On the mortality of patients treated with dental implants: Association to age, degree of tooth loss, and treatment modality

Jan Kowar

Department of Prosthodontics/Dental Materials Science,
Institute of Odontology at
Sahlgrenska Academy
University of Gothenburg

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UNIVERSITY OF
GOTHENBURG

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jan.kowar@vgregion.se

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“No one should die with their teeth sitting in a glass of water”
Per-Ingvar Brånemark (1929–2014)

Abstract

Rehabilitation of partially or completely edentulous patients with implant-supported prostheses is a common treatment in dentistry. Clinical studies evaluating this type of treatment have largely focused on technical and biological complications. To date, only a few studies have investigated the survival of edentulous patients and the possible effects of prosthetic treatments and age at time of edentulism.

The overall aim of this thesis was to analyse the mortality of partially or completely edentulous patients in different age groups treated with implant-supported prostheses. The mortality of a large group of patients who were either treated at the Brånemark clinic, Region Västra Götaland (I-III), or in other parts of Sweden (IV) was studied with regard to degree of tooth loss and compared with a reference population matched for age and gender. Comparisons of mortality were performed on the basis of the treatment modality in relation to the degree of tooth loss (I, II) and between two treatments for edentulous patients (IV). Causes of death, as described by ICD10, were analysed in the edentulous patients and compared with the expected frequency of death cause in a reference population (III). The patients' socio-economic situation was extracted from Statistics Sweden and the implant and denture groups were compared (IV).

The results indicated that completely edentulous patients had a higher mortality compared to partially edentulous individuals. Compared to a matched reference population, elderly patients (≥80 years) treated with implant-supported prostheses had lower mortality and younger edentulous patients (≤59 years) had higher mortality. A majority of the patients died due to diseases in the circulatory system (CVD) and the incidence of CVD-related deaths was highest in the younger patient group. Patients treated with implant-supported prostheses had, in general, a lower ten-year mortality rate compared to patients who received a removable denture irrespective of socioeconomic status.

In Sweden, edentulous patients, especially younger patients, belong to a special group of dentistry patients. As these patients often have poor general health, they should receive special attention. Although this thesis does not assume being treated with implant-supported prothesis per se causes lower mortality, the thesis does assume it contributes to better nutrition, improved masticatory function, and an increased quality of life.

Keywords

Mortality, age, edentulous, dental implant, socioeconomic status

Sammanfattning på svenska

Rehabilitering av partiellt eller helt tandlösa patienter med implantatstödda proteser är idag en vanlig behandlingsmetod inom tandvården. Kliniska studier som utvärderar denna typ av behandlingen har utvärderat tekniska och biologiska komplikationer. Det finns idag få studier som har studerat överlevnaden av patienter med olika tillstånd av tandlöshet och som en möjlig effekt av olika protetiska behandlingar.

Det övergripande målet med föreliggande avhandling var att analysera mortaliteten hos patienter i olika åldersgrupper som var helt eller delvis tandlösa och behandlades med implantatstödda broar.

Mortaliteten hos en stor grupp av patienter som antingen har behandlats på Brånemarkkliniken, FTV Västra Götaland (I-IV) eller i hela Sverige (IV) följdes upp med avseende på tandlöshet och jämfördes med en referenspopulation som matchades efter ålder och kön. Jämförelse av mortaliteten utfördes med utgångspunkt från protetisk behandlingsmetod i relation till typ av tandförlust (I, II) samt mellan två olika typer av protetisk behandling av total tandlöshet (IV). Kartläggning av dödsorsaker utfördes (III) genom att ta fram data med utgångspunkt från ICD10 och jämföra med ett statistiskt sett förväntat utfall av olika dödsorsaker i en referenspopulation. Patienternas socio-ekonomiska situation hämtades fram ur SCB´s databas och jämförelse mellan grupperna analyserades (IV).

Resultaten indikerade att helt tandlösa patienter har en högre mortalitet jämfört med partiellt tandlösa. Äldre patienter (≥80år) som behandlades med implantatstödda konstruktioner hade en lägre mortalitet jämfört med referenspopulationen. Yngre tandlösa patienter (≤59år) uppvisade en högre mortalitet jämfört med en matchande referenspopulation. De flesta patienterna avled till följd av sjukdomar i det cirkulatoriska systemet (CVD) och förekomsten av CVD relaterade dödsfall var högst i den yngre patientgruppen. Patienter som behandlades med implantatstödda konstruktioner hade generellt en lägre tioårsmortalitet jämfört med patienter som fick en avtagbar helprotes utan implantatförankring oberoende av socio-ekonomisk status.

Tandlösa patienter i Sverige tillhör idag en speciell patientgrupp inom tandvården och framförallt för yngre tandlösa patienter bör allmänhälsan uppmärksammas på grund av risk för ökad mortalitet. Behandling med implantatstödda konstruktioner tros inte vara orsak till den lägre mortaliteten per se men antas bidrar till förbättrat tuggfunktion vilket kan bidra till förbättrad nutrition samt förhöjd livskvalitet för den patientgruppen.

List of papers

This thesis is based on the following studies, which are referred to in the text by their Roman numerals.

I. Kowar J, Stenport V, Jemt T.

Mortality patterns in partially edentulous and edentulous elderly patients treated with dental implants.

Int J Prosthodont. 2014 May-Jun;27(3):250-6

II. Jemt T, Kowar J, Nilsson M, Stenport V.

Patterns of mortality in patients treated with dental implants: A comparison of patient age groups and corresponding reference populations.

Int J Prosthodont. 2015 Nov-Dec;28(6):569-76

III. Kowar J, Stenport V, Nilsson M, Jemt T.

Causes of death in implant patients treated in the edentulous jaw: A comparison between 2098 deceased patients and the Swedish national cause of death register.

Int J Dent. 2019 Mar 11;2019:7315081

IV. Kowar J, Stenport V, Nilsson M, Jemt T.

Mortality in edentulous patients: A registry-based cohort study in Sweden comparing 8463 patients treated with removable dentures or implant-supported dental prostheses.

Manuscript Submitted.

Content

Abbreviation

CI	Confidence interval
CNC	Computer numeric controlled
CSR	Cumulative survival rate
CVD	Cardiovascular disease
DG	Denture group
EDI	Equalized disposable income
EMG	Electromyography
ICD	International classification of diseases
IG	Implant group
ISCED	International Standard Classification of Education
KM	Kaplan-Meier
NUTS	Nomenclature of territorial units for statistics
OHIP	Oral health impact profile
OHRQoL	Oral health related quality of life
OR	Odds ratio
PL	Product limit
PMMA	Polymethylmethacrylate
QoL	Quality of life
SCB	Statistics Sweden
SES	Socioeconomic status
SMR	Standardized mortality ratio
SSIA	Swedish social insurance agency
SUN	Classification of Swedish education
WHO	World Health Organisation

1. Introduction

1.1 Mortality in Sweden

In Sweden, all-cause mortality has decreased over the last decades. In 2019, 88,822 people died [1], which is the lowest number of deaths in the Swedish population since 1977 and gives an annual mortality rate of 8.7 deaths per 1000 individuals. Compared to 2016 through 2018, the number of deaths in 2019 decreased by 3.3%. This reduction is more pronounced for women (4.5) than for men (2.0%) [2].

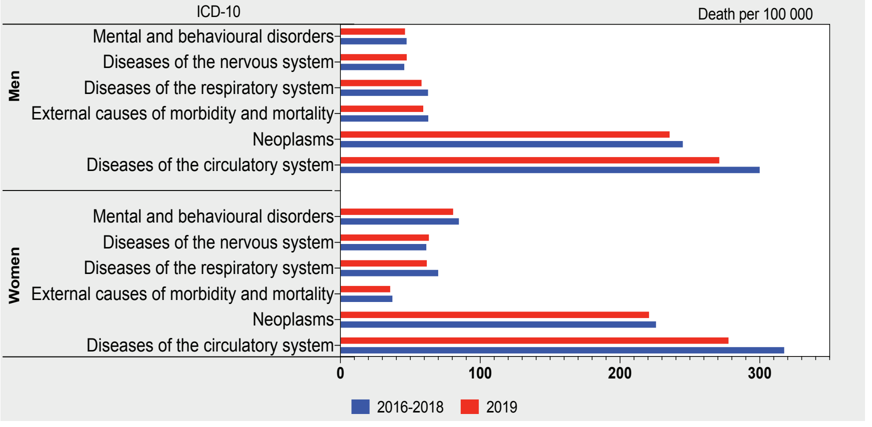

Figure 1. Frequency for the main causes of death according to ICD-10 diagnoses in 2019 and between 2016–2018 in Sweden (data from Cause of Death Register [2]).

Figure 1 shows the most common causes of death in Sweden. Compared to the period 2016–2018, the number of deaths due to cardiovascular diseases per 100 000 inhabitants decreased in 2019 (12.5% for women an 9.6% for men) [2]. In addition, the number of deaths due to respiratory system diseases or failures decreased for both women and men with an incidence of 11.7% and 7.4%, respectively [2].

In general, women live longer than men in Sweden. The mean expected remaining life time in 2019 was 84.7 and 81.3 years for women and men, respectively [3]. Cardiovascular disease (CVD) is the most common cause of death for both women and men. In 2019, 31% of all deaths were related to CVD followed by neoplasm, which accounted for 25% and 28% of all deaths for women and men, respectively [1].

However, the cause of death differs between different age groups. The most common cause of death in younger and middle-aged adults (20–59 years old) are neoplasms and death due to external causes such as violence, accidents, suicide, and self-harming behaviours [2]. Death due to mental and behavioural disorders is more common in the oldest population (>80 years old) [2]. Different types of dementia are included in this category and women are overrepresented in this subgroup. The distribution of the most common causes of death in the adult population in Sweden with regard to age groups are shown in Figure 2.

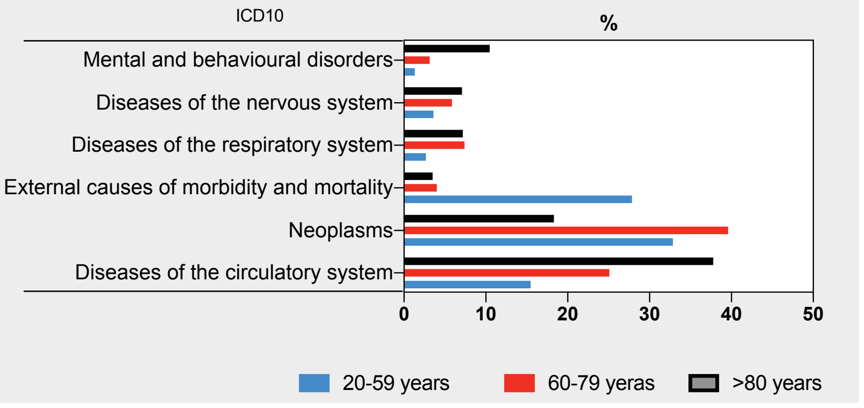

Figure 2. Frequencies of the main causes of death according to ICD-10 diagnoses in 2019 in three different age groups (data from Cause of Death Register [2]).

Reports about mortality related to dental treatment are rare. A review from 2017, including 56 studies published between 1960 until October 2015, reported that on average about three deaths occur per year as a consequence of a dental treatment. Almost half of these deaths (47%)

were related to complications due to anaesthesia, sedation, and/or medication. Bleeding, infections, cardiovascular events, and airway respiratory complications are other causes of death related to dental treatment [4].

1.1.1 Oral health related to mortality

One of the health topics within the World Health Organisation (WHO) is oral health. About 3,5 billion people are affected by diseases related to the oral cavity. Dental caries is the most common disease worldwide with a prevalence of 2,3 billion cases in 2017, where the prevalence of periodontal diseases was about 800 million cases the same year [5]. Neither disease is lethal; however, if untreated, both could lead to tooth loss and edentulism.

Moreover, several studies have reported an association between periodontitis and cardiovascular disease [6-9]. A possible association between endodontic infections and CVD is discussed in the literature. Although Cowan et al. [10] did not find an independent association between endodontic infections and different diagnoses related to CVD, Aminoshariae et al. [11] suggested that CVD could be a risk factor for negative endodontic outcomes.

Individuals missing over ten teeth or having less than five masticatory units were associated with increased all-cause mortality and dental plaque, and gingival inflammation was associated with all-cancer mortality [12]. Moreover, Adolph et al. [12] report that the risk for all-cause and all-cancer mortality increased when ≥3 oral diseases were cumulated using a Cox regression model. However, causal relationships between oral health-related diseases and mortality are still unclear.

1.2 Tooth loss

Tooth loss could be described as a result of a patient's history of dental diseases and treatments. However, tooth loss is not only an outcome of oral diseases; it could reflect other factors such as the treatment choices of patients and dentists, access to dental services, and socio-economic status [13-15]. Defining tooth loss is complex and could include missing one tooth or a complete absence of natural teeth, usually called edentulism [16, 17].

There are different classifications to describe partially edentulous situations. The most common are the Kennedy classification (1932) [18] and the Eichner index (1955) [19]. The Kennedy classification is based on both the location of lost teeth and in relation to the remaining teeth in one jaw. The Eichner index describes the presence of masticatory units between both jaws. The masticatory units are described as four supporting zones: the left premolars, the right premolars, the left molars, and the right molars. The Eichner index is divided into three main categories, whereas the Kennedy classification is divided into four classes (Table 1) [18, 19]. Completely edentulous situations are not included in the classifications.

Table 1. Description of the classification of dental jaws.

Classification	Class/Category	
Kennedy	I	Edentulous area bilateral and posterior to the remaining teeth
	II	Edentulous area unilateral and posterior to the remaining teeth
	III	Edentulous area between anterior and posterior teeth (unilateral or bilateral)
	IV	Single edentulous area crosses the midline and anterior to the remaining teeth
Eichner index	A	Four support zones posterior
	B	One to three support zones posterior or occlusal contacts anterior
	C	No occlusal contact on remaining teeth

Between 1990 and 2010, the worldwide prevalence of edentulous individuals decreased from 4,4% to 2,4% and the incidence rate almost halved (from 374 to 205 cases per 100 000 person years) [20]. The same report found a sharp increase of prevalence around the age of 70, which was associated with a peak in incidence at the age of 65.

The number of remaining teeth can be used to describe oral health in a population. In general, compared to other countries, in Sweden the median number of remaining teeth is high in all age groups [21]. In 2018, individuals younger than 60 years old had 29 remaining teeth (median) [22]. The corresponding number of remaining teeth for the age group 60–79 years old and ≥80 years old is 26 and 22, respectively [22]. In addition to the median number of remaining teeth, even the 10th and 90th percentile could be used to distinguish between individuals with better (90th percentile) and poorer (10th percentile) oral health. Between 2010 and 2018, the number of remaining teeth in the younger age group (≤59 years of age) was unchanged, but the number of remaining teeth increased by five for individuals with poorer oral health between 60 and 79 years of age (10th percentile) (Figure 3).

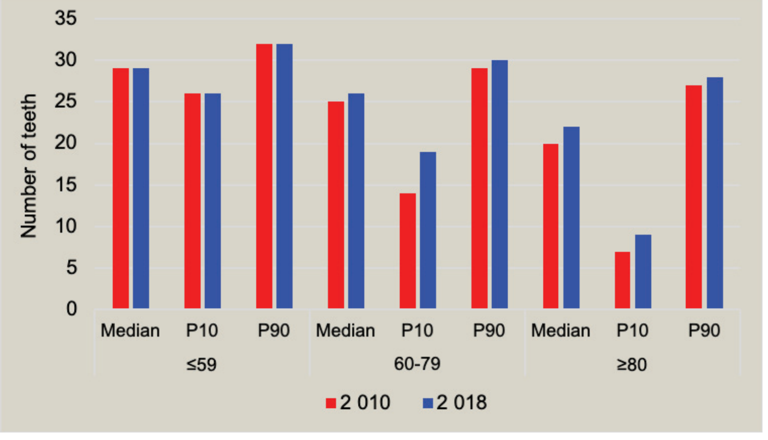

Figure 3. Number of remaining teeth (median, 10th and 90th percentiles) among Swedish patients between 2010 and 2018 for three age groups (≤59 years old; 60–70 years old; ≥80 years old). Data are from The National Board of Health and Welfare in Sweden [22].

That is, the oral health in elderly patients (≥60 years old) improved in Sweden over the last several years.

Thus, edentulism is a relatively rare disease in Sweden today. During the last several decades, a national approach to preventive dental care has improved oral health in the population. The prevalence of edentulism in 40 to 70 year olds has decreased from 16% in 1973 to 0,3% in 2013 [23] with an annual incidence rate of 23 persons per 100 000 adults. In the age group 65 to 74, it is estimated that 2,7% are edentulous, and Sweden is, together with Denmark and Switzerland, one of the few countries to reach the WHO goal of having 20 remaining natural teeth left in at least half of the population who are 80 years old [24].

1.2.1 Reasons for edentulism

Dental caries is the most common reason for tooth extraction. It is also the most common non-communicable disease worldwide, affecting about 2,3 billion people [5]. Avoiding free sugars combined with good oral hygiene can prevent dental caries. A recent study focusing on the genetic risk for caries has suggested that biological processes can influence different clusters of caries presentation and explain the variation of the disease [25].

However, dental caries can be prevented through individual and population-wide strategies although treatment is expensive, resource intensive, and can even lead to tooth extraction. Children and adolescents are most at risk for dental caries, but the fragile elderly are also at risk as they often require medications that hinder saliva production and have poor oral hygiene due to motor disabilities [25-27]. Socioeconomic status is associated with the disease and higher risk for dental caries in poor and disadvantage groups in the Swedish population [28, 29]. In addition, living in urban areas has been associated with higher risk for caries [30]. In 2018, about 4,1 million adults (≥23 years of age) in Sweden requested dental care. From this population, the number of patients treated for dental caries decreased from 28.8% to 22,9% between 2010 and 2018 and those with severe caries decreased from 14,8 % to 7,2 % in the same period [31].

Periodontitis is a disease of the tissues surrounding the teeth and severe untreated conditions may result in tooth loss. It is also a very common disease and it is estimated to affect 10% of the global population [5]. Periodontitis is suggested to be caused by specific bacteria in dental plaque. The severity of the disease depends on the number and type of bacteria together with the individual immune response, risk factors such as smoking and diabetes, and certain types of medications [32]. With adequate treatment, it is possible to eliminate dental plaque and halt the progression of tooth-supporting bone loss, but the treatment is costly and time intensive. Periodontitis is a very rare disease in children and adolescence and most of the cases develop after the age of 35. The progression of the disease is usually slow but cumulative and in older age can become more serious sometimes resulting in tooth loss [32]. Of the 4,1 million patients (≥23 years of age) seeking dental care each year in Sweden, the treatment of severe periodontitis has decreased from 2,9% to 2,2% between 2010 and 2018 [31].

Another reason for tooth loss is oro-dental trauma. Globally, about 20% of individuals encounter or undergo an injury to the teeth, mouth, or oral cavity in their life time [33]. Children and adolescence are most affected by oro-dental trauma; however, because the treatment often is complicated and with a uncertain prognosis, problems could occur later in life with tooth extraction as the result [33].

Tooth loss can also be the result of oral cancer when surgical treatment of the mandibula or maxilla is required. In 2018, the global incidence of oral cancer was estimated at 4 cases per 100 000 people [34], although in some Asian countries oral cancer is one of the most common cancers [35].

1.3 Treatment modalities

The rehabilitation of tooth loss can simply be divided into treatment with either removable or fixed tooth-supported or implant-supported prostheses. Some conditions of tooth loss can also be left untreated. The patients in the included studies of this thesis were treated with implant-supported prostheses or removable complete dentures. Study I and II included patients with different degrees of tooth loss, whereas study III and IV included a group of patients with complete edentulism. Treatment with tooth-supported prostheses is an option, but these were not examined or analysed in the studies.

Within the Swedish national dental care subsidy, administrated by the Swedish social insurance agency (SSIA), about 17 million dental treatments were performed each year between 2009 and 2019 [36]. In the same period, between 44 642 and 65 096 dental implants were placed each year, and the number has increased slightly over the last several years [36]. Figure 4 shows the frequency of prosthetic treatment in the complete edentulous jaw with dental implant-supported prostheses or removable complete dentures. Although the treatment with implant-supported prostheses is relatively stable, the rehabilitation with removable dentures has strongly decreased between 2009 and 2019.

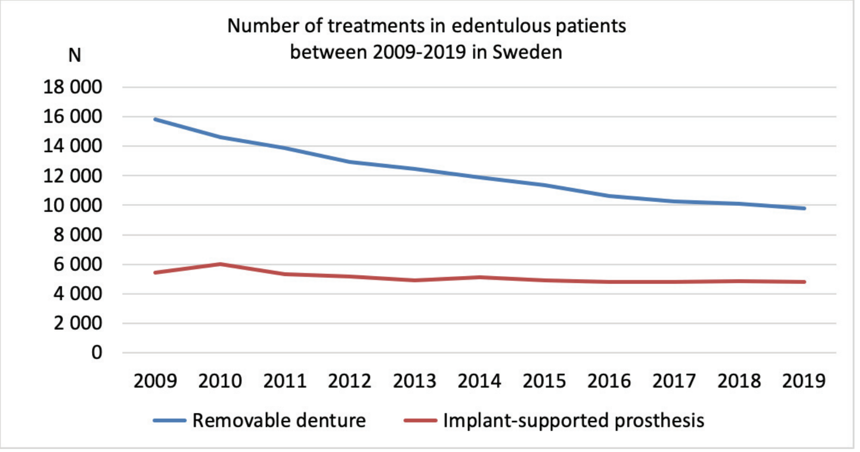

Figure 4. Number of treatments of the edentulous jaw with removable dentures or implant-supported prostheses in Sweden between 2009 and 2019 (data from SSIA register [36]).

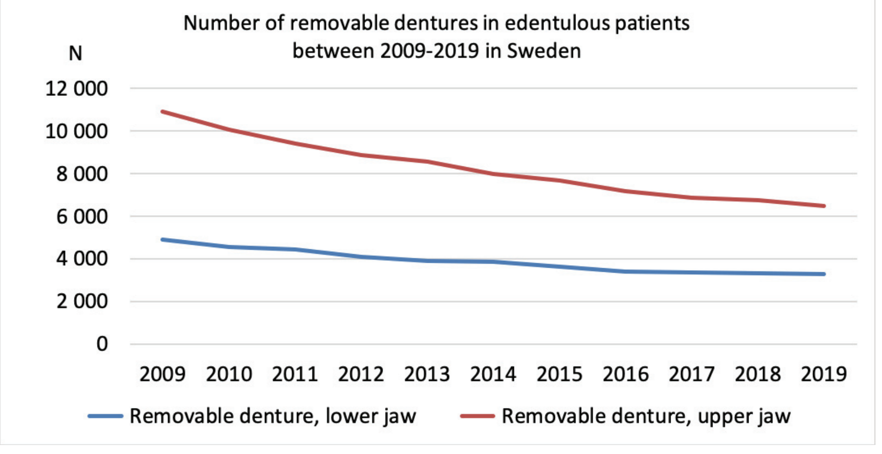

Figure 5. Number of removable dentures between 2009 and 2019 in Sweden (data from SSIA register [36]).

1.3.1 Removable denture

The history of removable dentures is long and as early as the 16th century wooden dentures were used in Japan [37]. In the 18th century, the first porcelain dentures were introduced, and the first patent was given to a French dentist [38]. Today, dentures are produced using polymethyl-methacrylate (PMMA) powders in combination with prefabricated acrylic teeth available in different shapes and tooth colours (Figure 6) [39]. Compared to other implant-supported alternatives, the treatment is moderately time-consuming and relatively cheap [40].

Darvell and Clark [41], describing the physical mechanism of the retention of a complete removable denture, postulated that factors like atmospheric pressure, vacuum, adhesion, cohesion, wettability of the PMMA, surface roughness, gravity, and muscular control are not important for the retention of a complete denture. However, the surface tension between the denture and the underlying soft tissue and the viscosity of the saliva were assumed to be important factors for the retention and function of removable dentures [41]. An advantage for the retention and function of the maxillary compared to the mandibular complete denture has been described in the literature [42]. Difficulties establishing satisfying lingual border seal through movement of the tongue and the underlying mouth floor and resorption of the alveolar ridge decrease the stability of the mandibular complete denture [42].

However, some studies show that patients are satisfied with their complete dentures [43, 44], but some studies report the opposite [45, 46]. The number of patients treated with removable dentures has decreased over the last several years in Sweden (Figure 5). This decrease in the use of removable dentures could be the result of improved masticatory function and prosthesis stability of implant-supported treatments in combination with lower prevalence of edentulism.

To evaluate dentistry treatments and their impact on oral Health-related Quality of Life (OHRQoL), health measurement scales have been developed and validated [47]. The self-administrated questionnaire Oral Health Impact Profile (OHIP) [48] includes several items that can be used to analyse the possible impact of oral health on an individual's daily life, including scores for functional limitations, oral handicap, physical disability, pain, psychological discomfort, and social disability. Specifically, patients treated with removable dentures in the edentulous mandibula were less satisfied than patients treated with implant-retained prostheses [49]. However, Awad et al. [50, 51] reported that the OHRQoL was improved from baseline to post treatment, including OHIP scores for functional limitations and physical disability, but no improvement was found for physical pain, psychological discomfort, and social disability. The possible impact on general health is still unclear [49].

Figure 6. Removable denture for the maxilla and mandible.

1.3.2 Implant-supported prosthesis

In the 1960s, the first osseointegrated oral implants were introduced as a treatment alternative to conventional complete dentures with unsatisfying function. Especially treatment of the edentulous lower jaw with osseointegrated oral implants improved masticatory functions and increased the Quality of Life (QoL) [52, 53].

Various criteria describe and define implant-supported prostheses (Table 2). The focus in the following section is on the patient's ability to remove the prosthesis (i.e., whether the prosthesis is fixed or removable).

Table 2. Treatment options with implant-supported prostheses.

Type of support	Retention	Patient's ability to remove
Implant	Screw	Fixed
Tissue	Cement	Removable
	Attachment	
	Combination	

During 2009 and 2019, about 50 000 implant-supported prostheses for treatment of the complete edentulous jaw were registered in the SSIA database [36]. The most common implant treatment of the edentulous patient in Sweden is the implant-supported fixed bridge. Only about 8% of the registered cases were removable implant-supported prostheses (Figure 7) [36].

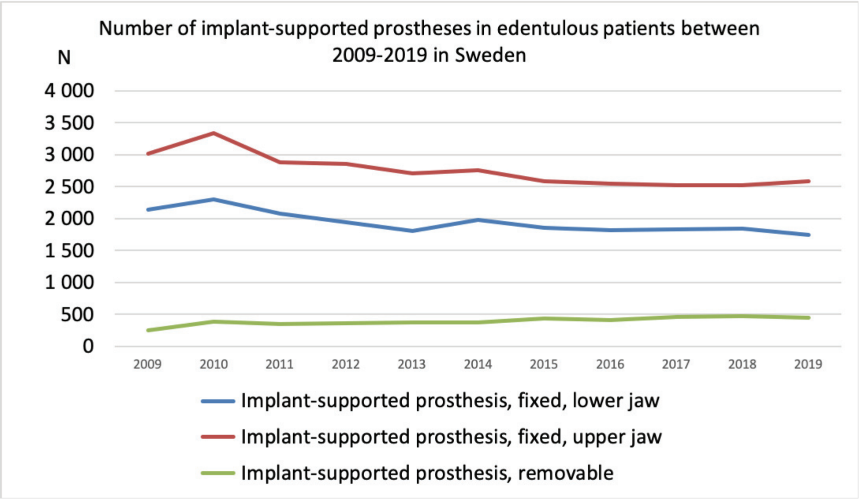

Figure 7. Frequencies of different treatments in the edentulous patient in Sweden between 2009 and 2019 (data from SSIA register [36]).

1.3.2.1 Fixed implant-supported prosthesis

An implanted-supported prosthesis is fixed to dental implants and cannot be removed by the patient. The fixation to the implants could be screw-retained or cemented. The screw-retained alternative can be removed by the dentist, but cemented alternative is not intended for removal, and if needed, removal often leads to destruction of the prosthesis.

The prosthesis could be performed using metal or ceramic frameworks provided with resin teeth or porcelain veneers (Figure 8). The frameworks could be manufactured from gold alloy, titanium, cobalt chromium, or Zirconia. The technique has changed over the last decades from cast frameworks to computer numeric control (CNC) milled or laser sintered frameworks. The latter improves the precision and fit of the components [54].

Figure 8. Implant-supported fixed prosthesis in the maxilla with a framework in Zirconia and porcelain veneers.

The treatment of the edentulous mandible [55] and maxilla [56] with fixed implant-supported prostheses has shown to be a successful alternative, with high survival of both implants and prosthetic construction. The positive impact on OHRQoL and patient satisfaction was reported in several studies [57-60]. Also, the positive impact on improved masticatory function has been demonstrated [61-63]. Significantly higher values for bite forces and muscular activity during clenching has been reported compared to dentate individuals, and the chewing efficiency to prepare food for swallowing has been comparable to persons with natural dentition [63].

1.3.2.2 Removable implant-supported prosthesis

If the implant dental prosthesis can be removed by the patient, it is considered to be a removable alternative. A wide range of attachments to retain the prosthesis to the implants is available. The most common attachments are the implant bar, the Ball attachment, and the Locator attachment (Figure 9). The implant bar provides good stability for the attached prosthesis, and the Ball attachment is prefabricated, easily replaceable, and has hygienic advantages. The Locator attachment, a more recent alternative, has the possibility to adapt the retention forces through different colour-defined components.

Figure 9. Three types of attachment (implant bar, Locator, and Ball). Pictures provided courtesy of Dentsply Sirona.

Especially in the edentulous mandible, the removable implant-supported prothesis has been shown to be a viable treatment alternative for the conventional removable denture. Different studies have shown high survival of the constructions and implants and a high patient satisfaction [64, 65]. Measurements of the OHIP scores demonstrated higher values after treatment with mandibular overdentures for all subscales, including psychological discomfort, functional limitations, and physical and social disability [50, 51].

Also, the positive impact on improved masticatory function has been demonstrated [61, 62]. The maximum bite forces during bilateral clenching was doubled compared to individuals wearing conventional removable dentures, and the chewing process was more efficient when measuring the chewing cycles of test food [46, 66]. However, in Sweden removable implant-supported prostheses are rare (Figure 7). The wear of the attachments and the requirement to replace components make the initial benefits less favourable compared to the fixed implant-supported prosthesis [67-69].

1.4 Tooth loss associated to different conditions

Age has a major impact on tooth loss. Due to a cumulative effect of diseases in the oral cavity, such as dental caries and periodontitis, tooth loss is more evident in older adults [26]. While individuals in Sweden younger than 60 years old have 29 remaining teeth (median), the corresponding number for persons older than 80 years is 22 [22].

Several studies have suggested an association between tooth loss and general health [58, 70-76]. The risk for Alzheimer's disease or dementia seems to increase in patients with reduced numbers of remaining teeth [77]. Elderly patients with chewing difficulties have shown higher risk for cognitive impairment [78]. However, the strength of the evidence is weak, and a causal relationship was not established.

Risk for cardiovascular disease – e.g., myocardial infarct, heart failure, and stroke – seems to increase in individuals with ≥5 missing teeth [79]. This association have been shown especially strong among the younger individuals (<65 years old) and those with a history of periodontitis [8, 9, 79]. The incidence of CVD-related diseases seems to increase with number of missing teeth and edentulous individuals generally showed the highest risk for mortality due to CVD-related diseases [80]. Nevertheless, tooth loss could be associated to different lifestyles and behavioural factors, and a clear correlation to CVD-related mortality is missing.

Severe tooth loss could influence the masticatory function, which is an important aspect of oral health. Mastication can be divided into phases, and studies using electromyography (EMG) on jaw movement tracking have illustrated the normal physiology of mastication [81, 82].

Furthermore, the response from the brain to different types of prosthetic treatment have been reported, suggesting that the sensory and motor feedback to the brain can be restored with implant-supported prostheses [83]. This could be of importance to understanding and clarifying the processes underlying patients' behavioural responses to oral prosthetic treatment. Trulsson et al. [62] reported that the bite force increased in completely edentulous patients treated with implant-retained prostheses compared to conventional complete dentures, but decreased when comparing the bite forces in a full natural dentition.

Also, patients treated with implant-retained prostheses showed better chewing efficiency compared to complete denture wearers [62]. Swallowing dysfunction has been reported to be a risk factor for undernutrition in elderly [84] and has been associated with poor oral health and higher risk for early death in older people [85]. Moreover, replacing missing teeth to protect against all-cause mortality has been discussed in the literature. Studies on edentulous patients indicate that patients using dentures have a decreased risk for all-cause mortality compared to untreated individuals not using dentures [17, 86]. The effect of treatment choice on mortality is still unclear and remains to be established.

In addition to oral function, tooth loss impact OHRQoL [87]. Speech difficulties due to tooth loss and after prosthetic treatment might influence psychosocial functioning [62]. Specifically, tooth loss in the anterior region could influence orofacial aesthetics and impact a patient's quality of live (QoL) [88]. Several studies have shown that prosthetic treatment of edentulous patients improves their QoL [52, 53, 89], and it has been stated that the treatment with implant-supported fixed prostheses "means an odontological and psycho-social restitutio ad integrum" [89].

2. Aim

The overall aim of the current thesis was to investigate the mortality in patients treated with dental implants with different degrees of tooth loss.

2.1 Specific aims

a) To compare the patient survival of partially and completely implant-treated edentulous elderly patients (≥80 years old at implant surgery) with a reference population of comparable age in Sweden.
b) To report the mortality pattern in patients treated with implant-supported prostheses in different age groups and compare these with a reference population.
c) To examine the cause of death in a group of patients treated with implant-supported prostheses in the edentulous jaw and to compare the results for different age groups with the mortality pattern in the Swedish population.
d) To analyse the association between age at the time of complete tooth loss and all-cause mortality in edentulous patients treated with different prosthetic alternatives.

3. Patients and Methods

3.1 Study design

The present thesis is based on four retrospective cohort studies that include patients in different age groups with different degrees of tooth loss.

Table 3. Overview of the patients and methods analysed in the present papers.

	Study I	Study II	Study III	Study IV
Design	Retrospective cohort studies			
Sample	>79 years old from one clinic (1986–2003)	All treated patients from one clinic (1986–1997) and (2004–2008)	>19 years old from one clinic (1986–2014)	>19 years old from SSIA (2009–2013)
Participants (N)	266	4231	3902	8463
Study period	1986-2013	Baseline (1986, 2004) to 2014	1986–2018	2009–2019
Max follow-up time	10 years	15 years	30 years	10 years
Exposure variable	Partial or completely edentulous	Partial or completely edentulous	Completely edentulous	Completely edentulous
Outcome variable	All-cause mortality	All-cause mortality	Cause-specific mortality	All-cause mortality

3.2 Participants

The participants in study I-III were treated at one specialist clinic (Brånemark Clinic, Public Dental Health Service, Region Västra Götaland, Sweden). All included patients were provided with implant-supported prostheses in one or both jaws (study I-IV) and in partial (study I and II) or complete (study I-IV) edentulous conditions. Patients were divided in subgroups based on age at implant surgery, time of inclusion, and treatment modality. The study population for study IV included patients who were completely edentulous in both jaws identified via a register from the Swedish Social Insurance Agency (SSIA). The included patients were treated either with conventional removable dentures or implant-supported prostheses and were divided into two study groups: the denture group (DG) and the implant group (IG). The number of participants, time of inclusion, and follow-up time for the four studies are shown in Table 3.

The treatment protocol for the patients (study I-III) include placement of Brånemark system implants (Nobel Biocare AB) in partial (study I and II) and/or complete edentulous (study I-III) situations [56]. Most of the treatments followed a two-stage surgical protocol [90]. After abutment connection, the patients were provided with fixed implant-supported prostheses [91]. During the time of inclusion for study I-III (1986-2018), the way the frameworks were manufactured changed. Initially, the prostheses for both partially and edentulous conditions were cast in gold alloy and veneered with acryl (partial edentulism) or artificial resin teeth (complete edentulism). Later, the frameworks were made from titanium milled using computer numeric control (CNC) and veneered with porcelain (partial edentulism) or artificial resin teeth (complete edentulism) [54, 92, 93].

After delivery of the prostheses, patients in study I-III were invited to participate in a follow-up according to a standardized protocol [91, 94]. Clinical examinations, which included radiologic examinations, were scheduled at prosthesis placement, after one year, after five years, and then every five years. Patients could also be invited for individual check-ups if needed, but all patients were also encouraged to schedule an examination themselves if they experienced a problem [94, 95].

The prosthetic treatment for the patients in study IV is not accounted for in detail. The patients in the implant group (IG) were treated with either a fixed or removable implant-supported prostheses, and the patients in the denture group (DG) were treated with conventionally removable dentures.

3.2.1 Reference group

The Cumulative survival rate (CSR) was calculated in studies I, II, and IV to describe the pattern of patient's mortality. For comparison of the expected and observed lifetime for each patient, data from Statistics Sweden of the remaining lifetime of the Swedish population were collected [96-100]. Baseline for study I-III was the time of implant surgery, and in study IV the patients were included at the time point when they became edentulous as recorded in the SSIA register [36]. The data covered gender, age at the time of inclusion in the study, and the time period (1986–2018). This information was used to calculate an expected mean CSR for a reference population with comparable age and gender at the time of inclusion.

The reference population for study III was obtained from the Swedish National Cause of Death Register. Matching age at inclusion to the study, sex, and the calendar year specific mortality rate for different diseases of an expected number of deceased patients were calculated and defined as the reference population [101, 102].

3.3 Methods

Because every citizen in Sweden has a unique identification number, records of different variables could be linked between different databases. In study I and II, the national Swedish population database was used to collect information regarding date of death. The data were used to determine the patient's lifetime and to calculate the CSR for the study groups.

The Swedish National Cause of Death Register was searched for all included patients to obtain the date of death (study III and IV) and the underlying cause of death (study III). This register uses the International Classification of Diseases (ICD), version 10 [103]. This version was first used in 1994. If the date of death for the included patients occurred before 1994, earlier versions – i.e., ICD-8 or ICD-9 – were used to code the underlying cause of death. Conversion tables from the National Board of Health and Welfare were used to translate ICD-8 or ICD-9 codes into ICD-10 codes. The observed cause of death classification for each patient was registered in study III and IV, and the most common causes of death in study III were compared with the expected death causes in the reference population and used for statistical analysis.

In study IV, the population was identified from the SSIA database using codes for dental treatment. The SSIA uses a specific code to identify individuals who have become edentulous in both jaws. To avoid including patients who had been edentulous for a long time and had replaced an earlier complete denture, at least one tooth extraction had to be reported to the SSIA register within the inclusion period. The SSIA register includes codes for implant surgery; if one of these implant codes were registered in any jaw after inclusion of the patient (through 31 December 2018), the patient was placed in the implant group (IG). The remaining patients were identified as edentulous treated with removable dentures and therefore were included in the denture group (DG). In addition to the data for all-cause mortality from the Swedish Cause of Death Register, socioeconomic data were obtained for all patients in study IV. Thus, information regarding education, country of birth, place of residence, and the disposable income were collected from separate registers.

The highest level of education for each patient in study IV was collected from the Register of Education of the Swedish Population. A three-digit code according to the Classification of Swedish Education (SUN 2000 [104]) was used to divide the included edentulous patients in study IV into three groups: primary, secondary, or tertiary. The SUN 2000 is adapted to the International Standard Classification of Education (ISCED 97 [105]).

The country of birth and the place of residence for each included edentulous patient in study IV was searched in the Total Population Register from Statistics Sweden. The patients were divided into two groups: born in Sweden and born abroad. The place of residence was obtained for the included individuals in study IV on a municipality level according to the Nomenclature of Territorial Units for Statistics (NUTS [106]). Three subgroups were identified based on the proportion of people in a municipality living in rural areas: subgroup 1 (predominantly urban regions) – less than 20% living in rural areas; subgroup 2 (intermediate region) – up to 50% living in rural areas; and subgroup 3 (predominantly rural region) – more than 50% of its population living in rural areas [107].

To analyse the annual income for each individual, Equalized Disposable Income (EDI) data were collected from Statistics Sweden. The EDI is the total income of a household per year after taxes and other deductions divided by the number of household members converted into equalized adults. The EDI makes it possible to compare income between individuals in different family situations. Income levels were defined for three groups. The limit for the lowest annual income (133 867 SEK) was defined as an income that is 50% lower than the median income of the whole study group and the limit for the highest annual income (307 518 SEK) was 50% higher than the median income. The intermediate group was defined between these two levels.

3.4 Statistical analysis

Descriptive statistics for all included patients in studies I-IV were presented as numbers and percentages. Data were also presented as 25^{th} percentile, median, and 75^{th} percentile as well as min and max values.

The analysis of the time to an event (T) – i.e., date for implant surgery, date patient became edentulous, or date of death – can be used to calculate survival time. Because the survival time is a random variable, it can be described with a distribution function. The distribution of the survival time can be described using a survival function [108]:

Survival function S(t) = P (a patient survives longer than a time t) = P(T>t). (1)

This can also be written as S(t) = 1 - P (a patient fails before time t) = 1 – F(t), where F(t) = the cumulative distribution function of T: for t = 0, S(t) = 1, and for t = ∞, S(t) = 0.

This means that the probability of surviving at least at time 0 is 1, and the probability of surviving "forever" is zero. S(t) is also called the cumulative survival rate (CSR), and the graph of the function is called a survival curve (Figure 10).

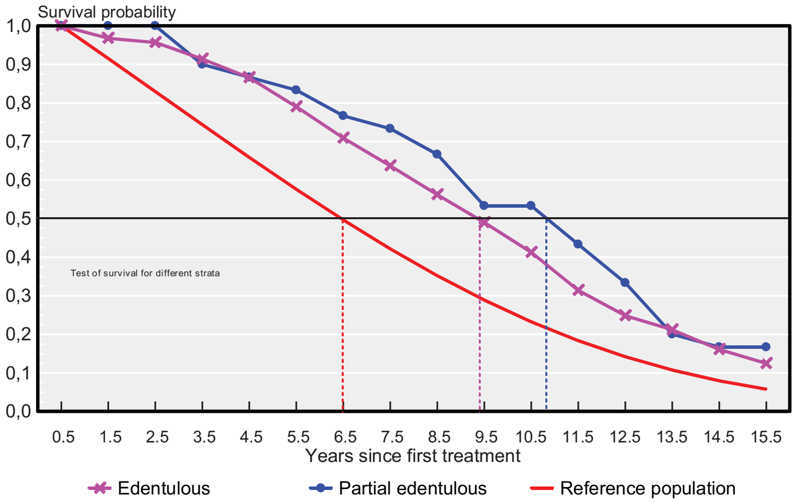

Figure 10. Example of a survival curve. The curve shows that the median survival time for the reference population is 6.5 years, for partial edentulous approx. 9.5 years, and for the edentulous patients approx. 11 years.

In clinical studies, start of the study and the follow-up time are often restricted to a specific start and closing date (e.g., 1 January 2000 to 31 December 2019), and the patients enter the study at different times after their treatment. If patients die before the study ends, the exact survival time is known. If patients drop out before the study ends, they are lost to follow-up. If patients are alive at the closing date of the study, the survival time is known at least until that point. For the lost patients, the survival time is known at least from entry until last contact. For the surviving patients, the survival time is known at least from entry to closing date of the study. The last two categories of patients are examples of censored observations.

If no data were censored (i.e., all patients are available for follow-up until failure at time t), the survival function is straight forward and estimated as follows:

$$\hat{S}(t) = \frac{\text{the number of patients surviving longer than the time } t}{\text{Total number of patients}}. \quad (2)$$

That is, the survival function reveals the proportion of observations in the population with an event time greater than t. If t = five years and 50 of 100 patients survive more than five years, the proportion survivors is 50%.

If data are censored, the numerator in (2) might not always be definable. This means that (2) is not a proper estimator for S(t). The solution to this situation is to use a nonparametric estimator such as a product-limit (PL) estimator (e.g., the probability of surviving k(≥t) or more years from study start is calculated as the product of k observed survival rates) or a Kaplan-Meier (KM) estimator [108]:

$$\hat{S}(k) = p_1 \times p_2 \times p_3 \times \ldots\ldots \times p_k \quad (3)$$

where p_1 is proportion of patients surviving at least one year, p_2 is proportion surviving at least two years having survived the first year, p_3 is proportion surviving at least three years having survived the first two years, and p_k is proportion surviving at least k years having survived k - 1 years.

This means that the PL estimates the probability of surviving *k-1* number of years from study start and the survival rate for year *k*:

$$\hat{S}(t) = \hat{S}(t-1)p_t \quad (4)$$

If data for survival times from n patients are collected irrespective of being censored, the n survival times are as $t_{(1)} \leq t_{(2)} \leq t_{(3)} \leq \ldots \leq t_{(n)}$. This results in the following estimator:

$$\hat{S}(t) = \prod_{t(r) \leq t} \times \frac{n-r}{n-r+1}. \quad (5)$$

This estimator (5) is based on individual survival times, whereas the so-called life table method is based on survival times grouped into intervals, and each interval can have data for more than one patient. The PL estimator can be considered a special case of the life table estimate where each time interval consists of only one patient. An advantage of using a non-parametric estimator is that it makes no assumption about the distribution of the outcome variable [108].

In studies I, II, and IV, the KM estimator was used to analyse survival time from date of the last registered treatment to either death or last day of follow-up. How survival, stratified by age and treatment, differs among patients was calculated.

The CSR was used to compare survival among patients and a reference population. The reference population was the Swedish population over the study period in the studied age groups. The difference (in percent) in survival between patients and reference population was calculated. Also, a difference in survival over the follow-up time stratified by age groups was calculated. To analyse the deviation in percent between reference population and treated patients, the level for the reference population was set as zero.

The Standardized Mortality Ratio (SMR) was calculated in study III. The SMR for the different diseases was the observed number of deaths for the specific disease in the study population divided by the expected number of deaths for the standardized Swedish reference population. The data were retrieved from the databases provided by the Swedish National Board of Health [101, 102]. Population figures were retrieved from Statistics Sweden [101]. The results were considered to be statistically significant if the 95% confidence interval of the SMR did not include one.

Since the patient data for study IV were extracted from Statistics Sweden, the proportion of missing data is regarded as low, less than 0.2%, except for one of the variables, education level: 4.2% of the education level data is missing, mainly for patients born abroad (e.g., Asia, Africa, and Europe) and majority of these were 60 years or older. For educational level, sensitivity analysis was conducted where missing data were assumed to be either primary school or secondary school. There were no changes in the results due to the sensitivity analysis [109].

To evaluate the connection between mortality and socioeconomic factors, the data were analysed with the uni- and multivariable logistic regression models [109]. The probability for an outcome, p_i in a linear probability model varies between zero and one, while linear functions to its nature are unbounded functions. To solve this problem one can transform the probability, so it is no longer bounded between zero and one. This can be done by using the logarithm of the odds (logit or log-odds):

$$\log \left[\frac{p_i}{1-p_i}\right] \quad (6)$$

Where p_i is the probability of the event ($y_i = 1$) and $1\text{-}p_i$ is the probability that the event does not occur ($y_i = 0$).
Where $0 \leq p_i \leq 1$, and $0 \leq \left[\frac{p_i}{1-p_i}\right] \leq \infty$

The model estimated in the univariable case for i=1, ……n individuals and one explanatory variable (univariable model) is as follow:

$$\log \left[\frac{p_i}{1-p_i}\right] = \alpha + \beta x_i \quad (7)$$

This model can be extended to a multivariable model for $I = 1, \ldots\ldots. n$ individuals and k explanatory variables to:

$$\log\left[\frac{p_i}{1-p_i}\right] = \alpha + \beta x_{i1} + \beta_2 x_{i2} + \beta_3 x_{i3} + \ldots. + \beta_k x_{ik} \quad (8)$$

Where p_i is the probability that $y_i = 1$. In contrast to the traditional regression model, there is no random error term in a logistic model. The random variation comes from the probabilistic relationship between p_i and y_i.

Equation (8) can be solved for pi and is equal as

$$p_i = \frac{e^{\alpha+\beta x_{i1}+\beta_2 x_{i2}+ \beta_3 x_{i3}+\ldots..+ \beta_k x_{ik}}}{1+ e^{\alpha+\beta x_{i1}+\beta_2 x_{i2}+ \beta_3 x_{i3}+\ldots..+ \beta_k x_{ik}}} \quad (9)$$

Since $\log(e^x) = x$, (9) can be written as

$$p_i = \frac{1}{1+ e^{-\alpha-\beta x_{i1}-\beta_2 x_{i2}- \beta_3 x_{i3}-\ldots..- \beta_k x_{ik}}} \quad (10)$$

Equation (10) has the desired properties, that no matter the value of the β's and the x's, the probability p_i will always be between zero and one.

In the analysis, the univariable logistic regression model (7) was first used to evaluate which variables were to be included in the multivariable model (8). All explanatory variables with a P-value ≤ 0.2 were included in the first multivariable analysis, and those variables that had a P-value ≤ 0.05 were included in the semi-final model. If some of the variables in the semi-final model had a P-value>0.5, they were excluded in the final run of the model [109]. No "automatic" forward or backward elimination of explanatory variables were used in the analysis. This procedure was used to avoid "fishing" for significances. Odds ratios and 95% confidence intervals were calculated, and Benjamini-Hochberg Procedure was used to compensate for multiple comparisons [110].

In the uni- and multivariable logistic regression analysis, the event (deceased, coded=1) versus the non-event (alive, coded=0) were used as outcome. A logit model to estimate the probability of deceased were analysed as the probability to decease before the end of the study, which takes a value between 0 and 1.

The explanatory variables were categorized as follows: treatment with implant (Yes=0, and No=1); gender (male=0 and female=1); educational level (tertiary=0, secondary=1, primary=2); income (high EDI=0, intermediate EDI=1, low EDI=2); regional typology (rural area=0, intermediate area=1, urban area=2); and country of birth (abroad=0, Sweden=1). Interaction effects were analysed, especially between education level, country, and income level. The results in study IV are presented as Odds Ratios (ORs) with 95% confidence intervals (95% CI), and *P*-values for the explanatory variables were used in the estimated model. No interaction effects were found. Since age might be a confounder, results are stratified by age in the uni- and multivariable analysis as well as in the Kaplan-Maier analysis.

The calculated *P*-values in the present studies were considered statistically significant if $P<0.05$ with 95% confidence interval.

SAS® Stat version 13.1 software, Proc Logistic (Copyright© 2002–2012 by SAS Institute Inc., Cary, NC, USA) was were used for the Kaplan-Meier and logistic regression data analysis. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp IBM was used for some of the descriptive analysis.

3.5 Ethical considerations

Study I-III were approved by the Regional Ethical Review Board in Gothenburg (Dnr 197-12 and 460-15) and study IV by the Swedish Ethical Review Authority (Dnr 2019-02118). The STROBE guidelines [111] for observational studies were followed in the design of the studies.

4. Results

4.1 All-cause mortality

4.1.1 Association to degree of tooth loss

Altogether, 266 patients were identified for inclusion in study I. However, only 230 patients completed the ten-year follow-up period. (Figure 11).

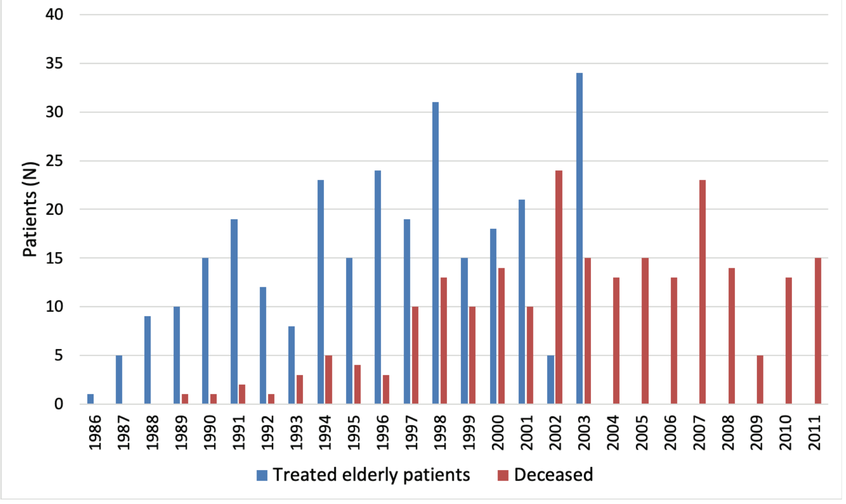

Figure 11. **Study I**: Number of treated and deceased elderly patients (≥79 years old) between 1986 and 2011.

In the elderly population in study I (≥80 years old at time of implant surgery), an increased CSR was observed compared to the reference population ($P<0.05$). The 10-year mortality was 14% and 22.7% lower in the edentulous and partially edentulous patients compared to their corresponding reference population. The partially edentulous patients showed a statistically significant lower mortality compared to the edentulous patients (−10.4%) over the ten years of follow-up (Figure 12).

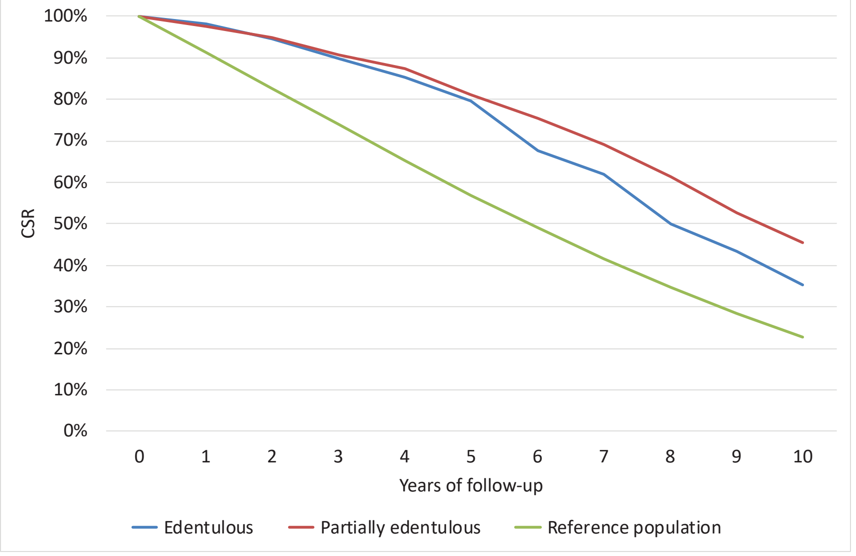

Figure 12. **Study I**: Cumulative survival rate (CSR) of edentulous and partially edentulous patients compared to the corresponding reference population.

The study population in study II consisted of 4267 consecutively treated patients (11–101 years old at implant surgery). During the 15 years of follow-up, 1241 patients were deceased, 236 partially edentulous patients and 1005 edentulous patients. The 15-year mortality, stratified by degree of tooth loss (partially or completely edentulous), showed a similar pattern as in study I. Thus, an increased mortality was observed for the completely edentulous group of patients compared to the partially edentulous individuals irrespective of age at the time of inclusion to the study ($P<0.05$)

4.1.2 Association to age

The study population in study II-IV was stratified by age at time of inclusion to the study.

Study II

The difference in mortality age between the edentulous study group and the reference population showed a systematic decrease for the whole group with increased age at surgery (Figure 13). In contrast, higher mortality rates were observed for the completely edentulous patients from the younger age groups (40–69 years old) compared to the older edentulous individuals (≥70 years old), who showed lower 15-year mortality compared to the reference population ($P<0.05$). A similar pattern has been displayed for the different age groups of the partially edentulous patients with exceptions for partially edentulous patients younger than 50 years old, who had a similar death rate compared to the reference population.

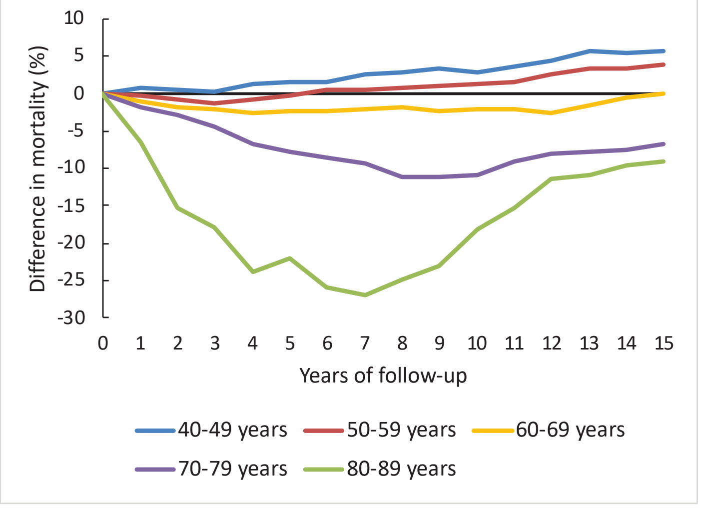

Figure 13. **Study II**: Difference in mortality between the reference population and edentulous patients stratified by age. The difference in mortality was highest for the youngest age group followed by a consistent shift towards lower mortality in the older age groups [112]. Figure provided courtesy of Quintessence Publishing Co., Inc.

Study III

The observed all-cause mortality among patients younger than 60 years old was generally higher compared to the expected mortality in the reference population (SMR=2.2; $P<0.05$). In the age group 60–79 years old, the observed number of deceased patients was lower than expected (SMR=0.9; $P<0.05$), and a similar pattern was shown in the age group >79 years old (SMR=0.6; $P<0.05$) (Table 4).

Table 4. **Study III**: Expected and observed mortality rate among 3902 (2142 females and 1760 males) edentulous patients treated with implant-supported prostheses 1986-2014 stratified by age.

Age group	Number of deaths (all causes)			
	Observed	Expected	SMR*	95% CI†
40-59 years (N=1262)	363	164	2.2‡	2.0-2.4
60-79 years (N=2350)	1497	1627	0.9‡	0.8-0.9
≥80 years (N=290)	236	362	0.6‡	0.5-0.7
All patients (N=3902)	2098	1377	1.5‡	1.5-1.6

* SMR, standardised mortality ratio
† 95% CI, 95% confidence interval
‡ statistically significant

Study IV

For the edentulous patients in the youngest age group (≤59 years old), a higher mortality compared to the reference population was observed ($P<0.05$) irrespective of prosthetic treatment. Furthermore, patients between 60–79 years old treated with removable dentures had an increased mortality rate compared to the reference population and a comparable death rate was found for the patients treated with implant-supported prostheses in the same age group.

However, the group of patients ≥80 years old showed an increased mortality compared to the reference population if treated with removable dentures and a lower mortality if treated with implant-supported prostheses ($P<0.05$) (Figure 14).

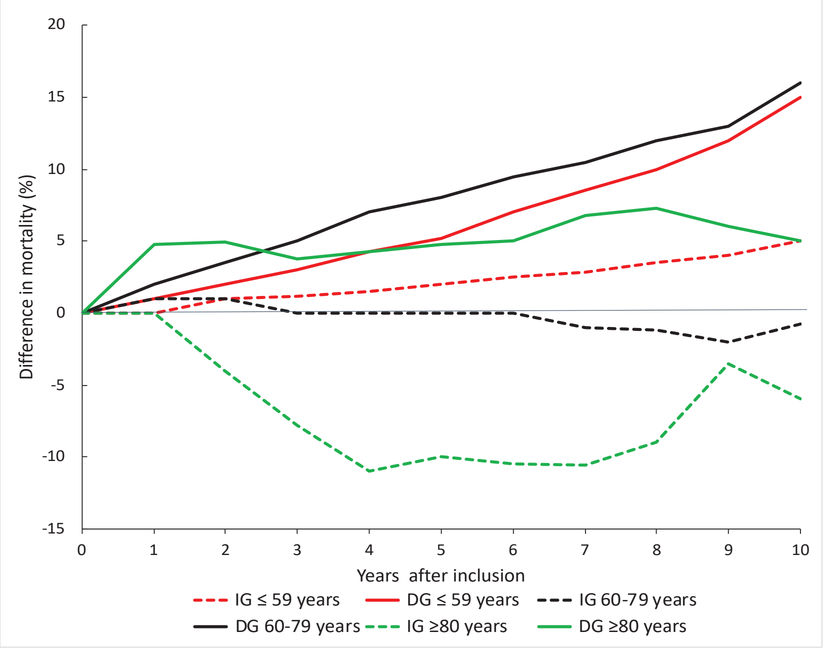

Figure 14. **Study IV**: The difference in mortality between reference populations and patients treated with implant (IG group) and removable dentures (DG group) stratified by age.

4.1.3 Time period of implant surgery

Different time periods, based on the choice of prosthetic treatment, were analysed in studies II and III. In study II, the differences in mortality for edentulous patients between 40 and 89 year olds treated with implant-supported prostheses were related to three periods: 1986–91, 1992–97, and 2004–08. In the oldest age group (80-89 years old), a reduced mortality compared to reference population was observed for all periods. Patients between 50 and 79 years old at the time of implant surgery had a mortality rate comparable to the reference populations for all three periods. Younger edentulous patients (40–49 years old) treated during the last period (2004–08) had a statistically significant higher mortality rate compared to their peers treated between 1986 and 1997 and compared to the reference population ($P<0.05$).

Table 5 presents the mortality among all patients (N=3902) in study III for two periods. The patients treated in the earlier period (1986–1997) showed a lower mortality (SMR 0.9; $P<0.05$) compared to the reference population in contrast to the patients treated in the later period (1997–2014), which demonstrated a higher mortality rate (SMR 2.4; $P<0.05$). However, patients in the younger age group (40–59 years old) displayed an increased mortality for both periods, whereas the elderly patients (≥80 years old) had a lower mortality rate compared to the reference population ($P<0.05$).

Table 5. **Study III**: Mortality among 3902 (2142 females and 1760 males) treated edentulous patients who received treatment with implant-supported prostheses, 1986–1996 or 1997–2014.

	Number of deaths (all causes)				
Time period	N	Observed	Expected	SMR*	95% CI†
1986-1996	2496	245	278	0.9‡	0.8-0.9
1997-2014	1406	459	187	2.4‡	2.2-2.7

* SMR, standardised mortality ratio

† 95% CI, 95% confidence interval

‡ statistically significant

4.1.4 Treatment modality

The association of prosthetic treatment modality in different clinical conditions in relation to mortality was analysed in study I, II, and IV. In study I and II, a difference in mortality was reported between patients treated with implant-supported prostheses in partially edentulous and complete edentulous situations. The results from both studies showed that the all-cause mortality was statistically significantly lower for patients treated with partial implant-supported prostheses compared to the completely edentulous patients treated with implant-supported prostheses ($P<0.05$).

Study IV investigated the difference in mortality between edentulous patients treated with dental implants (implant group, IG) or removable dentures (denture group, DG). A consistently higher mortality rate for the DG group compared to the IG group was observed irrespective of age, gender, and socioeconomic status ($P<0.05$). The results of the multivariable analysis between the groups (stratified by age) demonstrated that patients treated with dental implants showed a lower risk of mortality in all age groups ($P<0.05$) (Table 6).

Table 6. Results of the multivariable logistic analysis of edentulous patients in the implant group (IG) and denture group (DG) stratified by age (**Study IV**).

	Age-group ≤59 years (N=2709)			Age-group 60 -79 years (N=4584)			Age-group ≥ 80 years (N=1170)		
	OR*	95% CI†	*P*-value	OR*	95% CI†	*P*-value	OR*	95% CI†	*P*-value
IG	1.0			1.0			1.0		
DG	1.7	1.2-2.4	<0.05‡	1.7	1.4-2.0	<0.05‡	1.8	1.2-2.6	<0.05‡
Male	1.0			1.0			1.0		
Female	0.8	0.6-1.0	0.05	0.7	0.6-0.8	<0.05‡	0.5	0.4-0.7	<0.05‡

* OR, Odds-ratio

† 95% CI, 95% confidence interval

‡ statistically significant

4.1.5 Association to socioeconomic status (SES)

The variables used to illustrate SES in study IV were education level, residence, equalized disposable income (EDI), and country of birth. The overall proportion of patients with tertiary education level was higher in the IG group compared to the DG group (16% vs. 8%). Almost half (42%) of the population in the IG group lived in an urban area and had high EDI, whereas the corresponding numbers for the DG group were 27% and 19%, respectively. More patients were born abroad in the IG group (42%) than the DG group (31%).

The mortality rate was generally higher for all included variables related to SES in the DG group compared to the IG group. Univariable logistic analysis comparing age at inclusion, EDI, and country of birth showed the highest association to mortality in both study groups ($P<0.05$). Male patients and participants from the implant group who lived in rural areas had statistically significant higher mortality ($P<0.05$). The univariable analyses did not reveal statistically significant differences for the education level and residence for patients in the IG group, so these variables were excluded. The remaining variables contributed to a statistically significant difference in the final multivariable logistic analysis ($P<0.05$). Low EDI and born in Sweden were the most important factors in relation to patient mortality.

4.2 Cause-specific mortality

Study III analysed the cause-specific mortality for 3902 edentulous patients treated with implant-supported prostheses. Of the included patients, 2098 died before 31 December 2014 (54%). The most common causes of death in the study group over the entire inclusion period (1986–2014) are shown in Figure 15.

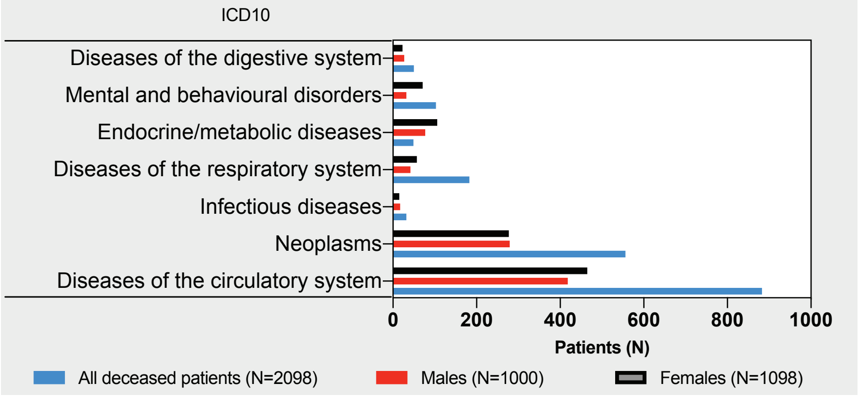

Figure 15. **Study III**: Number of deceased patients divided by main causes of death for the 2098 edentulous patients treated with implant-supported prostheses between 1986 and 2014.

Differences in cause of mortality between the early (1986–1996) and late (1997–2014) periods were observed. Specifically, cause of death due to cardiovascular diseases (CVD) decreased over time. The risk of mortality caused by CVD-related diseases increased from SMR=0.7 in the early period to SMR=4.2 in the late period. However, elderly patients (≥80 years old) showed a statistically significant lower mortality in almost all causes of death compared to the expected cause of death in the reference population irrespective of period. The younger group of edentulous patients (<60 years old) had increased SMR in all causes of death (SMR=2.2; $P<0.05$).

Moreover, if treated in the later period (1997–2014), the younger patient group had a five times higher mortality due to CDV-related diseases compared to the reference population (SMR=5.4; $P<0.05$).

5. Discussion

5.1 Study I and II

The overall aim in study I and II was to compare mortality patterns in patients treated with implant-supported prostheses with a reference population regarding age at implant surgery, gender, and degree of tooth loss. However, in study I all the patients were elderly (≥80 years old at implant surgery) compared to study II, where the participants were patients of all age groups.

The prosthetic treatment of elderly patients has been discussed in the literature. Although some researchers suggest increased implant failure rates and other biological complications related to the treatment in elderly patients [113-115], some researchers report similar or improved results compared to younger age groups [116-118]. A recent study showed an increased risk of implant failure in younger edentulous patients many years after treatment compared to edentulous patients treated with implants at an older age [119]. Moreover, study I demonstrated a statistically significant lower all-cause mortality in treated elderly implant patients (≥80 years old) compared to the corresponding reference population.

When comparing the two study groups in study I and II (partially edentulous and completely edentulous), partially edentulous patients had significantly lower mortality. This finding agrees with previous studies where a decreased number of remaining teeth and poor dental health in elderly was found to be a predictor for higher mortality [120-123]. In addition, the findings in study II confirmed the results from study I: lower mortality rates for the older part of the study population. However, the expected higher mortality associated with edentulism in elderly patients reported in previous studies [76, 120, 122-125] was not confirmed in the patient group treated with implant-supported prostheses in study I and II.

In contrast, the younger group of edentulous patients (≤59 years old) treated with implant-supported prostheses between 1986 and 1997 showed a statistically significant higher mortality compared to the reference population. Complete tooth loss in the younger study group seems to be associated with a higher risk for compromised general health. When comparing the mortality patterns in the younger age groups (≤49 years old) in different periods in study II, a higher mortality was observed in the later period (2004–2008) compared to the earlier period (1986–1997). These findings were confirmed in study III with higher risk for all-cause mortality in the later period (1997–2014) compared to the earlier period (1986–1996). These observations could mean that complete tooth loss in younger patients (≤59 years old) in Sweden is associated with compromised general health.

The association between mortality and replacement of missing teeth has been debated in the literature [86, 126]. The question has been whether there is any advantage for the survival of the patient if missing teeth are replaced with prosthetic constructions. Compared to the corresponding reference population, the older edentulous patients (≥70 years old) treated with implant-supported prostheses had a consistent lower mortality and the younger group of edentulous patients (≤59 years old) had a constant higher mortality.

The observed difference in mortality between partially and completely edentulous patients in study I and II could be explained as an effect of improved masticatory efficiency resulting in a better diet, as shown in previous studies [75, 127, 128]. Haraldson et al. [61] did not find any differences in bite forces between patients treated with implant-supported prostheses and natural dentition. A decrease of the maximum bite forces was reported in patients with implant-supported dentures and conventional dentures compared to natural dentition [62]. Also, the chewing efficiency in the group of patients with natural teeth was much higher compared to patients treated with removable dentures [62].

Another interpretation of the prolong lifetime of the elderly patient group with implant-supported prosthesis was that these patients were recruited from a healthier group of edentulous individuals who were more motivated to replace missing teeth and go through a more invasive and protracted treatment compared to conventional denture treatment. Therefore, the dental treatment per se might indirectly influence mortality pattern.

However, the observed mortality pattern in the elderly (≤80 years old) in study I and II showed a lower mortality for the first five years of follow-up compared to the corresponding reference population. These findings were also confirmed in study IV, where another study group was analysed.

The positive impact of implant-supported prosthesis treatment could be interpreted as an immediate effect of subjective well-being and improved QoL, and it could be assumed that these elderly edentulous individuals were motivated to improve speech and masticatory and oral function to enhance self-confidence and socializing. Recent research has investigated whether social well-being might have a protective role in association to survival [129]. Steptoe at al. [129] divided social well-being into three different aspects – evaluative well-being (overall life satisfaction), eudemonic well-being (meaning in life), and hedonic well-being (different kind of feelings). They found that high levels of eudemonic well-being was associated with increased survival independent of age, sex, and physical health [130]. Edentulous elderly patients (≥79 years old) with implant-supported prostheses might have better general health and might have a personality associated with factors that improve eudemonic well-being, which could contribute to a higher survival rate in this group of patients.

5.2 Study III

In study III, the results demonstrated a decreased number of treated edentulous implant patients between the early (1986–1996) and late (1997–2014) period. At the same time, the proportion of treated elderly implant patients (≥79 years old) increased from 4.8% to 12%. Although this observation is not in line with previous studies reporting that the number of edentulous individuals decreased in the aging western world over the last decades [16, 21, 23, 43, 128], it could be interpreted as a result of more edentulous elderly patients being capable and motivated to undergo the treatment with implant-supported prostheses.

The results from study III indicating that edentulism in the study group is associated with higher risk for all-cause mortality are in accordance with the observations in study I and II as well as with previous publications [131, 132].

Moreover, patients treated in the earlier study period (1986–1996) demonstrated a lower risk for all-cause mortality compared to the group of edentulous patients treated between 1997 and 2014. The reasons for the differences between the periods are unknown, but it could be speculated that edentulous patients in Sweden belong to a more vulnerable group in society and therefore have inferior general health and that the patients in the early period (1986–1996) became edentulous due to lack of adequate prophylactic treatment or for behavioural reasons [52].

The findings from study III also demonstrated that CVD-related diseases were the most common cause of death in the edentulous study population. Specifically, compared to the reference population, the younger edentulous age group (≤59 years old) showed statistically significant increased mortality caused by CVD-related diseases. These results are in align with the results from a US study that followed 41 000 adults for 16 years. They showed that complete edentulism in individuals <65 years old was associated with higher mortality [133].

Higher risk for cardiovascular mortality was found in patients with periodontitis [7] and osteoarthritis [134, 135], both chronic inflammatory diseases [136, 137]. Females with severe periodontitis and younger than 65 years old showed increased risk for myocardial infarction [9]. Therefore, since severe periodontitis is one the most common reasons for tooth extraction in adults [26, 138, 139], the younger edentulous patient (≤59 years old) may represent the patient group with an increased risk for early mortality due to CVD-related diseases.

In contrast, the older group of edentulous patients (≥80 years old) in study III showed a statistically significant lower mortality risk due to the most common diseases (CVD, neoplasms, mental illness, and respiratory diseases) compared to the corresponding reference population, confirming the findings from study I and II – i.e., when treated with implant-supported prostheses, this age group had decreased mortality. However, because a causal relationship is still missing, further investigations are required.

5.3 Study IV

The results from study IV showed that edentulous patients in Sweden had an increased risk for mortality (18%) compared to the corresponding reference population. These findings confirm the results from study I, II, and III regarding edentulous implant patients and agree with findings from previous studies [120, 122, 133, 140, 141].

The age groups of edentulous patients in study IV were similar to the age groups of edentulous patients in study II and III: younger edentulous patients (≤59 years old) have a higher mortality and older edentulous patients (≥80 years old) a lower mortality compared to their peers in the reference population.

The observations of the entire Swedish edentulous population presented in study IV correspond well with the results in study II for edentulous patients treated with implant-supported prosthesis (Figure 13). A possible association between age and all-cause and cause-specific mortality in edentulous patients has been included in a review by Koka et al. [142]. Inconsistent results were reported in that review. In contrast to the findings in this thesis (studies I-IV), some of the included studies reported a stronger association between degree of tooth loss and mortality in the older age group [142] and some studies found that younger age was associated with higher risk for mortality [143, 144]. The latter studies also supported the findings in study II, III, and IV.

From the findings in study IV, the estimated annual incidence of edentulism in Sweden between 2009 and 2013 was calculated to be 23 cases in 100 000 adults. As reported by Norderyd et al. [23], complete edentulism is a rare diagnosis in Sweden today. The prevalence of edentulism decreased in the adult population (40–70 years old) from 16% in 1973 to 0.3% in 2015 [23]. In the age group 65 to 74 years old, the prevalence of edentulous individuals is estimated to be 2.7% [24]. The highest incidence of the 8463 edentulous patients in study IV was observed at 65 years old. This is in accordance with a report from Kassebaum et al. [20] who noted that the age of 65 is the peak age for the incidence of edentulism worldwide. Accumulated number of edentulous patients results in a higher prevalence in older age [20].

In study IV, patients treated with implant-supported prostheses showed statistically significant lower risk for mortality compared to the patients treated with conventional removable dentures independent of age at inclusion to the study and regardless of variables related to SES.

The association between replacing missing teeth and therefore improving masticatory function and QoL and prolonged life has been discussed in the literature. Wearing dentures was associated with a decreased mortality in an elderly population [145]. It was suggested that the lower risk of mortality was a result of better masticatory function and nutrition, which could contribute to avoiding asphyxiation [145].

Moreover, regarding maximum bite forces and chewing efficiency, a group of patients treated with implant-supported dentures has shown improved chewing capabilities compared to a group of patients treated with conventional removable dentures [61, 62]. The improvement of the masticatory function in patients treated with implant-supported prostheses (IG) in study IV might contribute to the lower mortality compared to the denture group (DG). However, it remains unclear whether the choice of the treatment itself has some significant impact.

Alternatively, the decreased mortality risk for the patients treated with implant-supported prostheses from study IV might be a result of healthier patients with improved life situation satisfaction that results in a higher motivation to undergo a more invasive treatment. These suggestions are supported by Boven et al. [146] who reported that implant-supported dentures improved the chewing ability and clearly had a positive effect on QoL.

In the 1980s, Blomberg et al. found that implant-supported prostheses were associated with improved self-confidence, psycho-social health, and QoL [89]. Throughout the last decades, the importance of oral health for overall health and QoL has been discussed. Different health measurement scales have been developed and validated [47]. The self-administrated questionnaire Oral Health Impact Profile (OHIP) [48] is one of the instruments used in dentistry to analyse the possible impact of the oral health on an individual's daily life. The original OHIP consists of 49 items, but shorter versions with either 14 (OHIP-14) or five (OHIP-5) items have been developed and validated [147]. In an edentulous population treated with removable implant-supported dentures, the OHIP-14 significantly improved after treatment and after five years of follow-up [64]. The studies in this thesis do not include qualitative measurements, but future investigations should consider their use.

Furthermore, the findings in study IV showed that the mortality risk was significantly higher for the edentulous patients born in Sweden compared to those born abroad. This finding agrees with the results from a demographic report from 2016 [148], but contradicts the results of a Swedish population study from 2005 [149] where the group born in Sweden had significantly lower mortality compared to foreign-born individuals. However, the data in that study were not based on only edentulous patients, and there might be a difference in the prevalence of edentulism between those born in Sweden and those born abroad. From the data in study IV, it was estimated that the annual incidence of edentulism is 18 and 45 cases per 100 000 adults in the two groups, indicating that fewer individuals born in Sweden suffer edentulism. Severe tooth loss and edentulism is a result of many factors, but it could be suggested that a higher proportion of persons born abroad lose their teeth due to caries, limited economy, and limited access to dentistry rather than severe treatment-resistant periodontitis, which has been reported to be associated with an increased risk of mortality [150].

In general, individuals with high SES and live in urban areas have better access to advanced dental care. They can afford more costly treatments and often present better oral health [151]. In study IV, measurements of SES (income, education, and residence) have been included and analysed related to mortality. The findings from study IV show that edentulous individuals with high income and higher education level have lower mortality compared to the group of less educated patients with low income. The possible association between all-cause mortality and SES variables with regard to degree of tooth loss and edentulism are diffuse and often difficult to interpret [17, 142]. However, no significant differences in mortality were observed between the group of patients treated with implant-supported prostheses and the patients treated with conventional removable dentures related to education, disposable income, and residence. Further investigations for improved understanding are needed.

6. Conclusion

Edentulous patients showed higher risk for mortality compared to dentate individuals and a corresponding reference population in Sweden.

Younger edentulous patients (≤59 years old) demonstrated higher all-cause and CVD-related mortality compared to their peers in the reference population.

Elderly patients (≥79 years old), if treated with implant-supported prostheses, have lower mortality, whereas those treated with removable dentures have higher mortality compared to the reference population.

Edentulous patients treated with implant-supported prostheses present a lower mortality compared to individuals treated with conventional removable dentures irrespective of age, gender, SES, and country of birth.

In Sweden today, as edentulous patients belong to a vulnerable group of dentistry patients and especially at a younger age, the general health of these patients should be paid attention to. Implant-supported treatment per se is not believed to be the cause of the lower mortality, although it is assumed to contribute to improved masticatory function, better nutrition, and an increased quality of life.

7. Future Perspective

The findings of the present thesis exposed the mortality patterns in edentulous patients and demonstrated that the time a person becomes edentulous influences overall mortality. The observed higher mortality in younger edentulous patients should be a reason for increased attention to general health problems in dentistry. In-depth cooperation between medical and dental care providers might improve long-term survival for these patients and help provide the best cost-benefit analysis for society.

Qualitative research, such as in-depth interviews with the participants, could help explain the prolong lifetime of the elderly implant patients. However, more knowledge is needed about why some elderly avoid implant-based treatments, and some elderly seek sophisticated rehabilitation. Moreover, measurements of OHRQoL could complement the results of the present studies. The OHIP could be used to measure the impact of the treatment on a patient's daily life.

Finally, it could be of interest to study the cause-specific mortality in the edentulous Swedish population, accounted for in study IV, and to analyse possible differences between the group treated with implant-supported prostheses and the group of removable denture wearers. This type of study could provide valuable information for decision-making regarding treatment choice for this specific patient group.

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