in the maxillary compared to the mandibular sites (Couso-Queiruga et al., 2021), resulting in less bone quantity available for implant placement. In addition, posterior maxillary regions may exhibit limited vertical bone height due to maxillary sinus pneumatization (Cha et al., 2019). Therefore, maxillary sites are more likely to require bone augmentation for implant placement.

Site → Dimensions

Implant length may be restricted in the posterior region due to anatomical structures such as the inferior alveolar canal and the maxillary sinus. Furthermore, narrow implants are often required in the anterior region (e.g., lower incisors and upper lateral incisors), whereas wider implants are indicated in the posterior region to withstand masticatory forces.

Site → Bone quality

The bone quality varies across various sites of the jaws. The upper jaw generally has relatively thin cortical plates and less dense medullary bone than the lower jaw (Nanci, 2018), and the anterior region of each jaw has denser bone than the posterior(Truhlar et al., 1997).

Diabetes

Diabetes → Smoking

It could be argued that if a patient is diagnosed with diabetes, they are more likely to reduce or quit smoking to minimize health risks.

Diabetes → Healing mode

Surgeons may be less likely to choose transmucosal implant healing mode for diabetic patients.

Diabetes → Implant timing

Implants that are placed immediately after tooth extraction may have a greater chance of complications compared to delayed implants (Esposito et al., 2010). Therefore, clinicians may be more likely to choose a more conservative, delayed healing approach in patients with diabetes.

Diabetes → Augmentation

Surgeons may be reluctant to recommend bone augmentation for diabetic patients due to the potential complications associated with this disease, such as delayed healing (Dubey et al., 2022), microvascular complications (Khalil, 2017), and higher risk of infection (Chang et al., 2019).

Diabetes → Bone quality

Diabetes can impact bone quality through impaired bone metabolism, low bone turnover, and microvascular complications associated with the disease (Hygum et al., 2019).

Diabetes → Periodontitis

Patients with diabetes are at a higher risk of developing periodontitis (Preshaw and Bissett, 2019).

Smoking

Smoking → Healing mode

Surgeons may be less likely to choose transmucosal implant healing mode with smokers.

Smoking → Implant timing

Implants that are placed immediately after tooth extraction may have a greater chance of complications compared to delayed implants (Esposito et al., 2010). Therefore, it seems that smokers may not be ideal candidates for immediate implant placement, as smoking can have additional detrimental effects on the healing process.

Smoking → Bone quality

Smoking was shown to interfere with osteoblast function, bone remodelling and mineralization (Deng et al., 2008, Ma et al., 2011). Individuals who smoke tend to have lower bone mineral density compared to those who do not smoke (Law and Hackshaw, 1997, Ward and Klesges, 2001). According to Saldanha et al. (2006), after six months of tooth extraction, smokers had significantly lower radiographic bone density in the extraction socket compared to non-smokers.

Smoking → Augmentation

Tobacco smoking is a well-established risk factor that decreases local vascularization, as well as having impaired healing (Ma et al., 2010). Therefore, surgeons may be reluctant to recommend certain types of bone augmentation for smokers.

Smoking → Periodontitis

Smoking is a well-recognised risk factor for periodontitis (Leite et al., 2018).

Implant timing

Implant timing → Healing mode

Immediate implants are more likely to be allowed to heal transmucosally, as submerged healing would require additional flap mobilisation.

Implant timing → Primary stability

Placing an implant in a fully healed ridge will more likely provide higher primary stability, compared to placement into more immature bone in case of early implantation or compared to immediate implants.

Implant timing → Bone quality

As the extraction socket heals, the quality of the bone changes over time due to the maturation and remodelling of newly formed bone (Farina and Trombelli, 2011).Therefore, the quality of bone at implant insertion may be affected by the timing of implant placement relative to the time of tooth extraction.

Implant timing → Augmentation

The timing of implant placement may affect the need for and type of bone augmentation. For example, bone grafting materials are often used to fill the jumping gap between the immediately placed implants and the buccal wall of the alveolar socket. In many cases of late implantation, extensive augmentation may be necessary to facilitate implant placement.

Periodontitis

Periodontitis → Bone quantity

It has been demonstrated that periodontitis can lead to the destruction of the alveolar bone (Brunetti et al., 2015, Usui et al., 2021).

Bone quantity

Bone quantity → Augmentation

An insufficient amount of bone may require bone augmentation to place the implant in the optimal position.

Bone quantity → Implant dimensions

The amount of alveolar bone available (height and width) can determine the length and diameter of the implant to be placed.

Bone quantity → Primary stability

It has been reported that wider alveolar ridges can provide higher primary implant stability (de Elío Oliveros et al., 2020).

Augmentation

Augmentation →Healing mode

Surgeons likely prefer a two-stage approach (submerged healing) than a one-stage approach (transmucosal healing) when placing implants in augmented sites.

Augmentation → Loading time

It is more likely to wait longer before loading implants that have been placed in the augmented sites.

Augmentation → Dimensions

Bone augmentation enables the insertion of larger dental implants. On the other hand, patients who have limited or insufficient bone quantity and are unwilling or unable to be submitted to bone augmentation procedures are usually treated with shorter and narrower implants.

Augmentation → Primary stability

Some augmentation procedures, such as ridge splitting, may result in decreased primary implant stability.

Augmentation → Bone quality

Bone augmentation results in the formation of new bone with a different density and proportion of vital bone compared to sites where no augmentation was performed (Kühl et al., 2012, Chan et al., 2013).

Implant dimensions

Implant dimensions → primary stability

The size of the implant (length and diameter) reflects the surface area in contact with the bone and can therefore affect the primary stability of the implant. Furthermore, it has been shown that higher insertion torque values were associated with increased implant length and diameter (Gómez-Polo et al., 2016, Farronato et al., 2020).

Bone quality

Bone quality → Primary stability

The thickness of the cortical bone is an important factor in determining the primary stability of dental implants. Thicker cortical bone results in increased primary stability (Miyamoto et al., 2005). Furthermore, more immature bone in cases of early implantation may result in lower primary stability.

Primary stability

Primary stability ⟶ healing mode

Submerged implant placement is usually recommended If the primary implant stability is low.

Primary stability ⟶ Loading

In order to load the implant immediately or early (before two months), it is usually necessary to ensure that the implant has achieved good primary stability. Otherwise, conventional loading (after two months) may be necessary.

3.4.12. Limitations of the present study

The results of the present study need to be interpreted with caution due to its limitations. The main limitations of this study are:

- The majority of the included studies had a retrospective study design that may inherently be subject to biases such as selection bias and thus may have an impact on the validity of our findings.

- Many of the included studies had a relatively small sample size, which may have limited their ability to detect small effects.

- The analyses in this study were based on crude (unadjusted) estimates and did not account for potential confounding factors that may influence the exposures and the outcome. This is because the included studies either did not adjust for confounders or used an approach for adjustment that does not allow for causal interpretation.

- Half of the included studies did not use a statistical approach that accounts for the clustering of implants within patients. Therefore, we calculated an approximate cluster-adjusted estimate for these studies, which may differ from the actual one.

- Including only studies in the English language may have caused us to miss potentially relevant studies published in other languages.

3.5. Conclusion

Within the limitations of this study, we found that the main factors associated with an increased risk of early implant failure were male sex, smoking habit, previous history of periodontitis, placement of the implant in the upper jaw, transmucosal healing mode, bone augmentation at the implant site, and the use of short implants or narrow implants. On the other hand, the current evidence was inconclusive with respect to diabetes and the posterior region of the jaws as factors that may increase the risk of early implant failure. However, in order to better identify and investigate potential risk factors for early implant failure, further studies with larger sample sizes are required. Moreover, it is necessary to control for confounding factors based on an appropriate causal model to reduce bias in selecting confounding variables and enable causal interpretation.

CHAPTER 4: PATIENT, IMPLANT, AND SURGICAL CHARACTERISTICS IN A LARGE MULTI-CENTRE PRACTICE-BASED NETWORK

4.1. Aims

-To describe patient, implant and procedure-related characteristics of implants placed in a network of specialist oral surgery and oral and maxillofacial surgery practices in Germany between 2010 and 2022.

-To assess the incidence of early implant failure in the ECDI implant dataset.

4.2. Methods

The European Centres for Dental Implantology (ECDI) are a group of Oral & Maxillofacial Surgery and Oral Surgery practices (centres) who constituted themselves in 2009. The purpose of the ECDI is to provide members a forum for collegiate exchange of knowledge and experience regarding clinical, organisational and scientific matters relating to oral implantology. With very few exceptions, the participating centres are busy referral practices covering all aspects of outpatient dentoalveolar surgery, including oral implantology. Typically, each centre uses a variety of implant systems, depending on the preferences of the referring dentists. From the outset, participating centres committed to documenting their implant treatments using a commercially available database software for the purpose of quality control (ImpDat, Kea Software GmbH). ImpDat is a database programme specifically designed for the documentation of implantological data. The software allows a degree of customarization and a specific set of data collection was implemented for the ECDI. Hence, between 2010 and 2015 (period 1), a number of patient, procedure and implant related data were recorded by participating centres for all implant surgeries. The database was later reviewed and revised in order to improve the recording of some data, in particular data on the medical history and some parameters were added and/or recorded in different way. These changes came into effect in January 2016

(period 2). Most centres consistently contributed data between 2010 to 2023; however, a few left the network while others joined after 2010. The database software links in with most practice management software packages, which allows for the automatic transfer of certain patient data (i.e., date of birth, sex) into the database. The programme also allows for most implant components and biomaterials to be scanned into the database, which facilitates its use during busy routine clinical practice and reduces data entry errors. It is important to note that, while the clinicians in the ECDI centres agreed on the set of parameters to be routinely recorded, no formal calibration exercises were undertaken. Furthermore, not all centres recorded all parameters in the database. For example, some centres did not record the medical history data even after changes were made to the database before 2016. As the vast majority of implants were restored by the referring general dentist, data on timing and type of restoration were not recorded. Furthermore, patients were not routinely recalled to the surgery after discharge back to the referrer and therefore no outcome/follow-up data were recorded. However, it is reasonable to assume that patients who experienced significant problems with their implants during the first year after placement would have been re-referred or returned to the implant surgeon. This is particularly true for failing implants/implant loss, as usually a repeat implantation would be offered to such patients at no cost. However, we cannot rule out that some early implant failures were not recorded where there was a complete breakdown of trust or where the implant failure had not significantly impacted on the prosthetic rehabilitation.

The ImpDAT software stores the complete database locally in each centre and allows the upload of completely anonymised data onto a central server. These data were used for the secondary data analyses presented here. As these data were collected

as part of routine care and completely anonymised, no review by an ethics committee was required.

Study variables and statistical analysis

Variables for this study were classified as patient-related variables and implant-related variables. Patient-related variables included age, sex and medical history (smoking habit, diabetes). Implant-related variables included implant site, implant dimensions (length, diameter), implant brand, timing of implant placement, healing mode, bone quality at the implant site, implant insertion torque, alveolar ridge defects, bone augmentation, augmentation materials and techniques, time of augmentation relative to implant placement and frequency of augmentation per implant site.

Age and sex were recorded for every patient. For the medical history data, this study focused on the diabetes status (type I or II, treatment: insulin or tablets) and smoking status (Never smoked, former or current smoker). Patients who smoked were assigned to one of the following three categories: <5 cigarettes/day, 5–15 cigarettes/ day or >15 cigarettes/day.

Implant placement sites were categorised based on two variables: the jaw (maxillary or mandibular) and the location of the tooth that was replaced by the implant (central incisor, lateral incisor, canine, first premolar, second premolar, first molar, and second molar).

Implant dimensions were categorised into variables of three categories for implant length and diameter, where the length of the implants was classified as short (<10 mm), standard (≥10-<13 mm), or long (13-18 mm), and the diameter was classified as narrow (≥3-<3.75 mm), standard (≥3.75-<5 mm), or wide (5-7 mm) (Al-Johany et al., 2017).

Implant placement protocols were categorised into three main groups according to the time gap between tooth extraction and implantation (Gallucci et al., 2018). These include *immediate placement*, where the implant is inserted into the fresh extraction socket on the same day as the tooth extraction; *early placement*, where the implant is placed within 16 weeks after tooth extraction; and *late placement*, in which the implant is placed more than 16 weeks after the tooth extraction.

The healing modes of implants were categorised as either submerged healing for implants placed according to the two-stage surgical technique in which the implant is placed in one procedure and the abutment is connected in another, or transmucosal healing for implants placed according to the one-stage surgical technique in which implant placement and abutment connection are performed in the same procedure (Hämmerle et al., 2012).

Bone quality at the implant placement site was classified into four categories according to Lekholm and Zarb (1985) classification, which is based on the proportion of compact and cancellous bone, with type 1 consisting mainly of homogenous cortical bone, type 2 consisting of a thick layer of cortical bone surrounding a core of dense trabecular bone, type 3 consisting of a thin layer of cortical bone surrounding a core of dense trabecular bone, and type 4 consisting of a very thin layer of cortical bone surrounding a core of low-density trabecular bone. Bone quality was assessed by the surgeons at implant placement using tactile evaluation during bone drilling in addition to the clinical and radiographical assessment of the alveolar crest. Additionally, surgeons recorded implant insertion torques as a measure of primary stability, which were grouped into four categories: <8, 8-19, 20-50, and >50 N/cm.

Alveolar bone defects at the implant site were classified according to Terheyden (2010) classification based on the relationship between the bone defect and the planned implant position (Figure 4.1). The classification is as follows:

-Type 1/4 defect: Buccal bone defect up to 50% of the length of the planned implant.

-Type 2/4 defect: Buccal bone defect over 50% of the length of the planned implant.

-Type 3/4 defect: Buccal bone defect over 50% and palatal/lingual bone defect up to 50% of the length of the planned implant.

-Type 4/4 defect: Buccal and palatal/lingual bone defect of more than 50% of the length of the planned implant.

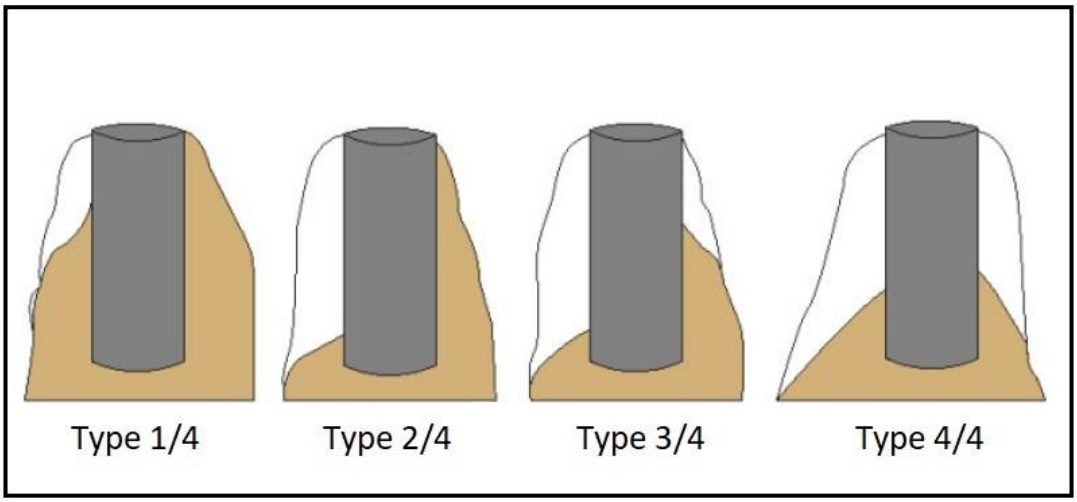


Figure 4.1 Classification of alveolar bone defects (Terheyden, 2010), used with permission

Bone augmentation procedures were grouped according to the timing of bone grafting relative to the time of implant placement into three groups: prior, simultaneous and staged (including both prior and simultaneous graftings). The type of augmentation procedure and the frequency of augmentation per implant site were also reported. Bone augmentation materials used were categorized as autologous bone grafts, bone substitutes (BSM), or a combination of both.

Data were tabulated and analysed using Stata 17.0 statistical software (Stata Corporation, College Station, TX, USA). Descriptive statistics (mean, median, standard deviation (SD), range, frequency and per cent) were used to summarise data and characterise the distribution of values for study variables. To evaluate linear trends over time or associations between variables, we fitted appropriate multilevel mixed models to account for clustering of implants within patients and centres. Where 3 level models didn't converge, 2-level models (implant and patient) were fitted as the intraclass correlation coefficients were generally very low for centres.

4.3. Results

The available dataset included a total of 150,896 dental implants, which were placed in 63,414 patients in 21 different dental practices during the period from 1st January 2010 to 31st December 2022 (Tables 1 and 3). The median number of implants placed per patient during the study period was 2 (range 1 to 24) (Figure 4.2). More data (90,700 implants / 38,918 patients) was obtained for the period from 2016 to 2022 compared to the period from 2010 to 2015 (60,196 implants / 24,496 patients). Furthermore, some patients' characteristics data, such as medical history and smoking status, and implant-related characteristics data, such as bone quantity at the implant site, were only available for patients who received dental implants from January 2016 onwards (period 2).

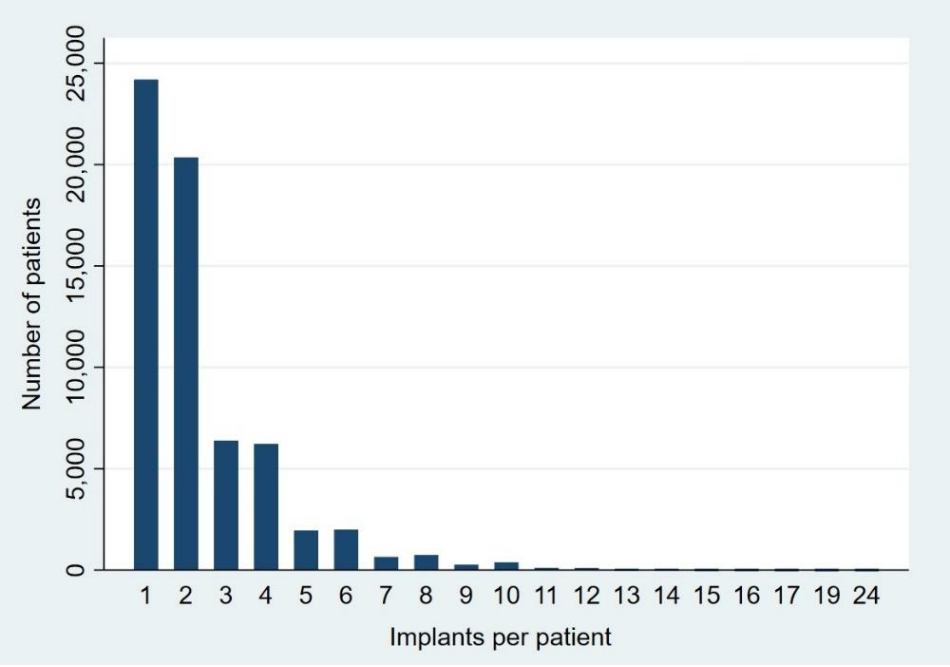


Figure 4.2 Number of implants placed per patient

4.3.1. Patient-related characteristics

Patients' characteristics are presented in Table 4.1.

Table 4.1- Patients' characteristics

Characteristics	2010-2015	2016-2022	Overall
Patients__No.	24,496	38,918	63,414
Age			
(Mean ± SD) yrs	58.5±12.6	60.5±12.4	59.7±12.5
Sex__no(%)			
Males	11,348 (46.3%)	18,560 (47.7%)	29,908 (47.2%)
Females	13,148 (53.7%)	20,358 (52.3%)	33,506 (52.8%)
Diabetes__no(%)			
No		26,076 (67%)	26,076 (67%)
Yes		1,582 (4.1%)	1,582 (4.1%)
Missing		11,260 (28.9%)*	11,260 (28.9%)
Diabetes type__no(%)			
Type 1		204 (13%)	204 (13%)
Type 2		1,052 (66.5%)	1,052 (66.5%)
Not specified		326 (20.5%)	326 (20.5%)
Diabetes treatment__no(%)			
Insulin injection		226 (14.3%)	226 (14.3%)
Tablets		729 (46.1%)	729 (46.1%)
Both		89 (5.6%)	89 (5.6%)
Not specified		538 (34%)	538 (34%)
Smoking status__no(%)			
Never		18,348 (47.2%)	18,348 (47.2%)
Former		5,079 (13%)	5,079 (13%)
Current		4,077 (10.5%)	4,077 (10.5%)
Missing		11,414 (29.3%)*	11,414 (29.3%)

Table 4.1- Continued			
Characteristics	**2010-2015**	**2016-2022**	**Overall**
Smoking dose__no(%)**			
Former smokers			
<5 cig		924 (18.2%)	924 (18.2%)
5-15 cig		1,980 (39%)	1,980 (39%)
15+ cig		1,632 (32.1%)	1,632 (32.1%)
Missing		543 (10.7%)	543 (10.7%)
Current smokers			
<5 cig		773 (19%)	773 (19%)
5-15 cig		1,906 (46.7%)	1,906 (46.7%)
15+ cig		1,052 (25.8%)	1,052 (25.8%)
Missing		346 (8.5%)	346 (8.5%)

* Four centres 1, 6, 11, 17) with large patient numbers did not record medical history in the implant database.
** Ever smokers only.

4.3.1.1. Age and sex

Patients included in this dataset were composed of 29,908 males (47.2%) and 33,506 females (52.8%), ranging in age from 18 to 90 years, with a mean age of 59.7 years (SD = 12.5) at the time of implantation. There were slightly more dental implants inserted in females than in males in this dataset (77,564 (51.4%) and 73,332 (48.6%), respectively).

Out of the 63,414 patients who received dental implants, approximately 74% were older than 50 years at the time of implant placement, with a mean age of 64.3 years (SD = 8.6) (Table 4.2, Figure 4.3). Moreover, there was an upward trend in the age of the patients receiving dental implants over the 13-year data collection period (Figures 4.4 A, B, p for trend <0.001).

Table 4.2 Age distribution of patients receiving dental implants during the years 2010–2022

Age	No. of patients (%)	Males	Females	No. of implants (%)
18-30	2234 (3.5%)	1034	1200	3281 (2.17%)
30-40	4703 (7.4%)	2089	2614	7456 (4.94%)
40-50	9901 (15.6%)	4519	5382	18860 (12.50%)
50-60	18012 (28.4%)	8440	9572	43539 (28.85%)
60-70	16765 (26.5%)	8019	8746	46312 (30.69%)
70-80	9729 (15.3%)	4797	4932	26212 (17.37%)
80-90	2070 (3.3%)	1010	1060	5236 (3.47%)
Total	63414 (100%)	29908	33506	150896 (100%)

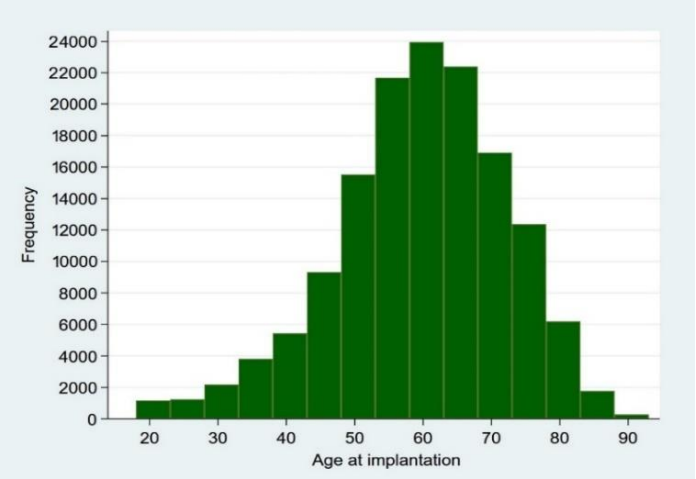


Figure 4.3 Distribution of age at the time of implantation

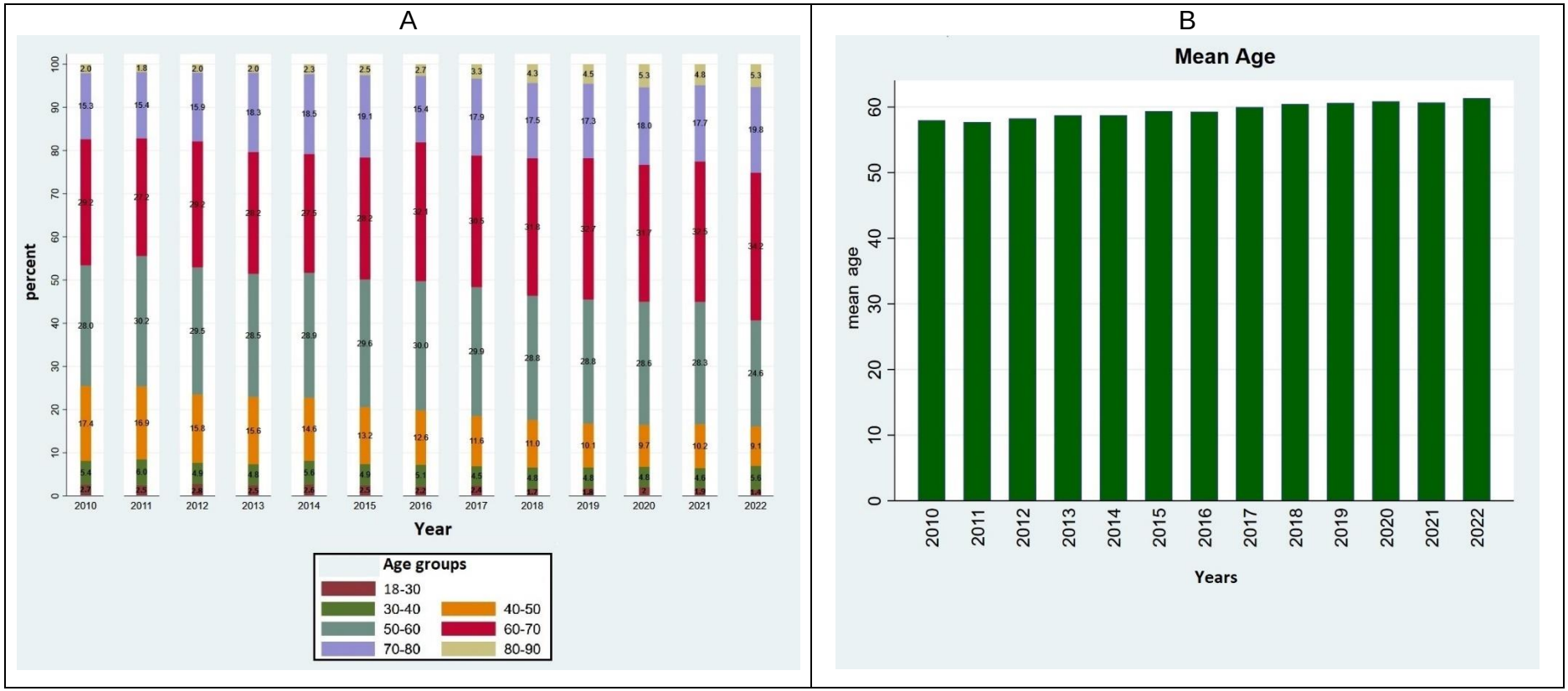


Figure 4.4 (A) Proportional representation of age categories by year. (B) Mean age by year

4.3.1.2 Diabetes and Smoking

For the 2016-2022 part of the dataset, in which we have the patients' medical history and smoking status, 38,918 patients, representing about 61% of all patients across the dataset, were treated during this period and received a total of 90,700 implants. Of these patients, 1,582 (4.1%) had diabetes, with 204 patients (13%) having type 1 diabetes, 1,052 patients (66.5%) having type 2 diabetes, and the diabetes type was not specified in 362 (20.5%) patients (Table 4.1). The diabetes treatment mode (insulin therapy or tablets) was also reported in Table 4.1.

Regarding smoking status, subjects with current or past smoking history were reported in this dataset. There were 4,077 (10.5%) smokers and 23,427 (60.2%) non-smoking patients at the time of implant placement. 5,079 (13%) patients reported being former smokers, whereas 18,348 (47.2%) patients reported having never smoked. Smoking status data was missing for 11,414 (29.3%) patients (Table 4.1).

Current smokers reported the number of cigarettes smoked daily and were further classified by the average number of cigarettes smoked per day (<5, 5-15, >15) (Table 4.1). The majority of current smokers (46.7%) reported smoking between 5 and 15 cigarettes per day. For former smokers, previous smoking doses were also reported in this dataset (Table 4.1).

4.3.2. Implant-related characteristics

Implants characteristics are described in Table 4.3.

Table 4.3 Implant-related characteristics

Characteristics	2010-2015	2016-2022	Overall
Implants__no	60,196	90,700	150,896
Site (Max-Mand) __no(%)			
Maxilla	33,025 (55%)	49,815 (55%)	82,840 (55%)
Mandible	27,171 (45%)	40,885 (45%)	68,056 (45%)
Site (Ant-Post) __no(%)			
Anterior	14,881 (24.7%)	21,797 (24%)	36,678 (24.3%)
Posterior	45,315 (75.3%)	68,903 (76%)	114,218 (75.7%)
Implant length			
Mean__mm	11.2±1.9	10.9±1.8	11±1.8
Length class__no(%)			
short(<10)	11,760 (19.5%)	20,244 (22.3%)	32,004 (21.2%)
Standard(≥10-<13)	32,317 (53.7%)	52,192 (57.6%)	84,509 (56%)
long(13-18)	16,119 (26.8%)	18,264 (20.1%)	34,383 (22.8%)
Implant diameter			
Mean__mm	4.15±0.52	4.12±0.49	4.13±0.5
Diameter class __no(%)			
Narrow(≥3-<3.75)	11,328 (18.8%)	13,969 (15.4%)	25,297 (16.8%)
Standard(≥3.75-<5)	41,606 (69.1%)	67,712 (74.7%)	109,318 (72.4%)
Wide(5-7)	7,262 (12.1%)	9,019 (9.9%)	16,281 (10.8%)
Implant brand			
Camlog	16865 (28%)	32289 (35.6%)	49154 (32.6%)
Straumann	10497 (17.4%)	17020 (18.8%)	27517 (18.2%)
Neoss	10542 (17.5%)	15926 (17.6%)	26468 (17.5%)
Nobel Biocare	6318 (10.5%)	11278 (12.4%)	17596 (11.7%)
Ankylos	6173 (10.3%)	6434 (7.1%)	12607 (8.4%)
Astra Tech	6457 (10.7%)	2807 (3.1%)	9264 (6.1%)
Other	3344 (5.6%)	4946 (5.5%)	8290 (5.5%)

Table 4.3- Continued

Characteristics	2010-2015	2016-2022	Overall
Implant placement timing			
Immediate	3,407 (5.7%)	9,551 (10.5%)	12,958 (8.6%)
Early (<16 wks)	844 (1.4%)	8,351 (9.2%)	9,195 (6.1%)
Late (>16 wks)	54,069 (89.8%)	72,796 (80.3%)	126,865 (84.1%)
Missing	1,876 (3.1%)	0	1,878 (1.2%)
Healing mode			
Submerged	41,820 (69.5%)	69,198 (76.3%)	111,018 (73.6%)
Transmucosal	11,760 (19.5%)	19,271 (21.2%)	31,031 (20.6%)
Missing	6,616 (11%)	2,231 (2.5%)	8,847 (5.8%)
Bone quality__no(%)			
Type 1	9,767 (16.2%)	15,076 (16.6%)	24,843 (16.5%)
Type 2	22,139 (36.8%)	41,086 (45.3%)	63,225 (41.9%)
Type 3	15,081 (25%)	25,281 (27.9%)	40,362 (26.7%)
Type 4	4,677 (7.8%)	6,687 (7.4%)	11,364 (7.5%)
Missing	8,532 (14.2%)	2,570 (2.8%)	11,102 (7.4%)
Primary implant stability (Insertion torque_N/cm)			
<8	456 (0.8%)	1,479 (1.7%)	1,935 (1.3%)
8-19	3,110 (5.2%)	10,737 (11.8%)	13,847 (9.2%)
20-50	36,480 (60.6%)	54,422 (60%)	90,902 (60.2%)
>50	3,743 (6.2%)	21,317 (23.5%)	25,060 (16.6%)
Missing	16,407 (27.2%)	2,745 (3%)	19,152 (12.7%)
Bone defects__no(%)*			
No (sufficient bone)		42,679 (47%)	42,679 (47%)
Yes		34,916 (38.5%)	34,916 (38.5%)
Type 1/4		16,312 (46.7%)	16,312 (46.7%)
Type 2/4		7,532 (21.6%)	7,532 (21.6%)
Type 3/4		2,707 (7.8%)	2,707 (7.8%)
Type 4/4		5,451 (15.6%)	5,451 (15.6%)
Other		2,914 (8.3%)	2,914 (8.3%)
Missing		13,105 (14.5%)	13,105 (14.5%)

Table 4.3- Continued			
Characteristics	**2010-2015**	**2016-2022**	**Overall**
Augmentation__no(%)			
No	36,531 (60.7%)	42,679 (47.1)	79,210 (52.5%)
Yes	23,665 (39.3%)	48,021 (52.9%)	71,686 (47.5%)
Augmentation Timing __no(%) (Relative to implantation)			
Same	16,469 (69.6%)	39,418 (82.1%)	55,887 (77.9%)
Before	6,519 (27.5%)	6,932 (14.4%)	13,451 (18.8%)
Both (Before+Same	677 (2.9%)	1,671 (3.5%)	2,348 (3.3%)
Augmentation Frequency__Mean (Per implant site)	1±0.18	1±0.19	1±0.19
1 time	22,949 (97%)	46,250 (96.3%)	69,199 (96.5%)
2 times	693 (2.9%)	1,714 (3.6%)	2,407 (3.4%)
3 times	21 (0.1%)	52 (0.1%)	73 (0.1%)
4 times	0	3	3
5 times	2	2	4
Augmentation Materials__no(%)			
Autlologous	7,389 (31.2%)	13,749 (28.6%)	21,138 (29.5%)
BSM	5,522 (23.3%)	10,703 (22.3%)	16,225 (22.6%)
Both	9,503 (40.2%)	21,265 (44.3%)	30,768 (42.9%)
Missing	1,251 (5.3%)	2,304 (4.8%)	3,555 (5%)
Augmentation techniques			
Sinus lift	11100 (34.8%)	19073 (29.5%)	30173 (31.2%)
Apposition(Horizontal)	12598 (39.5%)	26564 (41%)	39162 (40.5%)
Onlay	4126 (12.9%)	7339 (11.3%)	11465 (11.9%)
Inlay	1573 (4.9%)	5415 (8.4%)	6988 (7.2%)
Socket preservation	1091 (3.4%)	3923 (6.1%)	5014 (5.2%)
Spreading	471 (1.5%)	826 (1.3%)	1297 (1.3%)
Splitting	634 (2%)	887 (1.4%)	1521 (1.6%)
Distraction	136 (0.4%)	194 (0.3%)	330 (0.3%)
Shell technique	34 (0.1%)	309 (0.5%)	343 (0.4%)
Sandwich technique	133 (0.4%)	136 (0.2%)	269 (0.3%)

* Data on bone defects was only available for the (2016-2022) period.

4.3.2.1. Implant site

The location of the implant was determined by the tooth it replaced (Figure 4.5). The most common site for implant placement was the first molar region of the mandible (24,550 implants/16.3%), followed by the first molar region (21,839 implants/14.5%) and the first premolar region (15,486 implants/10.3%) of the maxilla (Table 4.4). More implants were reported to be placed in the upper jaw than in the lower jaw (82,840 implants (55%) versus 68,056 implants (45%)). In addition, there were more implants placed in the posterior regions (premolars and molars) of both jaws (114,218 implants/75.7%) than in the anterior regions (canine to canine) (36,678 implants/24.3%). Implant-related characteristics based on the site of implantation are presented in Table 4.4

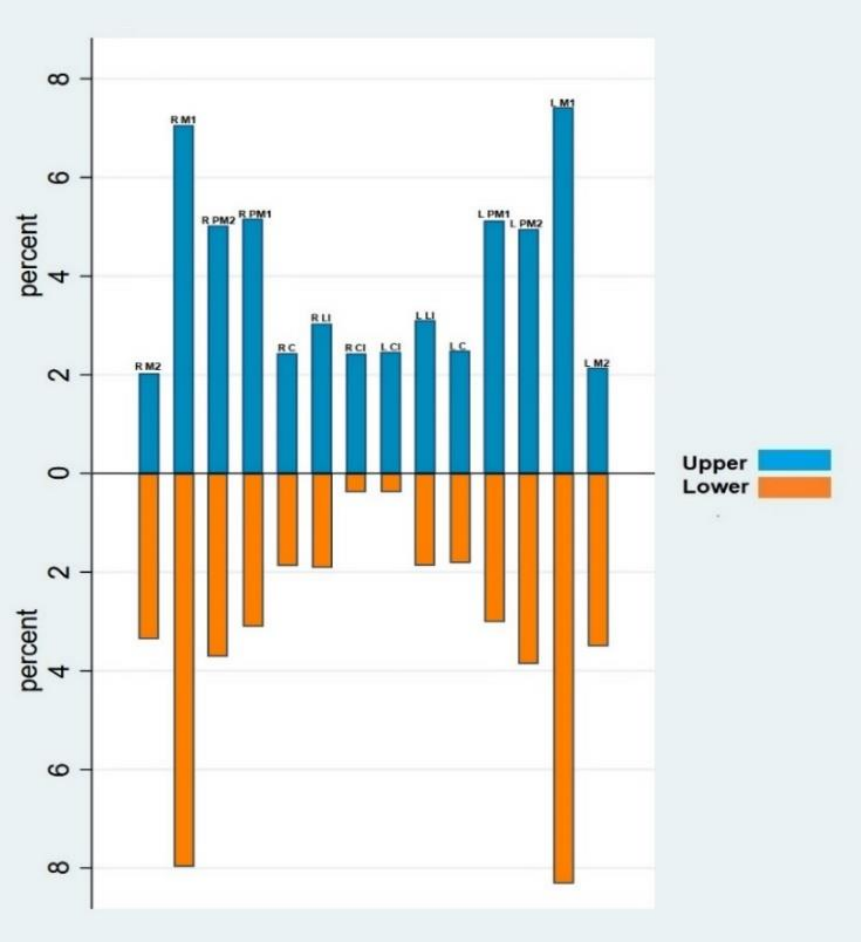


Figure 4.5 Chart-like representation of the distribution of implants according to their locations

Table 4.4- Implant characteristics for each site

Characteristics	Maxilla							Mandible						
	Central Incisor	Lateral Incisor	Canine	1st premolar	2nd Premolar	1st Molar	2nd Molar	Central Incisor	Lateral Incisor	Canine	1st premolar	2nd Premolar	1st Molar	2nd Molar
Implants__no	7402	9295	7469	15486	15035	21839	6314	1165	5785	5562	9237	11420	24550	10337
Implant length														
Mean__mm	12.1±1.8	12.1±1.9	12±1.9	11.5±1.7	11.1±1.8	10.6±1.5	10.4±1.5	11.9±1.8	12.1±1.9	11.8±1.9	11.2±1.7	10.6±1.9	10.3±1.5	9.8±1.5
Length class__no(%)														
Short(<10)	566 (7.7%)	676 (7.3%)	729 (9.8%)	1738 (11.2%)	2741 (18.2%)	5575 (25.5%)	1909 (30.2%)	108 (9.3%)	497 (8.6%)	631 (11.3%)	1536 (16.6%)	3383 (29.6%)	7252 (29.5%)	4663 (45.1%)
Standard (≥10-<13)	3441 (46.5%)	4249 (45.7%)	3621 (48.5%)	8841 (57.1%)	8963 (59.6%)	13435 (61.5%)	3782 (59.9%)	566 (48.6%)	2598 (44.9%)	2704 (48.6%)	5256 (56.9%)	6447 (56.5%)	15321 (62.4%)	5285 (51.1%)
long(13-18)	3395 (45.9%)	4370 (47%)	3119 (41.7%)	4907 (31.7%)	3331 (22.2%)	2829 (13%)	623 (9.9%)	491 (42.2%)	2690 (46.5%)	2227 (40%)	2445 (26.5%)	1590 (13.9%)	1977 (8.1%)	389 (3.7%)
Implant diameter														
Mean__mm	3.96±0.39	3.77±0.39	3.92±0.38	3.95±0.38	4.06±0.42	4.44±0.51	4.52±0.49	3.57±0.42	3.80±0.36	3.92±0.36	3.92±0.36	4.01±0.4	4.35±0.49	4.41±0.48
Diameter class __no(%)														
Narrow (≥3-<3.75)	1697 (22.9%)	4023 (43.3%)	1895 (25.4%)	3380 (21.8%)	2416 (16.1%)	1232 (5.6%)	185 (2.9%)	704 (60.4%)	2004 (34.6%)	1256 (22.6%)	2105 (22.8%)	2038 (17.9%)	1808 (7.4%)	554 (5.4%)
Standard (≥3.75-<5)	5488 (74.1%)	5157 (55.5%)	5421 (72.5%)	11649 (75.2%)	11713 (77.9%)	15348 (70.2%)	4375 (69.23%)	451 (38.7%)	3747 (64.8%)	4195 (75.4%)	6968 (75.4%)	8883 (77.8%)	18209 (74.2%)	7714 (74.6%)
Wide(5-7)	217 (2.9%)	115 (1.2%)	153 (2.1%)	457 (3%)	906 (6%)	5259 (24.1%)	1754 (27.8%)	10 (0.9%)	34 (0.6%)	111 (2%)	164 (1.8%)	499 (4.4%)	4533 (18.5%)	2069 (20%)

Table 4.4- Continued

Characteristics	Maxilla							Mandible						
	Central Incisor	Lateral Incisor	Canine	1st premolar	2nd Premolar	1st Molar	2nd Molar	Central Incisor	Lateral Incisor	Canine	1st premolar	2nd Premolar	1st Molar	2nd Molar
Implant brand														
Camlog	1283 (30.9%)	1251 (28%)	1052 (29%)	2461 (32.9%)	2645 (31.5%)	5445 (35.5%)	1526 (36%)	134 (25.1%)	367 (21.3%)	364 (21.6%)	920 (27.8%)	1251 (28.1%)	2615 (30.5%)	1020 (29.7%)
Straumann	738 (17.8%)	888 (19.9%)	693 (19.1%)	1511 (20.2%)	1605 (19.1%)	2862 (18.7%)	786 (18.5%)	105 (19.7%)	506 (29.3%)	345 (20.5%)	823 (24.8%)	943 (21.2%)	2050 (23.9%)	845 (24.6%)
Neoss	874 (21.1%)	908 (20.2%)	949 (26.2%)	1668 (22.3%)	1860 (22.1%)	2955 (19.3%)	820 (19.3%)	120 (22.5%)	424 (24.6%)	609 (36.1%)	778 (23.5%)	1186 (26.6%)	2143 (25%)	855 (24.9%)
Nobel Biocare	635 (15.3%)	751 (16.8%)	392 (10.8%)	759 (10.2%)	1013 (12.1%)	1455 (9.5%)	391 (9.2%)	73 (13.7%)	171 (9.9%)	129 (7.7%)	310 (9.4%)	451 (10.1%)	722 (8.4%)	287 (8.4%)
Ankylos	233 (5.6%)	246 (5.5%)	238 (6.6%)	421 (5.6%)	538 (6.4%)	1090 (7.1%)	262 (6.2%)	14 (2.6%)	78 (4.5%)	89 (5.3%)	156 (4.7%)	224 (5%)	355 (4.1%)	136 (4%)
Astra Tech	247 (6%)	229 (5.1%)	153 (4.2%)	324 (4.3%)	366 (4.4%)	823 (5.4%)	271 (6.4%)	53 (9.9%)	55 (3.2%)	44 (2.6%)	131 (4%)	197 (4.4%)	335 (3.9%)	161 (4.7%)
Other	143 (3.4%)	189 (4.2%)	145 (4%)	327 (4.4%)	373 (4.4%)	704 (4.6%)	188 (4.4%)	34 (6.4%)	126 (7.3%)	106 (6.3%)	195 (5.9%)	204 (4.6%)	351 (4.1%)	135 (3.93%)
Implant placement timing														
Immediate	1333 (18%)	1905 (20.5%)	876 (11.7%)	1436 (9.3%)	1194 (7.9%)	998 (4.%)	246 (3.9%)	190 (16.3%)	1164 (20.1%)	532 (9.6%)	932 (10.1%)	926 (8.1%)	867 (3.5%)	359 (3.5%)
Early (<16wks)	680 (9.2%)	610 (6.6%)	510 (6.8%)	963 (6.2%)	870 (5.8%)	1143 (5.2%)	349 (5.5%)	94 (8.1%)	271 (4.7%)	307 (5.5%)	558 (6%)	707 (6.2%)	1512 (6.2%)	621 (6%)
Late (>16 wks)	5271 (71.2%)	6717 (72.3%)	5925 (79.3%)	12895 (83.3%)	12804 (85.2%)	19397 (88.8%)	5634 (89.2%)	873 (74.9%)	4300 (74.3%)	4644 (83.5%)	7648 (82.8%)	9662 (84.6%)	21877 (89.1%)	9218 (89.2%)
Missing	118 (1.6%)	63 (0.7%)	158 (2.1%)	192 (1.2%)	167 (1.1%)	301 (1.4%)	85 (1.4%)	8 (0.7%)	50 (0.9%)	79 (1.4%)	99 (1.1%)	125 (1.1%)	294 (1.2%)	139 (1.3%)

Table 4.4- Continued

Characteristics	Maxilla							Mandible						
	Central Incisor	Lateral Incisor	Canine	1st premolar	2nd Premolar	1st Molar	2nd Molar	Central Incisor	Lateral Incisor	Canine	1st premolar	2nd Premolar	1st Molar	2nd Molar
Healing mode														
Submerged	5545 (74.9%)	6611 (71.1%)	5817 (77.9%)	11691 (75.5%)	11360 (75.6%)	17394 (79.7%)	5192 (82.2%)	836 (71.8%)	3746 (64.8%)	3929 (70.6%)	6409 (69.4%)	7877 (67%)	17217 (70.1%)	7394 (71.5%)
Transmucosal	1377 (18.6%)	2226 (24%)	1126 (15.1%)	2904 (18.8%)	2806 (18.7%)	3146 (14.4%)	747 (11.8%)	265 (22.8%)	1719 (29.7%)	1282 (23.6%)	2246 (24.3%)	2916 (25.5%)	5944 (24.2%)	2327 (22.5%)
Missing	480 (6.5%)	458 (4.9%)	526 (7%)	891 (5.8%)	869 (5.8%)	1299 (6%)	375 (5.9%)	64 (5.5%)	320 (5.5%)	351 (6.3%)	582 (6.3%)	627 (5.5%)	1389 (5.7%)	616 (6%)
Bone quality__no(%)														
Type 1	804 (10.9%)	1015 (10.9%)	616 (8.3%)	1289 (8.3%)	1070 (7.1%)	1551 (7.1%)	317 (52%)	318 (27.3%)	1707 (29.5%)	1309 (23.5%)	2536 (27.5%)	3110 (27.2%)	6372 (26%)	2829 (27.4%)
Type 2	2920 (39.5%)	4102 (44.1%)	2836 (38%)	6567 (42.4%)	5970 (39.7%)	8424 (38.6%)	2006 (31.8%)	489 (42%)	2436 (42.1%)	2538 (45.6%)	4164 (45.1%)	5058 (44.3%)	11283 (46%)	4432 (42.9%)
Type 3	2348 (31.7%)	2974 (32%)	2469 (33.1%)	5148 (33.2%)	5166 (34.4%)	7666 (35.1%)	2406 (38.1%)	216 (18.5%)	1013 (17.5%)	955 (17.2%)	1495 (16.2%)	2102 (18.4%)	4450 (18.1%)	1954 (18.9%)
Type 4	716 (9.7%)	699 (7.5%)	814 (10.9%)	1396 (9%)	1711 (11.4%)	2585 (11.8%)	1094 (17.3%)	51 (4.4%)	239 (4.1%)	239 (4.3%)	314 (3.4%)	407 (3.6%)	722 (2.9%)	377 (3.7%)
Missing	614 (8.3%)	505 (5.4%)	734 (9.8%)	1086 (7%)	1118 (7.44%)	1613 (7.4%)	491 (7.8%)	91 (7.8%)	390 (6.7%)	521 (9.4%)	728 (7.9%)	743 (6.5%)	1723 (7%)	745 (7.2%)
Primary implant stability (Insertion torque_N/cm)														
<8	31 (0.4%)	48 (0.5%)	20 (0.3%)	51 (0.3%)	76 (0.5%)	166 (0.8%)	94 (1.5%)	4 (0.3%)	5 (0.1%)	8 (0.1%)	8 (0.1%)	27 (0.2%)	71 (0.3%)	42 (0.4%)
8-19	360 (4.9%)	416 (4.5%)	401 (5.4%)	668 (4.3%)	833 (5.5%)	1491 (6.8%)	654 (10.4%)	30 (2.6%)	95 (1.6%)	206 (3.7%)	217 (2.3%)	403 (3.5%)	808 (3.3%)	440 (4.3%)
20-50	4215 (56.9%)	5294 (57%)	4184 (56%)	8973 (57.9%)	8701 (57.9%)	12229 (56%)	3485 (55.2%)	679 (58.3%)	3087 (53.4%)	3096 (55.7%)	5077 (55%)	6559 (57.4%)	13977 (56.9%)	5919 (57.3%)
>50	482 (6.5%)	920 (9.9%)	364 (4.9%)	958 (6.2%)	805 (5.4%)	777 (3.6%)	130 (2.1%)	68 (5.8%)	687 (11.9%)	501 (9%)	663 (7.2%)	1126 (9.9%)	1968 (8%)	845 (8.2%)
Missing	2314 (31.3%)	2617 (28.2%)	2500 (33.5%)	4836 (31.2%)	4620 (30.7%)	7176 (32.9%)	1951 (30.9%)	384 (33%)	1911 (33%)	1751 (31.5%)	3272 (35.4%)	3305 (28.9%)	7726 (31.5%)	3091 (29.9%)

Table 4.4- Continued

Characteristics	Maxilla							Mandible						
	Central Incisor	Lateral Incisor	Canine	1st premolar	2nd Premolar	1st Molar	2nd Molar	Central Incisor	Lateral Incisor	Canine	1st premolar	2nd Premolar	1st Molar	2nd Molar
Bone defects__no(%)*														
No (sufficient bone)	1683 (38.6%)	2641 (46.8%)	1991 (45.7%)	4391 (46.5%)	3609 (40.2%)	3357 (25.2%)	972 26.1%)	325 (48.3%)	2294 (64.8%)	2048 (63.5%)	3317 (58.6%)	3685 (54.5%)	8745 (58.8%)	3621 (59%)
Yes	2030 (46.6%)	2372 (42%)	1819 (41.8)	3794 (40.2%)	3716 (41.4%)	6439 (48.3%)	1750 (47.1%)	261 (38.8%)	996 (28.1%)	862 (26.8%)	1840 (32.5)	2378 (35.2%)	4729 (31.7%)	1930 (31.5%)
Type 1/4	868 (42.8%)	992 (41.8%)	828 (45.5%)	1624 (42.8%)	1446 (38.9%)	2177 (33.8%)	537 (30.7%)	130 (49.8%)	481 (48.3%)	481 (55.8%)	1080 (58.7%)	1420 (59.7%)	3055 (64.6%)	1193 (61.8%)
Type 2/4	570 (28.1%)	583 24.6%)	481 (26.4%)	876 (23.1%)	646 (17.4%)	1187 (18.4%)	309 (17.7%)	67 (25.7%)	209 (20.9%)	210 (24.4%)	399 (21.7%)	573 (24.1%)	997 (21.1%)	425 (22%)
Type 3/4	238 (11.7%)	223 (9.4%)	190 (10.5%)	294 (7.8%)	263 (7.1%)	448 (6.9%)	141 (8.1%)	35 (13.4%)	91 (9.1%)	45 (5.2%)	137 (7.5%)	133 (5.6%)	320 (6.8%)	149 (7.7%)
Type 4/4	100 (4.9%)	125 (5.3%)	128 (7%)	622 (16.4%)	1051 (28.3%)	2275 (35.3%)	669 (38.2%)	10 (3.8%)	44 (4.4%)	29 (3.4%)	72 (3.9%)	90 (3.8%)	166 (3.5%)	70 (3.6%)
Other	254 (12.5%)	449 (18.9%)	192 (10.6%)	378 (9.9%)	310 (8.3%)	352 (5.5%)	94 (5.4%)	19 (7.3%)	171 (17.2%)	97 (11.3%)	152 (8.3%)	162 (6.8%)	191 (4%)	93 (4.8%)
Missing	644 (14.8%)	634 (11.2%)	543 (12.5%)	1256 (13.3%)	1649 (18.4%)	3528 (26.5%)	997 (26.8%)	87 (12.9%)	253 (7.1%)	314 (9.7%)	506 (8.9%)	699 (10.3%)	1411 (9.5%)	584 (9.5%)
Augmentation__no(%)														
Yes	4163 (56.2%)	4469 (48.1%)	3632 (48.6%)	7501 (48.4%)	8434 (56.1%)	15421 (70.6%)	4267 (67.6%)	534 (45.8%)	1728 (29.9%)	1690 (30.4%)	3318 (35.9%)	4468 (39.1%)	8606 (35.1%)	3455 (33.4%)
No	3239 (43.7%)	4826 (51.9%)	3837 (51.4%)	7985 (51.6%)	6601 (43.9%)	6418 (29.4%)	2047 (32.4%)	631 (54.2%)	4057 (70.1%)	3872 (69.6%)	5919 (64.1%)	6952 (60.9%)	15944 (65%)	6882 (66.6%)

Table 4.4- Continued

Characteristics	Maxilla							Mandible						
	Central Incisor	Lateral Incisor	Canine	1st premolar	2nd Premolar	1st Molar	2nd Molar	Central Incisor	Lateral Incisor	Canine	1st premolar	2nd Premolar	1st Molar	2nd Molar
Augmentation Timing __no(%) (Relative to implantation)														
Same	3055 (73.4%)	3578 (80.1%)	2839 (78.2%)	5827 (77.7%)	6546 (77.6%)	11139 (72.2%)	3100 (72.7%)	404 (75.7%)	1543 (89.3%)	1491 (88.2%)	2841 (85.6%)	3609 (80.8%)	7081 (82.3%)	2834 (82%)
Before	880 (21.1%)	738 (16.5%)	673 (18.5%)	1446 (19.3%)	1628 (19.3%)	3747 (24.3%)	1019 (23.9%)	98 (18.4%)	143 (8.3%)	157 (9.3%)	385 (11.6%)	715 (16%)	1282 (14.9%)	540 (15.6%)
Both (Before+Same	228 (5.5%)	153 (3.4%)	120 (3.3%)	228 (3%)	260 (3.1%)	535 (3.5%)	148 (3.5%)	32 (6%)	42 (2.4%)	42 (2.5%)	92 (2.8%)	144 (3.2%)	243 (2.8%)	81 (2.3%)
Augmentation Frequency__Mean (Per implant site)														
1 time	3922 (94.2%)	4307 (96.4%)	3506 (96.5%)	7262 (96.8%)	8158 (96.7%)	14856 (96.3%)	4111 (96.3%)	500 (93.6%)	1685 (97.5%)	1645 (97.3%)	3218 (97%)	4312 (96.5%)	8350 (97%)	3367 (97.5%)
2 times	232 (5.57%)	157 (3.51%)	120 (3.30%)	228 (3.04%)	267 (3.17%)	549 (3.56%)	153 (3.6%)	30 (5.6%)	41 (2.4%)	41 (2.43%)	96 (2.89%)	152 (3.40%)	253 (2.94%)	88 (2.55%)
3- times	9 (0.2%)	5 (0.1%)	6 (0.2%)	11 (0.15%)	9 (0.1%)	16 (0.10%)	3 (0.1%)	4 (0.8%)	2 (0.1%)	4 (0.2%)	4 (0.1%)	4 (0.1%)	3 (0.03%)	3367 (97.5%)
Augmentation Materials__no(%)														
Autologous	1380 (33.15%)	1255 (28.08%)	1128 (31.06%)	1786 (23.81%)	1983 (23.51%)	2715 (17.61%)	707 (16.57%)	219 (41.01%)	696 (40.28%)	869 (51.42%)	1409 (42.47%)	1884 (42.17%)	3607 (41.91%)	1500 (43.42%)
BSM	864 (20.75%)	1159 (25.93%)	818 (22.52%)	1769 (23.58%)	1823 (21.61%)	3515 (22.79%)	794 (18.61%)	115 (21.54%)	492 (28.47%)	318 (18.82%)	817 (24.62%)	975 (21.82%)	1980 (23.01%)	786 (22.75%)
Both	1770 (42.52%)	1897 (42.45%)	1509 (41.55%)	3585 (47.79%)	4035 (47.84%)	8149 (52.84%)	2450 (57.42%)	176 (32.96%)	489 (28.30%)	434 (25.68%)	994 (29.96%)	1466 (32.81%)	2733 (31.76%)	1081 (31.29%)
Missing	149 (3.58%)	158 (3.54%)	177 (4.87%)	361 (4.81%)	593 (7.03%)	1042 (6.76%)	316 (7.41%)	24 (4.49%)	51 (2.95%)	69 (4.08%)	98 (2.95%)	143 (3.20%)	286 (3.32%)	88 (2.55%)

Table 4.4- Continued

Characteristics	Maxilla							Mandible						
	Central Incisor	Lateral Incisor	Canine	1st premolar	2nd Premolar	1st Molar	2nd Molar	Central Incisor	Lateral Incisor	Canine	1st premolar	2nd Premolar	1st Molar	2nd Molar
Augmentation techniques														
Sinus lift	0	0	0	3972 (37.5%)	6457 (54.3%)	14221 (66.8%)	3926 (66.5%)	0	0	0	0	0	0	0
Apposition (Horizontal)	3014 (53.5%)	3184 (55.8%)	2416 (55.9%)	3881 (36.7%)	3170 (26.7%)	3869 (18.2%)	1047 (17.7%)	409 (56.3%)	1254 (57.9%)	1217 (57.8%)	2592 (61.9%)	3530 (63%)	6866 (64.3%)	2713 (63.5%)
Onlay	1143 (20.3%)	963 (16.9%)	751 (17.4%)	1019 (9.6%)	799 (6.7%)	1143 (5.4%)	337 (5.7%)	138 (19%)	340 (15.7%)	378 (17.9%)	709 (16.9%)	996 (17.8%)	1968 (18.4%)	781 (18.3%)
Inlay	622 (11%)	579 (10.2%)	471 (10.9%)	719 (6.8%)	665 (5.6%)	1097 (5.2%)	325 (5.5%)	87 (12%)	202 (9.3%)	202 (9.6%)	372 (8.9%)	434 (7.7%)	852 (8%)	361 (8.5%)
Socket preservation	504 (8.9%)	625 (11%)	357 (8.3%)	542 (5.1%)	441 (3.7%)	528 (2.5%)	147 (2.5%)	59 (8.1%)	276 (12.7%)	184 (8.7%)	312 (7.4%)	320 (5.7%)	477 (4.5%)	234 (5.5%)
Spreading	97 (1.7%)	102 (1.8%)	95 (2.2%)	194 (1.8%)	191 (1.6%)	249 (1.2%)	79 (1.3%)	9 (1.2%)	14 (0.6%)	13 (0.6%)	36 (0.9%)	68 (1.2%)	113 (1.1%)	37 (0.9%)
Splitting	138 (2.4%)	149 (2.6%)	160 (3.7%)	184 (1.7%)	109 (0.9%)	88 (0.4%)	20 (0.3%)	13 (1.8%)	62 (2.9%)	77 (3.7%)	103 (2.5%)	146 (2.6%)	206 (1.9%)	66 (1.5%)
Distraction	36 (0.6%)	35 (0.6%)	17 (0.4%)	32 (0.3%)	18 (0.2%)	31 (0.1%)	9 (0.2%)	5 (0.7%)	6 (0.3%)	16 (0.8%)	20 (0.5%)	33 (0.6%)	54 (0.5%)	18 (0.4%)
Shell technique	52 (0.9%)	41 (0.7%)	0	18 (0.2%)	14 (0.1%)	17 (0.1%)	0	4 (0.6%)	7 (0.3%)	0	22 (0.5%)	35 (0.6%)	56 (0.5%)	0

* Data on bone defects was only available for the (2016-2022) period.

4.3.2.2. Distribution of implants by length and diameter

Implants of different lengths and diameters were used and recorded in this dataset (Tables 4.3, 4.5, Figures 4.6, 4.7). About 56% of all implants were of standard length, and 72.5% were of standard diameter. Implants of both standard lengths and diameters were the most frequently used implants (62,293 implants/41.3%), followed by long implants with standard diameters (25,217 implants/16.7%), and the least used implants were the long ones with wide diameters (2,569 implants/1.7%) (Table 4.5).

Table 4.5 Distribution of implants based on their length and diameter

Length	Diameter			Total
	Narrow (>=3-<3.75)	Standard (>=3.75-<5	Wide (5-7)	
Short (<10)	5,176	21,808	5,020	32,004
Standard (>=10-<13)	13,524	62,293	8,692	84,509
Long (13-18)	6597	25,217	2,569	34,383
Total	25,297	109,318	16,281	150,896

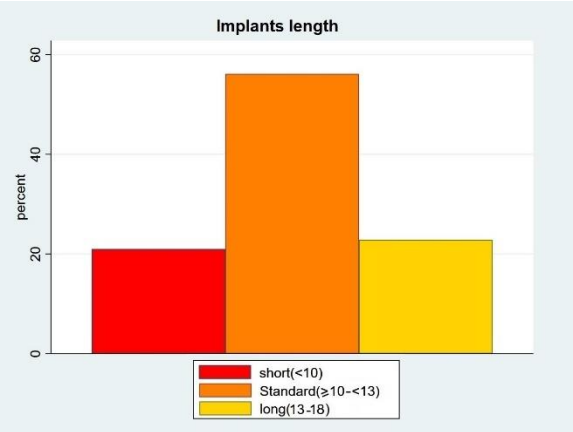


Figure 4.6 Implants' lengths

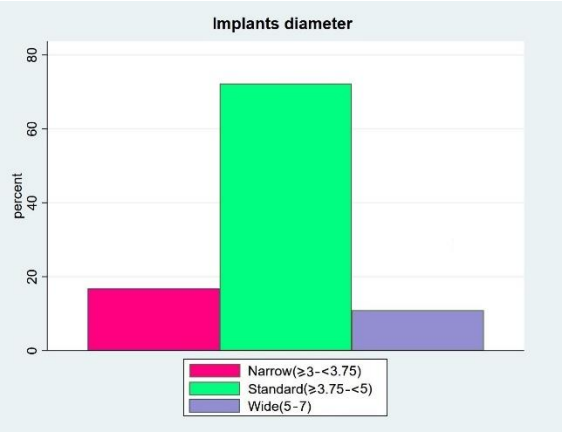


Figure 4.7 Implants' diameters

The lengths and diameters of the implants used varied according to the location in each jaw (Table 4.4, Figures 4.8, 4.9); long implants were more common in the anterior regions of both jaws (from canine to canine), while short implants were more common in the posterior regions (premolars and molars). Regarding implant diameter, narrow implants were more common in the anterior regions of both jaws, while wide implants were more common posteriorly.

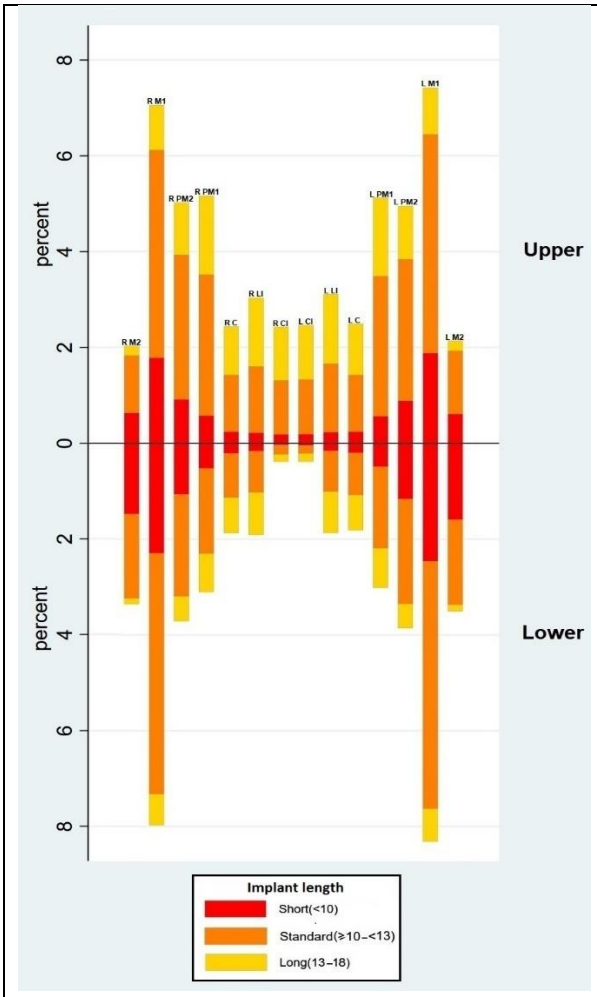


Figure 4.8 Chart-like representation of the distribution of implant lengths according to their locations

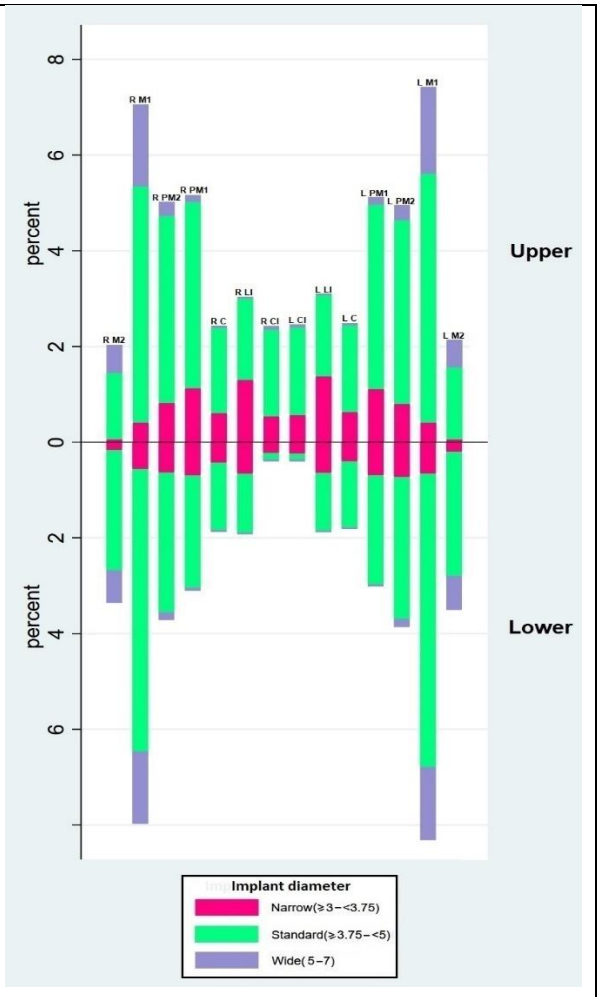


Figure 4.9 Chart-like representation of the distribution of implant diameters according to their locations

The proportion of different length and diameter classes was evaluated for each implant site. It was evident that implants of shorter lengths and wider diameters were used as we go posteriorly in the jaws (Table 4.4, Figures 4.10, 4.11).

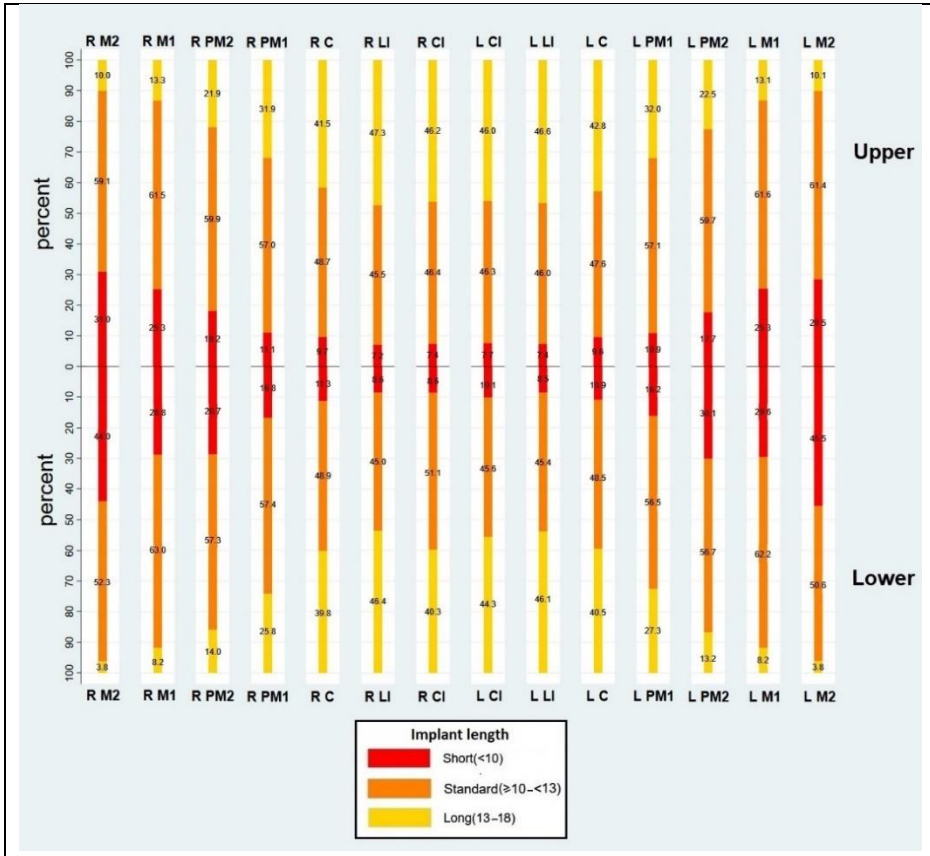


Figure 4.10 Chart-like representation of the proportion of implant lengths for each site

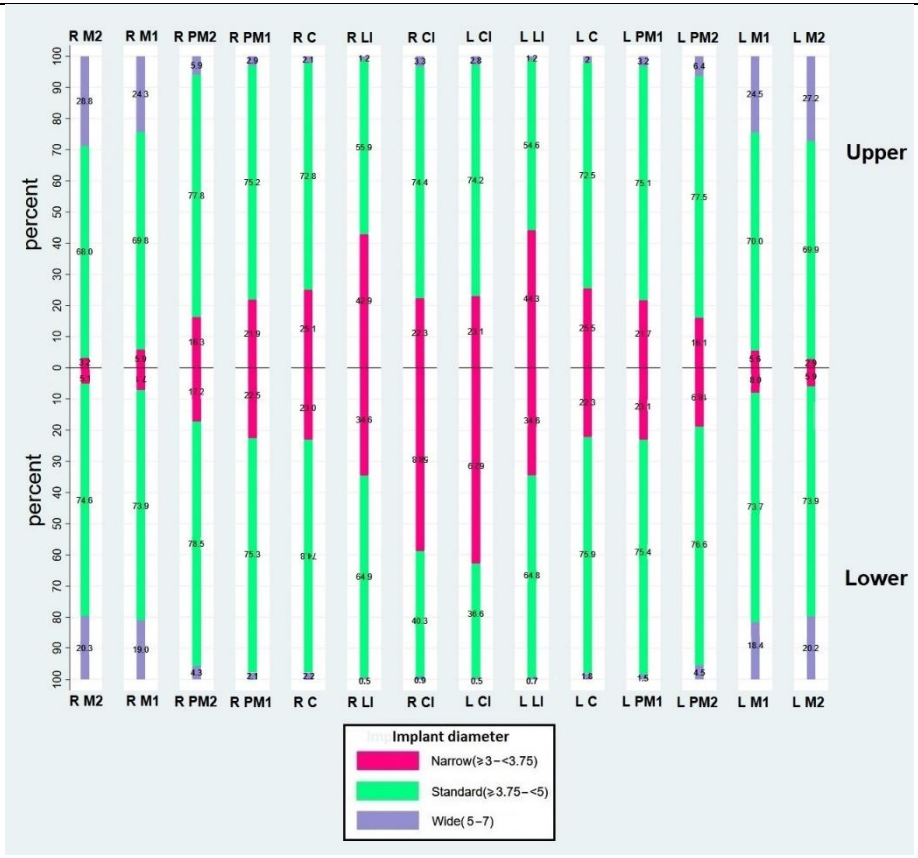


Figure 4.11 Chart-like representation of the proportion of implant diameters for each site

Over the 13-year data collection period, there was a clear trend towards using shorter implants (Figure 4.12). The reduction over time in implant lengths was statistically significant (p for trend <0.001, see Appendix 5). On the other hand, narrow and wide implants had become less used over the study years (Figure 4.13) (p < 0.001 for both trends, see appendix 5).

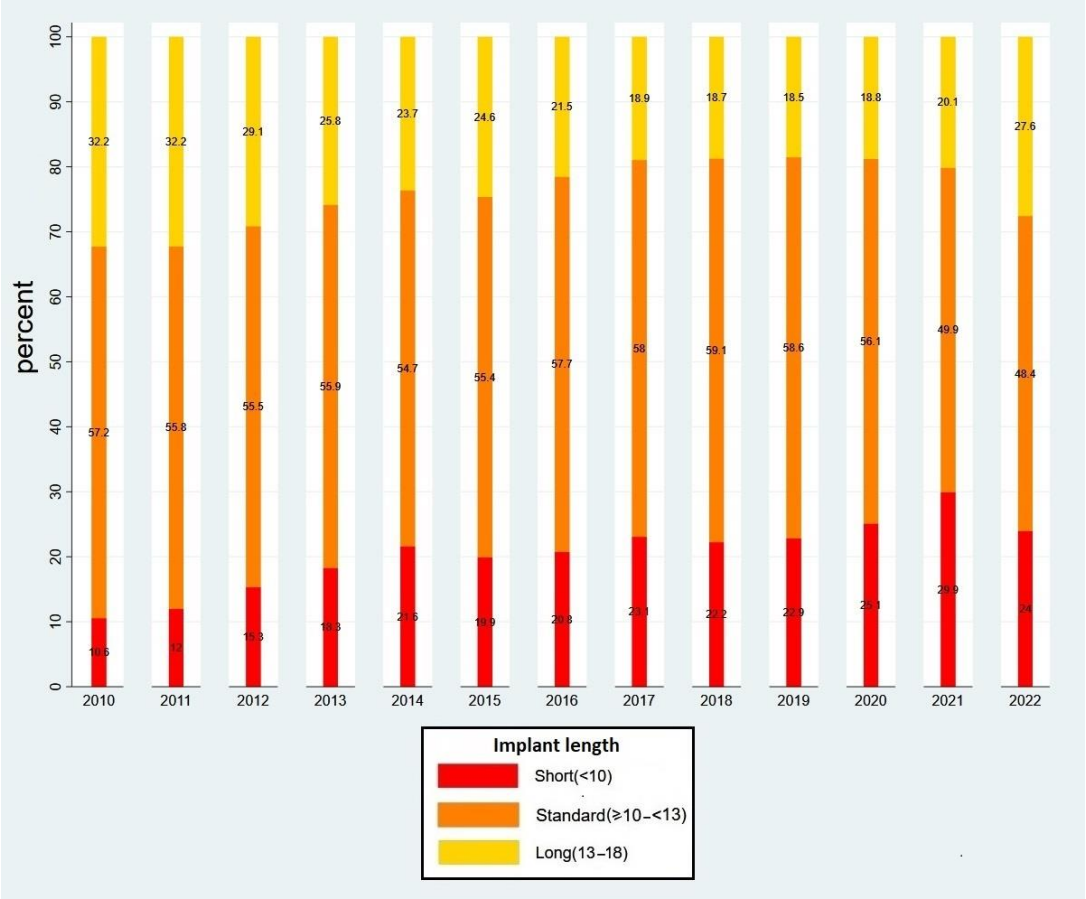


Figure 4.12 Proportional representation of implant lengths by year

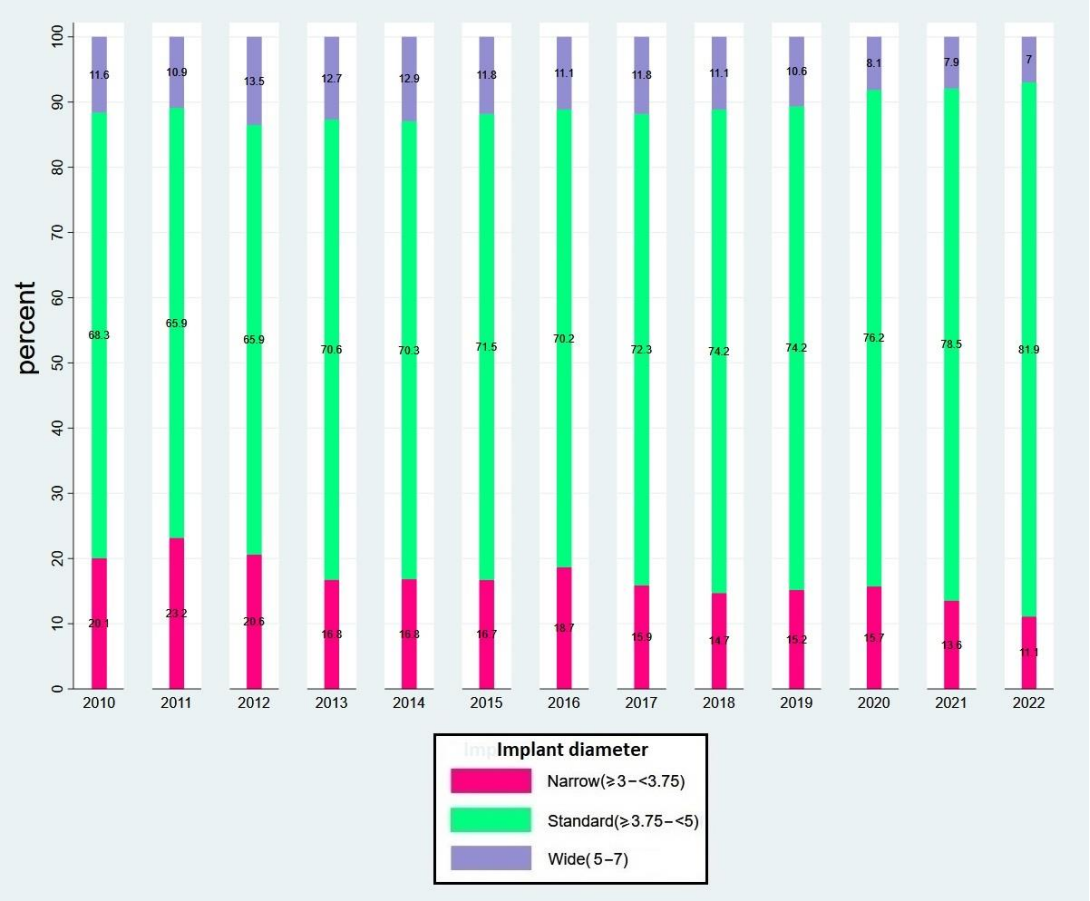


Figure 4.13 Proportional representation of implant diameters by year

4.3.2.3. Implant brands

This dataset included a wide range of implant systems that were grouped into seven categories based on their brand, as shown in Table 4.3. Four brands (Camlog, Straumann, Neoss, and Nobel Biocare) accounted for approximately 80% of all implants placed, with Camlog being the most common (32.6%), followed by Straumann (18.2%). Among the remaining 20%, Ankylos accounted for 8.4%, followed by Astra Tech with 6.1%.

4.3.2.4. Timing of implant placement

Out of all the implants placed,12,958 implants (8.6%) were placed immediately after extraction, while 9,195 implants (6.1%) were placed using the early placement protocol (within 16 weeks). Late implant placement, which refers to implant placement after 16 weeks, was the most frequently used protocol in this dataset, with 126,865 implants (84.1% of all implants placed) falling under this category (Tables 4.3, 4.4).

4.3.2.5. Healing mode

Healing mode data were reported for 142,049 (94.2%) and were missing in only a small proportion of cases (8,847 implants/5.8%) (Table 2,3). 111,018 implants (73.6%) were placed according to the two-stage surgical technique (Submerged implant), where the implant is inserted in one surgery, and the abutment is subsequently attached in another one. On the other hand, 31,031 implants (20.6%) were inserted according to the one-stage surgical technique (transmucosal implants), where both the implant placement and abutment connection are performed in the same procedure.

4.3.2.6 Bone quality

Bone quality was reported for 139,794 (92.6%) implants and was missing in 11,102 (7.4%) implant placement sites across this dataset (Table 4.3). Overall, bone quality type 2 was the most commonly reported bone quality (42%). However, different bone qualities were reported across different sites of patients' jaws (Table 4.4). Type 2 bone quality was the most common in both the maxilla and mandible, both anteriorly (canine to canine) and posteriorly (premolars and molars). Type 3 bone was more common in

maxillary sites than in mandibular sites, while type 1 was more common in mandibular sites than in maxillary sites (Figure 4.14).

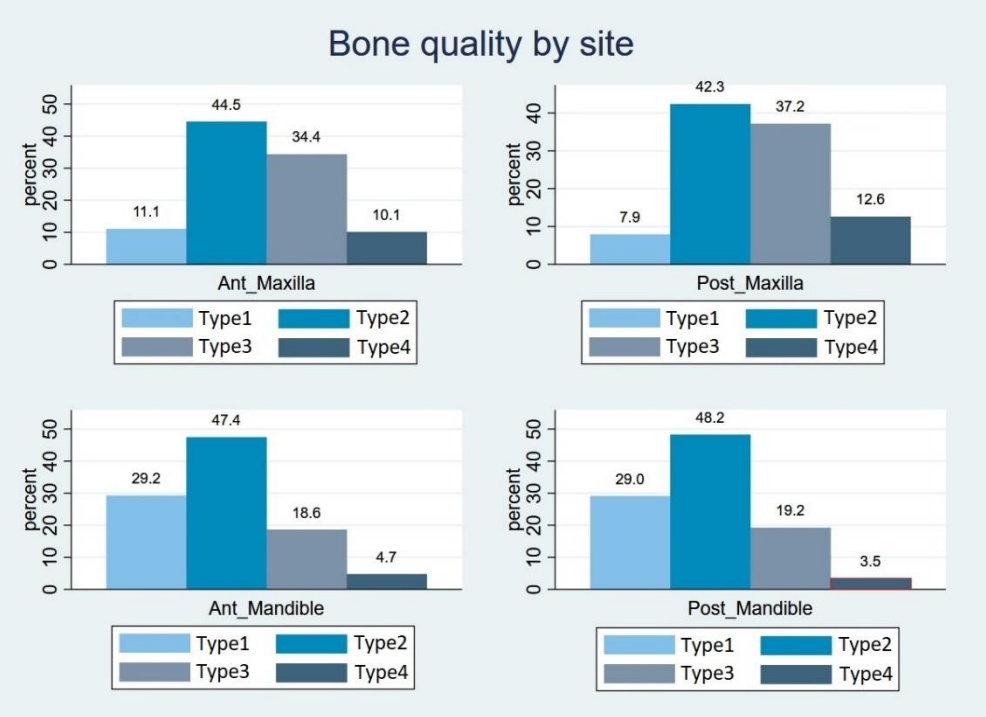


Figure 4.14 Bone quality by site

4.3.2.7. Primary stability

Primary implant stability was reported based on implant insertion torque for 131,744 implants, approximately 87% of all implants placed. Different insertion torques were reported for different implantation sites (Table 4.4). Of the implants with recorded insertion torques, 69% (90,902 implants) were inserted with torques ranging from 20-50 Ncm, 19% (25,060 implants) had torques greater than 50 N/cm, and 12% (15,782 implants) had insertion torques less than 20 Ncm.

Table 4.6 shows the distribution of insertion torque values over the four bone quality categories according to the classification of Lekholm and Zarb (1985). Higher torque values (>50 Ncm) were more common in type 1 bone (37.18%), followed by type 2

(19.07%), and less common in types 3 and 4 (11.10% and 8.92%, respectively). There was a significant positive association between insertion torque and bone quality ($p < 0.001$, see Appendix 6)

Table 4.6 Implants' insertion torques for different bone qualities

Bone quality	Insertion torque				
	<8	**8-19**	**20-50**	**>50**	**Total**
Type 1	79 (0.35%)	497 (2.19%)	13659 (60.28%)	8425 (37.18%)	22660 100%)
Type 2	400 (0.67%)	2935 (4.95%)	44655 (75.31%)	11306 (19.07%)	59296 100%)
Type 3	593 (1.56%)	7878 (20.79%)	25220 (66.55%)	4208 (11.10%)	37899 100%)
Type 4	841%) (8.37%)	2421 (24.09%)	5890 (58.62%)	896 (8.92%)	10048 100%)

4.3.2.8. Bone quantity

Data on bone quantity was only available for the 2016-2022 period, and it was reported for 77,595 implantation sites, representing approximately 85.5% of all reported implant sites from 2016-2022 (Table 4.3). About 55% (42,679) of these sites had a relatively adequate amount of bone with no bone defects, while 45% (34,916) had some type of bone defects based Terheyden (2010) classification of alveolar bone defects. The most common type of bone defect reported was type 1/4 (Buccal bone defect up to 50% of the length of the planned implant), accounting for 46.7% of all reported defects (Table 4.3). Table 4.4 shows the proportion of bone defects by implant site. The maxillary first and second molars sites had the highest proportion of type 4/4 defect (35.3% and 38.2%, respectively), which represents vertical bone defects, while the mandibular first and second molars sites had the highest proportion of type 1/4 defect (64.6% and 61.8% respectively).

4.3.2.9. Bone augmentation

A total of 71,686 implant sites (47.5%) required bone augmentation, and different augmentation techniques were used (Table 4.3). More augmentations were reported in the maxilla than in the mandible (67% vs. 33%) and posteriorly than anteriorly (77.4% vs. 22.6%) (Table 4.4, Figure 4.15).

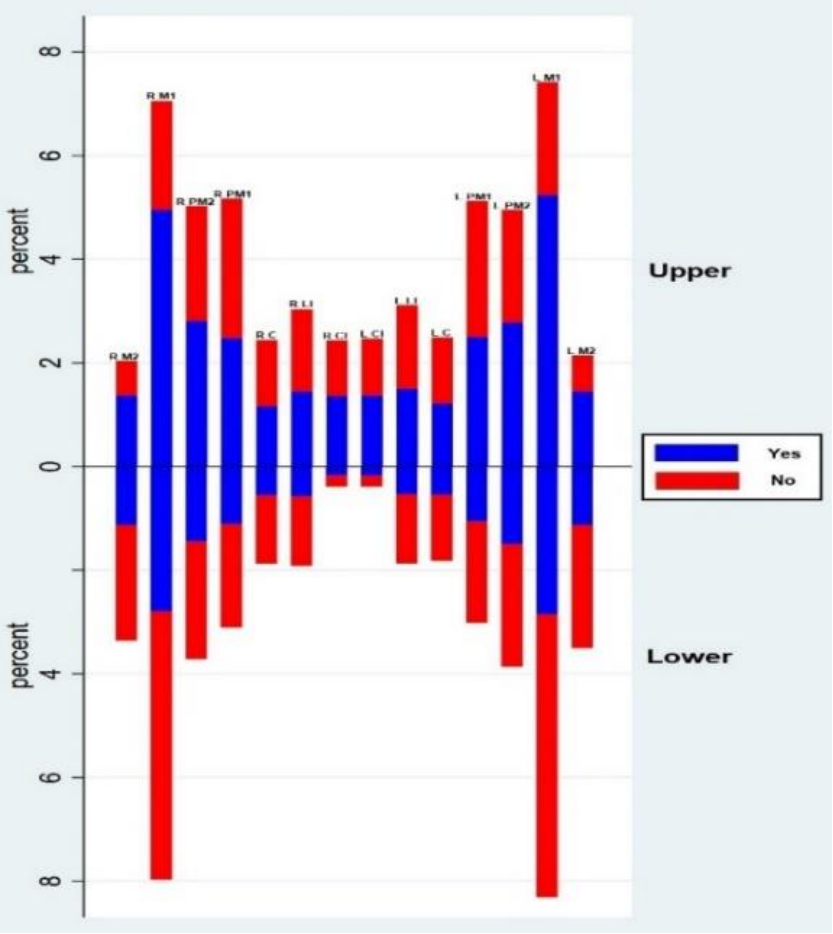


Figure 4.15 Chart-like representation of the distribution of bone augmentations by sites

The proportion of bone augmentation was evaluated for each implant site (Table 4.4, Figure 4.16). The maxillary first and second molar sites had the highest proportion of augmentation procedures performed (70.6% and 67.6%, respectively). In the mandible, the mandibular incisors sites had the highest proportion (45.8%).

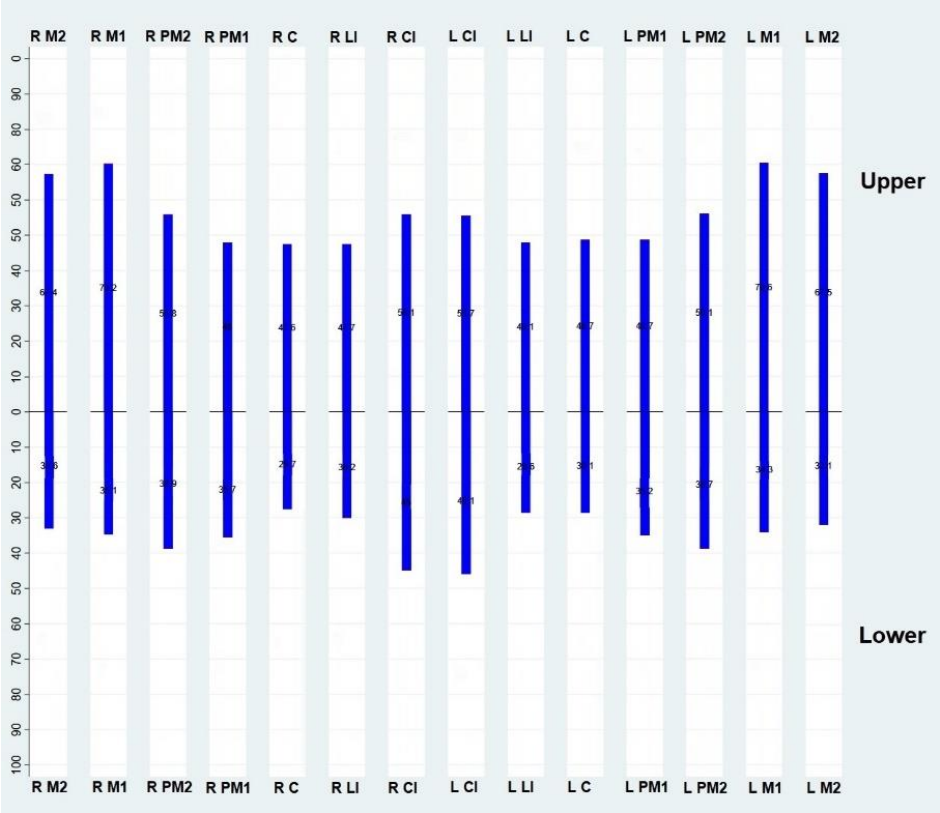


Figure 4.16 Chart-like representation of the proportion of bone augmentations for each site

Bone augmentation procedures were grouped according to the timing of bone grafting relative to the time of implant placement into three groups: prior, simultaneous or staged (including both prior and simultaneous) (Table 4.3). Simultaneous augmentation was the most frequently performed procedure, accounting for 77.9% (55,887) of augmented sites, while augmentation only before implant placement was reported for 18.7% (13,451) of the sites and only 3.3% (2,348) of sites were augmented using a staged approach that included augmentation prior to and at the same time as implantation.

Regarding the frequency of augmentation for each implant site, we found that 96.5% of the augmented sites were augmented once, 3.4% were augmented twice, and only a few were augmented three or more times. (Table 4.3).

The types of augmentation materials used were specified for about 95% (68,131) of all augmented implantation sites (Table 4.3). Implant sites augmented with autologous bone alone were slightly more frequent than those augmented with only BSM (29.5% vs. 22.6%, respectively). However, most implant sites were augmented with both autologous and BSM (43.1%).

4.3.3. Implant failures

From the treated patient population, a total of 2,708 implants (1.8%) out of the 150,896 implants installed were reported to have failed over various periods since placement. 2,133 implant failures in 854 patients happened within the first year of implant placement, with most occurring in the first 28 weeks (86%) (Figure 4.17). This corresponds to a 1.4% failure rate in the first year (95% CI: 1.0%, 1.6%). However, if there was a previous failure in the same site, the incidence of early implant failure was reported as 4.4% (95% CI: 3.2%, 5.4%) compared to 1.4% (95% CI: 1.1%, 1.7%) for first-time placements (Table 4.7). The distributions of the number of implants that failed per patient during the first year of implant placement were displayed in Figure 4.18.

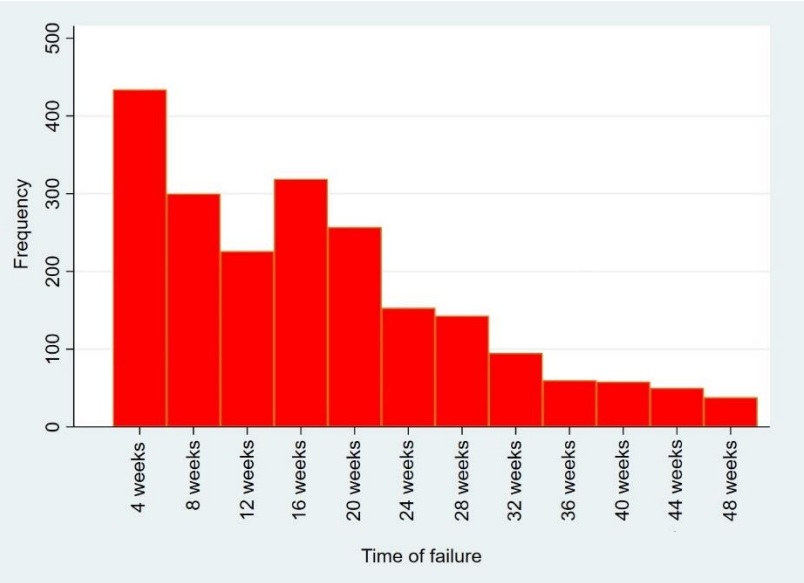


Figure 4.17 Distribution of implant failures during the first year

Implant placement	Early failure		Total
	No	Yes	
1st placement	147,515 (98.6%)	2,076 (1.4%)	149,591 (100%)
2nd placement	1,248 (95.6%)	57 (4.4%)	1,305 (100%)
Overall	148,763 (98.6%)	2,133 (1.4%)	150,896 (100%)

Table 4.7 Incidence of early implant failure

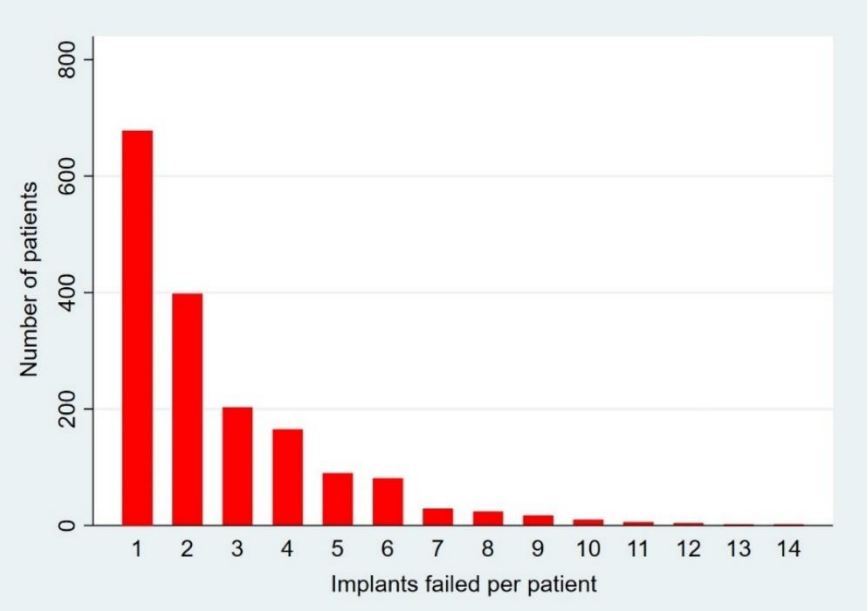


Figure 4.18 Number of failed implants per patient during the first year of implant placement

4.3.4. Patient and implant-related characteristics by different centres

Table 4.8 displays differences in patient and implant characteristics, as well as missing data across centres.

Regarding patient characteristics, age and sex distributions were similar between the different centres. However, medical history reporting varied among centres, with some centres having more missing medical history data than others, and four centres (1, 6, 11, and 17) did not record any medical history data.

In terms of implant-related characteristics, different centres used different implant systems. Although most centres used a variety of implant systems, only a few used mainly one system. For example, Centre 9 used the Neoss implant system almost exclusively, while Centres 12 and 15 primarily used the Straumann implant system (86.3% and 85.2%, respectively).

Late implant placement (>16 weeks) was the most commonly used placement protocol across all centres. However, some centres, such as Centre 1 and Centre 17, had a higher proportion of immediate implants than others (35.8% and 39%, respectively). Furthermore, most centres used a two-stage surgical approach to place implants (submerged healing), whereas some centres (e.g., Centres 15, 19, and 21) predominantly used a one-stage surgical approach (transmucosal healing).

Different centres had different approaches regarding the timing of bone augmentation relative to implant placement. While some centres, such as 3, 5, 9, and 16, predominantly performed augmentation simultaneously with implant placement and rarely before, other centres, such as centres 11 and 13, performed bone augmentation before implant placement in over half of their cases. Furthermore, bone augmentation

techniques also varied between centres. Some techniques, such as sinus lift and appositional bone augmentation, were performed by all centres, whereas other augmentation techniques, such as alveolar ridge splitting and distraction osteogenesis, were only performed by some centres (e.g., Centres 3, 4, and 18). In addition, the choice of augmentation materials also varied between centres, with some centres predominantly using bone substitute materials and few autologous bone grafts (e.g., Centres 4, 8, and 12), whereas others regularly used autologous bone and rarely used bone substitutes (e.g., Centres 9, and 20).

Table 4.8 - Data characteristics by centres

Centre	Patients_ No.	Age (Mean ± SD) yrs	Sex		Diabetes (2016-2022)			Smoking status (2016-2022)			
			Males	Females	No	Yes	Missing	Never	Former	Current	Missing
1	2752	59±13.6	1242 (45.2%)	1510 (54.8%)	0	0	1097 (100%)	0	0	0	1097 (100%)
2	1606	58.8±12.2	807 (50.3%)	799 (49.7%)	698 (94.5%)	24 (3.2%)	17 (2.3%)	348(47.1%)	249(33.7%)	119(16.1%)	23 (3.1%)
3	7766	60±12.4	3689 (47.5%)	4077 (52.5%)	3598 (82.6%)	279 (6.4%)	479 (11%)	2297 (52.7%)	967 (22.2%)	764 (17.5%)	328 (7.5%)
4	2460	59.7±13.2	1041 (42.3%)	1419 (57.7%)	889 (64.1%)	40 (2.9%)	458 (33%)	513 (37%)	255 (18.4%)	132 (9.5%)	487 (35.1%)
5	3290	60.7±13.3	1469 (44.7%)	1821 (55.3%)	1143 (47.6%)	77 (3.2%)	1189 (49.4%)	785 (32.6%)	247 (10.3%)	189 (7.9%)	1188 (49.3%)
6	2115	59.2±12.3	986 (46.6%)	1129 (53.4%)	0	0	2115 (100%)	0	0	0	2115 (100%)
7	4389	58.3±12.2	2130 (48.5%)	2259 (51.5%)	1745 (64.4%)	149 (5.5%)	817 (30.1%)	1194 (44.1%)	359 (13.2%)	328 (12.1%)	830 (30.6%)
8	3072	60±11.8	1449 (47.2%)	1623 (52.8%)	2760 (89.8%)	102 (3.3%)	210 (6.9%)	2331 (75.9%)	9 (0.3%)	524 (17.1%)	208 (6.8%)
9	5143	60.3±11.9	2429 (47.2%)	2714 (52.8%)	2590 (86.9%)	157 (5.3%)	234 (7.8%)	1896 (63.6%)	426 (14.3%)	427 (14.3%)	232 (7.9%)
10	6150	59.6±12.5	2871 (46.7%)	3279 (53.3%)	3815 (89.8%)	248 (5.8%)	187 (4.4%)	2754 (64.8%)	777 (18.3%)	518 (12.2%)	201 (4.7%)
11	498	60.3±12.6	250 (50.2%)	248 (49.8%)	7 (8%)	0	79 (92%)	5 (5.8%)	1 (1.2)	0	80 (93%)
12	4189	60.2±12.6	2012 (48%)	2177 (52%)	2840 (91.5%)	190 (6.1%)	75 (2.4%)	2005 (64.6%)	619 (19.9%)	359 (11.6%)	122 (3.9%)
13	4836	59.2±11.8	2239 (46.3%)	2597 (53.7%)	1724 (72.5%)	55 (2.3%)	600 (25.2%)	1652 (69.4%)	7 (0.3%)	58 (2.4%)	662 (27.8%)
14	2345	60.7±12.8	1046(44.6%)	1299 (55.4%)	501 (40%)	27 (2.2%)	726 (57.8%)	296 (23.6%)	81 (6.5%)	77 (6.1%)	800 (63.8%)
15	5736	58.8±13.3	2735 (47.%)	3001 (52.3%)	1074 (40.6%)	59 (2.2%)	1511 (57.2%)	621 (23.5%)	339 (12.8%)	148 (5.6%)	1536 (58.1%)
16	814	58.8±12.7	399 (49%)	415 (51%)	309 (53.5%)	21 (3.6%)	248 (42.9%)	183 (31.7%)	84 (14.5%)	57 (9.9%)	254 (43.9%)
17	1559	59.7±10.7	777 (49.8%)	782 (50.2%)	0	0	1559 (100%)	0	0	0	1559 (100%)
18	1128	60.2±12.6	645 (57.2%)	483 (42.8%)	213 (28.6%)	11 (1.5%)	521 (69.9%)	132 (17.7%)	45 (6%)	31 (4.2%)	537 (72.1%)
19	1984	60.7±12.6	904 (45.6%)	1080 (54.4%)	1585 (79.9%)	101 (5.1%)	298 (15%)	826 (41.6%)	568 (28.6%)	291 (14.7%)	299 (15.1%)
20	1042	61.6±12.8	523 (50.2%)	519 (49.8%)	546 (52.4%)	40 (3.8%)	456 (43.8%)	472 (45.3%)	45 (4.3%)	53 (5.1%)	472 (45.3%)
21	540	61.8±13.7	265 (49.1%)	275 (50.9%)	39 (7.2%)	2 (0.4%)	499 (92.4%)	38 (7%)	1 (0.2%)	2 (0.4%)	499 (92.4%)

Table 4.8 - Continued										
Centre	Implants_No.	Site		Implant placement timing				Healing mode		
		Maxilla	Mandible	Immediate	Early (<16 wks)	Late (>16 wks)	Missing	Submerged	Transmucosal	Missing
1	5679	3343 (58.9%)	2336 (41.1%)	2035 (35.8%)	324 (5.7%)	3215 (56.6%)	105 (1.9%)	4311 (75.9%)	1207 (21.3%)	161 (2.8%)
2	4451	2555 (57.4%)	1896 (42.6%)	52 (1.2%)	85 (1.9%)	4312 (96.8%)	2 (0.1%)	3061 (68.77%)	1389 (31.21%)	1 (0.02%)
3	20278	10648 (52.5%)	9630 (47.5%)	2753 (13.6%)	964 (4.8%)	16537 (81.5%)	24 (0.1%)	14918 (73.6%)	5323 (26.2%)	37 (0.2%)
4	5913	3309 (56%)	2604 (44%)	149 (2.5%)	239 (4%)	5516 (93.3%)	9 (0.2%)	5672 (95.9%)	181 (3.1%)	60 (1%)
5	7575	4264 (56.3%)	3311 (43.7%)	1250 (16.5%)	365 (4.8%)	5931 (78.3%)	29 (0.4%)	6098 (80.5%)	433 (5.7%)	1044 (13.8%)
6	5694	3466 (60.9%)	2228 (39.1%)	552 (9.7%)	199 (3.5%)	4921 (86.4%)	22 (0.4%)	4510 (79.2%)	1134 (19.9%)	50 (0.9%)
7	10120	5507 (54.4%)	4613 (45.6%)	541 (5.35%)	722 (7.13%)	8856 (87.51%)	1 (0.01%)	9092 (89.8%)	927 (9.2%)	101 (1%)
8	6623	3674 (55.5%)	2949 (44.5%)	100 (1.5%)	937 (14.2%)	5586 (84.3%)	0	6544 (98.8%)	73 (1.1%)	6 (0.1%)
9	12233	7053 (57.7%)	5180 (42.3%)	283 (2.31%)	1081 (8.84%)	10868 (88.84%)	1 (0.01%)	12012 (98.2%)	188 (1.5%)	33 (0.3%)
10	13465	7066 (52.5%)	6399 (47.5%)	386 (2.87%)	258 (1.92%)	12819 (95.20%)	2 (0.01%)	12767 (94.8%)	328 (2.4%)	370 (2.8%)
11	1908	1077 (56.4%)	831 (43.6%)	77 (4%)	113 (5.9%)	1717 (90%)	1 (0.1%)	1584 (83%)	182 (9.5%)	142 (7.5%)
12	9956	5570 (55.9%)	4386 (44.1%)	996 (10%)	363 (3.7%)	8573 (86.1%)	24 (0.2%)	8176 (82.1%)	27 (0.3%)	1753 (17.6%)
13	11229	6566 (58.5%)	4663 (41.5%)	802 (7.1%)	1888 (16.8%)	8354 (74.4%)	185 (1.7%)	7133 (63.5%)	2636 (23.5%)	1460 (13%)
14	5675	2883 (50.8%)	2792 (49.2%)	84 (1.5%)	207 (3.6%)	5384 (94.9%)	0	5617 (99%)	33 (0.6%)	25 (0.4%)
15	11092	5283 (47.6%)	5809 (52.4%)	196 (1.8%)	596 (5.4%)	10064 (90.7%)	236 (2.1%)	1894 (17.1%)	7387 (66.6%)	1811 (16.3%)
16	2059	1167 (56.7%)	892 (43.3%)	125 (6.1%)	75 (3.6%)	1859 (90.3%)	0	2049 (99.5%)	3 (0.2%)	7 (0.3%)
17	5496	2950 (53.7%)	2546 (46.3%)	2150 (39%)	79 (1.5%)	3267 (59.5%)	0	840 (15.3%)	4648 (84.6%)	8 (0.1%)
18	3629	2101 (57.9%)	1528 (42.1%)	164 (4.5%)	124 (3.4%)	2104 (58%)	1237 (34.1%)	1417 (39%)	497 (13.7%)	1715 (47.3%)
19	4300	2417 (56.2%)	1883 (43.8%)	45 (1.1%)	83 (1.9%)	4172 (97%)	0	1059 (24.6%)	3238 (75.3%)	3 (0.1%)
20	2341	1309 (55.9%)	1032 (44.1%)	137 (5.9%)	206 (8.8%)	1998 (85.3%)	0	1938 (82.8%)	371 (15.8%)	32 (1.4%)
21	1180	632 (53.6%)	548 (46.4%)	81 (6.9%)	287 (24.3%)	812 (68.8%)	0	326 (27.6%)	826 (70%)	28 (2.4%)

Table 4.8 - Continued

Centre	Implant length			Implant diameter			Implant brand						
	Short (<10)	Standard (>=10,<13)	Long (>=13)	Narrow (>=3,<3.75)	Standard (>=3.75,<5)	Wide (>=5,<=7)	Camlog	Straumann	Neoss	Nobel Biocare	Ankylos	Astra Tech	Other
1	1295 (22.8%)	3375 (59.4%)	1009 (17.8%)	1148 (20.2%)	4095 (72.1%)	436 (7.7%)	1282 (22.6%)	1921 (33.8%)	0	1616 (28.5%)	0	664 (11.7%)	196 (3.4%)
2	897 (20.1%)	3173 (71.3%)	381 (8.6%)	57 (1.3%)	3549 (79.7%)	845 (19%)	4447 (99.9%)	4 (0.1%)	0	0	0	0	0
3	1648 (8.1%)	9839 (48.5%)	8791 (43.4%)	3834 (18.9%)	15875 (78.3%)	569 (2.8%)	6 (0.03%)	24 (0.12%)	12905 (63.64%)	4629 (22.83%)	1273 (6.28%)	383 (1.89%)	1058 (5.22%)
4	399 (6.7%)	3648 (61.7%)	1866 (31.6%)	620 (10.5%)	4788 (81%)	505 (8.5%)	4398 (74.4%)	287 (4.9%)	270 (4.6%)	8 (0.14%)	4 (0.07%)	699 (11.8%)	243 (4.1%)
5	530 (7%)	3797 (50.1%)	3248 (42.9%)	1299 (17.1%)	5460 (72.1%)	816 (10.8%)	767 (10.2%)	234 (3.1%)	52 (0.7%)	5593 (74.2%)	0	206 (2.7%)	688 (9.1%)
6	3950 (69.4%)	1389 (24.4%)	355 (6.2%)	694 (12.2%)	3877 (68.1%)	1123 (19.7%)	1962 (34.6%)	392 (6.9%)	0	2 (0.1%)	0	3147 (55.5%)	164 (2.9%)
7	5768 (57%)	3656 (36.1%)	696 (6.9%)	6499 (64.2%)	3330 (32.9%)	291 (2.9%)	4 (0.1%)	488 (4.8%)	0	0	9541 (94.3%)	18 (0.2%)	69 (0.6%)
8	3778 (57%)	2496 (37.7%)	349 (5.3%)	128 (1.9%)	5607 (84.7%)	888 (13.4%)	6034 (91.1%)	136 (2.1%)	0	0	0	424 (6.4%)	29 (0.4%)
9	3699 (30.2%)	5041 (41.2%)	3493 (28.6%)	1347 (11%)	9917 (81.1%)	969 (7.9%)	0	2 (0.02%)	12227 (99.95%)	0	0	1 (0.01%)	3 (0.02%)
10	1628 (12.1%)	7104 (52.8%)	4733 (35.1%)	1056 (7.8%)	12067 (89.6%)	342 (2.6%)	11757 (87.3%)	4 (0.03%)	0	5 (0.04%)	0	1697 (12.6%)	2 (0.01%)
11	389 (20.4%)	1251 (65.6%)	268 (14%)	298 (15.6%)	1434 (75.2%)	176 (9.2%)	363 (19%)	929 (48.7%)	0	40 (2.1%)	112 (5.9%)	364 (19.1%)	100 (5.2%)
12	1417 (14.2%)	8411 (84.5%)	128 (1.3%)	3203 (32.2%)	6726 (67.5%)	27 (0.3%)	314 (3.2%)	8550 (86.3%)	0	46 (0.5%)	0	0	993 (10%)
13	1764 (15.7%)	5882 (52.4%)	3583 (31.9%)	1072 (9.6%)	5886 (52.4%)	4271 (38%)	6965 (65%)	983 (9.2%)	1 (0.01%)	368 (3.4%)	1553 (14.5%)	601 (5.6%)	247 (2.3%)
14	712 (12.5%)	4012 (70.7%)	951 (16.8%)	342 (6%)	3930 (69.3%)	1403 (24.7%)	3681 (64.9%)	705 (12.4%)	102 (1.8%)	27 (0.5%)	67 (1.2%)	312 (5.5%)	781 (13.7%)
15	479 (4.3%)	9955 (89.8%)	658 (5.9%)	1441 (13%)	9292 (83.8%)	359 (3.2%)	867 (7.8%)	9448 (85.2%)	41 (0.4%)	515 (4.6%)	0	0	221 (2%)
16	184 (8.9%)	904 (43.9%)	971 (47.2%)	653 (31.7%)	1328 (64.5%)	78 (3.8%)	71 (3.5%)	0	868 (42.2%)	188 (9.1%)	0	27 (1.3%)	905 (43.9%)
17	837 (15.2%)	3162 (57.5%)	1497 (27.3%)	276 (5%)	3877 (70.5%)	1343 (24.5%)	0	0	0	4211 (76.6%)	0	179 (3.3%)	1106 (20.1%)
18	802 (22.1%)	2597 (71.6%)	230 (6.3%)	742 (20.5%)	2598 (71.6%)	289 (7.9%)	526 (14.5%)	2362 (65.1%)	2 (0.1%)	68 (1.9%)	57 (1.5%)	445 (12.3%)	169 (4.6%)
19	1092 (25.4%)	3018 (70.2%)	190 (4.4%)	399 (9.3%)	2717 (63.2%)	1184 (27.5%)	3759 (87.4%)	274 (6.4%)	0	214 (5%)	0	0	53 (1.2%)
20	371 (15.8%)	1032 (44.1%)	938 (40.1%)	108 (4.6%)	1925 (82.2%)	308 (13.2%)	1949 (83.3%)	294 (12.5%)	0	0	0	0	98 (4.2%)
21	365 (30.9%)	767 (65%)	48 (4.1%)	81 (6.9%)	1040 (88.1%)	59 (5%)	2 (0.2%)	480 (40.7%)	0	66 (5.6%)	0	97 (8.2%)	535 (45.3%)

Table 4.8 - Continued												
Centre	Augmentation		Augmentation Timing (Relative to implantation)			Augmentation frequency			Augmentation Materials			
	Yes	No	Same	Before	Both	1 time	2 times	3-5 times	Autologous	BSM	Both	Missing
1	2408 (42.4%)	3271 (57.6%)	1667 (69.2%)	627 (26.1%)	114 (4.7%)	2284 (94.9%)	112 (4.6%)	12 (0.5%)	111 (4.6%)	853 (35.4%)	1341 (55.7%)	103 (4.3%)
2	2155 (48.4%)	2296 (51.6%)	1498 (69.5%)	510 (23.7%)	147 (6.8%)	2005 (93%)	149 (6.9%)	1 (0.1%)	479 (22.23%)	54 (2.5%)	1233 (57.2%)	389 (18.1%)
3	9719 (47.9%)	10559 (52.1%)	8683 (89.3%)	728 (7.5%)	308 (3.2%)	9403 (96.8%)	301 (3%)	15 (0.2%)	3654 (37.6%)	918 (9.5%)	4679 (48.1%)	468 (4.8%)
4	2753 (46.6%)	3160 (53.4%)	1275 (46.3%)	1281 (46.5%)	197 (7.2%)	2516 (91.4%)	222 (8.1%)	15 (0.5%)	231 (8.4%)	1934 (70.3%)	254 (9.2%)	334 (12.1%)
5	4564 (60.3%)	3011 (39.7%)	4125 (90.4%)	312 (6.8%)	127 (2.8%)	4434 (97.2%)	124 (2.7%)	6 (0.1%)	1587 (34.8%)	158 (3.5%)	2773 (60.7%)	46 (1.01%)
6	1711 (30.1%)	3983 (69.9%)	1321 (77.2%)	313 (18.3%)	77 (4.5%)	1629 (95.2%)	81 (4.7%)	1 (0.1%)	470 (27.5%)	100 (5.8%)	1118 (65.3%)	23 (1.4%)
7	3118 (30.8%)	7002 (69.2%)	2468 (79.2%)	591 (18.9%)	59 (1.9%)	3048 (97.8%)	67 (2.1%)	3 (0.1%)	1173 (37.6%)	191 (6.1%)	1331 (42.7%)	423 (13.6%)
8	2952 (44.6%)	3671 (55.4%)	1589 (53.8%)	1088 (36.9%)	275 (9.3%)	2666 (90.3%)	284 (9.6%)	2 (0.1%)	498 (16.9%)	1941 (65.8%)	124 (4.2%)	389 (13.1%)
9	8892 (72.7%)	3341 (27.3%)	8804 (99%)	27 (0.3%)	61 (0.7%)	8831 (99.31%)	58 (0.65%)	3 (0.03%)	8270 (93%)	0	0	622 (7%)
10	6115 (45.4%)	7350 (54.6%)	4047 (66.2%)	1911 (31.3%)	157 (2.5%)	5944 (97.2%)	170 (2.78%)	1 (0.02%)	945 (15.5%)	1604 (26.2%)	3524 (57.6%)	42 (0.7%)
11	573 (30%)	1335 (70%)	239 (41.7%)	326 (56.9%)	8 (1.4%)	563 (98.2%)	10 (1.8%)	0	21 (3.7%)	4 (0.7%)	538 (93.9%)	10 (1.7%)
12	9406 (94.5	550 (5.5%)	8834 (93.9%)	313 (3.3%)	259 (2.8%)	9143 (97.2%)	254 (2.7%)	9 (0.1%)	19 (0.2%)	6135 (65.2%)	3215 (34.2%)	37 (0.4%)
13	3820 (34%)	7409 (66%)	1096 (28.7%)	2722 (71.2%)	2 (0.1%)	3818 (99.9%)	2 (0.1%)	0	151 (3.9%)	200 (5.2%)	3452 (90.4%)	17 (0.5%)
14	2226 (39.2%)	3449 (60.8%)	1209 (54.3%)	832 (37.4%)	185 (8.3%)	2029 (91.15%)	196 (8.81%)	1 (0.04%)	248 (11.1%)	603 (27.1%)	1340 (60.2%)	35 (1.6%)
15	3084 (27.8%)	8008 (72.2%)	1851 (60%)	1156 (37.5%)	77 (2.5%)	3001 (97.31%)	82 (2.66%)	1 (0.03%)	1219 (39.5%)	273 (8.9%)	1458 (47.3%)	134 (4.3%)
16	1494 (72.6%)	565 (27.4%)	1479 (99%)	8 (0.5%)	7 (0.5%)	1487 (99.5%)	7 (0.5%)	0	125 (8.4%)	30 (2%)	1338 (89.5%)	1 (0.1%)
17	366 (6.7%)	5130 (93.3%)	292 (79.8%)	70 (19.1%)	4 (1.1%)	360 (98.4%)	6 (1.6%)	0	5 (1.4%)	308 (84.2%)	4 (1.1%)	49 (13.3%)
18	1462 (40.3%)	2167 (59.7%)	1080 (73.9%)	302 (20.6%)	80 (5.5%)	1377 (94.2%)	84 (5.7%)	1 (0.1%)	435 (29.8%)	90 (6.2%)	774 (52.9%)	163 (11.1%)
19	2436 (56.7%)	1864 (43.3%)	2229 (91.5%)	174 (7.1%)	33 (1.4%)	2400 (98.5%)	36 (1.5%)	0	277 (11.4%)	657 (27%)	1377 (56.5%)	125 (5.1%)
20	2076 (88.7%)	265 (11.3%)	1782 (85.8%)	127 (6.1%)	167(8.1%)	1909 (92%)	158 (7.6%)	9 (0.4%)	1162 (56%)	103 (4.9%)	788 (38%)	23 (1.1%)
21	356 (30.2%)	824 (69.8%)	319 (89.6%)	33 (9.3%)	4 (1.1%)	352 (98.9%)	4 (1.1%)	0	59 (16.6%)	69 (19.4%)	106 (29.8%)	122 (34.2%)

Table 4.8 - Continued										
Centre	Augmentation types									
	Sinus lift	Horizontal apposition	Onlay	Inlay	Socket preservation	Spreading	Splitting	Distraction	Shell technique	Sandwich technique
1	1015 (25.6%)	1480 (37.4%)	1076 (27.2%)	79 (2%)	118 (3%)	44 (1.1%)	138 (3.5%)	10 (0.3%)	0	0
2	1116 (30.1%)	1230 (33.4%)	301 (8.2%)	168 (4.6%)	6 (0.2%)	831 (22.6%)	21 (0.6%)	4 (0.1%)	0	7 (0.2%)
3	3950 (36.5%)	4432 (41%)	375 (3.5%)	262 (2.4%)	1287 (11.9%)	40 (0.4%)	397 (3.7%)	16 (0.1%)	11 (0.1%)	46 (0.4%)
4	1638 (35.3%)	1330 (28.6%)	1306 (28.1%)	31 (0.7%)	32 (0.7%)	7 (0.2%)	267 (5.7%)	32 (0.7%)	0	0
5	1496 (26.3%)	1994 (35%)	975 (17.1%)	755 (13.2%)	383 (6.7%)	26 (0.5%)	40 (0.7%)	27 (0.5%)	0	0
6	706 (22.5%)	1064 (34%)	878 (28%)	403 (12.9%)	47 (1.5%)	14 (0.4%)	11 (0.4%)	8 (0.2%)	0	2 (0.1%)
7	1695 (40%)	1185 (27.9%)	421 (9.9%)	422 (10%)	85 (2%)	75 (1.8%)	52 (1.2%)	37 (0.9%)	268 (6.3%)	0
8	1000 (21.7%)	185 (4%)	1058 (23%)	1277 (27.7%)	1054 (22.9%)	0	30 (0.7%)	0	0	0
9	3134 (23.5%)	7924 (59.4%)	1204 (9%)	980 (7.4%)	91 (0.7%)	0	0	0	0	0
10	2928 (34.5%)	3617 (42.7%)	1329 (15.7%)	408 (4.8%)	109 (1.3%)	3 (0%)	13 (0.2%)	30 (0.4%)	12 (0.1%)	27 (0.3%)
11	327 (34.7%)	192 (20.4%)	166 (17.6%)	42 (4.5%)	13 (1.4%)	5 (0.5%)	27 (2.9%)	43 (4.6%)	8 (0.8%)	120 (12.7%)
12	2660 (22.7%)	7906 (67.5%)	271 (2.3%)	0	813 (6.9%)	51 (0.5%)	0	8 (0.1%)	0	0
13	3001 (69.8%)	774 (18%)	391 (9.1%)	79 (1.8%)	6 (0.1%)	0	0	44 (1%)	0	4 (0.1%)
14	1223 (48.8%)	327 (13.1%)	112 (4.5%)	48 (1.9%)	781 (31.2%)	3 (0.1%)	11 (0.4%)	0	0	0
15	1430 (38.6%)	1696 (45.7%)	482 (13%)	26 (0.7%)	8 (0.2%)	54 (1.5%)	6 (0.2%)	2 (0.1%)	0	0
16	284 (15.4%)	40 (2.2%)	34 (1.8%)	1464 (79.6%)	9 (0.5%)	4 (0.2%)	6 (0.3%)	0	0	0
17	324 (84.6%)	20 (5.2%)	2 (0.5%)	4 (1.1%)	33 (8.6%)	0	0	0	0	0
18	588 (27%)	581 (26.6%)	232 (10.6%)	304 (14%)	49 (2.2%)	46 (2.1%)	270 (12.4%)	27 (1.2%)	39 (1.8%)	47 (2.2%)
19	911 (30%)	1623 (53.3%)	45 (1.4%)	149 (4.9%)	26 (0.9%)	73 (2.4%)	200 (6.6%)	8 (0.3%)	0	5 (0.2%)
20	552 (18.8%)	1445 (49.2%)	789 (26.8%)	69 (2.3%)	33 (1.1%)	4 (0.1%)	29 (1%)	4 (0.1%)	3 (0.1%)	11 (0.4%)
21	195 (45.9%)	117 (27.5%)	18 (4.2%)	16 (3.8%)	31 (7.3%)	17 (4%)	3 (0.7%)	28 (6.6%)	0	0

4.4. Discussion

Scientific documentation of dental implant treatment outcomes is mostly based on evaluations performed in convenience samples of selected patient groups or from clinical trials, where treatment is performed by clinicians in specialised health care or university settings. Such studies assess the intervention under somewhat idealised conditions when compared to the care provided to the general population in real-world dental practices, which limits the generalizability of the results.

As far as we know, most of the studies evaluating early and late implant failure were based on convenience samples, with treatment most often provided in a single clinical centre, which limits their external validity. In contrast, our study is based on the data drawn from 21 independent dental centres, with different clinicians and different treatment philosophies, which likely reflects a broader range of implant treatment practices. Furthermore, this dataset includes a broad representation of implant systems, including both major and less commonly used brands. Most centres use more than one implant system, and the systems used vary between centres depending on their preferences, what they are used to, and the preferences of the referring dentists. However, this data is not representative as almost all of these practices are referral practices providing specialised surgical dental services by trained and experienced oral surgeons (OS) and oral & maxillofacial surgeons (OMFS). Therefore, some variables may have been over-represented in this study, such as bone augmentation, which involves some complex types of augmentation that are not routinely performed in dental practices. Furthermore, more straightforward procedures, such as the placement of two implants in the edentulous anterior mandible

to support a mandibular overdenture, may be under-represented as such patients may not be referred to specialist practices.

Dental implant treatment is generally considered a predictable treatment method for replacing missing teeth, with a success rate of up to 98% in some studies (Lindquist et al., 1996, Carr et al., 2003, Östman et al., 2012, Jemt, 2017, Howe et al., 2019); this means that Implant failure, whether early or late, is a relatively rare outcome. Accordingly, any study investigating implant failure needs to have a large sample size and be adequately powered to detect small effects and enable meaningful interpretation of results. However, the vast majority of identified studies looking into risk factors of early implant failure had small sample sizes, and only a few available studies had large sample sizes (see Chapter 3). One of these relatively large studies, by Derks et al. (2015), which was based on the national data registry of the Swedish Social Insurance Agency, identified a cohort of 2,765 patients treated with 11,311 implants in 2003. In another retrospective study conducted by Lin et al. (2018), databases from two hospitals in Hangzhou, China, were used to identify a total of 18,199 patients treated with 30,959 implants over a 5-year period. In the same context, Chrcanovic et al. (2016) conducted a single-centre retrospective study on a large sample of 2,670 patients who received a total of 10,096 dental implants between 1980 and 2014. So, to the best of our knowledge, the dataset in the current study is the largest dental implants dataset that can be used when examining risk factors associated with early failure of dental implants, as it includes data on 150,896 implants placed in 63,414 patients over a 13-year period, along with potential risk factors associated with implant failure at the patient and implant level. This large volume of data obtained is mainly due to its multicentre origin (21 centres), in addition to the fact that these data were collected over a long period of 13 years.

Scientific evidence, treatment philosophies, clinical practices, and preferences may evolve, change, or even reverse over time. Studies extending over long periods of time usually allow for the detection and examination of such trends in clinical practices. The current dataset spans a reasonably long period of time(13 yrs) during which significant time trends could be detected.

One notable example is the trend towards changing practice towards more use of short implants (see section 4.3.2.2). The use of short implants or bone augmentation procedures are two common options to overcome limitations of reduced alveolar bone height due to resorption of the alveolar ridge after tooth extraction or proximity to anatomical structures such as the maxillary sinus and inferior alveolar nerve. The main advantage of short implant placement is avoiding invasive bone augmentation surgery and associated additional treatment duration, costs, and potential complications such as donor site morbidity or even graft failure. Therefore, when such a trend is observed in a data set like this obtained from specialised centres with qualified surgeons who have the ability to perform augmentation procedures whenever needed, yet tend to place more short implants over the years of study, it all supports the trend mentioned above. Furthermore, this trend towards more use of short implants is consistent with recent changes in the previous philosophy of using long implants whenever possible, and is also supported by positive clinical outcomes in the interests of short implants (Monje et al., 2013, Thoma et al., 2018, Felice et al., 2019).

In this study, we also observed an association between insertion torque and bone quality. This was consistent with what would be expected that higher bone quality, such as type 1 bone, is more likely to yield higher insertion torque and vice versa. However, the vast majority of implants placed in type 1 bone (60.3%) were inserted with medium torques ranging from 20-50 Ncm. That may reflect the efforts of the

surgeons to prepare the implant bed in a way that avoids high insertion torque, and in the majority of cases, they were successful. This is consistent with the current trend in clinical practice to avoid using high insertion torques as they can cause increased heat generation at the implant site (Marković et al., 2013), which may negatively impact the osseointegration process (Dhok et al., 2023).

Despite the fact that retrospective datasets are an important data source for outcome research, such datasets may display inherent weaknesses in data quality, such as missing or incomplete records. For this dataset, issues such as data quality may be lower in some aspects or some variables than in others. For example, data on age, gender, implant size and implant site were complete for all observations across the dataset, while some other variables, such as those related to medical history, were of lower quality. This was manifested by the gap in patients' medical history data for the period between January 2010 and December 2015. Furthermore, There was variation between centres in the consistency of medical history reporting. Some centres did better than others in reporting patients' medical history, while others did not report it at all (Table 4.8). A possible explanation for this is that some centers or surgeons typically use a different medical history recording system and do not wish to spend additional time entering data into this particular database.

On the other hand, there are differences between centres in the number and types of procedures performed. These differences are a reflection of the different case mixes depending on where centres are located, local competition between specialists, and the level of training of referring dentists. Simpler surgeries may be performed by the dentists themselves, and they may only refer complicated cases; however, the referral base may vary between different practices and different regions. Furthermore, and perhaps more importantly, these differences also illustrate that different surgeons

perform the treatment protocols that they are familiar with and that “work in their hands”. In implant dentistry, different approaches can often be used to achieve the same goal. One case in point is the fact that successful bone augmentation can be achieved with a variety of techniques and materials, which is reflected in the data presented here. For example, centre 9 exclusively uses titanium-reinforced ePTFE membranes in combination with autologous bone cores and concomitant implant placement, even in cases of substantial vertical defects. Hence, all augmentations are performed at the time of implant placement and no bone substitute materials are used in that centre.

4.5. Conclusions

-As far as we know, this is the largest dental implant dataset, documenting 150,896 implantations in 63,414 patients.

-The rate of early implant failure is low (1.4%).

-There is a broad representation of implant systems and surgical techniques in this dataset. Different practitioners used different approaches, which are likely to be a reflection of their preferences, training, and patient populations.

-There is a tendency to use shorter implants by experienced practitioners, who are less likely to avoid bone augmentation procedures.

CHAPTER 5: DETERMINANTS OF EARLY IMPLANT FAILURE IN A LARGE MULTICENTRE PRACTICE-BASED NETWORK

5.1. Aims

To assess the causal effect of the following factors reported in the ECDI implant dataset on the risk of early implant failure:

Patient's sex, age, implant site, diabetes, cigarette smoking, implant placement timing, bone quantity, bone quality, bone augmentation, implant dimensions, primary stability, and healing mode.

5.2. Methods

The statistical analysis plan was developed prior to conducting the analysis and was outlined as follows.

Summary statistics for the baseline characteristics of the used dataset were reported in Chapter 4.

Based on our hypothesized Directed acyclic graph (DAG) on the causal pathways linking potential risk factors with early implant failure (see Chapter 3, section 3.4.11), we constructed DAGs with each of these factors considered as an exposure of interest. This was done to make the underlying assumptions regarding the causal structure explicit and to guide variable selection for the statistical models to minimize bias in confounder selection by determining covariates adjustment sets required to block the non-causal paths (biasing paths) between exposure and outcome (Akinkugbe et al., 2016). Potential risk factors not present in the dataset were also included in DAGs and treated as unobserved variables. The DAGitty software was used to generate the DAGs and determine the required covariate adjustments (Textor et al., 2016).

Multilevel mixed-effects logistic regression models were used to estimate odd ratios (ORs) and two-sided 95% confidence intervals (95% CIs) for potential determinants of early implant failure. The implant was considered the statistical unit in these analyses. Early implant failure was the dichotomous outcome measure, defined as the total loss of the implant within the first year of its placement. All Models accounted for the clustering of observations at patient and centre levels and were adjusted for age and sex, and then fully adjusted for confounders sets that were determined using the directed acyclic graphs (DAGs). The intraclass correlation coefficient (ICC) was estimated for centres and patients from each model.

If any suggested confounder variable was only present in the (2016-2022) part of the dataset, we applied the 10% change-in-estimate criterion for confounding (Lee, 2014) by comparing the estimates between models that were adjusted or unadjusted for this confounder variable in the (2016-2022) part of the dataset. If the change in the estimate was less than 10%, we assumed that this variable had minimal or no confounding effect and excluded it from the final model, allowing for the combined dataset (2010-2022) to be used for analyses. If the change was greater than 10%, the model was only applied to the (2016-2022) parts of the dataset for which this confounder was available.

Similarly, if a covariate had more than 10% missing values, the estimates were compared between unadjusted and adjusted models for this covariate; if including this covariate was associated with less than 10% change in the estimate, it was excluded from the final model; otherwise, missing values were coded as “missing” and included in the model. Furthermore, for any given analysis, data from centres with more than 90% missing values for the variable of interest (exposure) or any covariate were excluded from that specific model.

The predicted probabilities (adjusted cumulative incidence estimates) and the 95% CI of early implant failure were computed for each risk factor from its respective multilevel mixed-effects logistic regression model. We also tested for interactions to examine potential effect modification between some variables in terms of the effect of one variable (the variable of interest) varying across the levels of another variable. The likelihood-ratio test was used to compare models with and without a multiplicative interaction term. The following potential interactions were considered: implant placement timing and bone augmentation, bone augmentation and implant dimensions, bone quality and primary stability, bone augmentation and healing mode.

Statistical analyses were performed using Stata 17.0 statistical software (Stata Corporation, College Station, TX, USA).

5.3. Results

5.3.1. Patient's sex

The baseline characteristics of the patients in this dataset are presented in Chapter 4 (see Table 4.1). Data on patients' sex was available for the entire 2010-2022 dataset with no missing values. Based on the DAG (Figure 5.1), no adjustment was required when looking at sex as a risk factor for early implant failure.

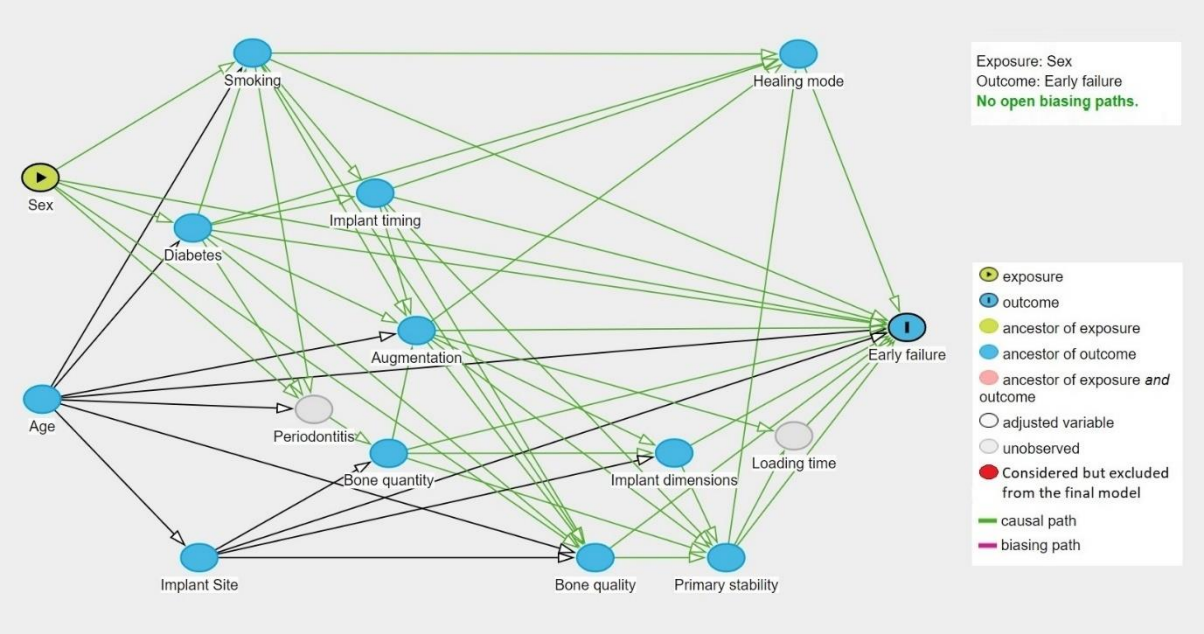


Figure 5.1 Directed acyclic graph (DAG) showing the association between exposure (patient sex) and outcome (early implant failure)

The results of the mixed-effects logistic regression model showed that the male sex was associated with an increased risk of early implant failure compared to females (OR: 1.40; 95%CI: 1.25, 1.56) (Table 5.1, see Appendix 8.1 for the full model). Based on the predicted probabilities calculated from this model, the cumulative incidence of early implant failure was 1.6% (95%CI: 1.2%, 2%) in males compared to 1.2% in females (95%CI: 1%, 1.4%) (Table 5.2).

The intraclass correlation coefficient (ICC) was estimated to be 0.04 for centres and 0.5 for patients.

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	21	1,180	20,278	7,185.5	150,896
Patient	63,414	1	24	2.4	

Independent variable	**Failed / Placed implants (n)**	**Odd ratio***	**(95% CI)**	**p-value**
Sex				
Females	924 / 77,564	1 (reference)		
Males	1209 / 73,332	1.40	(1.25, 1.56)	<0.001

*No adjustment is required

Table 5.1 Results of Mixed-effects logistic regression model evaluating associations between patient sex (independent variable) and early implant failure (dependent variable)

	Cumulative incidence of early implant failure (%)	**(95% CI)**
Sex		
Females	1.2%	(1.0%, 1.4%)
Males	1.6%	(1.2%, 2.0%)

Table 5.2 Cumulative incidences (predicted probabilities) of early implant failure with “Sex” as a predictor variable.

5.3.2. Age

The age distribution of patients who received dental implants between 2010 and 2022 is shown in Chapter 4 (see Table 4.2). There are no missing records regarding the age of patients in this dataset.

No adjustments were needed when investigating age as a risk factor for early implant failure (Figure 5.2).

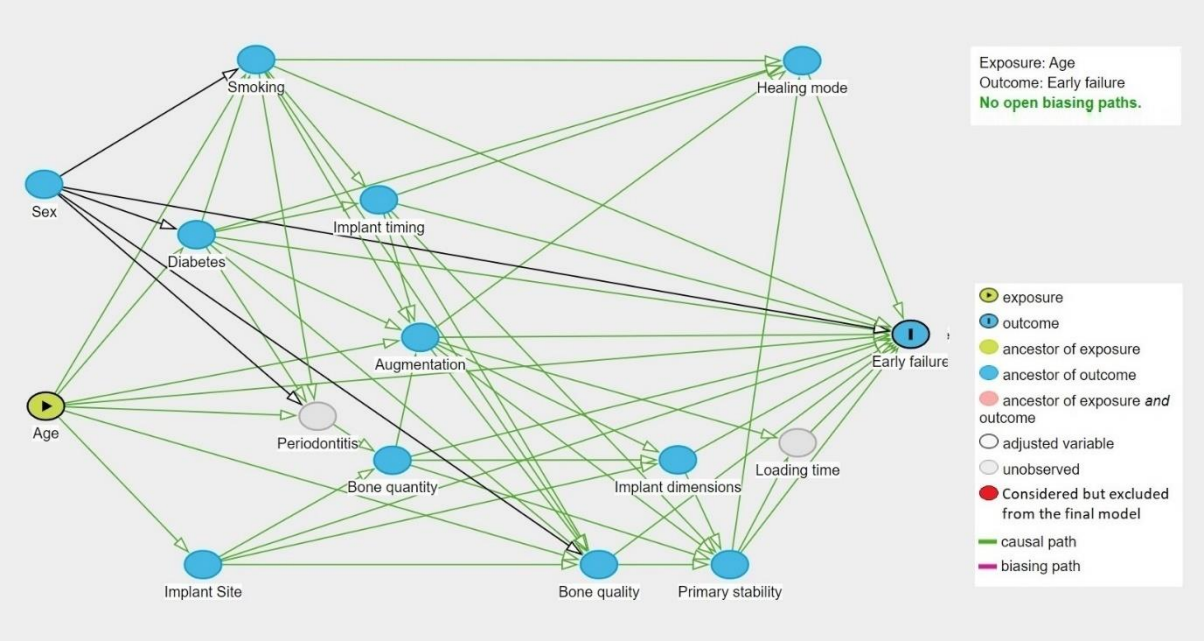


Figure 5.2 Directed acyclic graph (DAG) showing the association between exposure (age) and outcome (early implant failure).

The mixed-effects logistic regression model revealed that the risk of early failure was lower for all age groups than for the 18-30 age group (Table 5.3, see Appendix 8.2 for the full model). However, the only significant results were found in the 70-80 and 80-90 age groups with odds ratios of 0.64 (95% CI: 0.46, 0.90) and 0.62 (95% CI: 0.40, 0.95), respectively. In addition, the cumulative incidence of early failure for implants placed in patients aged 18-30 was highest at 1.8%, while for older age groups it ranged from 1.2% to 1.4% (Table 5.4, Figure 5.3).

The estimated intraclass correlation coefficient (ICC) for centres was 0.04, while for patients, it was 0.5.

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	21	1,180	20,278	7,185.5	150,896
Patient	63,414	1	24	2.4	

Independent variable	**Failed / Placed implants (n)**	**Odd ratio***	**(95% CI)**	**p-value**
Age				
18-30	60 /3,281	1 (reference)		
30-40	102/ 7,456	0.70	(0.48, 1.04)	0.080
40-50	265 / 18,860	0.71	(0.51, 1.00)	0.052
50-60	673 / 43,539	0.78	(0.57, 1.10)	0.145
60-70	661 / 46,312	0.76	(0.55, 1.04)	0.089
70-80	311 / 26,212	0.64	(0.46, 0.90)	0.01
80-90	61 / 5,236	0.62	(0.40, 0.95)	0.029

*No adjustment is required

Table 5.3 Results of Mixed-effects logistic regression model evaluating associations between age (independent variable) and early implant failure (dependent variable)

	Cumulative incidence of early implant failure (%)	(95% CI)
Age		
18-30	1.8%	(1.2%, 2.4%)
30-40	1.3%	(1.0%, 1.7%)
40-50	1.3%	(1.0%, 1.7%)
50-60	1.4%	(1.1%, 1.8%)
60-70	1.4%	(1.1%, 1.7%)
70-80	1.2%	(1.0%, 1.5%)
80-90	1.2%	(0.8%, 1.6%)

Table 5.4 Cumulative incidences (predicted probabilities) of early implant failure with “Age” as a predictor variable.

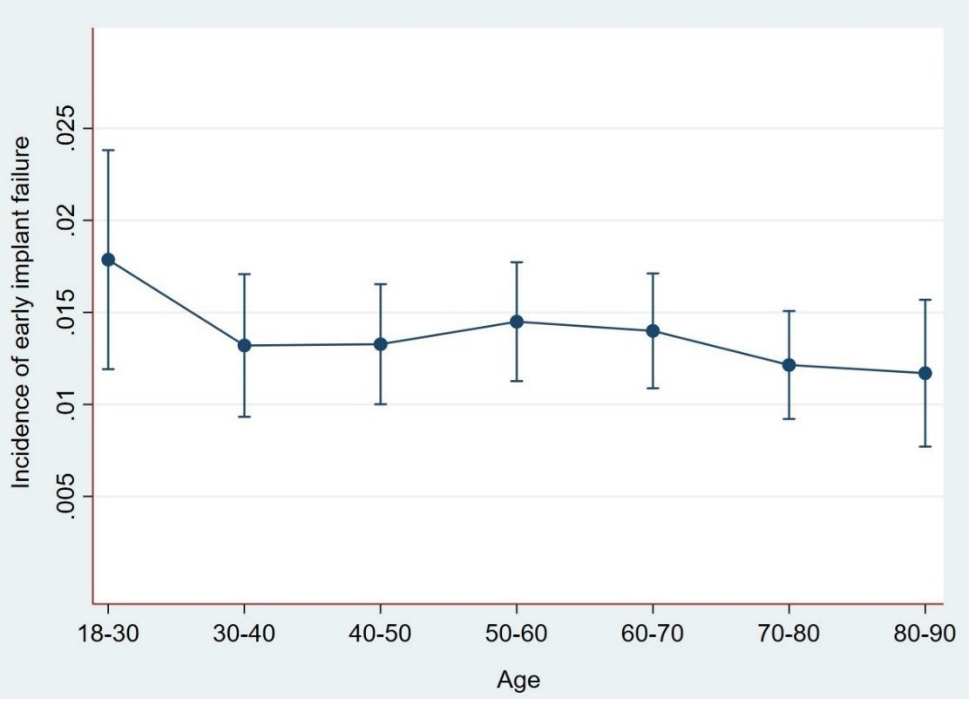


Figure 5.3 Cumulative incidence of early implant failure for each age group.

5.3.3. Implant site

The distribution of implants according to the placement sites in this dataset is illustrated in Chapter 4 (see Tables 4.3 and 4.4). The dataset contains complete information about the implant site with no missing data. The model assessing the effect of implant site on early implant failure was adjusted for age and sex based on the DAG (Figures 5.4-A, B).

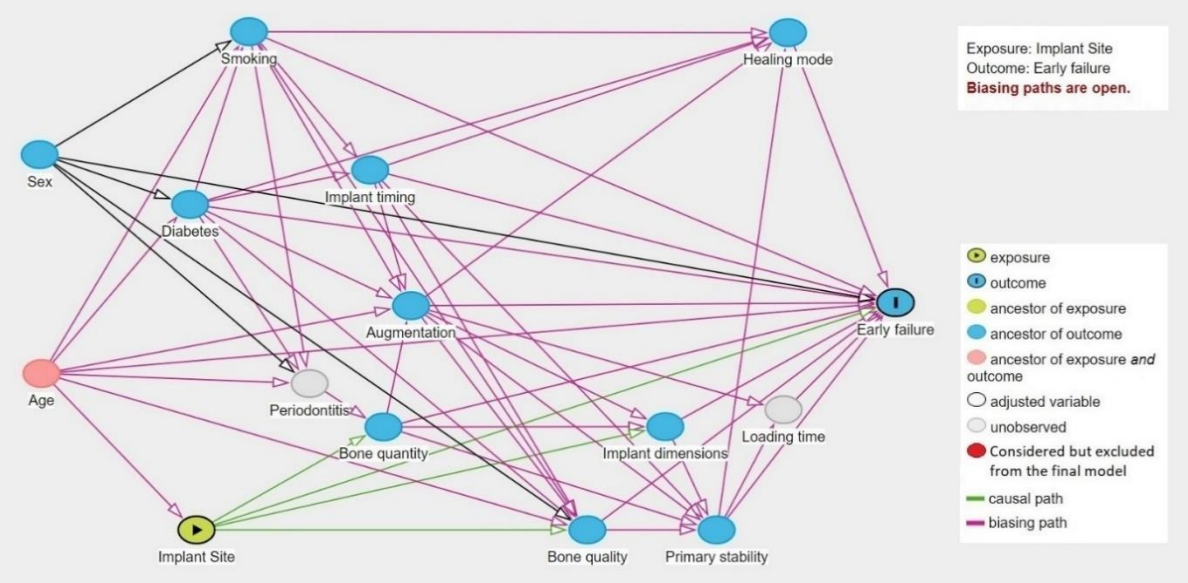


Figure 5. 4-A DAG (before adjustments) showing the association between exposure (Implant site) and outcome (early implant failure)), specifying the relationships among the covariates.

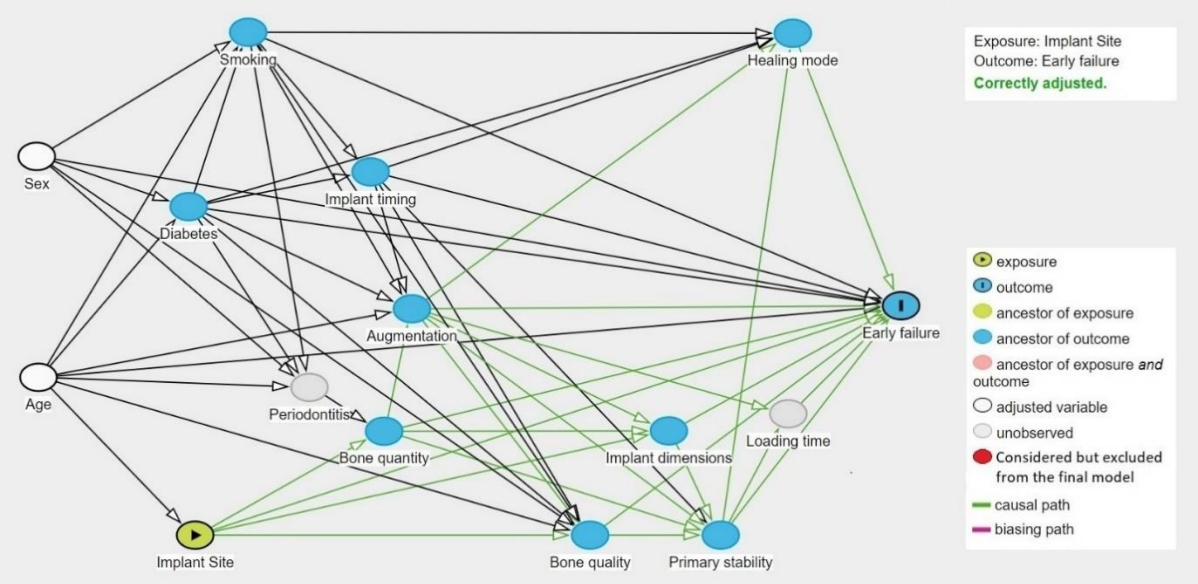


Figure 5.4-B DAG (after adjustment for age and sex) showing the association between exposure (Implant site) and outcome (early implant failure)), specifying the relationships among the covariates.

The mixed-effects logistic regression model revealed statistically significant higher odds of early implant failure for each implant site investigated compared to lower molars sites (Table 5.5, see Appendix 8.3 for the full model), with the highest odds observed in upper molar sites (OR:1.84; 95%CI: 1.57, 2.15) followed by lower anterior sites (OR: 1.80; 95%CI: 1.47, 2.19).

Figure 5.5 shows the predicted probabilities of early implant failure at the different implantation sites.

The estimated intraclass correlation coefficient (ICC) was 0.04 for centres and 0.5 for patients.

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	21	1,180	20,278	7,185.5	150,896
Patient	63,414	1	24	2.4	

Independent variable	**Failed / Placed implants (n)**	**Odd ratio**	**(95% CI)**	**p-value**
Lower molars	349 / 34,887	1 (reference)		
Lower anteriors	217 / 12,512	1.80	(1.47, 2.19)	<0.001
Lower premolars	329 / 20,657	1.67	(1.41, 1.97)	<0.001
Upper anteriors	388 / 24,166	1.58	(1.35, 1.88)	<0.001
Upper premolars	370 / 30,521	1.27	(1.08, 1.50)	<0.001
Upper molars	480 / 28,153	1.84	(1.57, 2.15)	<0.001

*Adjusted for age and sex

Table 5.5 Results of Mixed-effects logistic regression model evaluating associations between Implant site (independent variable) and early implant failure (dependent variable)

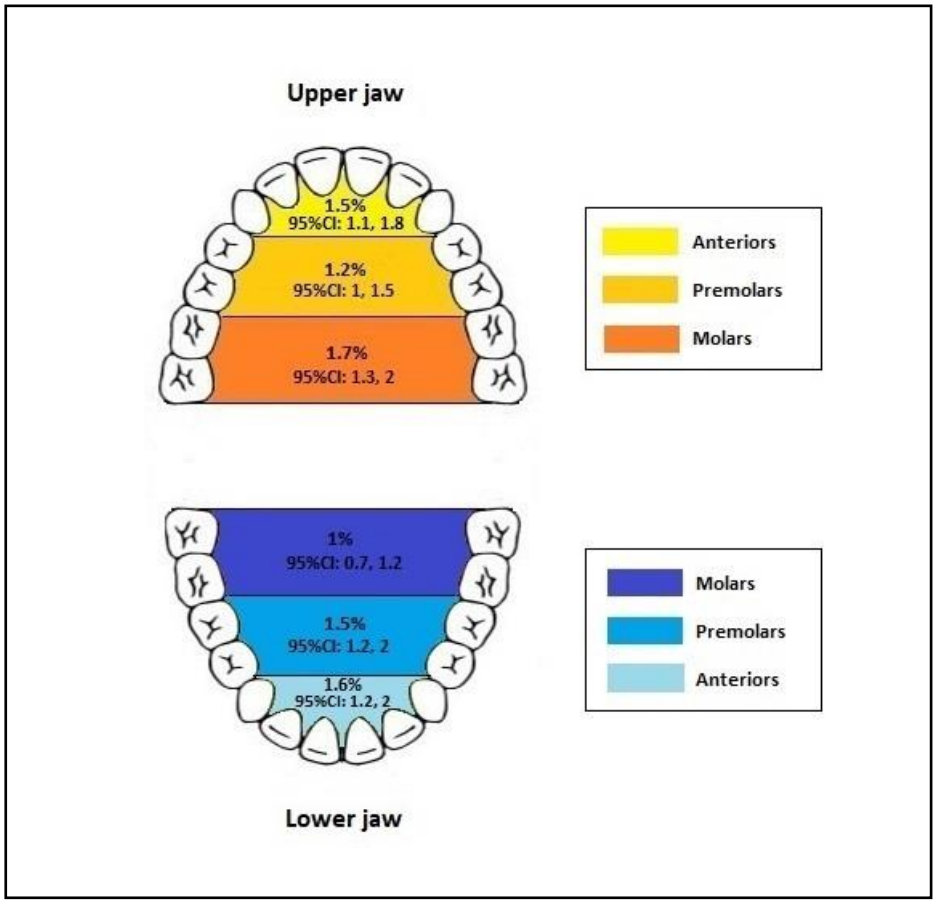


Figure 5.5 Predicted probabilities of early implant failure for implant sites

5.3.4. Diabetes

Data on diabetes was only available in the dataset from 2016-2022, limiting the analysis to this period. Detailed baseline data on diabetes is presented in Chapter 4 (see Table 4.1). The effect of diabetes on early implant failure was assessed by controlling for age and sex, as suggested by the DAG (Figures 5.6-A, B).

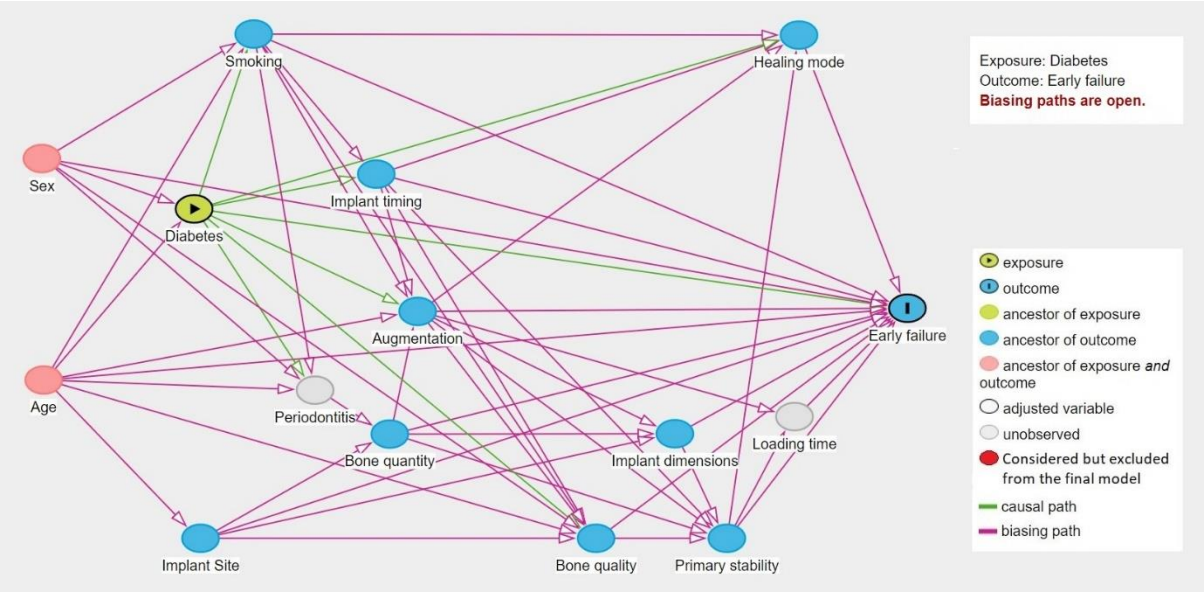


Figure 5.6-A DAG (before adjustments) showing the association between exposure (diabetes) and outcome (early implant failure), specifying the relationships among the covariates.

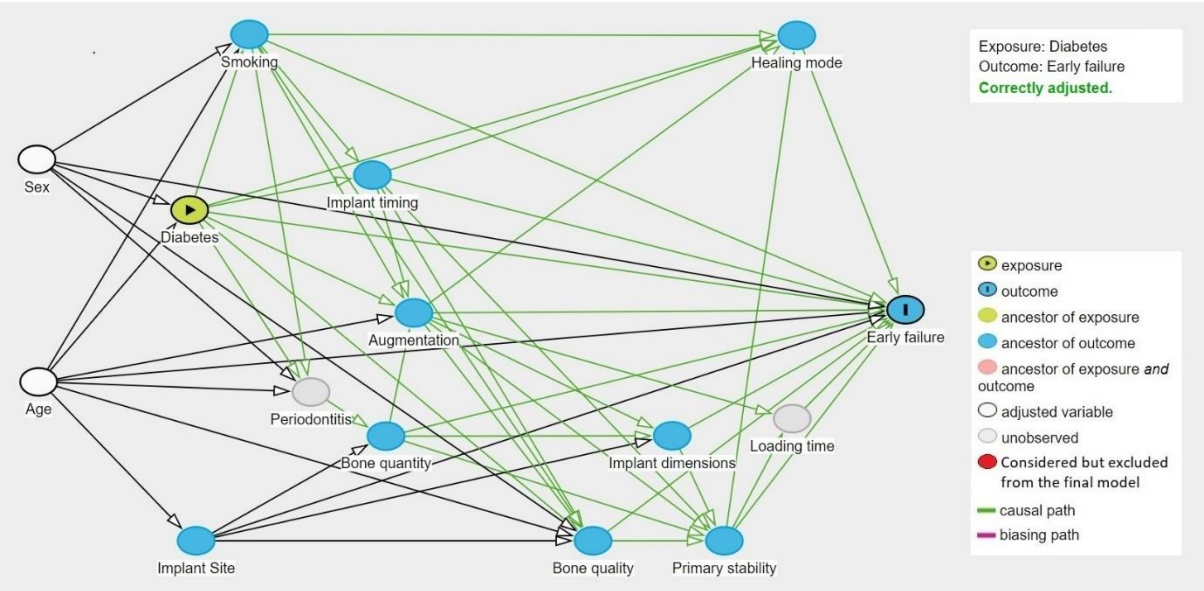


Figure 5.6-B DAG (after adjustment for age and sex) showing the association between exposure (diabetes) and outcome (early implant failure), specifying the relationships among the covariates.

Two centres (11 and 21) were excluded from the analysis due to over 90% missing diabetes data (See Appendix 7 for information on missing data by centres). The mixed-effects logistic regression model (Table 5.6, see Appendix 8.4 for the full model) suggested no evidence that diabetes is associated with a higher risk of early implant failure (OR:1.04; 95%CI 0.73, 1.48). The adjusted cumulative incidence estimated from this model for early failure of implants placed in diabetic patients is 1.4% compared to 1.3% for implants placed in non-diabetic patients (Table 5.7).

The intraclass correlation coefficient (ICC) was estimated to be 0.04 for centres and 0.5 for patients.

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	16	738	10,086	3,970.4	63,527
Patient	27,610	1	15	2.3	

Independent variable	**Failed / Placed implants (n)**	**Odd ratio***	**(95% CI)**	**p-value**
Diabetes				
No	747 / 59,352	1 (reference)		
Yes	52 / 4,286	1.04	(0.73, 1.48)	0.815

*Adjusted for age and sex

Table 5.6 Results of Mixed-effects logistic regression model evaluating associations between diabetes (independent variable) and early implant failure (dependent variable)

	Cumulative incidence of early implant failure (%)	**(95% CI)**
Diabetes		
No	1.3%	(1.0%, 1.7%)
Yes	1.4%	(1.0%, 2.0%)

Table 5.7 Adjusted cumulative incidences (predicted probabilities) of early implant failure with "Diabetes" as a predictor variable.

5.3.5. Smoking

Data about the smoking behaviour of patients who received dental implants was only available for the period 2016-2022 in the dataset. Baseline data on smoking status is presented in Chapter 4 (see Table 4.1). The impact of smoking on early implant failure was assessed by adjusting for age, sex, and diabetes, as recommended by the DAG (Figures 5.7-A, B).

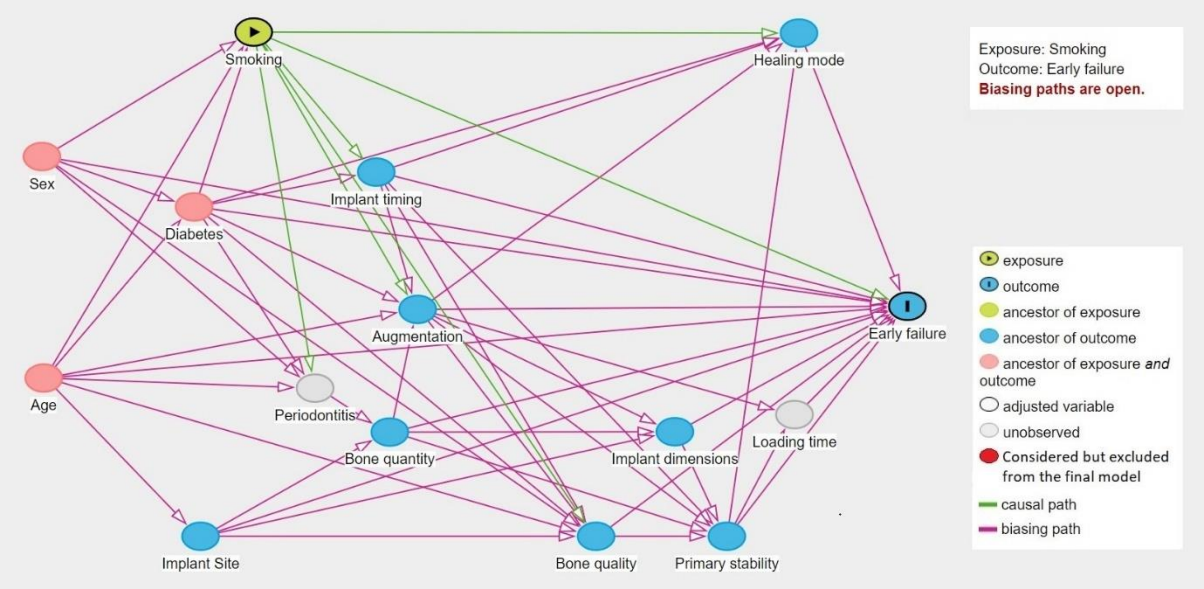


Figure 5.7-A DAG (before adjustments) showing the association between exposure (smoking) and outcome (early implant failure), specifying the relationships among the covariates.

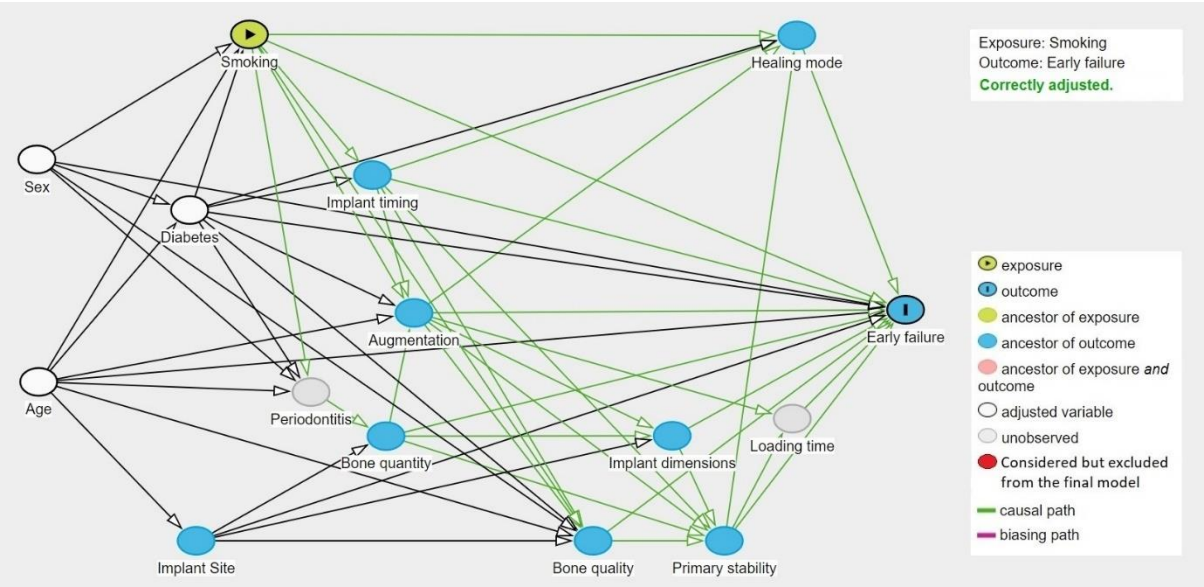


Figure 5.7-B DAG (after adjustment for age, sex, and diabetes) showing the association between exposure (smoking) and outcome (early implant failure), specifying the relationships among the covariates.

Two centres (11 and 21) were excluded from the analysis because they had over 90% missing smoking data (See Appendix 7 for information on missing data by centres). The mixed-effects logistic regression model shows that current smokers have significantly higher odds of early implant failure compared to non-smokers (OR: 1.62; 95%CI: 1.30, 2), while previous smoking habits do not appear to increase the risk of early failure (OR: 1.12; 95%CI: 0.88, 1.42) (Table 5.8, see Appendix 8.5 for the full model).

The estimated intraclass correlation coefficient (ICC) for centres was 0.04, while for patients it was 0.5.

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	16	676	10,067	3,898	62,368
Patient	27,141	1	15	2.3	

Independent variable	**Failed / Placed implants (n)**	**Odd ratio**	**(95% CI)**	**p-value**
Smoking status				
Never	433 / 39,828	1 (reference)		
Former	157 / 12,602	1.12	(0.88, 1.42)	0.347
Current	200 / 10,919	1.62	(1.30, 2.00)	<0.001

*Adjusted for age, sex and diabetes

Table 5.8 Results of Mixed-effects logistic regression model evaluating associations between smoking status (independent variable) and early implant failure (dependent variable)

We ran another model to investigate how varying smoking doses impact early implant failure in current smokers (Table 5.9, see Appendix 8.5 for the full model). The results of this model showed evidence of a dose-response relationship between smoking intensity and the odds of early implant failure, with higher odds associated with smoking more cigarettes per day.

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	16	660	10,018	3,846.8	61,549
Patient	26,805	1	15	2.3	

Independent variable	**Failed / Placed implants (n)**	**Odd ratio**	**(95% CI)**	**p-value**
Smoking status				
Never	433 / 39,828	1 (reference)		
Former	157 / 12,602	1.12	(0.88, 1.43)	0.338
Current (< 5 cigarettes/day)	23 / 1,697	1.26	(0.75, 2.13)	0.381
Current (5-15 cigarettes/day)	90 / 5,081	1.58	(1.16, 2.15)	0.004
Current (> 15 cigarettes/day)	69 / 3,290	1.85	(1.30, 2.64)	0.001

*Adjusted for age, sex and diabetes

Table 5.9 Mixed-effects logistic regression model for Smoking status (independent variable), including smoking doses for current smokers

The predicted probabilities from this model for early implant failure ranged from 1.4% (95%CI: 0.7%, 2.2%) in current smokers who smoke <5 cigarettes/day to 2% (95%CI: 1.2%, 2.7%) in current smokers who smoke >15 cigarettes/day. On the other hand, patients who never smoked had a 1.2% (95%CI: 0.8%, 1.5%) probability of early failure for their implants (Table 5.10, Figure 5.8).

	Cumulative incidence of early implant failure (%)	(95% CI)
Smoking status		
Never	1.2%	(0.8%, 1.5%)
Former	1.3%	(1.0%, 1.7%)
Current (< 5 cigarettes/day)	1.4%	(0.7%, 2.2%)
Current (5-15 cigarettes/day)	1.7%	(1.1%, 2.4%)
Current (> 15 cigarettes/day)	2.0%	(1.2%, 2.7%)

Table 5.10 Adjusted cumulative incidences (predicted probabilities) of early implant failure with "Smoking status" as a predictor variable.

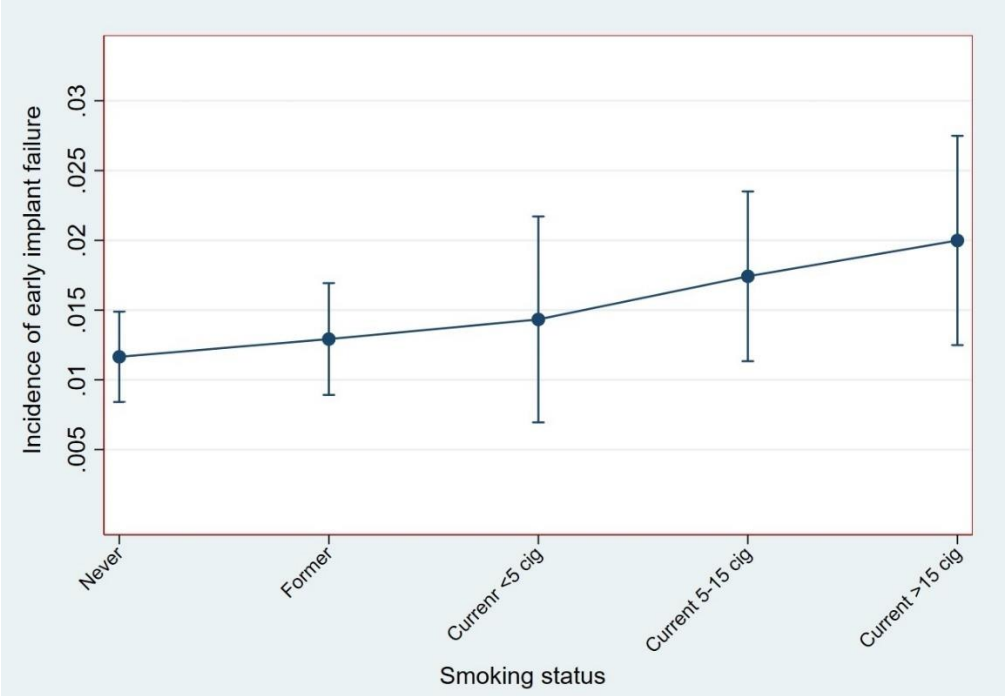


Figure 5.8 Cumulative incidences of early implant failure for smoking statuses

5.3.6. Timing of implant placement

The implant placement timing categories considered in this analysis were immediate (implants placed into fresh extraction sockets), early (implants placed up to 16 weeks after tooth extraction), and late (implants placed more than 16 weeks after tooth extraction). Summary statistics for implant placement timing in this dataset are presented in Chapter 4 (see Table 4.3). When investigating the impact of implant placement timing on early implant failure, age, sex, diabetes and smoking are the covariates that need adjusting for according to the DAG (Figures 5.9-A, B).

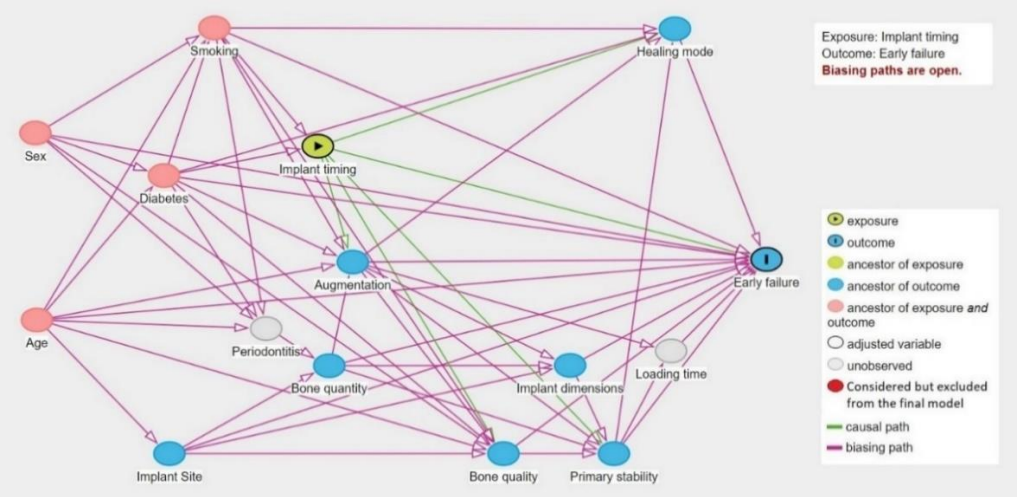


Figure 5. 9-A DAG (before adjustments) showing the association between exposure (timing of implant placement) and outcome (early implant failure)), specifying the relationships among the covariates

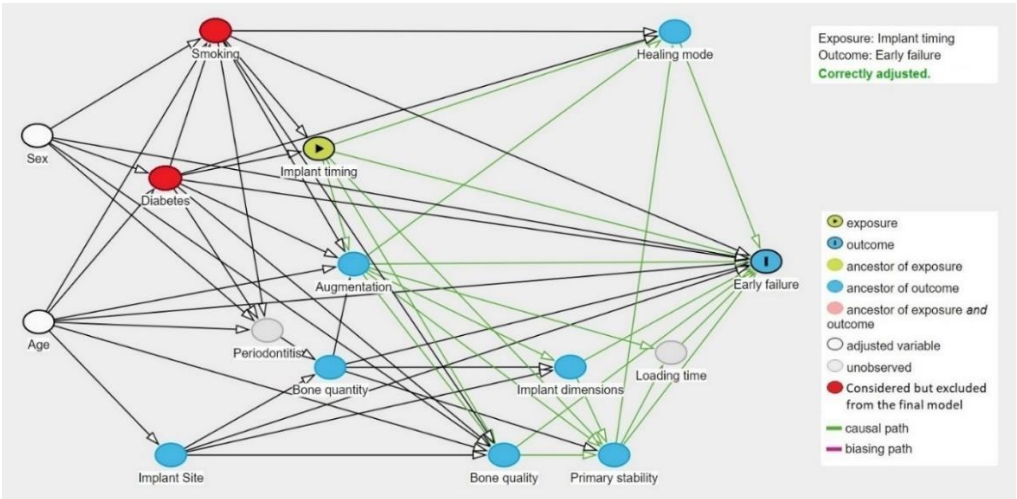


Figure 5.9-B DAG (after adjustment for age, sex, diabetes and smoking) showing the association between exposure (timing of implant placement) and outcome (early implant failure)), specifying the relationships among the covariates

As the data on diabetes and smoking were only available for the (2016-2022) period, we compared the unadjusted and adjusted models for these variables in this part of the dataset (Table 5.11, see Appendix 8.6 for the full models). We found that diabetes and smoking did not meet the pre-determined 10% change-in-estimate criterion for important confounders and were therefore excluded from the final model. As a result, we were able to fit a more parsimonious model without diabetes and smoking for the entire dataset from 2010 to 2022 (Table 5.12, see Appendix 8.6 for the full model).

According to the final model (Table 5.12), immediate implant placement was associated with increased odds of early implant failure compared to late implant placement (OR: 1.94; 95%CI: 1.64, 2.28). However, early implant placement did not show a significant difference in the odds of early failure compared to late placement (OR: 0.86; 95%CI: 0.68, 1.08).

According to the predicted probabilities estimated from this model, immediate implant showed a 2.3% (95%CI: 1.8%, 2.9%) probability of early failure, whereas the probabilities of early implant failure were comparable for both early and late implant placement (1,2%, 1.3%, respectively) (Table 5.13, Figure 5.10).

The intraclass correlation coefficient (ICC) was estimated to be 0.04 for centres and 0.5 for patients.

Timing of implant placement (Data 2016-2022)

Not adjusted for diabetes & smoking

Grouping information					
Group variable	No. of groups	Observations per group			No. of observations
		Min	Max	Average	
Centre	16	676	10,067	3,897.9	62,366
Patient	27,140	1	15	2.3	

Independent variable	Failed/Placed implants (n)	Odd ratio*	(95% CI)	p-value
Timing of implant placement				
Late (>16 wks)	638 / 52,605	1 (reference)		
Immediate	75 / 3,902	1.86	(1.38, 2.50)	<0.001
Early (≤16 wks)	63 / 5,859	0.87	(0.64, 1.18)	P=0.368

*Adjusted for age and sex

Adjusted for diabetes & smoking

Grouping information					
Group variable	No. of groups	Observations per group			No. of observations
		Min	Max	Average	
Centre	16	676	10,067	3,897.9	62,366
Patient	27,140	1	15	2.3	

Independent variable	Failed/Placed implants (n)	Odd ratio**	(95% CI)	p-value
Timing of implant placement				
Late (>16 wks)	638 / 52,605	1 (reference)		
Immediate	75 / 3,902	1.85	(1.37, 2.48)	<0.001
Early (≤16 wks)	63 / 5,859	0.88	(0.65, 1.20)	P=0.424

**Adjusted for age, sex, diabetes & smoking

Table 5.11 Comparing model outcomes for implant placement timing (independent variable)) and early implant failure (dependent variable), with and without adjusting for smoking and diabetes (2016-2022 part of the dataset).

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	21	1,180	20,254	7,096.1	149,018
Patient	62,812	1	24	2.4	

Independent variable	**Failed/Placed implants (n)**	**Odd ratio***	**(95% CI)**	**p-value**
Timing of implant placement				
Late (>16 wks)	1,730 / 126,865	1 (reference)		
Immediate	281 / 12,958	1.94	(1.64, 2.28)	<0.001
Early (≤16 wks)	104 / 9,195	0.86	(0.68, 1.08)	0.201

*Adjusted for age and sex

Table 5.12 Results of Mixed-effects logistic regression model evaluating associations between placement timing (independent variable) and early implant failure (dependent variable)

	Cumulative incidence of early implant failure (%)	**(95% CI)**
Timing of implant placement		
Immediate	2.3%	(1.8%, 2.9%)
Early (≤16 wks)	1.2%	(0.8%, 1.5%)
Late (>16 wks)	1.3%	(1.0%, 1.6%)

Table 5.13 Adjusted cumulative incidences (predicted probabilities) of early implant failure with "Implant placement timing" as a predictor variable

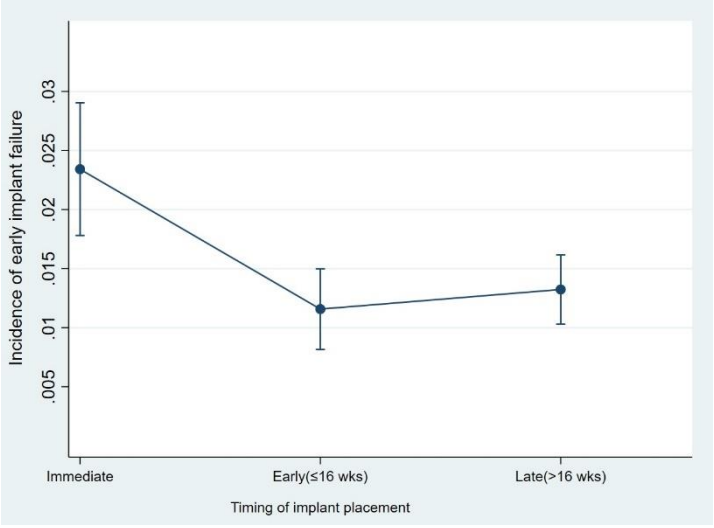


Figure 5.10 Adjusted cumulative incidences of early implant failure for Implant placement timing.

5.3.7. Bone quantity

Bone quantity in this study refers to the amount of available bone for implant placement, based on Terheyden (2010) classification of alveolar ridge defects (see Chapter 4, section 4.2). The analysis of bone quantity was limited to the dataset from 2016-2022, as this was the only period for which data was available. Baseline data on bone quantity is presented in Chapter 4 (see Table 4.3). When investigating the impact of bone quantity on early implant failure, age, sex, implant site, diabetes, and smoking are the covariates that need adjusting for according to the DAG (Figures 5.11-A, B).

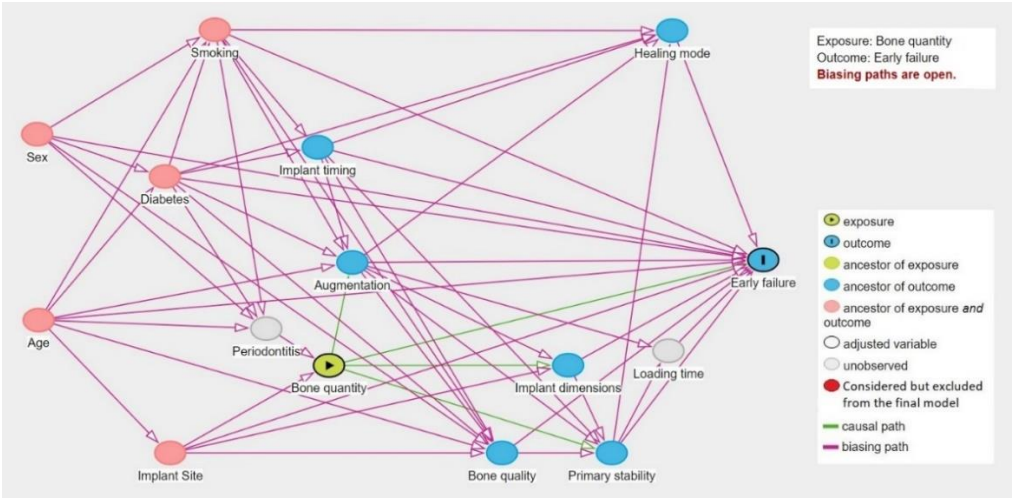


Figure 5.11-A DAG (before adjustments) showing the association between exposure (bone quantity) and outcome (early implant failure), specifying the relationships among the covariates.

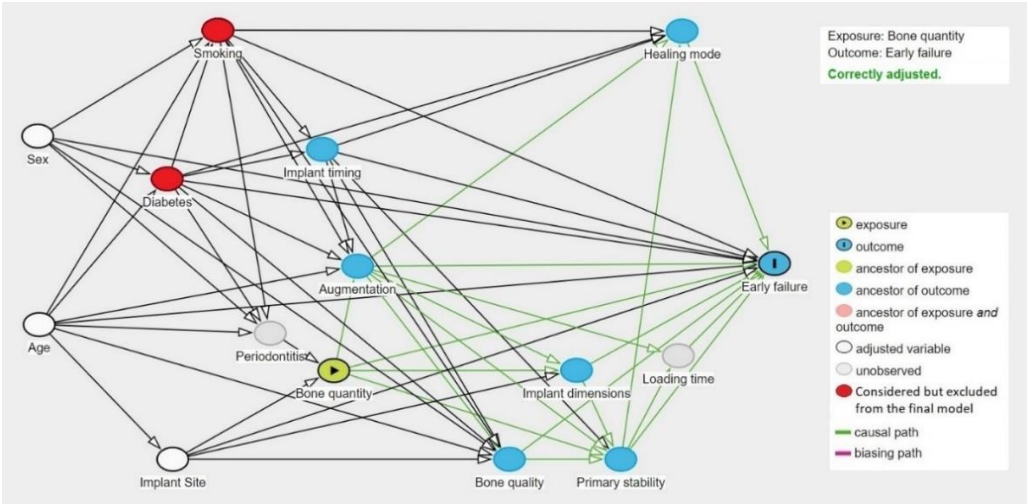


Figure 5.11-B DAG (after adjustment for age, sex, implant site, diabetes, and smoking) showing the association between exposure (bone quantity) andoutcome (early implant failure), specifying the relationships among the covariates

Although diabetes and smoking had more than 10% missing data as covariates, they were still considered for adjustment. However, the difference in estimates between the models adjusted and non-adjusted for them was minimal (<10%) (Table 5.14, see Appendix 8.7 for the full models). As a result, they were excluded from the final model, leading to a significant increase in sample size from 31,707 to 51,311.

The odds of early implant failures in the final fully adjusted model were found to be significantly higher only in the two categories of bone quantity representing vertical bone defects (Type 3/4 and Type 4/4), with odds ratios of 2.08 (95%CI: 1.34, 3.22) and 2.09 (95%CI: 1.01, 4.30), respectively. In addition, the estimates did not vary significantly between the minimally and fully adjusted models (Table 5.15, see Appendix 8.7 for the full models). Furthermore, the adjusted cumulative incidence of early failure for implants placed in bone with vertical defects was 2.5% (95%CI: 1.4%, 3.7%) for the Type 3/4 defect category and 2.6% (95%CI: 0.9%, 4.2%) for the Type 4/4 defect category, compared to 1.4% (95%CI: 0.9%, 1.8%) for implants placed in a relatively adequate amount of bone (Table 5.16, Figure 5.12).

The estimated intraclass correlation coefficient (ICC) for centres was 0.04, while for patients it was 0.5.

Adjustments excluded diabetes & smoking

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	11	93	7,898	2,882.6	31,709
Patient	15,121	1	15	2.1	

Independent variable	Failed/Placed implants (n)	Odd ratio*	(95% CI)	p-value
Bone quantity				
Sufficient bone	246 / 18,997	1 (reference)		
Type 1/4 defect	74 / 7,116	0.95	(0.68, 1.33)	0.771
Type 2/4 defect	32 / 3,560	0.79	(0.50, 1.24)	0.306
Type 3/4 defect	16 / 1,083	1.67	(0.90, 3.11)	0.107
Type 4/4 defect	5 / 227	2.26	(0.73, 6.94)	0.155
Other defects	7 / 726	1.10	(0.47, 2.58)	0.833

*Adjusted for age, sex, and implant site

Adjustments included diabetes & smoking

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	11	93	7,898	2,882.6	31,709
Patient	15,121	1	15	2.1	

Independent variable	Failed/Placed implants (n)	Odd ratio**	(95% CI)	p-value
Bone quantity				
Sufficient bone	246 / 18,997	1 (reference)		
Type 1/4 defect	74 / 7,116	0.94	(0.67, 1.32)	0.725
Type 2/4 defect	32 / 3,560	0.80	(0.50, 1.26)	0.334
Type 3/4 defect	16 / 1,083	1.69	(0.91, 3.14)	0.099
Type 4/4 defect	5 / 227	2.37	(0.77, 7.28)	0.132
Other defects	7 / 726	1.06	(0.45, 2.51)	0.887

**Adjusted for age, sex, implant site, diabetes & smoking

Table 5.14 Comparing model outcomes for bone quantity (independent variable) and early implant failure (dependent variable), with and without adjusting for diabetes and smoking

Adjusted for age and sex

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	15	166	8,401	3,420.9	51,313
Patient	23,450	1	16	2.2	

Independent variable	Failed/Placed implants (n)	Odd ratio	(95% CI)	p-value
Bone quantity				
Sufficient bone	488 / 34,571	1 (reference)		
Type 1/4 defect	98 / 8,962	0.90	(0.68, 1.17)	0.412
Type 2/4 defect	54 / 4,766	0.95	(0.67, 1.34)	0.765
Type 3/4 defect	36 / 1,561	2.3	(1.49, 3.55)	<0.001
Type 4/4 defect	13 / 456	2.21	(1.07, 4.56)	0.033
Other defects	13 / 997	1.40	(0.74, 2.64)	0.303

Fully adjusted*

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	15	166	8,401	3,420.9	51,313
Patient	23,450	1	16	2.2	

Independent variable	Failed/Placed implants (n)	Odd ratio	(95% CI)	p-value
Bone quantity				
Sufficient bone	488 / 34,571	1 (reference)		
Type 1/4 defect	98 / 8,962	0.81	(0.62, 1.07)	0.141
Type 2/4 defect	54 / 4,766	0.85	(0.60, 1.20)	0.359
Type 3/4 defect	36 / 1,561	2.08	(1.34, 3.22)	0.001
Type 4/4 defect	13 / 456	2.09	(1.01, 4.30)	0.046
Other defects	13 / 997	1.28	(0.67, 2.42)	0.454

*Adjusted for age, sex, and implant site

Table 5. 15 Results of Mixed-effects logistic regression model evaluating associations between bone quantity (independent variable) and early implant failure (dependent variable)

	Cumulative incidence of early implant failure (%)	(95% CI)
Bone quantity		
Sufficient bone	1.4%	(0.9%, 1.8%)
Type 1/4 defect	1.1%	(0.7%, 1.5%)
Type 2/4 defect	1.2%	(0.7%, 1.7%)
Type 3/4 defect	2.5%	(1.4%, 3.7%)
Type 4/4 defect	2.6%	(0.9%, 4.2%)
Other defects	1.7%	(0.6%, 2.7%)

Table 5.16 Adjusted cumulative incidences (predicted probabilities) of early implant failure with "Bone quantity" as a predictor variable.

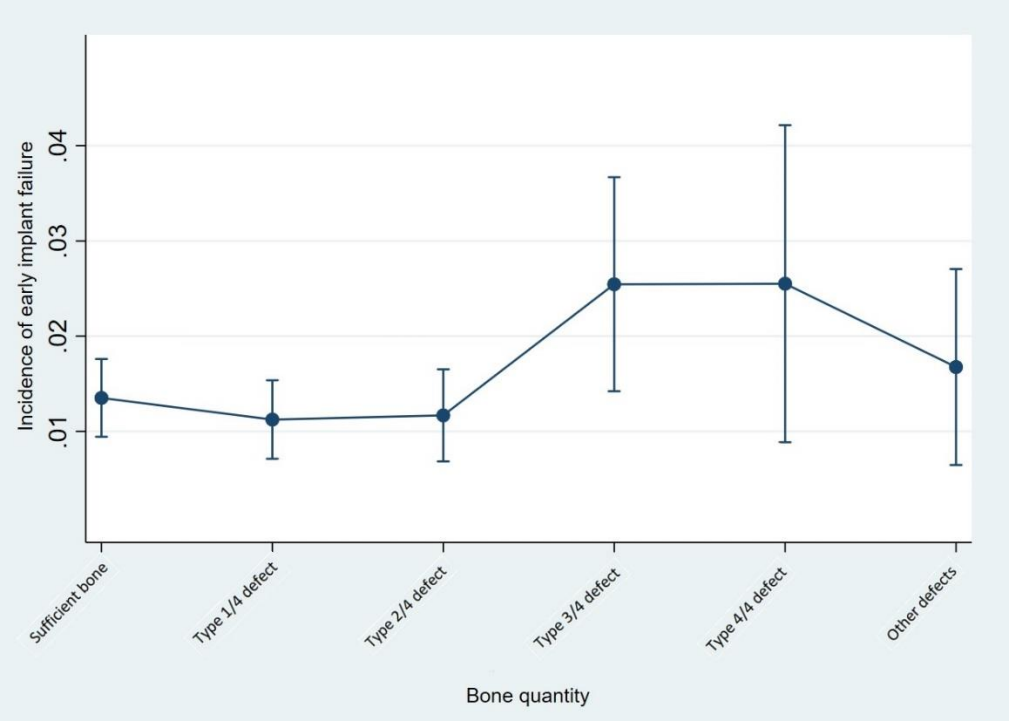


Figure 5.12 Adjusted cumulative incidence of early implant failure for different bone quantities

5.3.8. Bone augmentation

Bone augmentation refers to any type of bone augmentation, before or concomitant with implant placement, or both. Baseline data characteristics regarding bone augmentation in this dataset are presented in Chapter 4 (see Table 4.3). Based on the DAG (Figure 5.13-A, B), age, sex, implant site, implant placement timing, diabetes, smoking, and bone quantity are factors that should be considered when investigating the effect of bone augmentation on early implant failure.

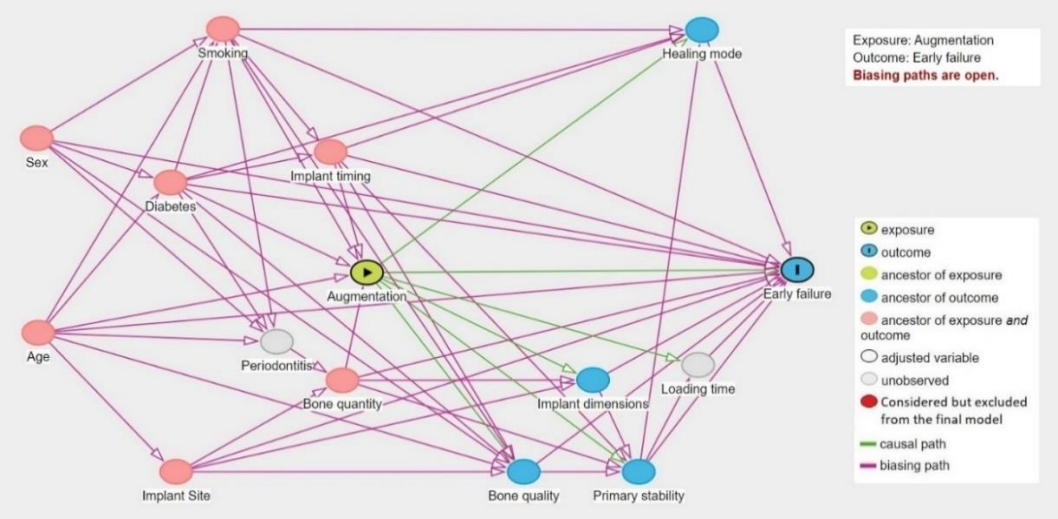


Figure 5.13-A DAG (before adjustments) showing the association between exposure (bone augmentation) and outcome (early implant failure), specifying the relationships among the covariates

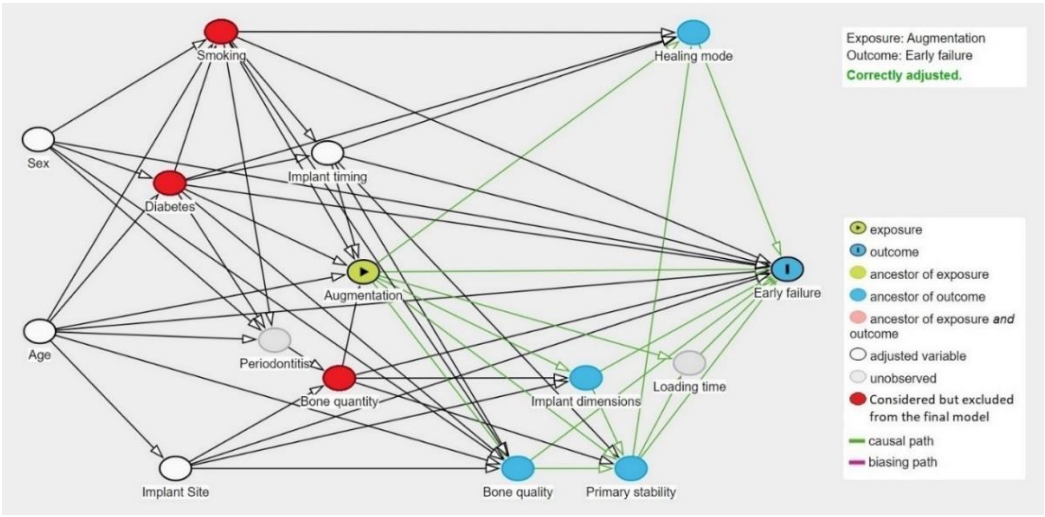


Figure 5.13-B DAG (after adjustment for age, sex, implant site, implant placement timing, diabetes, smoking, and bone quantity) showing the association between exposure (bone augmentation) and outcome (early implant failure), specifying the relationships among the covariates

Data on diabetes, smoking and bone quantity were only available for the (2016-2022) part of the dataset; therefore, we compared the unadjusted and adjusted models for these variables in this part (2016-2022) of the dataset (Table 5.17, see Appendix 8.8 for the full models). We found that these variables did not meet the 10% change-in-estimate criterion for important confounders and were therefore excluded from the final model; this allowed us to create a more parsimonious model for the entire dataset from 2010 to 2022, not including diabetes, smoking or bone quantity (Table 5.18, see Appendix 8.8 for the full model).

In the fully adjusted final model, bone augmentation was associated with a statistically significant higher risk of early implant failure compared to implants placed with no augmentation (OR: 1.13; 95%CI: 1.01, 1.27). However, the adjusted cumulative incidence of early implant failure estimated from this model was only slightly higher at 1.4% (95% CI: 1.1%, 1.8%) for cases with bone augmentation, compared to 1.3% (1.0%, 1.6%) for cases without bone augmentation (Table 5.19)

Regarding interaction analysis, the potential interaction of implant placement timing and bone augmentation was considered and tested using interaction terms. However, no evidence was found for such an interaction based on the likelihood-ratio test.

The estimated intraclass correlation coefficient (ICC) was 0.04 for centres and 0.5 for patients.

Adjustments excluded diabetes, smoking, bone quantity

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	11	93	7,897	2,882.5	31,707
Patient	15,120	1	15	2.1	

Independent variable	Failed/Placed implants (n)	Odd ratio*	(95% CI)	p-value
Bone augmentation				
No	246 / 18,995	1 (reference)		
Yes	134 / 12,712	1.01	(0.76, 1.34)	0.947

*Adjusted for age, sex, Implant site, and implant placement timing

Adjustments included diabetes, smoking, bone quantity

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	11	93	7,897	2,882.5	31,707
Patient	15,120	1	15	2.1	

Independent variable	Failed/Placed implants (n)	Odd ratio**	(95% CI)	p-value
Bone augmentation				
No	246 / 18,995	1 (reference)		
Yes	134 / 12,712	1.02	(0.43, 2.43)	0.956

**Adjusted for age, sex, Implant site, implant placement timing, diabetes, smoking, and bone quantity

Table 5.17 Comparing model outcomes for bone augmentation (independent variable) and early implant failure (dependent variable), with and without adjusting for diabetes, smoking and bone quantity

Adjusted for age and sex

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	21	1,180	20,254	7,096.1	149,018
Patient	62,812	1	24	2.4	

Independent variable	Failed/Placed implants (n)	Odd ratio	(95% CI)	p-value
Bone augmentation				
No	1,100 / 77,595	1 (reference)		
Yes	1,015 / 71,423	1.20	(1.08, 1.34)	0.001

Fully adjusted*

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	21	1,180	20,254	7,096.1	149,018
Patient	62,812	1	24	2.4	

Independent variable	Failed/Placed implants (n)	Odd ratio	(95% CI)	p-value
Bone augmentation				
No	1,100 / 77,595	1 (reference)		
Yes	1,015 / 71,423	1.13	(1.01, 1.27)	0.030

*Adjusted for age, sex, Implant site, and implant placement timing

Table 5.18 Results of Mixed-effects logistic regression model evaluating associations between Bone augmentation (independent variable) and early implant failure (dependent variable)

	Cumulative incidence of early implant failure (%)	(95% CI)	p-value
Bone augmentation			
No	1.3%	(1.0%, 1.6%)	<0.001
Yes	1.4%	(1.1%, 1.8%)	<0.001

Table 5.19 Adjusted cumulative incidences of early implant failure (predicted probabilities) with “Bone augmentation” as a predictor variable

5.3.9. Bone quality

Bone quality in this study refers to bone types as classified by Lekholm and Zarb (1985). Baseline data characteristics on bone quality in this dataset are presented in Chapter 4 (see Table 4.3). When examining the impact of bone quality on early implant failure, it is important to consider several factors, as illustrated in the DAG (Figures 5.14-A, B). These include age, sex, implant site, diabetes, smoking, implant placement timing, and bone augmentation.

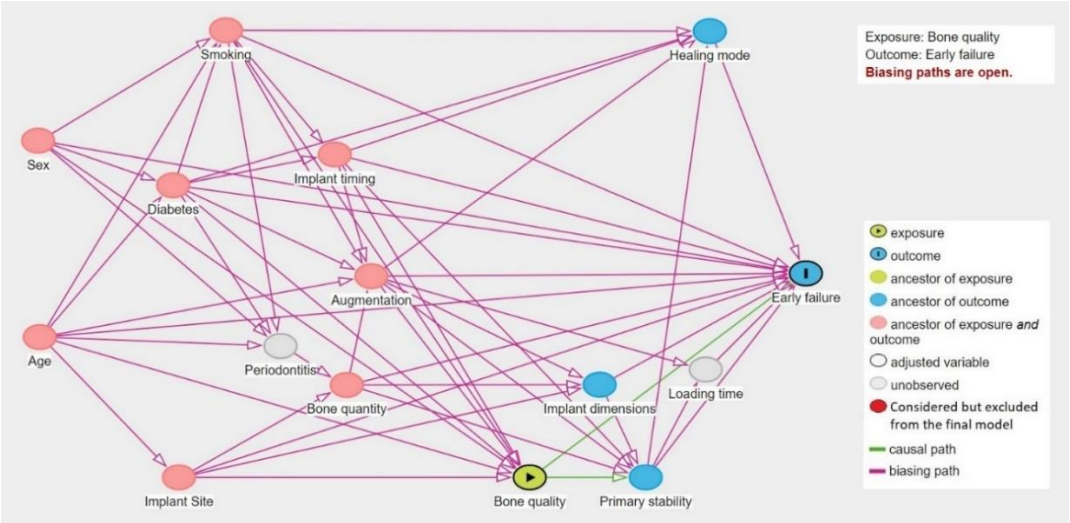


Figure 5.14-A DAG (before adjustments) showing the association between exposure (bone quality) and outcome (early implant failure)), specifying the relationships among the covariates

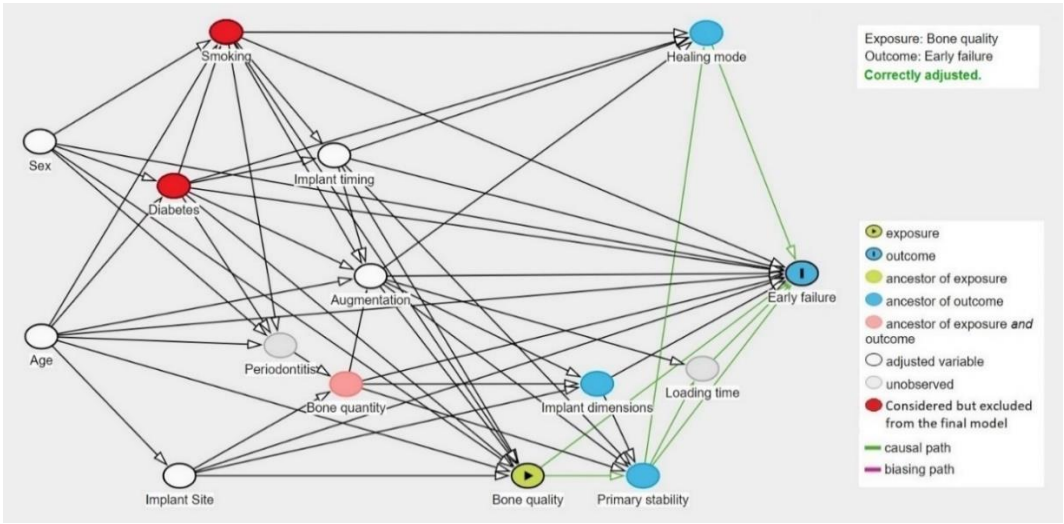


Figure 5.14-B DAG (after adjustment for age, sex, implant site, diabetes, smoking, implant placement timing, and bone augmentation) showing the association between exposure (bone quality) and outcome (early implant failure)), specifying the relationships among the covariates

Data on diabetes and smoking were only available for the 2016-2022 period of the dataset, with over 10% missing in each. Therefore, we compared the unadjusted and adjusted models for these covariates in the (2016-2022) part of the dataset (Table 5.20, see Appendix 8.9 for the full models). We found that these covariates did not meet the pre-determined 10% change-in-estimate criterion of confounding. As a result, we removed them from the final model; this enabled us to create a more parsimonious model for the complete dataset from 2010 to 2022 (Table 5.21, see Appendix 8.9 for the full model).

According to the final fully adjusted model, type 2 and type 3 bones were found to be associated with significantly lower odds of early implant failure compared to type 1 bone, with odd ratios of 0.79 (95%CI: 0.68, 0.92) and 0.69 (95%CI: 0.58, 0.82), respectively. On the other hand, the odds of early failure did not significantly differ between type 4 and type 1 bones (OR: 1.08; 95%CI: 0.85, 1.36).

The adjusted cumulative incidences of early implant failure estimated from this model were comparable for type 1 and type 4 bones at 1.7% and 1.8%, respectively. However, type 2 and type 3 bones showed relatively lower cumulative incidence of 1.4% and 1.2%, respectively (Table 5.22, Figure 5.15).

The intraclass correlation coefficient (ICC) was estimated to be 0.04 for centres and 0.5 for patients.

Adjustments excluded diabetes & smoking

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	16	596	10,060	3,849.3	61,589
Patient	26,900	1	15	2.3	

Independent variable	Failed/Placed implants (n)	Odd ratio*	(95% CI)	p-value
Bone quality				
Type 1	127 / 11,146	1 (reference)		
Type 2	345 / 28,441	0.85	(0.66, 1.09)	0.198
Type 3	215 / 17,387	0.73	(0.54, 0.98)	0.036
Type 4	78 / 4,615	1.31	(0.90, 1.91)	0.153

*Adjusted for age, sex, implant site, implant placement timing, and bone augmentation

Adjustments included diabetes & smoking

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	16	596	10,060	3,849.3	61,589
Patient	26,900	1	15	2.3	

Independent variable	Failed/Placed implants (n)	Odd ratio**	(95% CI)	p-value
Bone quality				
Type 1	127 / 11,146	1 (reference)		
Type 2	345 / 28,441	0.84	(0.65, 1.09)	0.190
Type 3	215 / 17,387	0.72	(0.53, 0.97)	0.032
Type 4	78 / 4,615	1.29	(0.90, 1.88)	0.176

**Adjusted for age, sex, implant site, diabetes, smoking, implant placement timing, and bone augmentation.

Table 5.20 Comparing model outcomes for bone quality (independent variable) and early implant failure (dependent variable), with and without adjusting for diabetes and smoking

Adjusted for age and sex

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	21	393	20,157	6,640	139,439
Patient	59,295	1	24	2.4	

Independent variable	Failed/Placed implants (n)	Odd ratio	(95% CI)	p-value
Bone quality				
Type 1	371 / 24,749	1 (reference)		
Type 2	891 / 63,070	0.83	(0.72, 0.97)	0.015
Type 3	529 / 40,299	0.76	(0.64, 0.90)	0.001
Type 4	178 / 11,321	1.26	(1, 1.58)	0.044

Fully adjusted*

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	21	393	20,157	6,640	139,439
Patient	59,295	1	24	2.4	

Independent variable	Failed/Placed implants (n)	Odd ratio	(95% CI)	p-value
Bone quality				
Type 1	371 / 24,749	1 (reference)		
Type 2	891 / 63,070	0.79	(0.68, 0.92)	0.003
Type 3	529 / 40,299	0.69	(0.58, 0.82)	< 0.001
Type 4	178 / 11,321	1.08	(0.85, 1.36)	0.538

*Adjusted for age, sex, implant site, implant placement timing, and bone augmentation

Table 5.21 Results of Mixed-effects logistic regression model evaluating associations between Bone quality (independent variable) and early implant failure (dependent variable)

	Cumulative incidence of early implant failure (%)	(95% CI)
Bone quality		
Type 1	1.7%	(1.3%, 2.1%)
Type 2	1.4%	(1.0%, 1.7%)
Type 3	1.2%	(0.9%, 1.5%)
Type 4	1.8%	(1.3%, 2.3%)

Table 5.22 Adjusted cumulative incidences (predicted probabilities) of early implant failure with “Bone quality” as a predictor variable

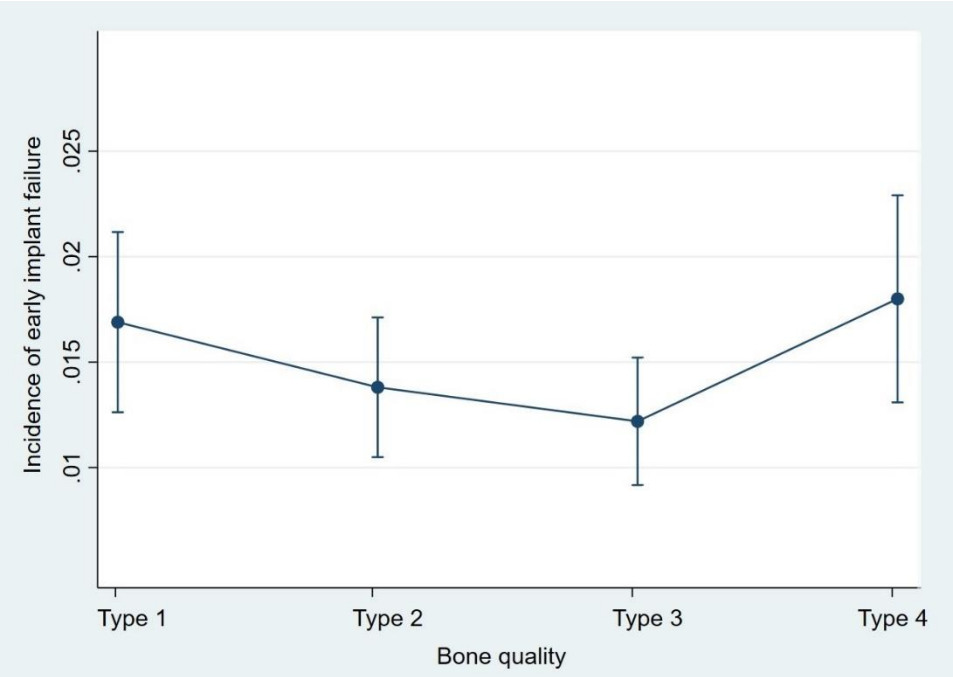


Figure 5.15 Adjusted cumulative incidence of early implant failure for different bone qualities.

5.3.10. Implant dimensions

The baseline characteristics of implant dimensions reported in this dataset are presented in Chapter 4 (see Table 4.3). In order to evaluate the relationship between implant dimensions and early implant failure, it is necessary to consider several covariates, including age, sex, implant site, bone quantity, and bone augmentation, as indicated by the DAG (Figures 5.16-A, B).

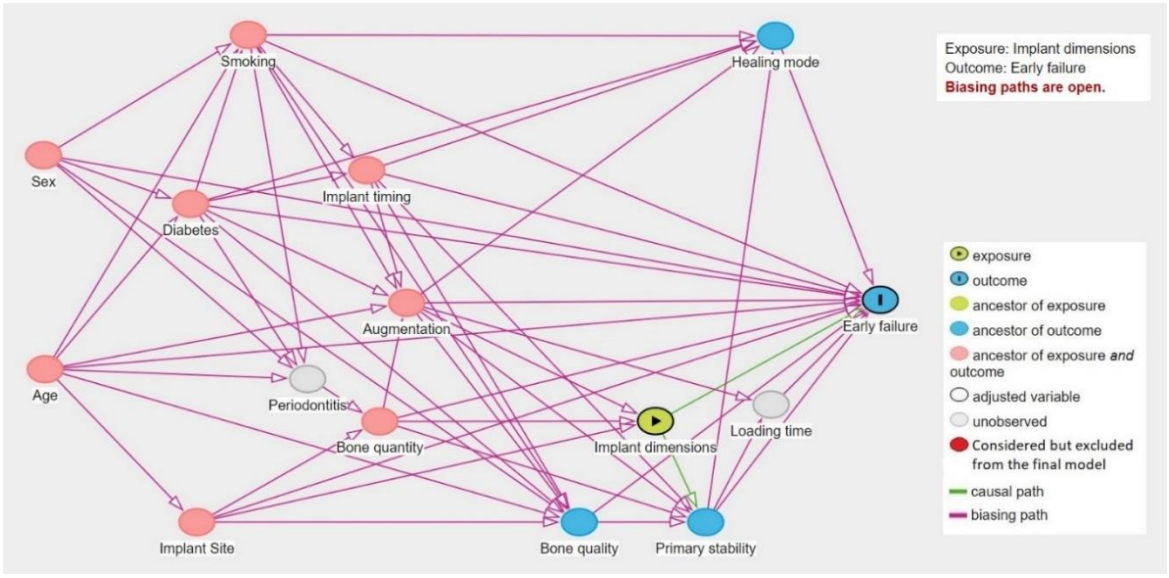


Figure 5.16-A DAG (before adjustments) showing the association between exposure (implant dimensions) and outcom (early implant failure), specifying the relationships among the covariates

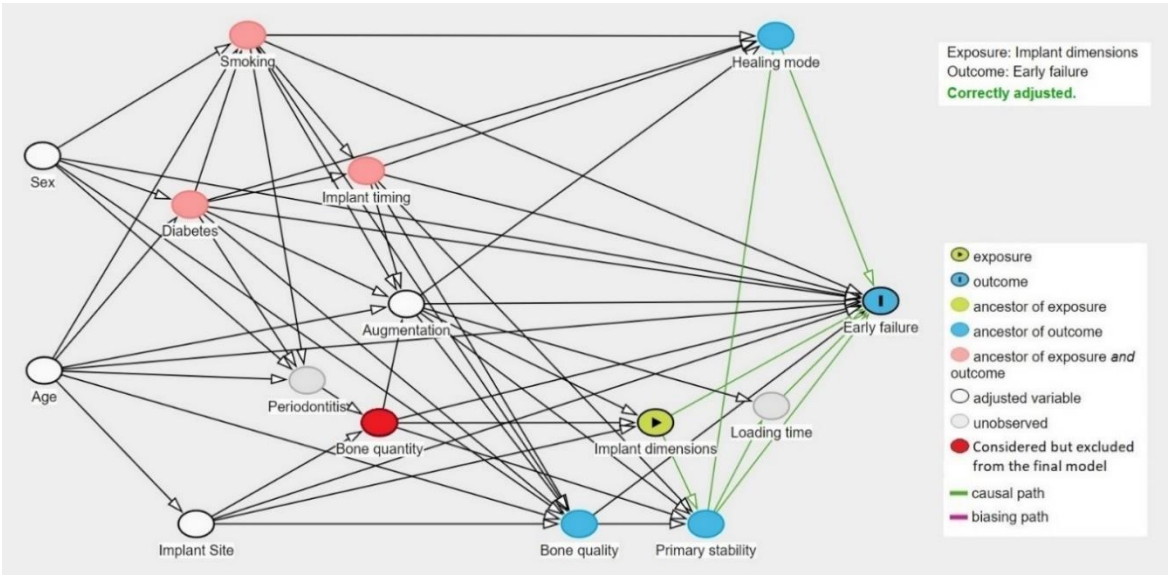


Figure 5.16-B DAG (after adjustment for age, sex, implant site, bone quantity, and bone augmentation) showing the association between exposure (implant dimensions) and outcome (early implant failure), specifying the relationships among the covariates

Data on bone quantity was only available for the (2016-2022) part of the dataset, and over 10% of this data was missing; therefore, we compared the unadjusted and adjusted models for this covariate in the (2016-2022) part of the dataset (Table 5.23, see Appendix 8.10 for the full models). We found that bone quantity as a confounder did not meet the pre-determined 10% change-in-estimate criterion and was therefore excluded from the final model; this allowed us to create a more parsimonious model for the entire dataset from 2010 to 2022 (Table 5.24, see Appendix 8.10 for the full model).

The results of the final model (Table 5.24) show that narrow-diameter implants across all length classes had significantly higher odds of early implant failure than implants of standard length and diameter (ORs: 1.70 for narrow/long, 1.78 for narrow/standard, and 2.66 for narrow/short implants). In addition, short implants of standard diameter were also associated with increased odds of early failure compared to the implants of standard length and diameter (OR: 1.45; 95%CI: 1.23, 1.70). The predicted probabilities of early failure based on implant dimensions are shown in (Table 5.25, Figure 5.17). It is clear that as both dimensions decrease, the probability of early failure increases. However, this trend is more pronounced with a reduction in implant diameter.

Regarding interaction analysis, the potential interaction of bone augmentation and implant dimensions was considered and tested using interaction terms. However, no evidence was found for such an interaction based on the likelihood-ratio test.

The estimated intraclass correlation coefficient (ICC) was 0.04 for centres and 0.5 for patients.

Adjustments excluded bone quantity

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	15	166	8,401	3,420.9	51,313
Patient	23,450	1	16	2.2	

Independent variable	Failed/Placed implants (n)	Odd ratio*	(95% CI)	p-value
Implant dimensions (length/diameter)				
Standard (≥10, <13) / Standard (≥3.75, <5)	247 / 20,740	1 (reference)		
Standard (≥10, <13) / Wide (≥5, ≤7)	28 / 3,527	0.67	(0.43, 1.05)	0.084
Standard (≥10, <13) / Narrow (≥3, <3.75)	80 / 4,217	1.44	(1.05, 1.98)	0.025
Short (<10) / Wide (≥5, ≤7)	29 / 1,709	1.55	(0.98, 2.46)	0.063
Short (<10) / Standard (≥3.75, <5)	132 / 9,484	1.27	(0.98, 1.65)	0.073
Short (<10) / Narrow (≥3, <3.75)	78 / 2,335	2.21	(1.50, 3.27)	<0.001
long (≥13, ≤18) / Wide (≥5, ≤7)	6 / 772	0.50	(0.19, 1.32)	0.162
long (≥13, ≤18) / Standard (≥3.75, <5)	82 / 7,267	1.06	(0.78, 1.44)	0.726
long (≥13, ≤18) / Narrow (≥3, <3.75)	20 / 1,262	1.68	(0.97, 2.92)	0.066

*Adjusted for age, sex, implant site, and bone augmentation

Adjustments included bone quantity

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	15	166	8,401	3,420.9	51,313
Patient	23,450	1	16	2.2	

Independent variable	Failed/Placed implants (n)	Odd ratio**	(95% CI)	p-value
Implant dimensions (length/diameter)				
Standard (≥10, <13) / Standard (≥3.75, <5)	247 / 20,740	1 (reference)		
Standard (≥10, <13) / Wide (≥5, ≤7)	28 / 3,527	0.68	(0.43, 1.07)	0.094
Standard (≥10, <13) / Narrow (≥3, <3.75)	80 / 4,217	1.45	(1.05, 2.00)	0.023
Short (<10) / Wide (≥5, ≤7)	29 / 1,709	1.53	(0.96, 2.43)	0.071
Short (<10) / Standard (≥3.75, <5)	132 / 9,484	1.26	(0.97, 1.64)	0.090
Short (<10) / Narrow (≥3, <3.75)	78 / 2,335	2.19	(1.48, 3.24)	<0.001
long (≥13, ≤18) / Wide (≥5, ≤7)	6 / 772	0.50	(0.19, 1.33)	0.165
long (≥13, ≤18) / Standard (≥3.75, <5)	82 / 7,267	1.06	(0.78, 1.44)	0.719
long (≥13, ≤18) / Narrow (≥3, <3.75)	20 / 1,262	1.66	(0.96, 2.89)	0.072

**Adjusted for age, sex, implant site, bone quantity, and bone augmentation

Table 5.23 Comparing model outcomes for implant dimensions (independent variable) and early implant failure (dependent variable), with and without adjusting for bone quantity

Adjusted for age and sex

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	21	1,180	20,278	7,185.5	150,896
Patient	63,414	1	24	2.4	

Independent variable	Failed/Placed implants (n)	Odd ratio	(95% CI)	p-value
Implant dimensions (length/diameter)				
Standard (≥10, <13) / Standard (≥3.75, <5)	741 / 62,293	1 (reference)		
Standard (≥10, <13) / Wide (≥5, ≤7)	83 / 8,692	0.89	(0.68, 1.15)	0.364
Standard (≥10, <13) / Narrow (≥3, <3.75)	275 / 13,524	1.80	(1.53, 2.14)	<0.001
Short (<10) / Wide (≥5, ≤7)	69 / 5,020	1.21	(0.91, 1.61)	0.180
Short (<10) / Standard (≥3.75, <5)	350 / 21,808	1.40	(1.19, 1.64)	<0.001
Short (<10) / Narrow (≥3, <3.75)	178 / 5,176	2.60	(2.03, 3.33)	<0.001
long (≥13, ≤18) / Wide (≥5, ≤7)	24 / 2,569	0.85	(0;53, 1.35)	0.485
long (≥13, ≤18) / Standard (≥3.75, <5)	283 / 25,217	1.04	(0.88, 1.22)	0.652
long (≥13, ≤18) / Narrow (≥3, <3.75)	130 / 6,597	1.77	(1.41, 2.23)	<0.001

Fully adjusted*

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	21	1,180	20,278	7,185.5	150,896
Patient	63,414	1	24	2.4	

Independent variable	Failed/Placed implants (n)	Odd ratio	(95% CI)	p-value
Implant dimensions (length/diameter)				
Standard (≥10, <13) / Standard (≥3.75, <5)	741 / 62,293	1 (reference)		
Standard (≥10, <13) / Wide (≥5, ≤7)	83 / 8,692	0.87	(0.67, 1.13)	0.297
Standard (≥10, <13) / Narrow (≥3, <3.75)	275 / 13,524	1.78	(1.49, 2.12)	<0.001
Short (<10) / Wide (≥5, ≤7)	69 / 5,020	1.17	(0.88, 1.57)	0.280
Short (<10) / Standard (≥3.75, <5)	350 / 21,808	1.45	(1.23, 1.70)	<0.001
Short (<10) / Narrow (≥3, <3.75)	178 / 5,176	2.66	(2.07, 3.42)	<0.001
long (≥13, ≤18) / Wide (≥5, ≤7)	24 / 2,569	0.80	(0.50, 1.28)	0.348
long (≥13, ≤18) / Standard (≥3.75, <5)	283 / 25,217	1.02	(0.86, 1.20)	0.853
long (≥13, ≤18) / Narrow (≥3, <3.75)	130 / 6,597	1.70	(1.33, 2.16)	<0.001

*Adjusted for age, sex, implant site, and bone augmentation

Table 5.24 Results of Mixed-effects logistic regression model evaluating associations between implant dimensions (independent variable) and early implant failure (dependent variable)

	Narrow	Standard	Wide
Short	2.7% (95%CI: 2.0%, 3.4%)	1.6% (95%CI: 1.2%, 2.0%)	1.3% (95%CI: 0.9%, 1.8%)
Standard	1.9% (95%CI: 1.5%, 2.4%)	1.2% (95%CI: 0.9%, 1.4%)	1.0% (95%CI: 0.7%, 1.3%)
Long	1.8% (95%CI: 1.3%, 2.3%)	1.2% (95%CI: 0.9%, 1.5%)	0.9% (95%CI: 0.5%, 1.4%)

Table 5.25 Adjusted cumulative incidences (predicted probabilities) of early implant failure with "Implant dimensions" as a predictor variable

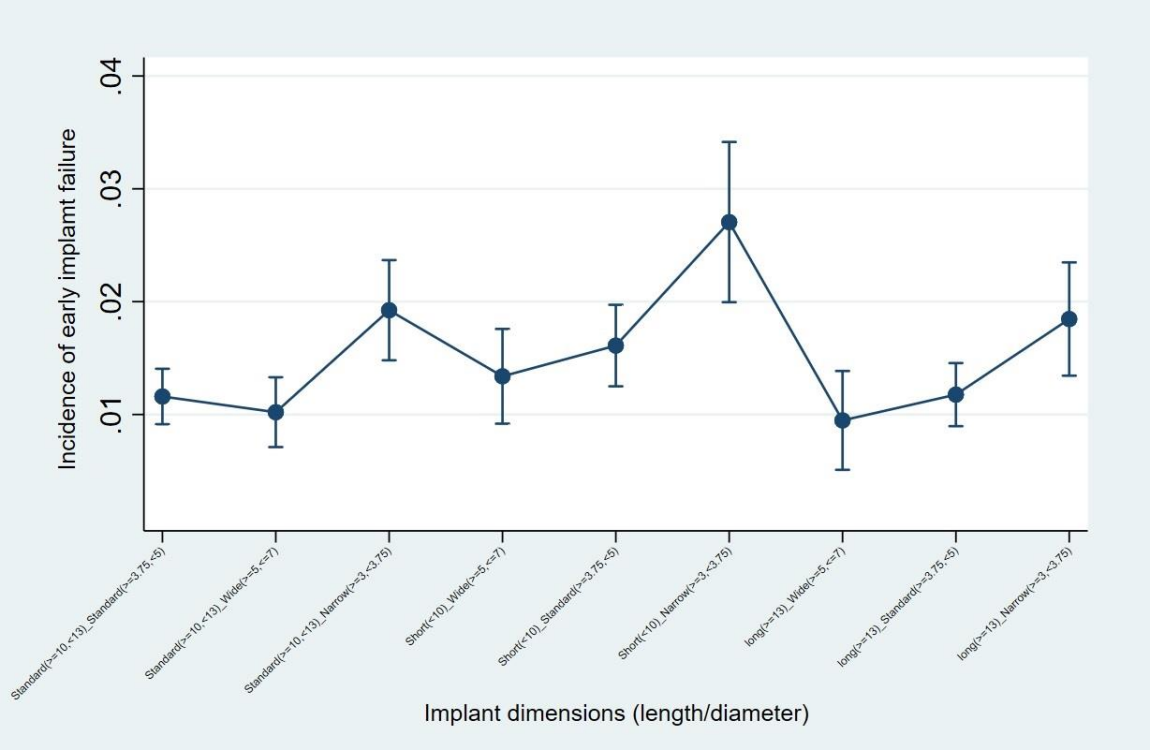


Figure 5.17 Adjusted cumulative incidence of early implant failure for different implant dimensions

5.3.11. Primary stability

Baseline data regarding the primary implant stability (measured by insertion torque) in this dataset is presented in Chapter 4 (see Table 4.3). Based on the DAG (Figure 5.18-A, B), age, sex, implant placement timing, bone quantity, bone augmentation, bone quality, and implant dimensions are factors that should be considered when investigating the effect of primary stability on early implant failure.

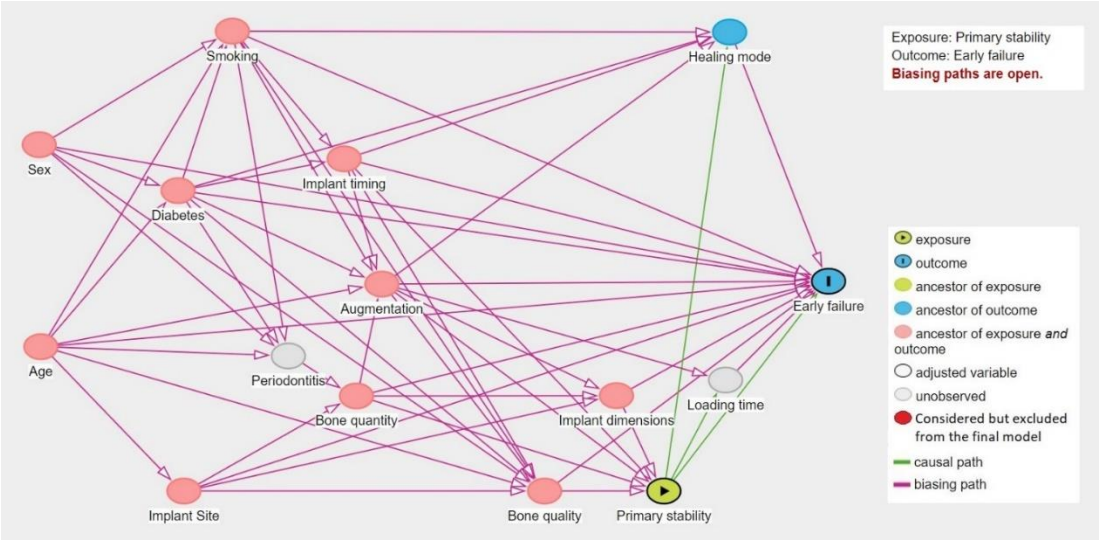


Figure 5.18-A DAG (before adjustments) showing the association between exposure (primary stability) and outcome (early implant failure), specifying the relationships among the covariates

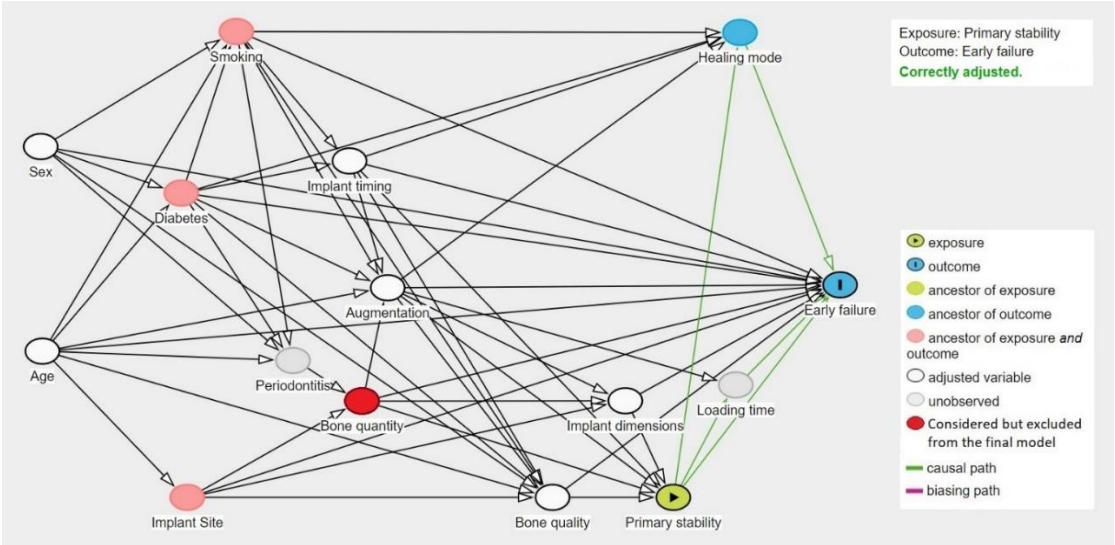


Figure 5.18-B DAG (after adjustment for age, sex, implant placement timing, bone quantity, bone augmentation, bone quality, and implant dimensions) showing the association between exposure (primary stability) and outcome (early implant failure), specifying the relationships among the covariates

Although the bone quantity was identified as a potential confounding factor by the DAG, data on this variable was only available for the period between 2016 and 2022, and more than 10% (about 15%) of this data was missing. To determine the impact of this covariate, we compared unadjusted and adjusted models in the (2016-2022) part of the dataset (Table 5.26, see Appendix 8.11 for the full models). Our analysis showed that bone quantity did not meet the 10% change-in-estimate criterion for important confounders, so it was excluded from the final model. This enabled us to create a more parsimonious model for the entire 2010-2022 dataset (Table 5.27, see Appendix 8.11 for the full model).

The three primary stability categories with insertion torques below 50 N/cm had significantly higher odds of early implant failure compared to the category with insertion torques above 50 N/cm (Table 5.27). Furthermore, the adjusted cumulative incidence of early implant failure decreased with increasing insertion torque (Table 5.28, Figure 5.19). For insertion torques below 8 N/cm, the cumulative incidence of early implant failure was 3.7% (95%CI: 2.6%, 4.8%), while for insertion torques exceeding 50 N/cm, the cumulative incidence dropped to 0.9% (95%CI: 0.6%, 1.1%).

Regarding interaction analysis, the potential interaction of bone quality and primary stability was considered and tested using interaction terms. However, no evidence was found for such an interaction based on the likelihood-ratio test.

The estimated intraclass correlation coefficient (ICC) for centres was 0.04, while for patients it was 0.5.

Adjustments excluded bone quantity

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	15	140	8,248	3,299.1	49,487
Patient	22,739	1	16	2.2	

Independent variable	Failed/Placed implants (n)	Odd ratio*	(95% CI)	p-value
Primary stability (Insertion torque N/cm)				
>50	94 / 12,151	1 (reference)		
20-50	462 / 31,947	1.66	(1.23, 2.23)	0.001
8-19	85 / 4,570	1.94	(1.30, 2.90)	0.001
<8	21 / 819	4.07	(2.19, 7.56)	< 0.001

*Adjusted for age, sex, implant placement timing, bone augmentation, bone quality and implant dimensions.

Adjustments included bone quantity

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	15	140	8,248	3,299.1	49,487
Patient	22,739	1	16	2.2	

Independent variable	Failed/Placed implants (n)	Odd ratio**	(95% CI)	p-value
Primary stability (Insertion torque N/cm)				
>50	94 / 12,151	1 (reference)		
20-50	462 / 31,947	1.65	(1.23, 2.22)	0.001
8-19	85 / 4,570	1.93	(1.29, 2.89)	0.001
<8	21 / 819	3.81	(2.04, 7.12)	< 0.001

**Adjusted for age, sex, implant placement timing, bone quantity, bone augmentation, bone quality and implant dimensions.

Table 5.26 Comparing model outcomes for primary stability (independent variable) and early implant failure (dependent variable), with and without adjusting for bone quantity

Adjusted for age and sex

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	21	259	19,491	6,178.1	129,741
Patient	55,396	1	24	2.3	

Independent variable	Failed/Placed implants (n)	Odd ratio*	(95% CI)	p-value
Primary stability (Insertion torque N/cm)				
>50	231 / 24,831	1 (reference)		
20-50	1,264 / 89,281	1.53	(1.29, 1.83)	>0.001
8-19	258 / 13,719	1.85	(1.47, 2.32)	>0.001
<8	74 / 1,910	5.31	(3.80, 7.40)	>0.001

Fully adjusted*

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	21	259	19,491	6,178.1	129,741
Patient	55,396	1	24	2.3	

Independent variable	Failed/Placed implants (n)	Odd ratio*	(95% CI)	p-value
Primary stability (Insertion torque N/cm)				
>50	231 / 24,831	1 (reference)		
20-50	1,264 / 89,281	1.67	(1.40, 2)	>0.001
8-19	258 / 13,719	2	(1.58, 2.54)	>0.001
<8	74 / 1,910	5.25	(3.70, 7.45)	>0.001

*Adjusted for age, sex, implant placement timing, bone augmentation, bone quality and implant dimensions.

Table 5.27 Results of Mixed-effects logistic regression model evaluating associations between primary stability (independent variable) and early implant failure (dependent variable)

	Cumulative incidence of early implant failure (%)	(95% CI)
Primary stability (Insertion torque N/cm)		
<8	3.7%	(2.6%, 4.8%)
8-19	1.7%	(1.2%, 2.1%)
20-50	1.4%	(1.1%, 1.7%)
>50	0.9%	(0.6%, 1.1%)

Table 5.28 Adjusted cumulative incidences (predicted probabilities) of early implant failure with "Primary stability" as a predictor variable

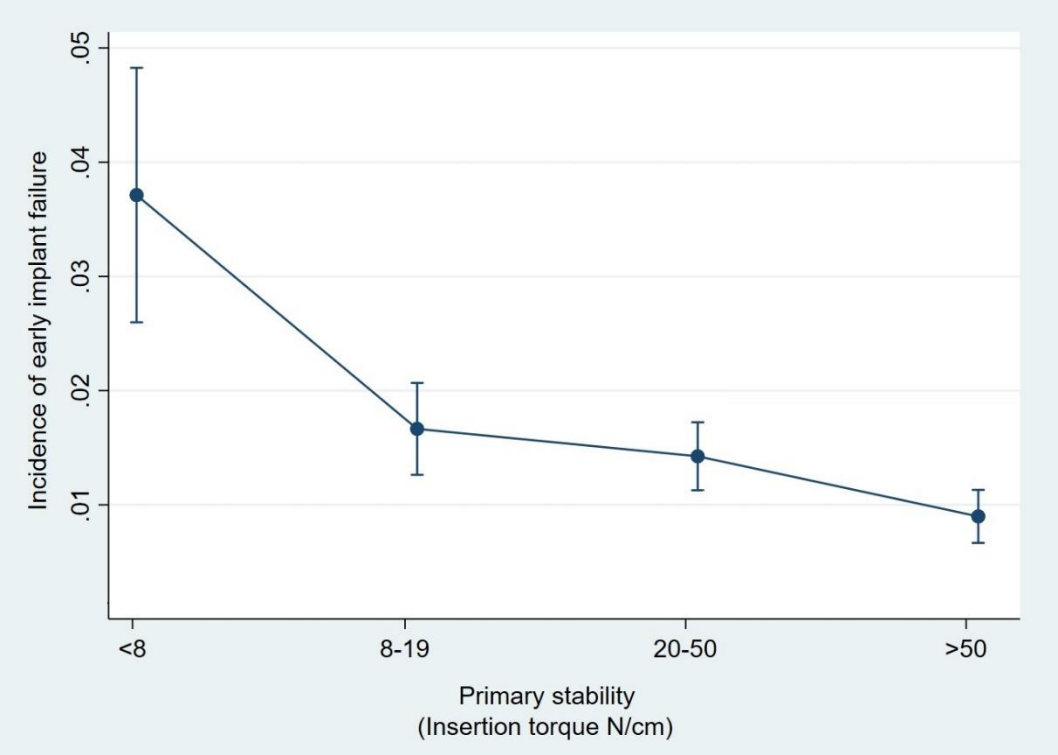


Figure 5.19 Adjusted cumulative incidences of early implant failure for primary stability variable

5.3.12. Healing mode

Baseline data characteristics regarding implant healing modes (submerged or transmucosal) in this dataset are presented in Chapter 4 (see Table 4.3). Based on the DAG (Figure 5.20-A, B), age, sex, diabetes, smoking, implant placement timing, bone augmentation, and primary stability are factors that should be considered when investigating the effect of bone augmentation on early implant failure.

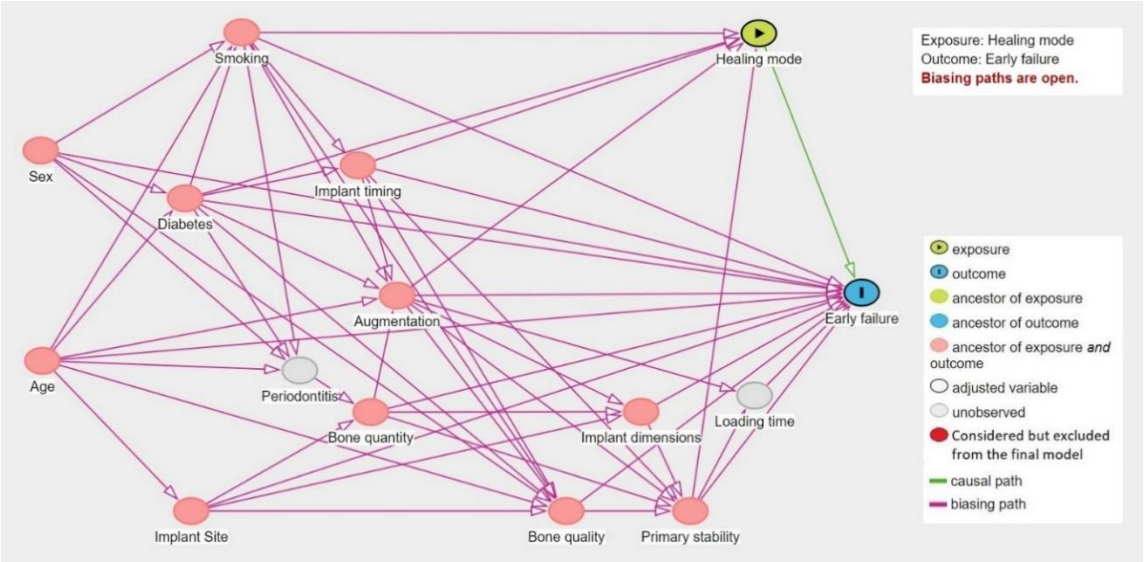


Figure 5.20-A DAG (before adjustments) showing the association between exposure (healing mode) and outcome (early implant failure), specifying the relationships among the covariates

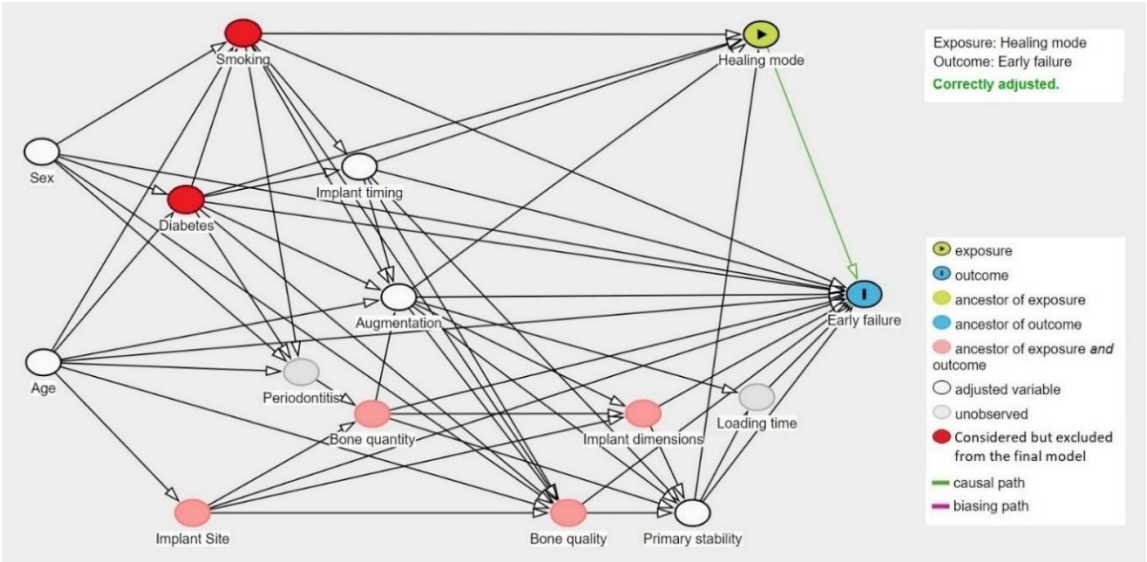


Figure 5.20-B DAG (after adjustment age, sex, diabetes, smoking, implant placement timing, bone augmentation, and primary stability) showing the association between exposure (healing mode) and outcome (early implant failure), specifying the relationships among the covariates.

The dataset only provided information on diabetes and smoking between 2016 and 2022, with more than 10% of the data missing for each. Consequently, we compared unadjusted and adjusted models for these covariates during this period (Table 5.29, see Appendix 8.12 for the full models). However, we found that these covariates did not meet our predetermined 10% change-in-estimate criterion of confounding. Thus, we eliminated them from the final model, resulting in a more parsimonious model for the complete dataset from 2010 to 2022 (Table 5.30, see Appendix 8.12 for the full model).

The results of the final model show that the transmucosal healing mode was associated with an increased risk of early implant failure compared to the submerged healing mode (OR: 1.21; 95%CI: 1.03, 1.42) (Table 5.30). However, based on the adjusted cumulative incidence calculated from this model, transmucosal healing had only a slightly higher chance of early implant failure than submerged healing (1.5% vs. 1.3%) (Table 5.31).

Regarding interaction analysis, the potential interaction of bone augmentation and healing mode was considered and tested using interaction terms. However, no evidence was found for such an interaction based on the likelihood-ratio test.

The estimated intraclass correlation coefficient (ICC) was 0.04 for centres and 0.5 for patients.

Adjustments excluded diabetes and smoking

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	16	602	9,971	3,791.3	60,660
Patient	26,572	1	15	2.3	

Independent variable	Failed/Placed implants (n)	Odd ratio*	(95% CI)	p-value
Healing mode				
Submerged	605 / 51,148	1 (reference)		
Transmucosal	148 / 9,512	1.50	(1.13, 1.98)	0.005

*Adjusted for age, sex, implant placement timing, bone augmentation, and primary stability

Adjustments included diabetes and smoking

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	16	602	9,971	3,791.3	60,660
Patient	26,572	1	15	2.3	

Independent variable	Failed/Placed implants (n)	Odd ratio**	(95% CI)	p-value
Healing mode				
Submerged	605 / 51,148	1 (reference)		
Transmucosal	148 / 9,512	1.49	(1.13, 1.98)	0.005

**Adjusted for age, sex, diabetes, smoking, implant placement timing, bone augmentation, and primary stability

Table 5.29 Comparing model outcomes for healing mode (independent variable) and early implant failure (dependent variable), with and without adjusting for diabetes and smoking

Adjusted for age and sex

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	21	355	19,553	6,165.4	129,473
Patient	55,334	1	24	2.3	

Independent variable	Failed/Placed implants (n)	Odd ratio	(95% CI)	p-value
Healing mode				
Submerged	1,355 / 100,192	1 (reference)		
Transmucosal	473 / 29,281	1.17	(1.00, 1.36)	0.048

Fully adjusted*

Grouping information					
Group variable	**No. of groups**	**Observations per group**			**No. of observations**
		Min	**Max**	**Average**	
Centre	21	355	19,553	6,165.4	129,473
Patient	55,334	1	24	2.3	

Independent variable	Failed/Placed implants (n)	Odd ratio	(95% CI)	p-value
Healing mode				
Submerged	1,355 / 100,192	1 (reference)		
Transmucosal	473 / 29,281	1.21	(1.03, 1.42)	0.022

*Adjusted for age, sex, implant placement timing, bone augmentation, and primary stability

Table 5.30 Results of Mixed-effects logistic regression model evaluating associations between healing mode (independent variable) and early implant failure (dependent variable)

	Cumulative incidence of early implant failure (%)	(95% CI)
Healing mode		
Submerged	1.3%	(1.0%, 1.6%)
Transmucosal	1.5%	(1.2%, 1.9%)

Table 5.31 Adjusted cumulative incidences (predicted probabilities) of early implant failure with “Healing mode” as a predictor variable

5.4. Discussion

5.4.1. Patient's sex

In this study, we observed that males were at a higher risk of early implant failure compared to females.

The present finding is consistent with a previous systematic review that found the placement of implants in male patients was associated with an increased risk of implant failure than in females (RR:1.21, 95% CI 1.07,1.37) (Chrcanovic et al., 2015a). This also accords with our systematic review and meta-analysis (see Chapter 3), which showed an 80% higher odds of early implant failure in male compared to female patients (OR: 1.80; 95% CI: 1.37, 2.37).

There are some possible explanations for the observed difference in the risk of early implant failure between the sexes. In general, men have a higher prevalence of cigarette smoking than women (Dai et al., 2022), which could increase their risk of implant failure compared to women. This is based on the available evidence that smoking has several negative effects on dental implants and could be associated with implant failure (see section 5.4.5). Moreover, it has been shown that men have a greater tendency to develop severe periodontal disease than women (Shiau and Reynolds, 2010b). Some evidence suggests that patients with a history of periodontitis may experience increased complications, such as higher bone loss and postoperative infection, and might be at greater risk of implant failure (Ong et al., 2008, Chrcanovic et al., 2014b). Our meta-analysis in this respect (see Chapter 3) also showed that the insertion of implants in patients with a prior history of periodontitis significantly increased the odds of early failure by 69% (OR:1.69; 95% CI: 1.18, 2.43) compared to implants inserted in patients with no prior history of periodontitis.

Following a specific program of supportive periodontal therapy (SPT) after receiving implant-supported restorations is important to control plaque accumulation, reduce inflammation, and lower the risk of peri-implant disease and implant failure and, thus, implant failure (Cortellini et al., 2019). Several studies have shown that females generally tend to have a higher level of compliance with SPT (Famili and Short, 2010, Gokulanathan et al., 2014, Jamison et al., 2014). This suggests that variations in compliance with SPT among patients of different sexes may contribute to the difference in implant failure rates. Furthermore, given the lower compliance with SPT in men compared to women, one might speculate that compliance with postoperative instructions is also inferior in men compared to women, which may also affect the outcome of implant treatment (Cortellini et al., 2019).

When considering the disparities in bite forces between males and females, a study conducted by Cosme et al. (2005) found that men have a significantly higher voluntary maximal bite force (MBF) (1,009 ± 290 N) compared to women (668 ± 179 N). The stronger bite force in men than women can be attributed to the larger diameter and cross-sectional area of type II fibres of their masseter muscles, which is suggested to be due to hormonal differences between sexes (Tuxen et al., 1999). This also suggests that men may exert stronger forces on their dental implants than women.

There is ongoing debate regarding the potential connection between excessive loading on dental implants and the development of marginal bone loss or loss of osseointegration (Chang et al., 2013, Sadowsky, 2019). It is possible for previously integrated dental implants to experience a complete loss of osseointegration if the applied force exceeds the biological adaptive limit (Chang et al., 2013). In normal conditions, the higher amount of load exerted on implants in men may not pose a problem; however, with complicating factors like poorly constructed prostheses,

parafunctional habit, or sudden onset of extra loads, such as the case of a sudden loss of teeth adjacent to an implant, the relatively higher amount of loads exerted by men compared to women may contribute to a higher rate of implant failure in men.

5.4.2. Age

The present study found no evidence that age is a risk factor for early implant failure. However, although there was a significantly lower risk of failure in the over-70 age groups than in the 18-30 age group, this may be due to a possible survival bias, as older patients may have died before the follow-up to determine whether the implant was successful, resulting in falsely lower failure rates for those age groups.

The present finding is consistent with our previous findings obtained through a systematic review meta-analysis of studies examining ageing as a risk factor for early implant failure (see Chapter 3), which showed no association between age and the risk of early implant failure. Furthermore, two other previous systematic reviews found that the risk of implant failure in older patients was not significantly higher when compared to younger patients, suggesting that age is not a limiting factor for dental implant treatment (Sendyk et al., 2017, Srinivasan et al., 2017).

These findings are somewhat unexpected given the fact that the process of osseointegration may be related, to some extent, to the ability of the host bone to achieve healing. In this regard, ageing could be considered a factor that may affect the outcome of dental implant treatment due to some age-related physiological changes in the healing process. The healing process in older people is relatively slower than in young (Guo and DiPietro, 2010); older adults generally have an increased inflammatory response during healing than younger adults, which prolongs the early inflammatory phase of the wound healing process; moreover, the proliferative phase of healing, which is responsible for new tissue formation, slows down due to the decrease in the number of stem cells and the amount of growth factors in older adults (Bartold et al., 2016). It has also been shown that ageing is associated with impaired

angiogenesis (Shimoda et al., 2014), an imbalanced bone remodelling process (Kloss and Gassner, 2006), and a decrease in bone mineral density (Riggs et al., 2004).

In addition, older patients are more likely to develop systemic disease than younger patients which may also have an impact on the success of dental implant treatment.

5.4.3. Implant site

In the present study, we observed an association between implant site and the risk of early implant failure. Placing implants in the lower molars sites was associated with a decreased risk of early implant failure compared to any other site. On the other hand, the upper molar sites followed by the lower anterior sites had the highest risk of early implant failure.

In contrast to our finding regarding lower failure risk for lower molar sites, Alsaadi et al. (2007) found that the early implant failure rate was significantly higher in the posterior regions (premolars and molars) of both jaws than in the anterior regions. Furthermore, Bahat (2000) reported a significantly higher failure rate for implants placed in the molar areas than those placed in the premolar areas (6.9% vs. 4.8%). However, these studies did not investigate the risk of early failure in lower and upper molars sites separately, as we did. Instead, they reported the overall risk associated with them, which may not accurately represent the risk for each site.

Several studies have demonstrated that implants placed in the maxilla are more likely to fail than implants placed in the mandible, with some studies reporting a significant difference between the two jaws (Strietzel et al., 2004, Balshi et al., 2007, Deng et al., 2010, Borba et al., 2017). Manzano et al. (2016) conducted a systematic review and meta-analysis of clinical studies reporting on early failure of dental implants; they found that the maxillary location was a significant risk factor for early implant failures. In a large retrospective study, Jemt et al. (2015) assessed the incidence of early failure for 39,077 implants placed in 8,528 patients over a period of 27 years; this study showed an incidence of early failures of 8.1% in the maxilla and 3.7% in the mandible, with a statistically significant difference between them.

The lower jaw generally has relatively thick cortical plates and more dense medullary bone than the upper jaw (Nanci, 2018). This more favourable type of bone in the lower jaw could result in increased primary stability of the inserted implants and makes them more resistant to mechanical stress, and thus may be less susceptible to failure. Furthermore, post-extraction alveolar bone resorption is generally higher in maxillary compared to the mandibular sites (Couso-Queiruga et al., 2021), resulting in less bone quantity available for implant placement. In addition, the maxillary molar region may exhibit limited vertical bone height due to maxillary sinus pneumatization (Cha et al., 2019); therefore, upper molar sites are more likely to require bone augmentation for implant placement which may be associated with an increased risk of early implant failure (Clauser et al., 2022)

In accordance with the present results regarding the risk of early implant failure for the mandibular anterior sites, some studies have reported a greater failure rate in the anterior region of the mandible than in the posterior region (Wagenberg and Froum, 2006, Lin et al., 2018). This finding could be attributed to a relatively poor blood supply in the anterior mandible. Additionally, the thicker cortical bone in the area could result in the generation of more heat during implant site preparation, which could negatively affect osseointegration (Dhok et al., 2023). Furthermore, narrower implants are often required in the anterior region, which may be associated with an increased risk of early implant failure (see section 5.4.9).

5.4.4. Diabetes

The current study found no evidence of an association between diabetes and early implant failure. This finding is not in line with a recent systematic review and meta-analysis conducted by Al Ansari et al. (2022) to evaluate the effect of diabetes on dental implant failure rates, which found a 78% increased risk of dental implant failure in diabetic patients compared to nondiabetic patients (OR: 1.77; 95% CI, 1.34, 2.35). However, this systematic review did not specifically investigate the impact of diabetes on early implant failure but on implant failure in general, including late failures.

Likewise, in contrast with the present study, the results of our systematic review and meta-analysis of studies looking into diabetes as a risk factor for early implant failure (see Chapter 3) suggest that implants placed in diabetic patients may have a 38% higher odds of early failure compared to those placed in nondiabetic patients (OR: 1.38; 95% CI: 0.70, 2.71; p=0.347). However, there was no statistical significance between the compared groups possibly due to the small number of studies included and the overall sample size being small.

A possible explanation for the lack of association between diabetes and early implant failure in this study may be that most diabetic patients in this cohort are likely to have well-controlled diabetes. Consequently, the potential adverse events associated mainly with uncontrolled diabetes, such as delayed healing (Dubey et al., 2022), impaired bone metabolism (Moreira et al., 2015), microvascular complications (Khalil, 2017), and impaired immunological response to infection (Berbudi et al., 2020), which may impact osseointegration, are minimised.

5.4.5. Smoking

In this study, we found that smoking was associated with an increased risk of early implant failure. This association showed a dose-response relationship, which strengthens the causal inference. On the other hand, no association was found between being a former smoker and the risk of early implant failure.

In accordance with the present findings, Several studies have shown that smoking has a significant negative effect on the success of implants in the early stages (Schwartz-Arad et al., 2002, DeLuca et al., 2006, Alsaadi et al., 2007, Chrcanovic et al., 2016, Grisar et al., 2017); furthermore, it has also been suggested that this effect is dose-related, meaning that it depends on the number of cigarettes smoked per day (Noguerol et al., 2006, Alsaadi et al., 2007). The findings of the current study are also consistent with the results of our systematic review and meta-analysis (see Chapter 3), which showed that the insertion of implants in smokers significantly increased the odds of early failure with an odds ratio of 1.98 (95% CI: 1.62, 2.48) compared to non-smokers. In another systematic review and meta-analysis of 107 clinical studies investigating the effect of smoking on implant failure rates, Chrcanovic et al. (2015b) showed that implants inserted in smokers were 2.23 times more likely to fail compared to implants inserted in non-smokers (95%CI: 1.96, 2.53) concluding that smoking a significant risk factor for implant failure. However, this review examined the impact of smoking on implant failure in general, but did not specifically focus on early implant failure.

The association between smoking and the increased risk of early implant failure may be explained by the negative effects of many chemical substances in tobacco products, especially nicotine, on the osseointegration process and the healing of peri-implant tissues. At the cellular level, nicotine affects the processes of osteogenesis and angiogenesis by hindering gene expression of some essential growth factors (Ma et al., 2011), such as bone morphogenic proteins (BMPs), which stimulate osteoblast differentiation and mineralisation (Rawadi et al., 2003); transforming growth factor (TGF), which regulate osteoblast proliferation and apoptosis during the bone remodelling process (Wu et al., 2016); and vascular endothelial growth factor (VEGF), which induces the formation of new blood vessels, recruitment of osteoblasts and regulation of their activities (Kleinheinz et al., 2005).

Nicotine also has sympathetic stimulating effects on microcirculation (Benowitz and Burbank, 2016). Exposure to nicotine increases epinephrine and norepinephrine release leading to vasoconstriction, which reduces blood perfusion in tissues and thus decreases the nutrients and oxygen supply to tissues, possibly leading to tissue ischemia and impaired healing (Jones and Triplett, 1992, Ma et al., 2010). On the other hand, nicotine-induces hypoxia and ischemia could result in the expression of hypoxia-inducible factor 1 (HIF-1), leading to the induction of VEGF expression, thereby promoting angiogenesis (Wang et al., 2007). Nevertheless, the resulting angiogenesis cannot compensate for the adverse effects of decreased blood flow that may be due to nicotine's induction of vasoconstriction (Ma et al., 2010). Furthermore, an excessive amount of VEGF can cause an increase in the recruitment of osteoclasts into bone regeneration sites, thereby generating excessive bone resorption (Keramaris et al., 2008).

5.4.6. Timing of implant placement

In this study, immediate implant placement was independently associated with an increased risk of early implant failure compared to late implant placement. On the other hand, there was no evidence of a difference in early failure risk between early and late implant placement.

Placing implants in fresh extraction sockets has been demonstrated to be a successful and predictable procedure (Polizzi et al., 2000, Schropp and Isidor, 2008). Some studies have shown that immediate implants have similar failure rates to those placed in healed sites (Grunder et al., 1999, Chen et al., 2004, Peñarrocha-Diago et al., 2008, Ribeiro et al., 2008). However, consistent with our findings, other studies found that inserting the implant into a fresh extraction socket may increase the risk of implant failure (Maló et al., 2000, Chaushu et al., 2001, Horwitz et al., 2007, Deng et al., 2010). Furthermore, a Cochrane systematic review conducted by Esposito et al. (2010) indicated that immediate implants may have a higher risk of failure than late implants.

It has been suggested that immediate implant placement into an infected socket may increase the risk of implant failure (Deng et al., 2010, Tarazona et al., 2014, Zhao et al., 2016). This may be one possible explanation for the reported higher risk of failure for immediate implants compared to late implants, given that late implants are placed in a healed ridge after any infection in the socket has healed. In addition, the primary stability is expected to be lower in immediate implants due to the existence of the jumping gap between the implant and the buccal wall of the alveolar socket.

5.4.7. Bone quality and quantity

In this study, we found that type 1 bone quality, according to the classification of Lekholm and Zarb (1985), was independently associated with an increased risk of early failure compared to type 2 and type 3. On the other hand, we found no evidence of a difference in the risk of early implant failure between type 1 and type 4 bones.

With regard to bone quantity, vertical bone defects (insufficient bone height) were found to be independently associated with an increased risk of early failure compared to placing implants in a sufficient amount of bone with no vertical or horizontal defects.

A systematic review and meta-analysis by Chrcanovic et al. (2017) investigating the risk of implant failure based on bone quality and quantity at the implant site showed that type 1 bone had a significantly higher risk of implant failure compared to type2 and type 3 bones (relative risk 1.67 and 1.19, respectively) which is consistent with the findings of the present study. However, in contrast to our findings, Chrcanovic et al. (2017) found that implants placed in type 4 bone had a significantly higher risk of failure compared to those placed in type 1 bone (RR:1.45; 95%CI: 1.12, 1.87); however, this may reflect a false-positive result due of the presence of uncontrolled confounding factors in the included studies, which was acknowledged as a limitation of this systematic review. Even in our study, we found that type 4 bone was associated with an increased risk of implant failure compared to type 1 bone in the model adjusted for age and sex only (Table 5.21); however, this association did not persist after full adjustment for potential confounders, including implant site, implant placement timing, and bone augmentation.

In accordance with the findings of the present study regarding the bone quantity, Chrcanovic et al. (2017) found that implant failure rates were highest in bone quantities

D and E, which represent a loss of alveolar bone height according to Lekholm and Zarb (1985) classification, compared to other bone quantities.

Although type 1 bone can provide good primary stability due to its thick cortical composition, its low blood supply can negatively impact osseointegration and may explain the higher risk of early implant failure in this type. Furthermore, implant site preparation in this type of bone could generate more heat and cause thermal injury to the bone tissue surrounding the implant, which may affect the osseointegration and lead to implant failure (Dhok et al., 2023). Regarding type 4 bone, which is composed of a thin cortical layer surrounding low-density trabecular bone, it is more likely to experience excessive bone resorption compared to other bone qualities. Furthermore, this type of bone may result in reduced primary stability of the inserted implants and make them less resistant to mechanical stress, and thus may be more susceptible to failure.

5.4.8. Bone augmentation

In the present study, we found that bone augmentation was independently associated with an increased risk of early implant failure compared to not having augmentation. However, this study investigated the risk of early implant failure associated with bone augmentation in general; therefore, the observed association may vary depending on other aspects of bone augmentation, such as the augmentation techniques and augmentation materials used, which are beyond the scope of this study.

In accordance with the present finding, a recent systematic review and meta-analysis by Clauser et al. (2022) found a significant association between bone augmentation procedure and increased risk of early implant failure (OR:1.50; 95% CI:1.06, 2.13). Similarly, our systematic review and meta-analysis (see Chapter 3) showed that bone augmentation significantly increased the odds of early implant failure by 96% compared to not having augmentation (OR: 1.96; 95% CI: 1.34, 2.86). The higher estimates of early implant failure relative effects in our previous systematic review and the Clauser et al. (2022) systematic review, compared to the present study (OR: 1.13; 95%CI: 1.01, 1.27), may be due to the use of crude (unadjusted) relative effects in these two studies, which could have inflated their estimates, while the estimate from the present study was based on an analysis that adjusted for potential confounders including age, sex, implant site, implant placement timing, and bone quantity.

There are several possible explanations for the increased risk of early implant failure associated with bone augmentation. Some potential adverse events associated with bone augmentation procedures, such as infection, wound dehiscence, or membrane exposure (Lim et al., 2018, Urban et al., 2019), may pose an additional risk for implant failure. It has been reported that when such complications arise, the outcomes of bone

augmentation are expected to be significantly impacted (Garcia et al., 2018), which might consequently increase the likelihood of implant failure in the augmented sites. In addition, bone augmentation results in the formation of new bone with a different density and proportion of vital bone in augmented sites compared to sites where no augmentation was performed (Kühl et al., 2012, Chan et al., 2013), which may have an effect on the osseointegration of implants placed in the augmented sites. Furthermore, it has also been shown that implant insertion in augmented sites was associated with lower insertion torque values and, therefore, lower primary stability compared to non-augmented sites (Huang et al., 2017).

5.4.9. Implant dimensions

In the present study, we found evidence that narrow-diameter implants, regardless of their length, and short implants with standard diameter were independently associated with an increased risk of early implant failure compared to implants of standard length and diameter.

Previous studies have shown that narrow implants have a higher risk of early implant failure (Ortega-Oller et al., 2014, Pommer et al., 2018). This is in line with our current findings, despite variations in the definition of narrow implant threshold. In a systematic review conducted by Pommer et al. (2018), it was found that implants with a diameter less than 3.3 mm had a lower success rate of 94.3% compared to those with a diameter of 3.3 mm or more, which had a success rate of 97.7%. Similarly, another systematic review and meta-analysis of prospective clinical studies (Ortega-Oller et al., 2014) showed that narrow implants with a diameter of less than 3.3 mm had significantly higher failure rates than wider implants (1.55% vs. 0.40%, respectively). In addition, our previous systematic review and meta-analysis (see Chapter 3) showed that using narrow implants with a diameter of less than 3.75mm significantly increased the odds of early implant failure compared to implants with wider diameters (OR: 1.71; 95% CI: 1.28, 2.28).

Our finding of increased early failure risk for short implants with standard diameter compared to standard dimensions implants also seems to be consistent with some other studies. A previous systematic review and meta-analysis of observational studies by Manzano et al. (2016) showed that implants less than 10 mm in length were at a significantly higher risk of early failure compared to longer implants (OR:1.60; 95%CI:1.15, 2.24). Another systematic review and meta-analysis showed that

inserting implants shorter than 7 mm in the maxilla and shorter than 5.5 mm in the mandible may increase the risk of early failure (Pommer et al., 2018). Our previous systematic review and meta-analysis (see Chapter 3) showed that implants shorter than 10mm had an 87% higher odds of early failure compared to longer implants (OR:1.87; 95%CI: 1.25, 2.78). However, these studies used different definitions for the threshold of defining short implants. Furthermore, they examined the risk of early failure for short implants, regardless of their diameter.

A possible explanation for the observed findings regarding implant dimensions is that when narrow or short implants are used, there is less contact between the bone and the implant due to their smaller surface area. As a result, they may have less osseointegration compared to larger implants. Furthermore, these implants may also have lower primary stability than larger implants (Gómez-Polo et al., 2016, Farronato et al., 2020).

5.4.10. Primary stability

In the present study, we found that insertion torques below 50Ncm were independently associated with an increased risk of early implant failure compared to higher insertion torques.

The observed association between lower insertion torques and early implant failure is consistent with previous studies that identified low primary stability, as evaluated by insertion torque, as a risk factor for implant failure (Ottoni et al., 2005, Cannizzaro et al., 2012). In a split-mouth randomised controlled trial, Cannizzaro et al. (2012) compared the failure rate between implants inserted with an insertion torque greater than 80 Nm and those inserted with a relatively low insertion torque (25 to 35 Ncm). Fifty implants were assigned to each group and followed up for six months after placement. The results of this study showed that implants inserted with higher insertion torques (>80) had significantly lower failure rates than implants inserted with low insertion torques (RD= -0.12; 95%CI: -0.21, -0.05). In the same context, Ottoni et al. (2005) reported that the risk of implant failure significantly decreased by 20% for each 9.8 Ncm increase in the insertion torque (RR: 0.79; 95%CI: 0.66, 0.93).

The findings of the present study may have clinical implications regarding the use of higher insertion torques. It is widely recommended in clinical practice to avoid using high insertion torques based on the fact that they are often achieved by under-preparing the implant bed, which may lead to compression of the peri-implant bone and increased frictional heat generation (Marković et al., 2013), thereby may increase the risk of bone necrosis and subsequently implant failure; However, the finding of the present study contradicts this idea as it shows that high insertion torques (>50Ncm) may be recommended to reduce the risk of early implant failure.

5.4.11. Healing mode

Submerged implant healing, in which the implant is placed in one procedure and the abutment connected in another, was originally proposed to minimise implant movement during the early stage of osseointegration to allow for proper new bone formation and remodelling process, minimise the risk of fibrous connective tissue formation between the bone and the implant (Fibrous encapsulation), and reduce contamination with oral microorganisms (Branemark, 1977, Albrektsson et al., 1981). However, the need for a second surgery to deliver the abutment and manage the soft tissues around the implant is associated with additional trauma, treatment time and cost for for patients. On the other hand, transmucosal (non-submerged) healing, which is based on a single-stage surgical approach where implant placement and abutment connection are performed in the same procedure, has recently become more popular as it provides less invasive treatment modality to patients and reduces the overall treatment time between implant placement and final prosthesis delivery (Ferrigno et al., 2002).

The current study found that transmucosal implant healing was independently associated with an increased risk of early implant failure compared to submerged healing. This finding is consistent with that of our systematic review and meta-analysis (see Chapter 3), which showed that implants placed according to the single-stage surgical approach (transmucosal healing) had a significantly higher odds of early failure compared to those placed according to the two-stage surgical approach (submerged healing), with an odds ratio of 1.80 (95% CI: 1.14, 3.28). Furthermore, in another systematic review and meta-analysis, Troiano et al. (2018) also found that non-submerged (transmucosal) implant healing was associated with a significantly

higher risk of early implant failure compared to submerged healing (RR: 2.34; 95% CI: 1.25, 4.39).

In contrast, some studies have reported no significant difference in the risk of implant failure between the submerged and transmucosal healing modes (Cecchinato et al., 2008, Eliasson et al., 2010, Hämmerle et al., 2012). However, these studies had a relatively smaller sample size compared to our study, which may have limited their ability to detect differences between investigated healing modes.

5.4.12. Strengths and limitations of the present study

The main strengths of our study are:

-This study has a very large sample size compared to previous studies concerned with early implant failure, providing high statistical power to detect even small differences, even though early implant failure is a relatively rare outcome. However, some detected differences in risk may not be considered clinically significant. To aid interpretation by the reader, we therefore report the cumulative incidence of early implant failure for each investigated risk factor, which represents the probability of early failure associated with these factors.

-Comprehensive adjustment for potential confounders in the performed analyses increases the relevance of this study as evidence concerning investigated risk factors of early implant failure. Confounder selection was based on a transparent approach making the underlying assumptions regarding causal pathways explicit using DAGs.

-The external validity of our findings is improved by the multicentre data origin and the use of different surgical techniques and implant systems.

Our study also has some limitations that need to be considered:

-As with any observational study, there is a possibility that the associations we observed may be explained by unmeasured or unknown confounding factors that were not considered in the DAG.

-The data used in this study was collected during routine clinical practice and not for research purposes. There was no calibrated protocol for data collection, which may have caused errors and misclassification in the data. However, some measures would have been more likely to be susceptible to misclassification than others. Subjective

measures like bone quality and quantity may have been more prone to misclassification, whereas measures like implant dimensions are unlikely to be misclassified, but data entry errors might be possible. Additionally, measures like insertion torque may have been estimated rather than exactly measured; furthermore, it might be measured in different ways depending on the measuring instrument and implant system used. However, the potential misclassifications in this study are likely to be non-differential (random error), which bias estimates towards the null, i.e., underestimates RRs.

-This study used data from high-volume surgical practices. The majority of these practices are referral practices providing specialist oral surgical services by highly trained and experienced oral surgeons and oral & maxillofacial surgeons, which may limit the generalisability of our findings. Furthermore, the case mix may not be representative of all implant patients. The referring practices are more likely to perform simpler procedures themselves and only refer more complex cases, such as those requiring extensive augmentation procedures.

- This study had a high amount of missing data for some variables, particularly for smoking, diabetes, and bone quantity; furthermore, data on these factors was only available in the dataset from 2016-2022, limiting their analyses to this period.

- Incidence of implant failure may have been underestimated as the presence of the implants after one year was not confirmed by a clinical examination or patient recall. The majority of participating clinical centres are referral practices, who would have performed the implant surgery (incl., where applicable the second stage surgery) and then referred the patient back to the general dentist for restoration. However, consistent with clinical experience, the assumption underlying the present study is that

patients who experience failure within the first year after placement will return to the surgeon. In fact, 86% of failures in this study occurred within the first 28 weeks. While we believe that this is a reasonable assumption, we cannot rule out that the incidence of early implant failure was slightly underestimated in this study.

5.5. Conclusion

Dental implant therapy is a highly successful treatment modality for replacing missing teeth with low early failure rates. There are a few factors that independently increase the risk of early implant failure, i.e., failure of osseointegration, including male sex, cigarette smoking, immediate implant placement, using narrow and short implants, placing implants in upper molar and lower anterior sites, poor bone quality, insufficient alveolar bone height, bone augmentation, and transmucosal healing mode. However, the most significant risk factor is low primary stability as measured by insertion torque. In contrast, there is no increased risk of early failure associated with older age or diabetes mellitus.

CHAPTER 6: CONCLUSIONS AND FUTURE WORK

6.1. Conclusions

Dental implant therapy continues to be a reliable and predictable treatment modality for replacing missing teeth in partially or fully edentulous patients, with a low incidence of failure within the first year of placement. However, Identifying the risk factors for early implant failure is still of great importance as losing the implant early after it has been placed can be frustrating for patients and clinicians, lead to additional costs and ultimately jeopardise the restoration of function and aesthetics that is the goal of implant surgery.

Several risk factors of early implant failure have been described in the literature. However, previous studies often have serious limitations in terms of sample size. Furthermore, the methods adopted in previous studies to assess risk factors for early implant failure were not based on a robust causal structure that allows for a causal interpretation of their findings. Therefore, it was of great importance to construct a causal model incorporating variables potentially related to early implant failure and defining their causal relationship based on available literature, expert knowledge, and plausible assumptions. This model reduces bias in selecting confounding variables by indicating which ones should be adjusted for when examining the relationship between a risk factor and early implant failure.

Our large retrospective cohort study using the proposed causal model identified several risk factors for early implant failure. These factors are male sex, cigarette smoking, immediate implant placement, low primary stability, using narrow and short implants, placing implants in upper molar and lower anterior sites, poor bone quality, insufficient alveolar bone height, bone augmentation and transmucosal healing mode.

On the other hand, age and diabetes mellitus do not appear to be associated with early implant failure.

6.2. Future work and recommendations

-Future studies investigating risk factors for early implant failure could update our causal model by incorporating additional potential risk factors and cofounders into the model based on appropriate causal assumptions This causal model can guide covariate selection for the statistical models when examining the relationship between a risk factor and early implant failure.

-Future studies could be planned based on the proposed causal model by specifying which variables need to be measured in addition to the exposure variable so that they can be adjusted for in the statistical analyses.

-Dentists with varying levels of training and experience, including both generalists and specialists, should be involved in future studies to enhance the generalizability of findings concerning the risk of early dental implant failure.

-Developing and using calibrated protocols for data collection in future studies is crucial to minimize measurement and classification errors.

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APPENDICES

Appendix 1: PubMed search strategy

#1	"Risk"[Mesh] OR "Risk Factors"[Mesh] OR Risk*[tiab] OR Factor*[tiab] OR Predispose*[tiab] OR Determinant*[tiab] OR Predictor*[tiab] OR “risk factor*”[tiab] OR (Risk[tiab] And factor*[tiab]) OR “Predisposing factor*”[tiab] OR (Predispos*[tiab] AND factor*[tiab])
#2	(((early[tiab]) OR (("up to"[tiab] OR "before"[tiab] "prior to"[tiab] OR "previous to"[tiab] OR "to"[tiab] "until"[tiab] OR till[tiab]) AND (load*[tiab] OR prosthes*[tiab] OR abutment*[tiab]))) OR (("within"[tiab] OR "during"[tiab] OR "in" OR "through*"[tiab]) (year[tiab] OR "first year"[tiab] OR "1st year"[tiab] OR "one year"[tiab] OR "1 year"[tiab]))) AND (fail*[tiab] OR loss*[tiab] OR lost[tiab] OR remov*[tiab])
#3	"Dental Implants"[Mesh] OR "Dental Implantation"[Mesh] OR "Dental Implantation, Endosseous"[Mesh] OR "dental implant*"[tiab] OR (dental[tiab] AND implant*[tiab]) OR "oral implant*"[tiab] OR (oral[tiab] AND implant*[tiab]) OR "osseointegrated implant*"[tiab] OR (Osseointegrat*[tiab] AND implant*[tiab])
#4	#1 AND #2 AND #3

Appendix 2: MEDLINE via OVID search strategy

1. exp Risk Factors/
2. exp Risk/
3. Risk factor$.mp.
4. (factor$ adj4 risk).mp.
5. (factor$ adj4 associated).mp.
6. (factor$ adj4 predisposing).mp.
7. (risk$ or determinant$).mp.
8. 1 or 2 or 3 or 4 or 5 or 6 or 7
9. (early adj4 (failure$ or loss$ or remov$)).mp.
10. (failure$ or loss$ or remov$).mp.
11. (("up to" or before or "prior to" or "previous to" or to or until or till) adj4 (load$ or prosthes$)).mp.
12. 10 and 11
13. ((within or during or in or through) adj5 (year or "first year" or "1st year" or "one year" or "1 year")).mp.
14. 10 and 13
15. 9 or 12 or 14
16. exp Dental Implants/
17. exp Dental Implantation/
18. dental implant$.mp.
19. (osseointegrat$ adj4 implant$).mp.
20. (endosseous adj4 implant$).mp.
21. ((oral or dental) adj4 implant$).mp.
22. 16 or 17 or 18 or 19 or 20 or 21
23. 8 and 15 and 22

Appendix 3: EMBASE via OVID Search Strategy

1. exp risk factor/
2. exp risk/
3. Risk factor$.mp.
4. (factor$ adj4 risk).mp.
5. (factor$ adj4 associated).mp.
6. (factor$ adj4 predisposing).mp.
7. (risk$ or determinant$).mp.
8. 1 or 2 or 3 or 4 or 5 or 6 or 7
9. exp implant complication/
10. (early adj4 (failure$ or loss$ or remov$)).mp.
11. (failure$ or loss$ or remov$).mp.
12. (("up to" or before or "prior to" or "previous to" or to or until or till) adj4 (load$ or prosthes$)).mp.
13. 11 and 12
14. ((within or during or in or through) adj5 (year or "first year" or "1st year" or "one year" or "1 year")).mp.
15. 11 and 14
16. 9 or 10 or 13 or 15
17. exp tooth implant/
18. exp tooth implantation/
19. dental implant$.mp.
20. (osseointegrat$ adj4 implant$).mp.
21. (endosseous adj4 implant$).mp.
22. ((oral or dental) adj4 implant$).mp.
23. 17 or 18 or 19 or 20 or 21 or 22
24. 8 and 16 and 23

Appendix 4: Cochrane Library search strategy

#1 MeSH descriptor: [Risk] explode all trees

#2 MeSH descriptor: [Risk Factors] explode all trees

#3 MeSH descriptor: [Precipitating Factors] explode all trees

#4 (risk AND factor*):ti,ab,kw

#5 (predispos* AND factor*):ti,ab,kw

#6 (factor*):ti,ab,kw

#7 (risk*):ti,ab,kw

#8 (determinant*):ti,ab,kw

#9 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8

#10 (early NEAR/5 (failure* or loss* or remov*)):ti,ab,kw

#11 (failure* or loss* or remov*):ti,ab,kw

#12 (("up to" or before or "prior to" or "previous to" or to or until or till) NEAR/5 (load* or prosthes*)):ti,ab,kw

#13 #11 or #12

#14 ((within or during or in or through) NEAR/5 (year or "first year" or "1st year" or "one year" or "1 year")):ti,ab,kw

#15 #11 or #14

#16 #10 or #13 or #15

#17 MeSH descriptor: [Dental Implants] explode all trees

#18 MeSH descriptor: [Dental Implantation] explode all trees

#19 dental next implant*

#20 osseointegrat* NEAR/5 implant*

#21 oral NEAR/5 implant*

#22 #17 or #18 or #19 or #20 or #21

#23 #9 and #16 and #22

Appendix 5: Multilevel mixed models for linear trends over time in the ECDI dataset

Implant length

Mixed-effects ML regression — Number of obs = **150,896**

Grouping information

Group variable	No. of groups	Observations per group: Minimum	Average	Maximum
centre	**21**	**1,180**	**7,185.5**	**20,278**
patientno	**63,414**	**1**	**2.4**	**24**

Wald chi2(**1**) = **1469.01**

Log likelihood = **-274572.67** — Prob > chi2 = **0.0000**

length	Coefficient	Std. err.	z	P>|z|	[95% conf.	interval]
year	**-.0642326**	**.0016759**	**-38.33**	**0.000**	**-.0675172**	**-.0609479**
_cons	**140.4174**	**3.383599**	**41.50**	**0.000**	**133.7857**	**147.0492**

Implant diameter (narrow <3.75mm)

Mixed-effects logistic regression — Number of obs = **150,896**

Group variable: **patientno** — Number of groups = **63,414**

Obs per group:
min = **1**
avg = **2.4**
max = **24**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**1**) = **173.36**

Log likelihood = **-54996.818** — Prob > chi2 = **0.0000**

narrow	Coefficient	Std. err.	z	P>|z|	[95% conf.	interval]
year	**-.0724117**	**.0054997**	**-13.17**	**0.000**	**-.0831908**	**-.0616325**
_cons	**140.7851**	**11.08182**	**12.70**	**0.000**	**119.0652**	**162.5051**

Implant diameter (wide >5mm)

Mixed-effects logistic regression — Number of obs = **150,896**
Group variable: **patientno** — Number of groups = **63,414**

Obs per group:
min = **1**
avg = **2.4**
max = **24**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**1**) = **184.45**
Log likelihood = **-45283.649** — Prob > chi2 = **0.0000**

thick	Coefficient	Std. err.	z	P>|z|	[95% conf.	interval]
year	**-.0753861**	**.0055508**	**-13.58**	**0.000**	**-.0862654**	**-.0645068**
_cons	**146.9706**	**11.18427**	**13.14**	**0.000**	**125.0498**	**168.8913**
patientno						
var(_cons)	**18.26693**	**.9311867**			**16.53005**	**20.18631**

LR test vs. logistic model: chibar2(01) = **12356.56** — Prob >= chibar2 = **0.0000**

Appendix 6: Multilevel mixed model for the association between insertion torque and bone quality in the ECDI dataset

Mixed-effects ologit regression — Number of obs = **129,903**
Group variable: **patientno** — Number of groups = **55,461**

Obs per group:
min = **1**
avg = **2.3**
max = **24**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**3**) = **9598.74**
Log likelihood = **-124548.13** — Prob > chi2 = **0.0000**

bone_quality_4groups	Coefficient	Std. err.	z	P>|z|	[95% conf.	interval]
primary_stability						
20-50	**1.692951**	**.0299379**	**56.55**	**0.000**	**1.634274**	**1.751628**
8-19	**4.033007**	**.0436973**	**92.29**	**0.000**	**3.947362**	**4.118653**
<8	**4.959235**	**.0825597**	**60.07**	**0.000**	**4.797421**	**5.121049**
patientno						
var(_cons)	**10.18104**	**.1297464**			**9.929888**	**10.43854**

Appendix 7: Missing data for each variable by centre in the ECDI dataset

Centre	% missing						
	Diabetes (Period2)	Smoking (Period2)	Insertion time	Bone quality	Bone quantity	Primary stability	Healing mode
1	100%	100%	1.9%	5.2%	8.8%	8.6%	2.8%
2	3.4%	4.2%	0.04%	0.1%	100%	0.1%	0.02%
3	11.4%	7.4%	0.1%	0.5%	100%	3.3%	0.2%
4	35.9%	38.3%	0.2%	37.6%	1.4%	46.6%	1%
5	48.5%	48%	0.4%	21.9%	100%	14.7%	13.8%
6	100%	100%	0.4%	0.6%	100%	8.8%	0.9%
7	29.3%	30%	0.01%	0.9%	7.4%	3.9%	1%
8	6.8%	6.7%	0	0.5%	44.5%	1.4%	0.1%
9	7.8%	7.7%	0.01%	0.2%	7%	0.6%	0.3%
10	4.9%	5.1	0.01%	0.3%	11.5%	1.2%	2.8%
11	92%	93.2%	0.05%	49.4%	3.7%	52.4%	7.4%
12	2.6%	4.5%	0.2%	0.5%	100%	24.5%	17.6%
13	23.9%	26.8%	1.7%	0.7%	0.5%	14.7%	13%
14	58%	63.7%	0	19.8%	36.5%	48%	0.4%
15	57%	57.8%	2.1%	15.9%	36.5%	23%	16.3%
16	41.5%	43.4%	0	17.3%	48.5%	17.6%	0.3%
17	100%	100%	0	0.2%	6.2%	0.4%	0.2%
18	69%	71.4%	34.1%	40.7%	10.7%	39%	47.3%
19	14%	14%	0	3.6%	38.3%	3%	0.1%
20	40.7%	42.7%	0	3.1%	100%	1.5%	1.4%
21	93%	93%	0	0	16.4%	0	2.4%

Appendix 8: Stata outputs for multilevel mixed-effects logistic regression models

Appendix 8.1: Patient's sex

Patient's sex

Mixed-effects logistic regression — Number of obs = **150,896**

Grouping information

Group variable	No. of groups	Observations per group: Minimum	Average	Maximum
centre	**21**	**1,180**	**7,185.5**	**20,278**
patientno	**63,414**	**1**	**2.4**	**24**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**1**) = **36.68**

Log likelihood = **-10486.29** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
sex						
male	**1.397917**	**.0773149**	**6.06**	**0.000**	**1.254307**	**1.55797**
_cons	**.002611**	**.000367**	**-42.31**	**0.000**	**.0019822**	**.0034392**
centre						
var(_cons)	**.2685936**	**.0910335**			**.1382295**	**.5219039**
centre>patientno						
var(_cons)	**3.054154**	**.166018**			**2.745498**	**3.397509**

Appendix 8.2: Age

Age

Mixed-effects logistic regression — Number of obs = **150,896**

Grouping information

Group variable	No. of groups	Observations per group: Minimum	Average	Maximum
centre	**21**	**1,180**	**7,185.5**	**20,278**
patientno	**63,414**	**1**	**2.4**	**24**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**6**) = **11.06**

Log likelihood = **-10499.252** — Prob > chi2 = **0.0867**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
age_7groups						
30-40	**.7081078**	**.1393961**	**-1.75**	**0.080**	**.4814312**	**1.041513**
40-50	**.7122996**	**.1241204**	**-1.95**	**0.052**	**.5062187**	**1.002276**
50-60	**.7869451**	**.1293697**	**-1.46**	**0.145**	**.5701791**	**1.086119**
60-70	**.7563688**	**.1243313**	**-1.70**	**0.089**	**.5480418**	**1.043887**
70-80	**.6446121**	**.1105168**	**-2.56**	**0.010**	**.4606409**	**.9020579**
80-90	**.6181754**	**.135775**	**-2.19**	**0.029**	**.4019345**	**.950754**
_cons	**.0041991**	**.0008647**	**-26.58**	**0.000**	**.0028047**	**.006287**
centre						
var(_cons)	**.2714223**	**.0919353**			**.1397428**	**.5271836**
centre>patientno						
var(_cons)	**3.06219**	**.1658359**			**2.753813**	**3.405099**

Appendix 8.3: Implant site

Implant site

Mixed-effects logistic regression — Number of obs = **150,896**

Grouping information

Group variable	No. of groups	Observations per group Minimum	Average	Maximum
centre	**21**	**1,180**	**7,185.5**	**20,278**
patientno	**63,414**	**1**	**2.4**	**24**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**7**) = **119.71**

Log likelihood = **-10443.036** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
site_upper_lower_Ant_PM_M4						
Lower anteriors	**1.795164**	**.1824349**	**5.76**	**0.000**	**1.470958**	**2.190827**
Lower premolars	**1.666066**	**.143097**	**5.94**	**0.000**	**1.407937**	**1.97152**
Upper anteriors	**1.589392**	**.1348557**	**5.46**	**0.000**	**1.345887**	**1.876952**
Upper premolars	**1.272333**	**.1066487**	**2.87**	**0.004**	**1.079573**	**1.499511**
Upper molars	**1.840782**	**.1471012**	**7.64**	**0.000**	**1.573914**	**2.1529**
age	**.9935924**	**.0021416**	**-2.98**	**0.003**	**.9894038**	**.9977987**
sex						
male	**1.405571**	**.0779019**	**6.14**	**0.000**	**1.260886**	**1.566857**
_cons	**.0026364**	**.000513**	**-30.52**	**0.000**	**.0018005**	**.0038603**
centre						
var(_cons)	**.2654107**	**.0901692**			**.1363753**	**.5165366**
centre>patientno						
var(_cons)	**3.039063**	**.1664152**			**2.729788**	**3.383377**

Appendix 8.4: Diabetes

Diabetes

(Data 2016-2022)

Mixed-effects logistic regression — Number of obs = **63,527**

Grouping information

Group variable	No. of groups	Observations per group: Minimum	Average	Maximum
centre	**16**	**738**	**3,970.4**	**10,086**
patientno	**27,610**	**1**	**2.3**	**15**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**3**) = **17.98**

Log likelihood = **-4003.6902** — Prob > chi2 = **0.0004**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
diabetes						
Yes	**1.04258**	**.18612**	**0.23**	**0.815**	**.7347746**	**1.479329**
age	**.9945266**	**.003478**	**-1.57**	**0.117**	**.9877332**	**1.001367**
sex						
male	**1.418696**	**.1256525**	**3.95**	**0.000**	**1.192613**	**1.687639**
_cons	**.0035319**	**.0010154**	**-19.64**	**0.000**	**.0020105**	**.0062046**
centre						
var(_cons)	**.3507427**	**.1448076**			**.1561571**	**.7877992**
centre>patientno						
var(_cons)	**2.952125**	**.2625151**			**2.479947**	**3.514205**

Appendix 8.5: Smoking status

Smoking status

(Data 2016-2022)

Mixed-effects logistic regression — Number of obs = **62,368**

Grouping information

Group variable	No. of groups	Observations per group: Minimum	Average	Maximum
centre	**16**	**676**	**3,898.0**	**10,067**
patientno	**27,141**	**1**	**2.3**	**15**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**5**) = **34.81**

Log likelihood = **-3902.5617** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
Smoking_status						
Former	**1.120576**	**.135594**	**0.94**	**0.347**	**.8839809**	**1.420496**
Current	**1.622525**	**.1863373**	**4.21**	**0.000**	**1.295495**	**2.032108**
age	**.9969422**	**.0036197**	**-0.84**	**0.399**	**.989873**	**1.004062**
sex						
male	**1.386012**	**.1254038**	**3.61**	**0.000**	**1.160786**	**1.65494**
diabetes						
Yes	**1.006828**	**.1853487**	**0.04**	**0.971**	**.7018692**	**1.44429**
_cons	**.0026703**	**.0007896**	**-20.04**	**0.000**	**.0014958**	**.0047673**
centre						
var(_cons)	**.3031233**	**.1265451**			**.1337419**	**.6870227**
centre>patientno						
var(_cons)	**2.994029**	**.2696255**			**2.509583**	**3.571992**

Smoking status including smoking doses

(Data 2016-2022)

Mixed-effects logistic regression — Number of obs = **61,549**

Grouping information

Group variable	No. of groups	Observations per group Minimum	Average	Maximum
centre	**16**	**660**	**3,846.8**	**10,018**
patientno	**26,805**	**1**	**2.3**	**15**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**7**) = **34.27**

Log likelihood = **-3820.3364** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
Smoking_status_dose						
Former	**1.123478**	**.1363933**	**0.96**	**0.338**	**.8855766**	**1.425288**
Currenr <5 cig	**1.263138**	**.3370768**	**0.88**	**0.381**	**.74869**	**2.131079**
Current 5-15 cig	**1.579642**	**.2476671**	**2.92**	**0.004**	**1.16172**	**2.147909**
Current >15 cig	**1.853674**	**.3354583**	**3.41**	**0.001**	**1.300145**	**2.642864**
age	**.9968613**	**.0036632**	**-0.86**	**0.392**	**.9897074**	**1.004067**
sex						
male	**1.372972**	**.1262886**	**3.45**	**0.001**	**1.14648**	**1.644208**
diabetes						
Yes	**1.011825**	**.1889934**	**0.06**	**0.950**	**.7016398**	**1.45914**
_cons	**.0026446**	**.0007869**	**-19.95**	**0.000**	**.001476**	**.0047384**
centre						
var(_cons)	**.2932712**	**.1228593**			**.1290262**	**.6665933**
centre>patientno						
var(_cons)	**3.041161**	**.2758854**			**2.54578**	**3.632938**

Appendix 8.6: Timing of implant placement

(Not adjusted for diabetes & smoking)

(Data 2016-2022)

Mixed-effects logistic regression — Number of obs = **62,366**

Grouping information

Group variable	No. of groups	Observations per group: Minimum	Average	Maximum
centre	**16**	**676**	**3,897.9**	**10,067**
patientno	**27,140**	**1**	**2.3**	**15**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**4**) = **35.41**

Log likelihood = **-3902.6047** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
placement_timing						
Immediate	**1.860558**	**.2809083**	**4.11**	**0.000**	**1.383974**	**2.501256**
Early(≤16 wks)	**.8693512**	**.1351311**	**-0.90**	**0.368**	**.6410403**	**1.178977**
age	**.9945231**	**.0034955**	**-1.56**	**0.118**	**.9876957**	**1.001398**
sex						
male	**1.418535**	**.12745**	**3.89**	**0.000**	**1.189496**	**1.691677**
_cons	**.0032996**	**.0009479**	**-19.89**	**0.000**	**.001879**	**.0057941**
centre						
var(_cons)	**.3128475**	**.1293893**			**.1390874**	**.7036841**
centre>patientno						
var(_cons)	**3.008741**	**.269424**			**2.524423**	**3.585976**

Timing of implant placement
(Adjusted for diabetes & smoking)
(Data 2016-2022)

Mixed-effects logistic regression — Number of obs = **62,366**

Grouping information

Group variable	No. of groups	Observations per group Minimum	Average	Maximum
centre	**16**	**676**	**3,897.9**	**10,067**
patientno	**27,140**	**1**	**2.3**	**15**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**7**) = **52.11**

Log likelihood = **-3894.3222** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
placement_timing						
Immediate	**1.845671**	**.2791321**	**4.05**	**0.000**	**1.372214**	**2.482485**
Early(≤16 wks)	**.882742**	**.1375663**	**-0.80**	**0.424**	**.6504034**	**1.198077**
age	**.9966198**	**.0036226**	**-0.93**	**0.352**	**.9895449**	**1.003745**
sex						
male	**1.38756**	**.1258473**	**3.61**	**0.000**	**1.161584**	**1.657498**
diabetes						
Yes	**1.004564**	**.185278**	**0.02**	**0.980**	**.6998183**	**1.442016**
Smoking_status						
Former	**1.122209**	**.1361261**	**0.95**	**0.342**	**.8847515**	**1.423397**
Current	**1.609329**	**.1853995**	**4.13**	**0.000**	**1.284056**	**2.017**
_cons	**.0026281**	**.000782**	**-19.97**	**0.000**	**.0014668**	**.0047088**
centre						
var(_cons)	**.3080272**	**.1280525**			**.1363732**	**.6957432**
centre>patientno						
var(_cons)	**3.007542**	**.2712666**			**2.520213**	**3.589106**

Timing of implant placement

(Final model)

Mixed-effects logistic regression — Number of obs = **149,018**

Grouping information

Group variable	No. of groups	Observations per group Minimum	Average	Maximum
centre	**21**	**1,180**	**7,096.1**	**20,254**
patientno	**62,812**	**1**	**2.4**	**24**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**4**) = **107.18**

Log likelihood = **-10360.976** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
placement_timing						
Immediate	**1.935819**	**.1613233**	**7.93**	**0.000**	**1.644103**	**2.279295**
Early(≤16 wks)	**.86008**	**.1013419**	**-1.28**	**0.201**	**.6827207**	**1.083514**
age	**.9948518**	**.0021258**	**-2.42**	**0.016**	**.990694**	**.9990271**
sex						
male	**1.406909**	**.0781883**	**6.14**	**0.000**	**1.261714**	**1.568813**
_cons	**.0034139**	**.000656**	**-29.56**	**0.000**	**.0023426**	**.0049753**
centre						
var(_cons)	**.2915935**	**.0982355**			**.1506659**	**.56434**
centre>patientno						
var(_cons)	**3.025705**	**.1666712**			**2.716052**	**3.370661**

Appendix 8.7: Bone quantity

Bone quantity
(Not adjusted for diabetes & smoking)
(Data 2016-2022)

Mixed-effects logistic regression — Number of obs = **31,709**

Grouping information

Group variable	No. of groups	Observations per group: Minimum	Average	Maximum
centre	**11**	**93**	**2,882.6**	**7,898**
patientno	**15,121**	**1**	**2.1**	**15**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**12**) = **28.90**

Log likelihood = **-1906.7763** — Prob > chi2 = **0.0041**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
bone_quantity						
Facial<=50%	.9512781	.1631249	-0.29	0.771	.6797414	1.331286
Facial>50%	.78731	.1839926	-1.02	0.306	.4979915	1.244714
Facial>50% + Oral<=50%	1.668931	.5302129	1.61	0.107	.8953957	3.110726
Facial>50% + Oral>50%	2.258479	1.293808	1.42	0.155	.7348364	6.941309
Other	1.096457	.4794473	0.21	0.833	.4653577	2.583427
age	.9971383	.0051369	-0.56	0.578	.9871208	1.007257
sex						
male	1.268234	.1613921	1.87	0.062	.9882749	1.6275
site_upper_lower_Ant_PM_M						
Lower anteriors	1.666958	.4053293	2.10	0.036	1.035025	2.684718
Lower premolars	1.687622	.3333808	2.65	0.008	1.145842	2.485567
Upper anteriors	1.455031	.2981523	1.83	0.067	.9737588	2.174168
Upper premolars	1.565166	.2930433	2.39	0.017	1.084405	2.259069
Upper molars	2.222922	.4216239	4.21	0.000	1.532766	3.223833
_cons	.0020177	.0008657	-14.46	0.000	.0008703	.0046782
centre						
var(_cons)	.3826633	.1945811			.1412498	1.036682
centre>patientno						
var(_cons)	2.959394	.3895337			2.286453	3.830391

Bone quantity

(Adjusted for diabetes & smoking)

(Data 2016-2022)

Mixed-effects logistic regression — Number of obs = **31,709**

Grouping information

Group variable	No. of groups	Observations per group Minimum	Average	Maximum
centre	**11**	**93**	**2,882.6**	**7,898**
patientno	**15,121**	**1**	**2.1**	**15**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**15**) = **43.99**

Log likelihood = **-1899.2782** — Prob > chi2 = **0.0001**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
bone_quantity						
Facial<=50%	.9413764	.1616756	-0.35	0.725	.6723178	1.318111
Facial>50%	.7977309	.1864366	-0.97	0.334	.5045721	1.261216
Facial>50% + Oral<=50%	1.687044	.5350686	1.65	0.099	.9060592	3.141206
Facial>50% + Oral>50%	2.368607	1.356191	1.51	0.132	.7711192	7.275529
Other	1.064503	.4668864	0.14	0.887	.4506234	2.514665
age	1.001077	.0053551	0.20	0.841	.9906358	1.011628
sex						
male	1.245507	.1599178	1.71	0.087	.9684021	1.601906
diabetes						
Yes	.804546	.2285786	-0.77	0.444	.4610171	1.404057
Smoking_status						
Former	1.09267	.1968611	0.49	0.623	.7675947	1.555414
Current	1.873495	.3060407	3.84	0.000	1.360211	2.58047
site_upper_lower_Ant_PM_M						
Lower anteriors	1.619564	.3940211	1.98	0.047	1.005335	2.609069
Lower premolars	1.658198	.3279472	2.56	0.011	1.12536	2.443325
Upper anteriors	1.432944	.2937031	1.76	0.079	.9588768	2.141389
Upper premolars	1.553327	.2909083	2.35	0.019	1.076091	2.242212
Upper molars	2.197526	.4171501	4.15	0.000	1.514792	3.187977
_cons	.0014545	.0006477	-14.67	0.000	.0006076	.0034816
centre						
var(_cons)	.3639021	.1868118			.1330497	.9953023
centre>patientno						
var(_cons)	2.931039	.3920385			2.255121	3.809547

Bone quantity

Final model (Adjusted for age and sex)

(Data 2016-2022)

Mixed-effects logistic regression — Number of obs = **51,313**

Grouping information

Group variable	No. of groups	Observations per group Minimum	Average	Maximum
centre	**15**	**166**	**3,420.9**	**8,401**
patientno	**23,450**	**1**	**2.2**	**16**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**7**) = **31.97**

Log likelihood = **-3460.0934** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
bone_quantity						
Facial<=50%	.8931189	.1229533	-0.82	0.412	.6819094	1.169747
Facial>50%	.9489892	.1662495	-0.30	0.765	.6731979	1.337765
Facial>50% + Oral<=50%	2.303888	.509764	3.77	0.000	1.493216	3.554679
Facial>50% + Oral>50%	2.20551	.8185621	2.13	0.033	1.065591	4.564861
Other	1.398071	.4545249	1.03	0.303	.7392587	2.644005
age	.9972878	.0036857	-0.73	0.462	.9900901	1.004538
sex						
male	1.364863	.1292292	3.29	0.001	1.133691	1.643173
_cons	.0032083	.0009978	-18.46	0.000	.0017439	.0059021
centre						
var(_cons)	.3455068	.1481352			.1491097	.8005848
centre>patientno						
var(_cons)	2.808329	.2788116			2.311748	3.41158

Bone quantity

Final model (Fully adjusted)

(Data 2016-2022)

Mixed-effects logistic regression — Number of obs = **51,313**

Grouping information

Group variable	No. of groups	Observations per group Minimum	Average	Maximum
centre	**15**	**166**	**3,420.9**	**8,401**
patientno	**23,450**	**1**	**2.2**	**16**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**12**) = **60.18**

Log likelihood = **-3445.5413** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
bone_quantity						
Facial<=50%	**.8138528**	**.1139466**	**-1.47**	**0.141**	**.6185433**	**1.070833**
Facial>50%	**.8495691**	**.1509034**	**-0.92**	**0.359**	**.5997985**	**1.20335**
Facial>50% + Oral<=50%	**2.080033**	**.4637358**	**3.29**	**0.001**	**1.343686**	**3.2199**
Facial>50% + Oral>50%	**2.085564**	**.7693312**	**1.99**	**0.046**	**1.012112**	**4.297522**
Other	**1.276739**	**.4163472**	**0.75**	**0.454**	**.6737886**	**2.41925**
age	**.9957135**	**.0037263**	**-1.15**	**0.251**	**.9884367**	**1.003044**
sex						
male	**1.354356**	**.1287107**	**3.19**	**0.001**	**1.124189**	**1.631648**
site_upper_lower_Ant_PM_M						
Lower anteriors	**1.579652**	**.2726663**	**2.65**	**0.008**	**1.126248**	**2.215586**
Lower premolars	**1.507551**	**.2184412**	**2.83**	**0.005**	**1.13484**	**2.002671**
Upper anteriors	**1.575057**	**.2246228**	**3.19**	**0.001**	**1.190979**	**2.082995**
Upper premolars	**1.243642**	**.1750797**	**1.55**	**0.121**	**.9437638**	**1.638805**
Upper molars	**1.997505**	**.2794413**	**4.95**	**0.000**	**1.51848**	**2.627646**
_cons	**.0025844**	**.000822**	**-18.73**	**0.000**	**.0013856**	**.0048205**
centre						
var(_cons)	**.336338**	**.144509**			**.1448951**	**.7807252**
centre>patientno						
var(_cons)	**2.814029**	**.2815523**			**2.312934**	**3.423686**

Appendix 8.8: Bone augmentation

Bone augmentation
(Adjustments excluded diabetes, smoking, bone quantity)
(Data 2016-2022)

Mixed-effects logistic regression — Number of obs = **31,707**

Grouping information

Group variable	No. of groups	Observations per group Minimum	Average	Maximum
centre	**11**	**93**	**2,882.5**	**7,897**
patientno	**15,120**	**1**	**2.1**	**15**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**10**) = **29.79**

Log likelihood = **-1906.4138** — Prob > chi2 = **0.0009**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
Augmentation						
Yes	**1.009649**	**.1456447**	**0.07**	**0.947**	**.7609958**	**1.339549**
age	**.9972549**	**.0051374**	**-0.53**	**0.594**	**.9872365**	**1.007375**
sex						
male	**1.254841**	**.1598326**	**1.78**	**0.075**	**.9776171**	**1.610678**
site_upper_lower_Ant_PM_M4						
Lower anteriors	**1.582897**	**.3862306**	**1.88**	**0.060**	**.9812001**	**2.553571**
Lower premolars	**1.640064**	**.3245132**	**2.50**	**0.012**	**1.112851**	**2.417045**
Upper anteriors	**1.356123**	**.2806256**	**1.47**	**0.141**	**.9039787**	**2.034418**
Upper premolars	**1.513374**	**.2837668**	**2.21**	**0.027**	**1.047951**	**2.185505**
Upper molars	**2.180941**	**.4136796**	**4.11**	**0.000**	**1.503795**	**3.163001**
placement_timing						
Immediate	**2.11064**	**.5797452**	**2.72**	**0.007**	**1.231993**	**3.61593**
Early(≤16 wks)	**1.009691**	**.2110576**	**0.05**	**0.963**	**.6702863**	**1.520956**
_cons	**.001976**	**.0008508**	**-14.46**	**0.000**	**.0008497**	**.0045952**
centre						
var(_cons)	**.3835114**	**.1950279**			**.1415516**	**1.039063**
centre>patientno						
var(_cons)	**2.984374**	**.3923259**			**2.306505**	**3.861466**

Bone augmentation

(Adjustments included diabetes, smoking, bone quantity)

(Data 2016-2022)

Mixed-effects logistic regression — Number of obs = **31,707**

Grouping information

Group variable	No. of groups	Observations per group Minimum	Average	Maximum
centre	**11**	**93**	**2,882.5**	**7,897**
patientno	**15,120**	**1**	**2.1**	**15**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**17**) = **51.13**

Log likelihood = **-1895.8215** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
Augmentation						
Yes	1.024721	.4507655	0.06	0.956	.432683	2.426842
age	1.001241	.0053671	0.23	0.817	.9907765	1.011816
sex						
male	1.239249	.1594852	1.67	0.096	.9629707	1.594791
diabetes						
Yes	.8070754	.2297182	-0.75	0.451	.4619939	1.409912
Smoking_status						
Former	1.10076	.1987329	0.53	0.595	.7727079	1.568086
Current	1.889217	.3094516	3.88	0.000	1.370428	2.6044
site_upper_lower_Ant_PM_M4						
Lower anteriors	1.542077	.3768361	1.77	0.076	.9552094	2.489508
Lower premolars	1.617768	.3208426	2.43	0.015	1.096736	2.386328
Upper anteriors	1.337998	.2774852	1.40	0.160	.8910996	2.009022
Upper premolars	1.510568	.2837924	2.20	0.028	1.045259	2.183015
Upper molars	2.179094	.4143597	4.10	0.000	1.501129	3.163253
placement_timing						
Immediate	2.14718	.5924173	2.77	0.006	1.25031	3.68739
Early(≤16 wks)	1.023754	.2145652	0.11	0.911	.678883	1.543818
bone_quantity						
Facial<=50%	.9383311	.4225855	-0.14	0.888	.3881594	2.268308
Facial>50%	.7975845	.3801442	-0.47	0.635	.3133846	2.029905
Facial>50% + Oral<=50%	1.688641	.8823717	1.00	0.316	.6063958	4.702391
Facial>50% + Oral>50%	2.378776	1.684372	1.22	0.221	.5937885	9.529616
Other	1	(omitted)				
_cons	.0014017	.0006277	-14.67	0.000	.0005827	.0033717
centre						
var(_cons)	.3650013	.1870491			.1336862	.9965574
centre>patientno						
var(_cons)	2.956616	.3947453			2.275878	3.840971

Bone augmentation

Final model (Adjusted for age and sex)

Mixed-effects logistic regression — Number of obs = **149,018**

Grouping information

Group variable	No. of groups	Observations per group Minimum	Average	Maximum
centre	**21**	**1,180**	**7,096.1**	**20,254**
patientno	**62,812**	**1**	**2.4**	**24**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**3**) = **52.49**

Log likelihood = **-10386.632** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
Augmentation						
Yes	**1.201051**	**.0660703**	**3.33**	**0.001**	**1.078292**	**1.337785**
age	**.9956779**	**.002132**	**-2.02**	**0.043**	**.991508**	**.9998654**
sex						
male	**1.408351**	**.0780453**	**6.18**	**0.000**	**1.263399**	**1.569933**
_cons	**.0031867**	**.0006252**	**-29.30**	**0.000**	**.0021694**	**.004681**
centre						
var(_cons)	**.2988659**	**.1005858**			**.1545245**	**.5780367**
centre>patientno						
var(_cons)	**3.001625**	**.1653092**			**2.694499**	**3.343759**

Bone augmentation

Final mode (Fully adjusted)

Mixed-effects logistic regression — Number of obs = **149,018**

Grouping information

Group variable	No. of groups	Observations per group Minimum	Average	Maximum
centre	**21**	**1,180**	**7,096.1**	**20,254**
patientno	**62,812**	**1**	**2.4**	**24**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**10**) = **183.38**

Log likelihood = **-10320.317** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
Augmentation						
Yes	**1.133744**	**.065494**	**2.17**	**0.030**	**1.012379**	**1.269659**
age	**.9936084**	**.0021572**	**-2.95**	**0.003**	**.9893894**	**.9978454**
sex						
male	**1.414966**	**.0789106**	**6.22**	**0.000**	**1.268457**	**1.578397**
site_upper_lower_Ant_PM_M4						
Lower anteriors	**1.68587**	**.1734504**	**5.08**	**0.000**	**1.377997**	**2.062527**
Lower premolars	**1.600016**	**.1392151**	**5.40**	**0.000**	**1.349157**	**1.897519**
Upper anteriors	**1.45605**	**.126613**	**4.32**	**0.000**	**1.227888**	**1.726609**
Upper premolars	**1.220726**	**.1040486**	**2.34**	**0.019**	**1.032919**	**1.442682**
Upper molars	**1.780434**	**.1481094**	**6.93**	**0.000**	**1.512575**	**2.095729**
placement_timing						
Immediate	**1.888634**	**.1609285**	**7.46**	**0.000**	**1.598151**	**2.231916**
Early(≤16 wks)	**.8568024**	**.1013083**	**-1.31**	**0.191**	**.6795707**	**1.080256**
_cons	**.0024704**	**.0004982**	**-29.77**	**0.000**	**.0016638**	**.003668**
centre						
var(_cons)	**.296572**	**.0998697**			**.1532819**	**.5738118**
centre>patientno						
var(_cons)	**3.027503**	**.1679038**			**2.715672**	**3.37514**

Appendix 8.9: Bone quality

Bone quality
(Adjustments excluded diabetes & smoking)
(Data 2016-2022)

Mixed-effects logistic regression — Number of obs = **61,589**

Grouping information

Group variable	No. of groups	Observations per group: Minimum	Average	Maximum
centre	**16**	**596**	**3,849.3**	**10,060**
patientno	**26,900**	**1**	**2.3**	**15**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**13**) = **82.70**

Log likelihood = **-3823.8919** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
bone_quality_4groups						
Type2	.8462811	.1097896	-1.29	0.198	.6562763	1.091296
Type3	.7256882	.1107088	-2.10	0.036	.5381376	.9786037
Type4	1.313354	.2502807	1.43	0.153	.9040064	1.908059
age	.991661	.0035953	-2.31	0.021	.9846393	.9987329
sex						
male	1.425925	.1300722	3.89	0.000	1.192478	1.705072
site_upper_lower_Ant_PM_M4						
Lower anteriors	2.102607	.3564152	4.38	0.000	1.508238	2.931205
Lower premolars	1.614674	.2393598	3.23	0.001	1.207542	2.159072
Upper anteriors	1.397829	.2129789	2.20	0.028	1.036959	1.884285
Upper premolars	1.590633	.2244615	3.29	0.001	1.206294	2.097427
Upper molars	1.932144	.2745265	4.64	0.000	1.462505	2.552593
placement_timing						
Immediate	1.787803	.2782722	3.73	0.000	1.317741	2.425546
Early(≤16 wks)	.8865453	.1390167	-0.77	0.443	.6519682	1.205523
Augmentation						
Yes	1.049673	.1011737	0.50	0.615	.8689813	1.267938
_cons	.0029051	.000944	-17.98	0.000	.0015366	.0054925
centre						
var(_cons)	.3526424	.144521			.1579401	.7873659
centre>patientno						
var(_cons)	3.025608	.2768193			2.528916	3.619853

Bone quality

(Adjustments included diabetes & smoking)

(Data 2016-2022)

Mixed-effects logistic regression — Number of obs = **61,589**

Grouping information

Group variable	No. of groups	Observations per group Minimum	Average	Maximum
centre	**16**	**596**	**3,849.3**	**10,060**
patientno	**26,900**	**1**	**2.3**	**15**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**16**) = **96.99**

Log likelihood = **-3816.4618** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
bone_quality_4groups						
Type2	.8435601	.109547	-1.31	0.190	.6539983	1.088066
Type3	.7211728	.110048	-2.14	0.032	.5347484	.9725887
Type4	1.294624	.2470285	1.35	0.176	.8906868	1.881751
age	.9937674	.0037229	-1.67	0.095	.9864974	1.001091
sex						
male	1.397059	.1286252	3.63	0.000	1.166395	1.673338
diabetes						
Yes	1.015185	.1884327	0.08	0.935	.7055862	1.46063
Smoking_status						
Former	1.102962	.1355311	0.80	0.425	.8668936	1.403316
Current	1.576576	.1839256	3.90	0.000	1.254332	1.981606
site_upper_lower_Ant_PM_M4						
Lower anteriors	2.039972	.3462728	4.20	0.000	1.462642	2.845185
Lower premolars	1.593484	.2364167	3.14	0.002	1.191405	2.131258
Upper anteriors	1.378255	.2101795	2.10	0.035	1.022172	1.858383
Upper premolars	1.576658	.2226986	3.22	0.001	1.195384	2.07954
Upper molars	1.913444	.2722264	4.56	0.000	1.447822	2.528812
placement_timing						
Immediate	1.781942	.2777701	3.71	0.000	1.312828	2.418686
Early(≤16 wks)	.900483	.1415556	-0.67	0.505	.6617088	1.225418
Augmentation						
Yes	1.050301	.1013195	0.51	0.611	.8693621	1.268898
_cons	.002359	.0007877	-18.12	0.000	.0012261	.0045389
centre						
var(_cons)	.3489645	.1436141			.1557667	.7817857
centre>patientno						
var(_cons)	3.025392	.2787728			2.525505	3.624224

Bone quality

Final model (Adjusted for age and sex)

Mixed-effects logistic regression — Number of obs = **139,439**

Grouping information

Group variable	No. of groups	Observations per group: Minimum	Average	Maximum
centre	**21**	**393**	**6,640.0**	**20,157**
patientno	**59,295**	**1**	**2.4**	**24**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**5**) = **67.63**

Log likelihood = **-9665.273** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
bone_quality_4groups						
Type2	**.8324099**	**.0627989**	**-2.43**	**0.015**	**.7179938**	**.9650589**
Type3	**.7580489**	**.0648169**	**-3.24**	**0.001**	**.6410845**	**.8963531**
Type4	**1.259015**	**.1438645**	**2.02**	**0.044**	**1.00639**	**1.575054**
age	**.9950136**	**.0022087**	**-2.25**	**0.024**	**.990694**	**.999352**
sex						
male	**1.413998**	**.0812805**	**6.03**	**0.000**	**1.263337**	**1.582625**
_cons	**.0041409**	**.0008623**	**-26.35**	**0.000**	**.0027532**	**.0062279**
centre						
var(_cons)	**.3167737**	**.1069524**			**.1634397**	**.6139607**
centre>patientno						
var(_cons)	**3.002818**	**.1727965**			**2.682544**	**3.361331**

Bone quality

Final model (Fully adjusted)

Mixed-effects logistic regression — Number of obs = **139,439**

Grouping information

Group variable	No. of groups	Observations per group: Minimum	Average	Maximum
centre	**21**	**393**	**6,640.0**	**20,157**
patientno	**59,295**	**1**	**2.4**	**24**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**13**) = **194.81**

Log likelihood = **-9600.0529** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
bone_quality_4groups						
Type2	.7927701	.0615127	-2.99	0.003	.6809272	.9229832
Type3	.6884408	.0624999	-4.11	0.000	.5762228	.8225129
Type4	1.076615	.1291519	0.62	0.538	.8510389	1.361982
age	.9936873	.0022481	-2.80	0.005	.9892908	.9981033
sex						
male	1.419174	.0822473	6.04	0.000	1.266791	1.589888
site_upper_lower_Ant_PM_M						
Lower anteriors	1.620148	.1747998	4.47	0.000	1.311347	2.001668
Lower premolars	1.619769	.1457768	5.36	0.000	1.357833	1.932235
Upper anteriors	1.511356	.1389743	4.49	0.000	1.262106	1.809829
Upper premolars	1.327074	.1194423	3.14	0.002	1.112457	1.583095
Upper molars	1.873709	.1673662	7.03	0.000	1.572787	2.232207
placement_timing						
Immediate	1.862318	.1630487	7.10	0.000	1.568664	2.210944
Early(≤16 wks)	.8709419	.1043937	-1.15	0.249	.6885914	1.101582
Augmentation						
Yes	1.107268	.0665847	1.69	0.090	.984162	1.245774
_cons	.0029261	.0006359	-26.84	0.000	.0019111	.00448
centre						
var(_cons)	.3276643	.1102693			.1694233	.633702
centre>patientno						
var(_cons)	3.040729	.1763011			2.714096	3.406672

Appendix 8.10: Implant dimensions

Implant dimensions
(Adjustments excluded bone quantity)
(Data 2016-2022)

Mixed-effects logistic regression — Number of obs = **51,313**

Grouping information

Group variable	No. of groups	Observations per group Minimum	Average	Maximum
centre	**15**	**166**	**3,420.9**	**8,401**
patientno	**23,450**	**1**	**2.2**	**16**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**16**) = **68.23**

Log likelihood = **-3440.8243** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
Implant_dimensions						
Standard(>=10,<13)_Wide(>=5,<=7)	.6701415	.1550668	-1.73	0.084	.4257978	1.054701
Standard(>=10,<13)_Narrow(>=3,<3.75)	1.439068	.234228	2.24	0.025	1.046012	1.979822
Short(<10)_Wide(>=5,<=7)	1.549697	.3646871	1.86	0.063	.9770919	2.457867
Short(<10)_Standard(>=3.75,<5)	1.271745	.1707805	1.79	0.073	.9774479	1.654651
Short(<10)_Narrow(>=3,<3.75)	2.212623	.4398063	4.00	0.000	1.498694	3.266646
long(>=13)_Wide(>=5,<=7)	.4992896	.2480609	-1.40	0.162	.1885611	1.322066
long(>=13)_Standard(>=3.75,<5)	1.056451	.1655898	0.35	0.726	.7770175	1.436376
long(>=13)_Narrow(>=3,<3.75)	1.679872	.4737828	1.84	0.066	.9665126	2.919745
age	.9959333	.0036957	-1.10	0.272	.9887161	1.003203
sex						
male	1.41934	.1351398	3.68	0.000	1.177717	1.710535
site_upper_lower_Ant_PM_M4						
Lower anteriors	1.43016	.260658	1.96	0.050	1.000568	2.044198
Lower premolars	1.380824	.205642	2.17	0.030	1.031268	1.848865
Upper anteriors	1.464516	.2258947	2.47	0.013	1.082431	1.981472
Upper premolars	1.1845	.1729394	1.16	0.246	.8897299	1.57693
Upper molars	2.002027	.2791846	4.98	0.000	1.523243	2.631303
Augmentation						
Yes	1.004448	.1102167	0.04	0.968	.810077	1.245457
_cons	.0023964	.0007628	-18.96	0.000	.0012842	.0044721
centre						
var(_cons)	.297454	.1304841			.1258993	.7027751
centre>patientno						
var(_cons)	2.709608	.2742028			2.222122	3.304039

Implant dimensions
(Adjustments included bone quantity)
(Data 2016-2022)

Mixed-effects logistic regression — Number of obs = **51,313**

Grouping information

Group variable	No. of groups	Observations per group Minimum	Average	Maximum
centre	**15**	**166**	**3,420.9**	**8,401**
patientno	**23,450**	**1**	**2.2**	**16**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**20**) = **87.30**

Log likelihood = **-3431.8726** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
Implant_dimensions						
Standard(>=10,<13)_Wide(>=5,<=7)	**.6785471**	**.157177**	**-1.67**	**0.094**	**.430933**	**1.06844**
Standard(>=10,<13)_Narrow(>=3,<3.75)	**1.448431**	**.2362133**	**2.27**	**0.023**	**1.052161**	**1.993947**
Short(<10)_Wide(>=5,<=7)	**1.532148**	**.3615819**	**1.81**	**0.071**	**.9647617**	**2.433221**
Short(<10)_Standard(>=3.75,<5)	**1.256978**	**.1694507**	**1.70**	**0.090**	**.9651143**	**1.637104**
Short(<10)_Narrow(>=3,<3.75)	**2.192952**	**.4369684**	**3.94**	**0.000**	**1.483947**	**3.240708**
long(>=13)_Wide(>=5,<=7)	**.5008835**	**.2492261**	**-1.39**	**0.165**	**.1888869**	**1.328225**
long(>=13)_Standard(>=3.75,<5)	**1.05807**	**.1660533**	**0.36**	**0.719**	**.7779062**	**1.439136**
long(>=13)_Narrow(>=3,<3.75)	**1.661606**	**.4691359**	**1.80**	**0.072**	**.9554342**	**2.889717**
age	**.9961443**	**.0037153**	**-1.04**	**0.300**	**.988889**	**1.003453**
sex						
male	**1.426824**	**.1363266**	**3.72**	**0.000**	**1.183155**	**1.720675**
site_upper_lower_Ant_PM_M4						
Lower anteriors	**1.440009**	**.2628694**	**2.00**	**0.046**	**1.006888**	**2.059442**
Lower premolars	**1.383974**	**.2065279**	**2.18**	**0.029**	**1.03301**	**1.854177**
Upper anteriors	**1.443316**	**.223591**	**2.37**	**0.018**	**1.065364**	**1.955353**
Upper premolars	**1.183475**	**.1732717**	**1.15**	**0.250**	**.8882503**	**1.576823**
Upper molars	**2.017355**	**.2822756**	**5.02**	**0.000**	**1.533484**	**2.653906**
Augmentation						
Yes	**1.314993**	**.4290578**	**0.84**	**0.401**	**.6937326**	**2.492612**
bone_quantity						
Facial<=50%	**.6263855**	**.2124791**	**-1.38**	**0.168**	**.3221823**	**1.217816**
Facial>50%	**.6626341**	**.2352222**	**-1.16**	**0.246**	**.3304561**	**1.328721**
Facial>50% + Oral<=50%	**1.560563**	**.5911443**	**1.17**	**0.240**	**.7427534**	**3.278824**
Facial>50% + Oral>50%	**1.546618**	**.7418597**	**0.91**	**0.363**	**.6040749**	**3.959819**
Other	**1**	(omitted)				
_cons	**.0023354**	**.000746**	**-18.97**	**0.000**	**.0012487**	**.0043678**
centre						
var(_cons)	**.2931644**	**.128772**			**.1239431**	**.693426**
centre>patientno						
var(_cons)	**2.73206**	**.2771095**			**2.239515**	**3.332933**

Implant dimensions

Final model (Adjusted for age and sex)

Mixed-effects logistic regression — Number of obs = **150,896**

Grouping information

Group variable	No. of groups	Observations per group Minimum	Average	Maximum
centre	**21**	**1,180**	**7,185.5**	**20,278**
patientno	**63,414**	**1**	**2.4**	**24**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**10**) = **143.21**

Log likelihood = **-10434.373** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
Implant_dimensions						
Standard(>=10,<13)_Wide(>=5,<=7)	**.8864784**	**.1177374**	**-0.91**	**0.364**	**.6833073**	**1.150059**
Standard(>=10,<13)_Narrow(>=3,<3.75)	**1.808324**	**.1569567**	**6.83**	**0.000**	**1.525438**	**2.143669**
Short(<10)_Wide(>=5,<=7)	**1.214068**	**.1758277**	**1.34**	**0.180**	**.9140453**	**1.61257**
Short(<10)_Standard(>=3.75,<5)	**1.39581**	**.1129393**	**4.12**	**0.000**	**1.191113**	**1.635685**
Short(<10)_Narrow(>=3,<3.75)	**2.602106**	**.3292641**	**7.56**	**0.000**	**2.030561**	**3.334524**
long(>=13)_Wide(>=5,<=7)	**.8472513**	**.200919**	**-0.70**	**0.485**	**.5323**	**1.348553**
long(>=13)_Standard(>=3.75,<5)	**1.03804**	**.0858278**	**0.45**	**0.652**	**.8827433**	**1.220656**
long(>=13)_Narrow(>=3,<3.75)	**1.772922**	**.2080762**	**4.88**	**0.000**	**1.408606**	**2.231462**
age	**.9958388**	**.0021106**	**-1.97**	**0.049**	**.9917107**	**.999984**
sex						
male	**1.484151**	**.0823578**	**7.12**	**0.000**	**1.331201**	**1.654675**
_cons	**.0028449**	**.0005321**	**-31.35**	**0.000**	**.0019719**	**.0041046**
centre						
var(_cons)	**.2336209**	**.0809098**			**.1184993**	**.4605829**
centre>patientno						
var(_cons)	**2.938914**	**.1623316**			**2.637366**	**3.274938**

Implant dimensions

Final model (Fully adjusted)

Mixed-effects logistic regression — Number of obs = **150,896**

Grouping information

Group variable	No. of groups	Observations per group Minimum	Average	Maximum
centre	**21**	**1,180**	**7,185.5**	**20,278**
patientno	**63,414**	**1**	**2.4**	**24**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**16**) = **222.93**

Log likelihood = **-10392.194** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
Implant_dimensions						
Standard(>=10,<13)_Wide(>=5,<=7)	**.8679524**	**.1179101**	**-1.04**	**0.297**	**.6650608**	**1.13274**
Standard(>=10,<13)_Narrow(>=3,<3.75)	**1.778541**	**.1600873**	**6.40**	**0.000**	**1.490894**	**2.121685**
Short(<10)_Wide(>=5,<=7)	**1.174421**	**.1747744**	**1.08**	**0.280**	**.8773036**	**1.572162**
Short(<10)_Standard(>=3.75,<5)	**1.449199**	**.1196435**	**4.49**	**0.000**	**1.232691**	**1.703734**
Short(<10)_Narrow(>=3,<3.75)	**2.660587**	**.3393442**	**7.67**	**0.000**	**2.072102**	**3.416205**
long(>=13)_Wide(>=5,<=7)	**.7999111**	**.1903408**	**-0.94**	**0.348**	**.5017602**	**1.275226**
long(>=13)_Standard(>=3.75,<5)	**1.016007**	**.0872953**	**0.18**	**0.853**	**.8585422**	**1.202353**
long(>=13)_Narrow(>=3,<3.75)	**1.695106**	**.2089135**	**4.28**	**0.000**	**1.331344**	**2.158258**
age	**.994842**	**.0021433**	**-2.40**	**0.016**	**.9906501**	**.9990517**
sex						
male	**1.491207**	**.0829753**	**7.18**	**0.000**	**1.337133**	**1.663035**
site_upper_lower_Ant_PM_M4						
Lower anteriors	**1.614024**	**.1740549**	**4.44**	**0.000**	**1.306524**	**1.993897**
Lower premolars	**1.525756**	**.1343449**	**4.80**	**0.000**	**1.283913**	**1.813154**
Upper anteriors	**1.437169**	**.133482**	**3.90**	**0.000**	**1.19798**	**1.724115**
Upper premolars	**1.195348**	**.1047742**	**2.04**	**0.042**	**1.006665**	**1.419396**
Upper molars	**1.835811**	**.1518535**	**7.34**	**0.000**	**1.561057**	**2.158923**
Augmentation						
Yes	**1.127086**	**.0644905**	**2.09**	**0.037**	**1.007516**	**1.260845**
_cons	**.0020585**	**.0004059**	**-31.37**	**0.000**	**.0013986**	**.0030296**
centre						
var(_cons)	**.2378801**	**.0822839**			**.1207601**	**.4685899**
centre>patientno						
var(_cons)	**2.939947**	**.1635938**			**2.636175**	**3.278723**

Appendix 8.11: Primary stability

Primary stability
(Adjustments excluded bone quantity)
(Data 2016-2022)

Mixed-effects logistic regression — Number of obs = **49,487**

Grouping information

Group variable	No. of groups	Observations per group Minimum	Average	Maximum
centre	**15**	**140**	**3,299.1**	**8,248**
patientno	**22,739**	**1**	**2.2**	**16**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**19**) = **72.29**

Log likelihood = **-3254.3245** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
primary_stability						
20-50	**1.659049**	**.2512738**	**3.34**	**0.001**	**1.232932**	**2.232437**
8-19	**1.939896**	**.3977611**	**3.23**	**0.001**	**1.297914**	**2.899419**
<8	**4.070046**	**1.286409**	**4.44**	**0.000**	**2.190595**	**7.561996**
age	**.9976818**	**.0038183**	**-0.61**	**0.544**	**.990226**	**1.005194**
sex						
male	**1.438624**	**.1418912**	**3.69**	**0.000**	**1.185751**	**1.745425**
placement_timing						
Immediate	**1.77683**	**.290727**	**3.51**	**0.000**	**1.289351**	**2.448615**
Early(≤16 wks)	**1.03101**	**.1699562**	**0.19**	**0.853**	**.7463582**	**1.424225**
Augmentation						
Yes	**1.097018**	**.1224353**	**0.83**	**0.407**	**.8814816**	**1.365256**
bone_quality						
Type2	**.874381**	**.1183767**	**-0.99**	**0.321**	**.6705978**	**1.14009**
Type3	**.7692445**	**.1235845**	**-1.63**	**0.102**	**.5614523**	**1.05394**
Type4	**.8687274**	**.1925253**	**-0.63**	**0.525**	**.5626551**	**1.341297**
Implant_dimensions						
Standard(>=10,<13)_Wide(>=5,<=7)	**.7007165**	**.1618459**	**-1.54**	**0.124**	**.4455932**	**1.10191**
Standard(>=10,<13)_Narrow(>=3,<3.75)	**1.379896**	**.2278255**	**1.95**	**0.051**	**.9984128**	**1.90714**
Short(<10)_Wide(>=5,<=7)	**1.606365**	**.3795659**	**2.01**	**0.045**	**1.010916**	**2.552546**
Short(<10)_Standard(>=3.75,<5)	**1.237713**	**.1684223**	**1.57**	**0.117**	**.9479653**	**1.616023**
Short(<10)_Narrow(>=3,<3.75)	**2.184011**	**.4448338**	**3.84**	**0.000**	**1.465157**	**3.255557**
long(>=13)_Wide(>=5,<=7)	**.4411806**	**.2305624**	**-1.57**	**0.117**	**.1584075**	**1.228732**
long(>=13)_Standard(>=3.75,<5)	**1.082239**	**.1697384**	**0.50**	**0.614**	**.7958311**	**1.471722**
long(>=13)_Narrow(>=3,<3.75)	**1.631904**	**.4644309**	**1.72**	**0.085**	**.9342158**	**2.850637**
_cons	**.0017979**	**.0006308**	**-18.02**	**0.000**	**.0009038**	**.0035762**
centre						
var(_cons)	**.2641724**	**.1180928**			**.1099957**	**.6344528**
centre>patientno						
var(_cons)	**2.806255**	**.2904653**			**2.290986**	**3.437415**

Primary stability

(Adjustments included bone quantity)

(Data 2016-2022)

Mixed-effects logistic regression — Number of obs = **49,487**

Grouping information

Group variable	No. of groups	Observations per group Minimum	Average	Maximum
centre	**15**	**140**	**3,299.1**	**8,248**
patientno	**22,739**	**1**	**2.2**	**16**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**23**) = **89.73**

Log likelihood = **-3246.0022** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
primary_stability						
20-50	**1.651672**	**.2507695**	**3.30**	**0.001**	**1.226557**	**2.224128**
8-19	**1.93424**	**.397577**	**3.21**	**0.001**	**1.292851**	**2.893824**
<8	**3.812042**	**1.215387**	**4.20**	**0.000**	**2.040659**	**7.121065**
age	**.9979419**	**.003838**	**-0.54**	**0.592**	**.9904477**	**1.005493**
sex						
male	**1.443459**	**.1429176**	**3.71**	**0.000**	**1.188849**	**1.752598**
placement_timing						
Immediate	**1.761626**	**.2895498**	**3.44**	**0.001**	**1.276456**	**2.431205**
Early(≤16 wks)	**1.04466**	**.172794**	**0.26**	**0.792**	**.755406**	**1.444673**
Augmentation						
Yes	**1.406961**	**.4662033**	**1.03**	**0.303**	**.7349074**	**2.693592**
bone_quantity						
Facial<=50%	**.654566**	**.2260368**	**-1.23**	**0.220**	**.3326702**	**1.287932**
Facial>50%	**.6525276**	**.2366615**	**-1.18**	**0.239**	**.3205394**	**1.328362**
Facial>50% + Oral<=50%	**1.667456**	**.6418445**	**1.33**	**0.184**	**.7841623**	**3.545705**
Facial>50% + Oral>50%	**1.308462**	**.6607651**	**0.53**	**0.594**	**.4863063**	**3.520567**
Other	**1**	(omitted)				
bone_quality						
Type2	**.8784306**	**.1192657**	**-0.95**	**0.340**	**.6731915**	**1.146242**
Type3	**.7731579**	**.1246335**	**-1.60**	**0.110**	**.5637078**	**1.060431**
Type4	**.8630233**	**.1920553**	**-0.66**	**0.508**	**.5579535**	**1.334895**
Implant_dimensions						
Standard(>=10,<13)_Wide(>=5,<=7)	**.7103925**	**.1643462**	**-1.48**	**0.139**	**.4514156**	**1.117944**
Standard(>=10,<13)_Narrow(>=3,<3.75)	**1.390654**	**.2301279**	**1.99**	**0.046**	**1.00545**	**1.923434**
Short(<10)_Wide(>=5,<=7)	**1.601975**	**.3797465**	**1.99**	**0.047**	**1.006652**	**2.549366**
Short(<10)_Standard(>=3.75,<5)	**1.229524**	**.1680062**	**1.51**	**0.130**	**.9406451**	**1.607118**
Short(<10)_Narrow(>=3,<3.75)	**2.162415**	**.4417414**	**3.78**	**0.000**	**1.448953**	**3.227185**
long(>=13)_Wide(>=5,<=7)	**.4473271**	**.2337743**	**-1.54**	**0.124**	**.1606146**	**1.245849**
long(>=13)_Standard(>=3.75,<5)	**1.082788**	**.1701752**	**0.51**	**0.613**	**.7957294**	**1.473403**
long(>=13)_Narrow(>=3,<3.75)	**1.612701**	**.4595926**	**1.68**	**0.094**	**.9225199**	**2.819239**
_cons	**.001743**	**.0006152**	**-18.00**	**0.000**	**.0008726**	**.0034813**
centre						
var(_cons)	**.2649181**	**.1184312**			**.110302**	**.6362679**
centre>patientno						
var(_cons)	**2.836711**	**.2940381**			**2.315177**	**3.47573**

Primary stability

Final model (Adjusted for age and sex)

Mixed-effects logistic regression — Number of obs = **129,741**

Grouping information

Group variable	No. of groups	Observations per group Minimum	Average	Maximum
centre	**21**	**259**	**6,178.1**	**19,491**
patientno	**55,396**	**1**	**2.3**	**24**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**5**) = **134.03**

Log likelihood = **-8930.6905** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
primary_stability						
20-50	**1.534003**	**.1376489**	**4.77**	**0.000**	**1.286608**	**1.828968**
8-19	**1.84657**	**.2137332**	**5.30**	**0.000**	**1.471779**	**2.316803**
<8	**5.305983**	**.9021782**	**9.81**	**0.000**	**3.802207**	**7.404504**
age	**.9953589**	**.0023088**	**-2.01**	**0.045**	**.9908439**	**.9998944**
sex						
male	**1.429931**	**.0855983**	**5.97**	**0.000**	**1.27163**	**1.607939**
_cons	**.0022665**	**.0004866**	**-28.36**	**0.000**	**.001488**	**.0034524**
centre						
var(_cons)	**.2440029**	**.0851457**			**.1231304**	**.4835316**
centre>patientno						
var(_cons)	**3.027873**	**.1798434**			**2.695131**	**3.401697**

Primary stability

Final model (Fully adjusted)

Mixed-effects logistic regression — Number of obs = **129,741**

Grouping information

Group variable	No. of groups	Observations per group Minimum	Average	Maximum
centre	**21**	**259**	**6,178.1**	**19,491**
patientno	**55,396**	**1**	**2.3**	**24**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**19**) = **298.65**

Log likelihood = **-8847.1466** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
primary_stability						
20-50	**1.674383**	**.1545992**	**5.58**	**0.000**	**1.39721**	**2.006541**
8-19	**2.001471**	**.2440403**	**5.69**	**0.000**	**1.57602**	**2.541772**
<8	**5.248919**	**.9367752**	**9.29**	**0.000**	**3.699609**	**7.447044**
age	**.9957422**	**.0023193**	**-1.83**	**0.067**	**.9912068**	**1.000298**
sex						
male	**1.534504**	**.0929758**	**7.07**	**0.000**	**1.36268**	**1.727995**
placement_timing						
Immediate	**2.095833**	**.1917155**	**8.09**	**0.000**	**1.751835**	**2.507379**
Early(≤16 wks)	**.9260821**	**.1119861**	**-0.64**	**0.525**	**.7306649**	**1.173764**
Augmentation						
Yes	**1.185429**	**.0714325**	**2.82**	**0.005**	**1.053375**	**1.334037**
bone_quality						
Type2	**.7956316**	**.0644158**	**-2.82**	**0.005**	**.6788866**	**.9324527**
Type3	**.6909842**	**.064545**	**-3.96**	**0.000**	**.5753833**	**.8298107**
Type4	**1.017303**	**.1300072**	**0.13**	**0.893**	**.7918995**	**1.306864**
Implant_dimensions						
Standard(>=10,<13)_Wide(>=5,<=7)	**.866095**	**.1260633**	**-0.99**	**0.323**	**.6511335**	**1.152023**
Standard(>=10,<13)_Narrow(>=3,<3.75)	**1.709974**	**.1653697**	**5.55**	**0.000**	**1.414721**	**2.066847**
Short(<10)_Wide(>=5,<=7)	**1.111065**	**.178827**	**0.65**	**0.513**	**.8104715**	**1.523145**
Short(<10)_Standard(>=3.75,<5)	**1.319451**	**.1160776**	**3.15**	**0.002**	**1.110477**	**1.567751**
Short(<10)_Narrow(>=3,<3.75)	**2.511491**	**.3371113**	**6.86**	**0.000**	**1.930532**	**3.26728**
long(>=13)_Wide(>=5,<=7)	**.7313492**	**.1957569**	**-1.17**	**0.242**	**.4328003**	**1.235839**
long(>=13)_Standard(>=3.75,<5)	**.9804089**	**.0893299**	**-0.22**	**0.828**	**.8200683**	**1.172099**
long(>=13)_Narrow(>=3,<3.75)	**1.686817**	**.2131098**	**4.14**	**0.000**	**1.316826**	**2.160764**
_cons	**.0018572**	**.0004254**	**-27.46**	**0.000**	**.0011855**	**.0029096**
centre						
var(_cons)	**.2480153**	**.0866218**			**.12508**	**.4917779**
centre>patientno						
var(_cons)	**2.960325**	**.1793326**			**2.628904**	**3.333528**

Appendix 8.12: Healing mode

Healing mode
(Adjustments excluded diabetes and smoking)
(Data 2016-2022)

Mixed-effects logistic regression — Number of obs = **60,660**

Grouping information

Group variable	No. of groups	Observations per group: Minimum	Average	Maximum
centre	**16**	**602**	**3,791.3**	**9,971**
patientno	**26,572**	**1**	**2.3**	**15**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**9**) = **98.45**

Log likelihood = **-3756.6877** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
healing_mode						
Transmucosal	**1.499765**	**.2144751**	**2.83**	**0.005**	**1.133173**	**1.984952**
age	**.9953411**	**.0036133**	**-1.29**	**0.198**	**.9882843**	**1.002448**
sex						
male	**1.461611**	**.1347157**	**4.12**	**0.000**	**1.220049**	**1.751002**
placement_timing						
Immediate	**1.781147**	**.2821535**	**3.64**	**0.000**	**1.30575**	**2.429627**
Early(≤16 wks)	**.8618513**	**.137213**	**-0.93**	**0.350**	**.6308336**	**1.17747**
Augmentation						
Yes	**1.146907**	**.1096242**	**1.43**	**0.152**	**.9509735**	**1.38321**
primary_stability						
20-50	**1.398195**	**.1849687**	**2.53**	**0.011**	**1.078851**	**1.812066**
8-19	**1.584993**	**.277392**	**2.63**	**0.008**	**1.124753**	**2.233559**
<8	**6.307083**	**1.530085**	**7.59**	**0.000**	**3.920386**	**10.14678**
_cons	**.0018235**	**.0005901**	**-19.49**	**0.000**	**.000967**	**.0034386**
centre						
var(_cons)	**.273199**	**.1139086**			**.1206635**	**.6185606**
centre>patientno						
var(_cons)	**3.087804**	**.2796103**			**2.585657**	**3.687472**

Healing mode

(Adjustments included diabetes and smoking)

(Data 2016-2022)

Mixed-effects logistic regression — Number of obs = **60,660**

Grouping information

Group variable	No. of groups	Observations per group: Minimum	Average	Maximum
centre	**16**	**602**	**3,791.3**	**9,971**
patientno	**26,572**	**1**	**2.3**	**15**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**12**) = **113.07**

Log likelihood = **-3748.9086** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
healing_mode						
Transmucosal	**1.493083**	**.2136644**	**2.80**	**0.005**	**1.127911**	**1.976484**
age	**.9973661**	**.0037443**	**-0.70**	**0.482**	**.9900543**	**1.004732**
sex						
male	**1.42747**	**.1328017**	**3.83**	**0.000**	**1.189535**	**1.712998**
diabetes						
Yes	**1.051877**	**.1961091**	**0.27**	**0.786**	**.7299099**	**1.515866**
Smoking_status						
Former	**1.115375**	**.138272**	**0.88**	**0.378**	**.8747787**	**1.422144**
Current	**1.602147**	**.1893154**	**3.99**	**0.000**	**1.270929**	**2.019684**
placement_timing						
Immediate	**1.768492**	**.2806794**	**3.59**	**0.000**	**1.29571**	**2.413783**
Early(≤16 wks)	**.8744335**	**.139549**	**-0.84**	**0.400**	**.6395659**	**1.195551**
Augmentation						
Yes	**1.147842**	**.109765**	**1.44**	**0.149**	**.9516647**	**1.384459**
primary_stability						
20-50	**1.409461**	**.1868355**	**2.59**	**0.010**	**1.086975**	**1.827623**
8-19	**1.586378**	**.2780541**	**2.63**	**0.008**	**1.125153**	**2.236671**
<8	**6.30696**	**1.532218**	**7.58**	**0.000**	**3.917676**	**10.1534**
_cons	**.001453**	**.0004847**	**-19.59**	**0.000**	**.0007557**	**.0027939**
centre						
var(_cons)	**.2685713**	**.1126016**			**.118082**	**.6108517**
centre>patientno						
var(_cons)	**3.084564**	**.2813056**			**2.579681**	**3.68826**

Healing mode

Final model (Adjusted for age and sex)

Mixed-effects logistic regression — Number of obs = **129,473**

Grouping information

Group variable	No. of groups	Observations per group: Minimum	Average	Maximum
centre	**21**	**355**	**6,165.4**	**19,553**
patientno	**55,334**	**1**	**2.3**	**24**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**3**) = **41.13**

Log likelihood = **-8982.7883** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
healing_mode						
Transmucosal	**1.168541**	**.0919834**	**1.98**	**0.048**	**1.001475**	**1.363476**
age	**.9945564**	**.0022899**	**-2.37**	**0.018**	**.9900784**	**.9990547**
sex						
male	**1.401787**	**.0835734**	**5.67**	**0.000**	**1.247195**	**1.575542**
_cons	**.0035086**	**.0007035**	**-28.19**	**0.000**	**.0023684**	**.0051976**
centre						
var(_cons)	**.2669109**	**.0928235**			**.1350033**	**.5277014**
centre>patientno						
var(_cons)	**3.03301**	**.1797287**			**2.700435**	**3.406544**

Healing mode

Final model (Fully adjusted)

Mixed-effects logistic regression — Number of obs = **129,473**

Grouping information

Group variable	No. of groups	Observations per group: Minimum	Average	Maximum
centre	**21**	**355**	**6,165.4**	**19,553**
patientno	**55,334**	**1**	**2.3**	**24**

Integration method: **mvaghermite** — Integration pts. = **7**

Wald chi2(**9**) = **213.45**

Log likelihood = **-8901.1261** — Prob > chi2 = **0.0000**

Early_failure	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
healing_mode						
Transmucosal	**1.20685**	**.099265**	**2.29**	**0.022**	**1.027167**	**1.417966**
age	**.9945264**	**.0023123**	**-2.36**	**0.018**	**.9900047**	**.9990688**
sex						
male	**1.44158**	**.0865406**	**6.09**	**0.000**	**1.281562**	**1.621578**
placement_timing						
Immediate	**1.995747**	**.1806871**	**7.63**	**0.000**	**1.671248**	**2.383252**
Early(≤16 wks)	**.8800532**	**.1067722**	**-1.05**	**0.292**	**.6938045**	**1.116299**
Augmentation						
Yes	**1.178571**	**.0711801**	**2.72**	**0.007**	**1.047002**	**1.326674**
primary_stability						
20-50	**1.643068**	**.1498756**	**5.44**	**0.000**	**1.374078**	**1.964715**
8-19	**1.99455**	**.2364293**	**5.82**	**0.000**	**1.58105**	**2.516195**
<8	**5.874885**	**1.011196**	**10.29**	**0.000**	**4.192654**	**8.232083**
_cons	**.0018143**	**.0004014**	**-28.53**	**0.000**	**.0011759**	**.0027992**
centre						
var(_cons)	**.2334399**	**.0813735**			**.1178852**	**.4622648**
centre>patientno						
var(_cons)	**3.047293**	**.181374**			**2.711758**	**3.424345**