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SEVERE ODONTOGENIC INFECTIONS—MEN IN THE DANGER ZONE?

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Jussi Furuholm

ACADEMIC DISSERTATION

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To my mother

ABSTRACT

BACKGROUND AND PURPOSE

Odontogenic infections (OIs) may, if they progress, lead to serious complications requiring hospitalization or even intensive care. This study aimed to investigate the background factors, clinical characteristics, and treatment of severe OIs (SOIs) requiring hospital care, with a particular focus on sex-related differences.

PATIENTS AND METHODS

This doctoral thesis comprises four retrospective sub-studies based on patients treated for OIs at the Department of Oral and Maxillofacial Surgery, Helsinki University Hospital. The sub-studies examined sociodemographic and general health-related factors, underlying dental infectious diseases (DIDs), and microbiological findings among patients with OIs.

RESULTS

The proportion of men among hospitalized patients was higher than that of women. Low income and being unmarried increased the risk of hospitalization due to OI. Impaired immune defense did not predict the need for intensive care, whereas smoking and heavy substance use were associated with a higher number of complications, the most common being sepsis and pneumonia. Infections originating in the mandible led to intensive care more often than those in the maxilla. The most common odontogenic cause of infections requiring intensive care was apical periodontitis (AP), which was also associated with higher C-reactive protein levels and a higher heart rate at hospital admission, compared with pericoronitis. *Streptococcus* species were the most frequently identified bacteria, and infections caused by the *Streptococcus anginosus* group (SAG) were associated with longer hospital stays and a higher likelihood of intensive care compared with infections caused by other bacterial species.

CONCLUSIONS

SOIs may reflect broader sex-related and social health disparities. The higher proportion of men among patients requiring hospitalization for OIs may suggest that, compared to women, men more often neglect oral health and delay seeking dental care. Most hospital-treated OIs occur in previously healthy individuals, however low socioeconomic status and social isolation appear to increase the risk of these infections. The findings highlight the importance of early diagnosis and effective primary care, as. The high prevalence of AP in these infections emphasizes the importance of recognizing and treating this DID promptly.

TIIVISTELMÄ

TAUSTA JA TAVOITTEET

Hammasperäiset infektiot voivat edetessään johtaa vakaviin seurauksiin, jotka edellyttävät sairaalahoitoa tai jopa teho-osastohoitoa. Tämän tutkimuksen tavoitteena oli selvittää vakavien sairaalahoitoa vaativien hammasperäisten infektioiden taustatekijöitä, kliinisiä piirteitä ja hoitoa erityisesti sukupuolten välisten erojen näkökulmasta.

AINEISTO JA MENETELMÄT

Väitöskirja koostuu neljästä retrospektiivisestä osatyöstä Helsingin yliopistollisen sairaalan suu- ja leukakirurgian päivystyksessä hoidetuista infektiopotilaista. Osatöissä tarkasteltiin hammasperäisten infektiopotilaiden sosiodemografisia ja yleiseen terveydentilaan liittyviä tekijöitä, taustalla olevia hammasinfektiosairauksia sekä mikrobiologisia löydöksiä.

TULOKSET

Miesten osuus sairastuneista oli naissukupuoleen verrattuna suurempi. Alhainen tulotaso ja naimattomuus lisäsivät hammasperäisten infektioiden sairaalahoidon riskiä. Heikentynyt immuunipuolustus ei ennustanut tehohoidon tarvetta, mutta tupakointi ja runsas päihteiden käyttö liittyivät useampiin komplikaatioihin, joista tavallisimpia olivat verenmyrkytys ja keuhkokuume. Alaleuan infektiopesäkkeet johtivat useammin tehohoitoon kuin yläleuan infektiot. Yleisin hammasperäinen syy tehohoitoa vaatineissa infektioissa oli apikaalinen parodontiitti, johon liittyivät myös korkeammat C-reaktiivisen proteiinin arvot ja syke sairaalaan tullessa kuin perikoroniitissa. *Streptococcus*-lajit olivat yleisimpiä bakteerilöydöksiä, ja *Streptococcus anginosus* -ryhmän bakteerien aiheuttamat infektiot liittyivät pidempään sairaalahoidon kestoon ja useammin tehohoidon tarpeeseen muihin bakteerilajeihin verrattuna.

JOHTOPÄÄTELMÄT

Vakaviin hammasperäisiin infektioihin voi liittyä laajempia sukupuolittuneita ja sosiaalisia terveyseroja. Miesten korkeampi osuus sairaalahoitoa vaativissa hammasperäisissä infektioissa voi viitata siihen, että etenkin miesväestössä on naisiin nähden enemmän suun terveyden laiminlyöntiä ja viivettä hoitoon hakeutumisessa. Valtaosa sairaalahoitoa vaativista hammasperäisistä infektioista ilmenee aiemmin terveillä potilailla, mutta alhainen sosioekonominen asema ja sosiaalinen eristäytyneisyys näyttävät lisäävän niiden riskiä. Varhaisen diagnostiikan ja tehokkaan perusterveydenhuollon merkitys korostuvat. Apikaaliparodontiitin yleisyys näissä infektioissa tähdentää sen tunnistamisen ja hoitamisen merkitystä ajoissa.

ABBREVIATIONS

AP	Apical periodontitis
BMI	Body mass index
BOP	Bleeding on probing
CAL	Clinical attachment level
CI	Confidence interval
CPITN	Community Periodontal Index of Treatment Needs
CRP	C-reactive protein
DID	Dental infectious disease
DMFT	Decayed, Missing, Filled Teeth
DNS	Dental Neglect Scale
HUSLAB	Helsinki University Hospital Laboratory Services
ICC	Immunocompromised condition
ICU	Intensive care unit
LOHS	Length of hospital stay
LOICUS	Length of intensive care unit stay
NA	Data not available
NSAID	Non-steroidal anti-inflammatory drug
OHRQoL	Oral health-related quality of life
OI	Odontogenic infection
OISS	Odontogenic Infection Severity Score
OR	Odds ratio
PPD	Probing pocket depth
RCT	Root canal treatment
SAG	*Streptococcus anginosus* group
SD	Standard deviation
SES	Socioeconomic status
SOI	Severe odontogenic infection
SPT	Supportive periodontal therapy
SRP	Scaling and root planing
WBC	White blood cell

CONTENTS

LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following publications:

I **Furuholm J**, Haapanen A, Snäll J.
The loneliness epidemic: Unveiling its impact on odontogenic infections. A retrospective cohort study.
Oral Health and Preventive Dentistry. 2025 Dec 2;23:773-778. doi: 10.3290/j.ohpd.c_2382.

II **Furuholm J**, Rautaporras N, Uittamo J, Saloniemi M, Snäll J.
Health status in patients hospitalised for severe odontogenic infections.
Acta Odontologica Scandinavica. 2021 Aug;79(6):436-442. doi: 10.1080/00016357.2021. 1876916. Epub 2021 Jan 27.

III **Furuholm J**, Uittamo J, Rautaporras N, Snäll J.
Are there differences between dental diseases leading to severe odontogenic infections requiring hospitalization? A retrospective study.
Quintessence International. 2022 May 11;53(6):484-491. doi: 10.3290/j.qi.b2793183.

IV **Furuholm J**, Uittamo J, Rautaporras N, Välimaa H, Snäll J.
Streptococcus anginosus: a stealthy villain in deep odontogenic abscesses.
Odontology. 2023 Apr;111(2):522-530. doi: 10.1007/s10266-022-00763-z. Epub 2022 Nov 8.

The publications are referred to in the text by their roman numerals.

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1 INTRODUCTION

Oral diseases constitute a major global health concern. The etiology of oral diseases is multifactorial, reflecting social inequalities and showing substantial variation between countries [1]. Adverse oral health outcomes are consistently linked to demographic and socioeconomic determinants. Men generally present with poorer overall and oral health indicators and less favorable health behavior [2, 3]. Furthermore, low socioeconomic status and inadequate dental hygiene habits exacerbate the burden of oral health conditions [4].

Occasionally, common dental infectious diseases (DIDs) such as caries, apical periodontitis (AP), marginal periodontitis, or pericoronitis may progress into acute odontogenic infections (OI) [5]. OIs are symptomatic, with clinical and radiological characteristic signs of infection, either alone or in combination. Mandibular molars are the most common sources of severe odontogenic infections (SOI) [6]. While most OIs are low-grade and well-localized, these infections occasionally extend into adjacent tissues, penetrate deeper in the neck, or disseminate to more distant sites through the bloodstream. In these cases of SOIs, hospital treatment is often necessary to prevent potentially serious consequences [7]. The frequency and severity of OIs has increased in recent decades [8]. Early recognition and elimination of the odontogenic source is associated with shorter hospital stay [9], whereas immunocompromised conditions and advanced age predispose to more complicated clinical courses [10].

The pathophysiology of SOIs involves a complex interplay between microbial virulence, host immune response, and anatomical pathways that facilitate the spread of infection. Microbiologically, SOIs are often polymicrobial, with anaerobic and microaerophilic *Streptococci* playing a prominent role. These organisms possess virulence factors that enhance tissue invasion, abscess formation, and resistance to host immune clearance, often contributing to more severe clinical manifestations [11].

This thesis examined the characteristics and outcomes of acute OIs, both with and without complications or distant spread. The study emphasized sociodemographic and general health-related background factors, underlying DIDs, and microbiological features of SOIs, with particular attention to sex-related differences.

2 REVIEW OF THE LITERATURE

2.1 Severe odontogenic infection

Acute OIs are usually mild, start locally around a tooth, and remain confined to the alveolar ridge vicinity. They are defined as having a sudden onset that can be confirmed clinically or radiologically and characterized primarily by pain and swelling that may be accompanied by systemic signs of infection, such as fever. OIs originate typically in the mandible, specifically in the molar region [12, 13]. Occasionally they spread to the surrounding tissues and even further to the deep structures of the neck. SOIs are those that originate in a tooth or its supporting structures that spread into adjacent fascial spaces and evoke systemic inflammatory responses. In this context they typically require hospital admission, intravenous antibiotics, and prompt surgical drainage [14]. The severity of acute OIs varies and can be quantified using the odontogenic infection severity score (OISS), which considers factors such as the number of affected anatomical spaces, presence of systemic symptoms, and airway compromise [15, 16].

The number of more severe OIs has increased in recent decades [8, 17-20]. Deep neck infections are often (20–50% of severe OIs) odontogenic in origin [18, 21-25] and may in the most severe cases be fatal [26-28]. Given that the primary clinical manifestations of infection overlap across diverse etiologies, establishing an accurate clinical diagnosis can be challenging [29].

2.1.1 Epidemiology

The overall incidence of SOIs and other maxillofacial-space infections requiring hospital admission in high-income countries ranges approximately between 1.7–11.6 per 100 000 person-years [17, 20, 30]. The observed variability in incidence reflects geographic, demographic, socioeconomic, and healthcare-resource differences, and discrepancies in the inclusion criteria of the studies. Overall, incidence rates have increased over the past two decades. Part of the increase in the incidence of SOIs can be explained by population aging and the growing number of elderly individuals retaining their natural teeth [20].

There is a preponderance of men among SOI patients, with previous studies describing that 51–63% are male [8, 11, 14, 17, 31, 32]. The reported mean ages of

SOI patients varied across earlier studies, partly reflecting differences in inclusion criteria. Mean age ranged from 30–51 years (Table 1), with most patients falling into the age group of 31–40 years [8, 11, 14, 17, 31-34].

Table 1 Reported age and sex distributions in previous studies of odontogenic infections.

Study	Period	Country	No. of patients	Mean age, years (SD)	Sex with most infections (%)
Sato *et al.* [31]	1999–2007	Brazil	210	30 (16.6)	Men (52%)
Seppänen *et al.* [17]		Finland			
	1994–1996		71	37 (13.4)	Men (59%)
	2004		101	42 (16.9)	Men (63%)
Fu *et al.* [8]		Australia		36 (14.7)	
	2003–2004		101		Men (58%)
	2013–2014		191		Men (57%)
Heim *et al.* [11]	NA	Germany	206	51 (20.0)	Men (51%)
Yankov *et al.* [34]	2018–2023	Bulgaria	705	41 (15.9)	Men (54%)
Overall	various		various	**30–51**	**Men (55%)**

NA=data not available, SD=standard deviation.

2.1.2 Anatomical aspects

OIs originate from dental structures and have the potential to disseminate extensively through the anatomical compartments of the head and neck [35-37]. The central anatomical structure in an OI is the tooth itself. As described in the books by Topazian *et al.* (2002) [36] and Hupp *et al.* (2019) [37], the maxillary and mandibular bones form the osseous framework of the teeth and oral cavity and provide the anatomic boundaries through which dental infections may erode. The infection develops locally in the structures immediately surrounding the tooth. If the infectious process progresses, perforation of the periosteum allows bacteria to enter adjacent soft tissues, where they spread along paths of least resistance defined by fascial planes and muscle attachments. The maxillary spaces include the buccal, palatal, vestibular, infraorbital (canine), and orbital spaces. The body of the mandible forms the mandibular space. The masticator spaces comprise the masseteric, pterygomandibular, superficial and deep temporal, submandibular, sublingual, submental, parotid, and peritonsillar spaces. Once the infection breaches the bone, its point of emergence depends on the thickness of the overlying bone and the position of nearby muscle attachments relative to the site of perforation. The maxilla consists of thin cortical plates and abundant cancellous bone, permitting relatively easy perforation of infections from tooth apices into the surrounding buccal and labial soft tissues. The palatal cortex, being dense and closely adherent to the periosteum, less frequently allows infection to pass into palatal soft tissues. The mandible has thicker cortical bone and a lower vascular density, rendering infections slower to perforate. The lingual cortical plate of the posterior mandible is particularly thin below the mylohyoid line, providing a common route for extension of molar infections into the submandibular space. Above the mylohyoid attachment, infections originating from premolars or anterior teeth more commonly track into the sublingual or submental spaces [36, 37]. The relevant anatomical structures are illustrated in Figure 1.

The soft tissues of the neck are organized into multiple compartments delineated by the superficial and deep cervical fasciae of fibrous connective tissue [36, 37]. The deep fasciae are further divided into superficial (investing), middle, and deep layers: the muscular and visceral layers form the middle layer, and the posterior prevertebral and alar layers form the deep layer. Occasionally, an SOI may progress to the advanced spaces of the neck: the lateral pharyngeal, retropharyngeal, carotid, pretracheal, visceral, danger, and mediastinal spaces. These infections represent deep, life-threatening extensions that may compromise the airway or descend into the mediastinum [36, 37].

The airway consists of the respiratory passages that carry air from the external environment to the alveoli. It runs from the nostrils and oral cavity to the terminal bronchioles, where gas exchange takes place in the alveolar units. The airway is divided into upper and lower segments, each with its own anatomy and specialized functions. The upper airway includes the nasal cavity, nasopharynx, and oropharynx [38]. With the larynx as the border, the lower respiratory tract comprises the trachea and bronchi [39]. Edema or abscess formation in the oropharyngeal region may displace or compress the pharynx and larynx, leading to airway narrowing, deviation, or total obstruction (Figure 1) [40].

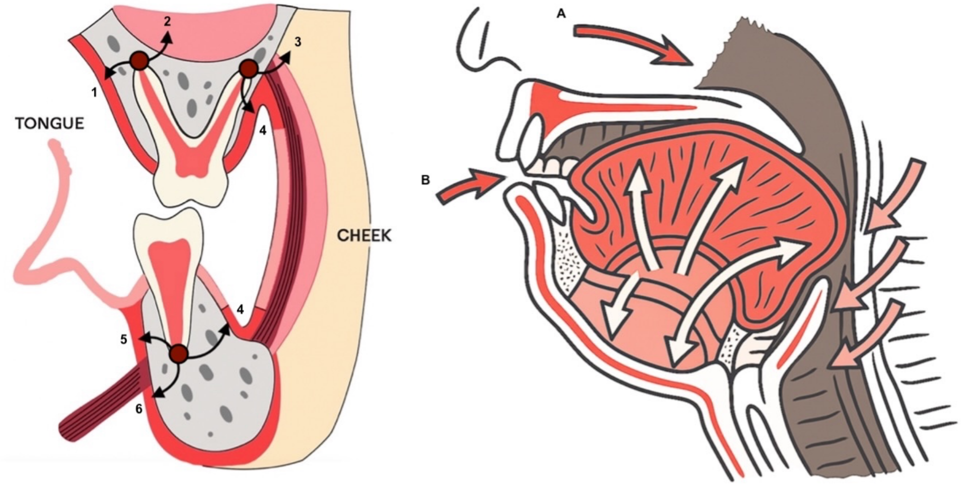

Figure 1 The black arrows depict anatomical routes for local spread of periapical infection: 1, palatal abscess; 2, maxillary sinus; 3, buccal space; 4, vestibular abscess; 5, sublingual space; 6, submandibular space (left, figure modified from Doving *et al*. [41]). The anatomical relations to involvement of spaces in bilateral cellulitis of the floor of the mouth are indicated with red, white, and pink arrows: areas of air intake through nasopharynx (A) and oropharynx (B) are indicated with red arrows, the sublingual abscess formation and edema with white arrows, and the critical sites of airway narrowing with pink arrows (right, figure by ChatGPT).

Beyond local progression, OIs can also disseminate hematogenously, resulting in systemic complications such as sepsis or infective endocarditis [42, 43]. Hematogenous dissemination may occur even in the absence of prominent local symptoms, underscoring the need for comprehensive clinical evaluation in suspected cases [44].

2.1.3 Clinical characteristics and diagnostics

As depicted in the book by Hupp *et al.* (2019) [37], when an OI extends into soft tissues, it typically progresses through four overlapping and clinically distinct stages, namely inoculation, cellulitis, abscess formation, and resolution. These phases reflect both the host immune response and the evolving microbial environment within the infected tissue. Inoculation marks the initial phase of infection. Clinically, it is characterized by mild edema, mild pain, and soft or dough-like tissue consistency. The skin may appear normal or slightly red. This stage is generally non-purulent and non-fluctuant and is microbiologically dominated by aerobic bacteria. Cellulitis represents a more advanced stage with diffuse edema, acute pain, erythema, and a firm, board-like consistency of the affected tissue. Unlike the inoculation phase, cellulitis involves a mixed microbial flora, reflecting a broader and more aggressive infection. Abscess formation is distinguished by the presence of pus and tissue fluctuation. Clinically, it is characterized by acute pain, red skin with a shiny center, and demarcated or diffuse edema. The tissue becomes firm but fluctuates due to purulent accumulation. The microbial profile is mixed flora with anaerobic bacteria predominating. Notably, cellulitis and abscesses can co-occur in different regions of the same infected area. Resolution is the final stage and signals the beginning of healing. This phase typically commences after successful drainage of the abscess and is marked by a decrease in inflammation and gradual restoration of normal tissue architecture [37].

Occasionally, an infection spreads extensively without clear boundaries or encapsulation in contrast with abscess-forming OIs; this type of infection is called a phlegmon. A phlegmonic infection extends easily into intermuscular spaces, the neck, and sometimes the mediastinum, and can be life-threatening [45].

Typical clinical features of SOIs include trismus, fever, dysphagia, pain, swelling, potential airway compromise, and signs of respiratory distress [31, 32, 46]. Trismus, often resulting from inflammation in the masticator space, is caused by spasm of the elevator muscles of the mandible, leading to reduced mouth opening. Trismus may also be the only visible sign of a deep pterygomandibular space infection, often linked to lower third molars, which can rapidly spread to the lateral pharyngeal space and compromise the airway [46]. Extraoral findings commonly include swelling, erythema, and tenderness, particularly in the buccal and submandibular regions. In advanced infections, crepitus or discoloration of the overlying skin (blotchy or darkened appearance) may be present. Clinically, the infected tooth often exhibits mobility, purulent discharge, deep caries, or signs of periapical infection, typically accompanied by localized dental pain. Intraoral swelling is frequently noted in the vestibule or floor of the mouth, especially near the source tooth. When the floor of the mouth is involved, the tongue may be visibly elevated [8].

The diagnostics of SOIs are based on a combination of medical history, clinical examination, and appropriate imaging [46]. Components of necessary anamnestic information entail symptoms, history of present illness, medical history and medications, social history (e.g., substance abuse, access to dental and medical care), and review of systems (oral cavity, head and neck, other parts of the body). For clinical evaluation, clinicians should start with general observations and vital signs, including temperature, heart rate, respiratory rate, blood pressure, and oxygen saturation before moving to regional and intraoral assessments. Tachycardia, tachypnea, fever (≥38.3°C), and low oxygen saturation may indicate systemic involvement and potential airway compromise. General appearance, such as fatigue, altered speech, drooling, or stridor, may indicate a severe infection and compromised airway. The head and neck should be examined for swelling, asymmetry, erythema, and consistency of affected tissues. Findings may correspond to different infection stages, such as doughy (inoculation), firm (cellulitis), or fluctuant (abscess). Assessment of mandibular opening is critical. Trismus may reflect involvement of masticator spaces and poses challenges for examination, surgical drainage, and airway management under anesthesia. An interincisal opening of 20 mm or less is commonly regarded as severe trismus and may indicate an infection requiring hospital-based management [47, 48]. Intraoral examination should follow, focusing on high-risk areas such as the floor of the mouth, pharynx, and palate. The dentition is evaluated for signs of caries, periodontal disease, restorations, fractures, or mobility. Identification of a likely source tooth is essential; if uncertain, further diagnostic tests, including radiographs or vitality testing, are recommended [37]. Imaging studies are commonly utilized in emergency settings to confirm the diagnosis, identify the precise location of the infection, and, most importantly, exclude abscess formation. Diagnostic imaging is especially valuable in cases where a deep neck infection is suspected and thorough clinical examination is challenging or limited. Computed tomography and magnetic resonance imaging are highly sensitive for detecting deep infections, especially in identifying abscess formation and accurately determining its location and extent [49]. Additional imaging modalities commonly used in the evaluation of OIs include periapical and panoramic radiographs and ultrasound. Panoramic radiographs provide a broad overview of the jaws, nasal cavity, maxillary sinuses, and dentition and are easily acquired with minimal patient discomfort; this is particularly beneficial in cases of trismus. Periapical radiographs offer a more detailed view of individual teeth and their periapical areas, with the advantage of lower radiation exposure [37]. Ultrasound is a supplementary imaging method for identifying fluid collections and soft-tissue edema in OI patients [50].

2.1.4 Treatment

OIs have afflicted humans for millennia. In fact, the earliest recognized hominid periapical lesion dates back over two million years [51]. In 17th century London, odontogenic causes ranked as the fifth or sixth leading cause of death [52]. The advent of antibiotics in the early 20th century, with the discovery of penicillin by Fleming and Gerhard Domagk's work on sulfonamides, dramatically reduced these mortality rates [53, 54]. Current treatment protocols emphasize the role of surgical management as the main treatment modality, and antimicrobial therapy only serves as adjunctive [12, 37]. In more severe cases, securing the airway and balancing hemodynamics act as supportive treatment.

Management of OIs depends on the following three key factors: eliminating the source of infection, establishing surgical drainage, and mobilizing the host defense system. Surgical intervention is therefore indispensable, since only operative techniques can achieve the first two objectives [37, 55]. In this setting, surgery not only encompasses incision and drainage along with extraction of the offending tooth or teeth, but also any procedure that removes the infectious focus, such as pulp extirpation followed by definitive root canal treatment and various forms of periodontal treatment. Surgical drainage is the second pillar of operative management. Incision and drainage promote healing through two key effects. The primary effect is reduction of bacterial burden; by removing the source and evacuating pus, drainage lowers the microbial load so that the host's immune defenses (the third management component) can clear any remaining infection. The secondary effect is relief of tissue pressure; decompressing the hydrostatic pressure in the infected area restores local blood flow, enhancing delivery of immune cells and adjunctive antibiotics to the site [37, 56].

Although surgery is essential for treating OIs, there are scenarios where adding antibiotic therapy can be beneficial. In such cases, clinicians should always balance the potential advantages against the inherent risks. Antibiotic treatment is particularly valuable in severe cases, such as infections of the deep fascial spaces or those accompanied by cellulitis, after controlling the infection source and completing incision and drainage [19]. Empirical antibiotic therapy should be initiated without delay, even before culture and sensitivity results, and then refined according to specific susceptibilities as soon as they become available [57]. Selection of agents must balance effective microbial eradication against preservation of gut microflora and the risk of cross-resistance. In moderate to severe OIs, postoperative antimicrobial coverage is generally indicated, if host defenses alone cannot reliably control residual bacteria. As the susceptibility patterns of the usual pathogens are well-characterized, an empirical regimen often includes penicillin to cover facultative organisms, together with metronidazole for obligate anaerobes. Antibiotic prescribing should follow key stewardship principles, namely use of the narrowest effective spectrum, the least toxic and least bactericidal agents, cost-benefit considerations, and optimal dose, duration, and route of administration [36, 37]. In SOIs, high-dose intravenous antibiotics are common practice, such as benzylpenicillin 4 000 000 IU six times daily and metronidazole 500 mg three times daily.

Deep-seated OIs adjacent to the upper airway can cause obstruction and subsequent respiratory function impairment [37]. Prompt endotracheal intubation or tracheostomy is essential to maintain adequate ventilation when the airway is compromised [58]. Male patients seem to require video laryngoscope for intubation and a procedural change in airway management more often than female patients [59].

Intensive care unit (ICU) support is occasionally required in SOIs when patients develop airway compromise, systemic inflammatory response, multi-space involvement, or organ dysfunction. The need for ICU due to OI severity is increasing; approximately 6–32% of SOI patients require ICU treatment [8, 17, 59]. Mean ICU treatment durations range from 3.8–7.2 days for SOIs and other deep neck space infections [18, 60]. Heavy alcohol use, increased number of spaces involved, time in operation room, peak blood sugar level, and dyspnea, elevated C-reactive protein (CRP) levels, and higher body mass index (BMI) increase the risk for treatment of SOI in ICU [59, 61, 62].

2.2 Sociodemographic aspects

2.2.1 Sociodemographics and oral health

Various sociodemographic factors may have an impact on oral health. These include ignorance or illiteracy of oral health issues, socioeconomic status, loneliness and social isolation, educational level, and marital status (Table 2) [3, 63-69].

Oral health-related quality of life (OHRQoL) is not randomly distributed; lower OHRQoL is closely tied to social disadvantage and low socioeconomic status (SES). This disparity has been observed regardless of age, socioeconomic indicator, or the country's economic classification [70]. In Finland, poor OHRQoL leads to irregular use oral health services, which in turn leads to poor subjective oral health [71].

In adolescents, low SES is associated with a higher likelihood of oral health-risk behaviors, such as infrequent toothbrushing and sugar-sweetened beverage consumption [72]. Lack of affordable dental care may deepen inequalities in dental caries prevalence [73]. Lower educational level is correlated with higher Decayed, Missing, Filled Teeth (DMFT), and Community Periodontal Index of Treatment Needs (CPITN) scores [74, 75]. In the elderly, a low educational level has an independent negative impact on OHRQoL [76].

Table 2 Effects of sociodemographic factors on oral health.

Study	Factor	Effect
Steele *et al.* 2014 [65]	SES and educational level	Lower income and educational levels associate with more decayed teeth.
Schwendicke *et al.* 2015 [66]	SES	Low SES associates with a higher risk of having caries lesions or experience.
Baskaradoss 2018 [68]	Ignorance or illiteracy of oral health issues	Limited oral health literacy associates with poorer periodontal health
Magno *et al.* 2020 [67]	SES	Lower income level associates with a higher chance of traumatic dental injury.
Lipsky et al. 2021 [3]	Sex/gender	Men typically have poorer oral health behaviours and oral hygiene practices, and they experience a higher prevalence of periodontal disease, oral cancer, and dental trauma.

Study	Factor	Effect
Hajek et al. 2022 [69]	Loneliness and social isolation	Loneliness and social isolation associate with poorer oral health.
Inoue *et al.* 2022 [63]	Marital status	Married men are more likely to receive dental treatment than unmarried men
Moltubakk *et al.* 2023 [64]	Educational level	Lower education associates with higher DMFT scores.

SES=socioeconomic status, DMFT=Decayed, Missing, Filled Teeth.

2.2.2 Sociodemographic factors in OIs

Studies on sociodemographic factors in OIs are scarce. Low income was associated with OIs in a Puerto Rican population [77]. Similar findings have been observed in the United Kingdom, where a higher incidence of OIs was observed among patients living in socially deprived areas [78, 79]. Less well-educated patients were more likely to be hospitalized for SOIs than patients in other education groups [80]. Lower areal population density or greater travel distance to hospital seem to associate with more severe OIs [81, 82]. Illiteracy and low SES have been linked to deep neck abscesses requiring hospitalization [83].

2.2.3 Loneliness and social isolation

Loneliness refers to subjectively feeling alone or isolated, whereas social isolation describes an objective state in which a person has little or no social contact or support [84]. Loneliness and social isolation are risk factors for several health conditions, such as coronary heart disease and premature death [85, 86]. Pooled evidence indicates 25—44% higher cardiovascular mortality for isolated adults [84]. Regarding overall mortality, no difference has been observed between measures of objective and subjective social isolation [86, 87]. Activation of the sympathetic nervous system and the hypothalamic-pituitary-adrenal axis has been proposed as a biological pathway linking social isolation and loneliness to increased cardiovascular morbidity and mortality [84]. Using a single direct question and after adjusting for social isolation and other covariates, loneliness independently predicts higher mortality in older men, implying that men may underreport loneliness unless it reaches a severe level [88].

Beyond its cardiovascular consequences, loneliness is linked to mental health disorders, such as depression and anxiety, across all age groups from adolescents and adults to older people [89-91]. In young adulthood, the risk for mental health impairment is particularly high in those with low resilience. Empirical evidence showing that intra-individual fluctuations in loneliness parallel concurrent shifts in mental-health status implies that population-level interventions aimed at reducing loneliness could yield clinically meaningful improvements in mental-health outcomes. Improving older adults' physical functioning, reinforcing their social support, and reducing loneliness, depression, and anxiety may improve their overall life satisfaction.

Oral health is associated with loneliness or social isolation. A meta-analysis revealed that poorer oral health was associated with greater loneliness and social isolation, although the authors noted that additional high-quality longitudinal studies are needed [69]. Among three latent classes of older adults defined by levels of loneliness, those in the loneliest class exhibited a greater number of risk factors and poorer oral health outcomes [92]. Loneliness, but not objective social isolation, has been independently linked to greater tooth loss in a community-dwelling cohort of older adults in Japan. The authors of the study suggested that the subjective distress of loneliness may have undermined individuals' motivation and ability to maintain oral hygiene, seek dental care, or adhere to preventive practices, thereby accelerating tooth loss over time [93]. A longitudinal study of Chinese older adults reported that higher levels of social isolation predicted both fewer remaining teeth at baseline and faster rates of tooth loss over follow-up. This finding underscores that when isolation manifests in reduced social support and barriers to care, it can translate into measurable declines in oral status [94]. Another systematic review focusing on community-dwelling older adults described a bidirectional relationship; not only does greater isolation lead to poorer oral health, but worsening oral health (e.g., pain, difficulty chewing) can in turn exacerbate feelings of social isolation. Of note, the perceived quality of social connectedness showed a stronger tie to oral outcomes than simple contact frequency [95].

2.2.4 Sex- or gender-based health differences

Extensive scientific research indicates that men on average have poorer health and die younger than women. The reasons behind men's heightened morbidity and mortality are complex and varied, resulting in a noticeably shorter life expectancy. Yet despite these statistics, initiatives aimed at closing the health gap for men remain sporadic and poorly defined [96]. Men's health outcomes pose challenges at global, regional, and national levels. Men are more prone to risk-taking behaviors, less likely than women to recognize disease symptoms, and use primary care services less often. These factors can negatively affect their overall health, particularly mental well-being. However, for certain conditions, men may seek help as promptly as women. Although men's health initiatives have grown in number, there is mounting evidence that "gender-sensitive" interventions tailored to men can yield positive results [97].

Gender- or sex-based health disparities also extend to oral health. Men are more likely to ignore their oral health, have poorer oral hygiene habits, and experience more periodontal disease, oral cancer, and dental trauma [3, 98]. Difficulty in describing feelings as a dimension of alexithymia associates with anticipatory and treatment-related dental anxiety in men [99]. Dental caries have anthropologically been more prevalent in women. Women have typically experienced higher caries rates than men for the following two reasons: their teeth erupt earlier, giving them longer exposure to acid-producing bacteria, and hormonal fluctuations during puberty, menstruation, and especially pregnancy alter saliva composition and flow in ways that make their oral environment more cariogenic [100]. However, among Finnish adults aged ≥30 years, dental caries are currently more common in men (39%) than in women (23%), and the prevalence of AP is also higher in men (31%) than in women (23%) [101, 102].

2.3 General risk factors

2.3.1 Medical comorbidities as risk factors for SOIs

While most OIs remain confined to the alveolar ridge vicinity, certain factors predispose to more serious disease. When host defense mechanisms are impaired, the normal response to infection is compromised, causing dental infections to advance more rapidly. Pre-existing health conditions often lead to these more severe OIs [103, 104]. Currently, research evidence on general health conditions that predispose to SOIs is limited. Diabetes is the most frequently encountered immunocompromising condition in dental practice and increases both susceptibility to infection and the severity of any existing oral disease. Even when glycemic control is satisfactory, moderate to severe dental infections can disturb glucose homeostasis, which advances hyperglycemia that impairs neutrophil function and broader immune defenses. Conversely, metabolic dysregulation inherent to diabetes can foster more aggressive and rapidly progressing infections. Furthermore, diabetic patients are predisposed to atypical bacterial pathogens, which complicates diagnostic assessment and selection of appropriate antimicrobial regimens [37]. Diabetes is widely recognized as a risk factor for SOIs [105-107].

Psychiatric disorders may predict more complex evolution of SOIs [108]. Mental illnesses are associated with poor oral health, specifically dental caries and tooth loss, and can complicate diagnosis of OI [62, 109, 110]. Malnutrition is also potentially associated with more severe OIs [111].

2.3.2 Other risk factors

OIs can affect individuals of any age; however, elderly patients are especially susceptible to more severe disease manifestations [10, 112, 113]. Patients aged >65 years often experience hyposalivation, which undermines oral host defenses by reducing both salivary flow and antimicrobial constituents and thus promotes the development of dental diseases. Moreover, advancing age impairs neutrophil chemotaxis, phagocytosis, and oxidative burst, and lowers secretory IgA-mediated mucosal immunity, collectively compromising pathogen clearance at the earliest stages of infection [114-116].

Smoking confers an elevated risk of developing SOIs [18, 79, 117]. Studies implicate alcohol abuse as a predisposing factor for SOIs and their complications [79, 118]. Like advancing age, obesity is associated with increased severity of OIs [59, 118]. In addition, poor oral health predisposes individuals to complicated SOIs [12, 118-120]. Inadequate prior local dental treatment increases the likelihood of patients developing more severe OIs [12, 33].

2.4 Dental diseases behind severe OIs

Ordinary dental diseases (Figure 2), such as marginal periodontitis [121, 122], pulp necrosis and AP [123-125], and pericoronitis [126, 127] are causes of OIs. Additionally, unfinished root canal treatments seem to increase the risk for further spread of endodontic infections [128]. The pathogenesis of these rather common diseases, such as marginal periodontitis and AP, is polymicrobial and triggers similar immunologic host responses [129, 130]. In some cases, a clear reason for the odontogenic source of infection remains unidentified [131].

Figure 2 A: Deep dental caries and apical periodontitis in a second lower molar. B: Lower molars with signs of marginal periodontitis-related attachment loss. C: Lower third molar with pericoronitis. (Figure by ChatGPT.)

2.4.1 Pulp necrosis, AP, and endodontic treatment

Dental caries are initiated when acidogenic bacteria (e.g., *Streptococcus mutans*) demineralize enamel; once the lesion breaches into dentine, the open dentinal tubules act as conduits that carry bacteria, their acids, and proteolytic enzymes toward the pulp chamber. Odontoblasts and resident immune cells mount an innate response, but persistent microbial invasion sustains an exaggerated inflammatory exudate inside the rigid pulp chamber. The rising tissue pressure collapses venules, producing local ischemia; the result is irreversible pulpitis that rapidly progresses to coagulative-liquefactive pulp necrosis when vascular supply is cut off. Bacteria then colonize the root-canal system and exit through the apical foramen into the periradicular tissues. The surrounding periodontal ligament and alveolar bone respond with inflammation, typically manifesting as an apical granuloma (i.e., AP) [132-134]. The molecular-level aspects of this cascade have been identified. Once the pulp is necrotic, its contents are colonized by a polymicrobial anaerobic biofilm rich in gram-negative species that release lipopolysaccharide, lipoteichoic acid, and other pathogen-associated molecular patterns. These virulence factors diffuse through the apical and lateral foramina to the periapical tissues, where they engage toll-like receptors on macrophages, dendritic cells, and osteoblasts, triggering a cytokine milieu dominated by TNF-α, IL-1β, and RANKL. The ensuing osteoclastic activation and matrix metalloproteinase release resorb periradicular bone and create the radiolucent lesion recognized clinically as AP [135, 136].

Root canal treatment (RCT), i.e., endodontic treatment, has been a method to relieve symptoms of odontogenic pain for centuries [137]. Pathogenic organisms were suggested as a cause of pulpal disease in 1878, and the rationale was demonstrated by Kakehashi *et al* in 1965 [137, 138]. In the 20th century, it was recognized that mechanical debridement of the root canals, together with chemical treatment, is essential to disinfect the canal space and allow for its proper obturation to prevent secondary infection. Accurate diagnosis forms the cornerstone of successful modern RCT. Clinicians should perform a systematic assessment encompassing patient history, clinical examination (palpation, percussion, mobility), sensibility testing (cold, electric pulp tests), and careful radiographic evaluation ideally combining periapical radiographs with cone-beam computed tomography when two-dimensional imaging is inconclusive [139]. Case complexity should be stratified using validated criteria, which integrate anatomical (canal curvature, calcification) and non-anatomical (patient cooperation, systemic health) factors to guide treatment planning and referral decisions [140]. After establishing a diagnosis, RCT follows a series of systematic steps. First, straight-line access is created through the crown, allowing extirpation of inflamed or necrotic pulp tissue; small hand files are then used to establish and confirm canal patency. Next, the working length of each canal is determined using an electronic apex locator or radiographs taken to verify the precise position of the instrument tip relative to the root apex. Following this, the root canals are mechanically shaped to progressively enlarge and taper the canals, thereby facilitating deeper irrigant penetration into the apical third. During and after the shaping, canal irrigation is performed [141]. In multi-visit treatment, an intracanal medicament is placed, and finally the canal system is sealed with an appropriate obturation technique. Endodontically treated teeth must also be restored to ensure proper function and to prevent coronal leakage [142]. After the treatment, the tooth is followed up to ensure the healing of the AP, the absence of secondary infection, or both. The successful outcome of RCT varies between 31% and 96% based on several factors including pre-operative periapical status, the quality of root filling and coronal restoration, and tooth type [143, 144].

2.4.2 Marginal periodontitis

Periodontal diseases have long been a leading cause of tooth loss [145]. They comprise a wide range of inflammatory conditions that affect the supporting structures of the teeth, such as the gingiva, bone, and periodontal ligament [146]. The prevalence of periodontal diseases, such as gingivitis and periodontitis, is high; worldwide these diseases may affect up to 90% of the population [147]. Gingivitis, a relatively harmless gum inflammation marked by bleeding and exudation, can progress to periodontitis, which is a destructive disease characterized by alveolar bone resorption, collagen destruction with fibrosis, and deep periodontal pocket formation [148]. The pathogenesis of periodontitis is triggered by microbial plaque accumulation and exudative vasculitis in the gingiva, perivascular collagen loss, and consecutive evolution into the chronic inflammatory destruction characteristic of periodontitis [149]. Historically, this process has been described as an interaction between local, modifying, and systemic factors [150]. In general, periodontitis develops and progresses based on both bacterial plaque accumulation and the individual’s innate susceptibility [151] and on environmental and genetic factors [152].

Effective management of marginal periodontitis begins with accurate diagnosis and staging. Clinicians should combine clinical measurements—probing pocket depth (PPD), clinical attachment level (CAL), bleeding on probing (BOP)—with radiographic assessment to determine bone-loss patterns. The 2017 World Workshop framework stratifies disease into stages (I–IV) and grades (A–C) based on severity, complexity, and progression risk [153]. The initial or cause-related periodontal therapy aims to halt disease progression by mechanical debridement to remove supra- and subgingival biofilm and calculus by scaling and root planing (SRP) [154]. In select cases, such as generalized severe periodontitis or refractory sites, systemic antibiotics improve clinical outcomes. A 2020 meta-analysis revealed that adjunctive amoxicillin + metronidazole with SRP produced significant additional PPD reductions (mean difference 0.5 mm; 95% confidence interval [CI]: 0.3–0.7 mm) and CAL gains (mean difference 0.4 mm; 95% CI: 0.2–0.6 mm) compared with SRP alone, albeit with a higher risk of adverse events [155]. When non-surgical measures fail to resolve deep pockets (≥6 mm) or complex defects, periodontal surgery is indicated after adequate pre-surgical re-evaluation and patient suitability assessment. The surgical methods include flap debridement, regenerative procedures, and resective surgery [153, 156]. Long-term success depends on structured maintenance. Supportive periodontal therapy (SPT) visits every 3–6 months include professional debridement, reinforcement of oral-hygiene techniques, and monitoring of PPD and BOP. Patients receiving regular SPT exhibit 80–90% tooth-retention rates over 10 years, compared with 50–60% in irregular attenders [153]. Host-modulation therapy using sub-antimicrobial-dose doxycycline (20 mg twice daily) targets matrix metalloproteinases and improves CAL by approximately 0.3 mm compared with SRP alone in chronic periodontitis. Probiotics and prebiotics have demonstrated modest reductions in PPD and BOP in early trials, although larger, long-term studies are needed to confirm these effects. Laser and photodynamic therapies may provide additional microbial reduction, but their clinical advantages over conventional SRP remain inconclusive [157-159]. Overall, well-executed non-surgical and surgical therapies followed by consistent SPT can achieve mean PPD reductions of 2.0–3.0 mm and CAL gains of 1.0–2.0 mm. Key predictors of favorable outcomes include good patient compliance, smoking cessation, optimal glycemic control in diabetics, and high-quality restorations that minimize plaque retention [153, 160].

2.4.3 Pericoronitis

Pericoronitis is an acute or chronic inflammation of the gingival tissues that overlie a partially erupted tooth—most often a mandibular third molar [161]. The soft-tissue operculum traps plaque and food debris, initiating a mixed anaerobic infection and a host-mediated inflammatory cascade. Bacterial biofilms dominated by oral streptococci, *Prevotella*, *Fusobacterium,* and other anaerobes proliferate in the oxygen-poor space beneath the operculum. Local anatomy, such as depth and shape of the flap and systemic immune responsiveness determine whether the inflammatory response remains localized or progresses. Early disease presents with localized erythema, swelling, halitosis, and foul taste. Progression causes intense pain radiating to the ear or temple, trismus, lymphadenopathy, and low-grade fever. When local therapy is instituted promptly and, if indicated, the causative third molar is removed, prognosis is excellent. Without intervention, the infection may spread along fascial planes, producing cellulitis, abscesses, or rarely Ludwig's angina [162]. Several independent predictors of more severe pericoronitis episodes have been identified. In women, these include right-side lesions, distal radiolucency, and menstruation, whereas concurrent upper-respiratory-tract infection increases the risk in men. For both sexes, stress-related immunomodulation, flap trauma from the maxillary antagonist, and crowded teeth are perilous [163, 164]. The position of the third molar affects the occurrence of pericoronitis; molars in the vertical position are more often associated with pericoronitis than molars in horizontal position [165].

Initial or conservative management of acute pericoronitis aims to relieve symptoms when immediate surgical treatment is not possible. This includes cleaning of the operculum by gentle flushing of the pericoronal space with warm saline or chlorhexidine, which reduces microbial load and alleviates pain. Nonsteroidal anti-inflammatory drugs (NSAIDs) effectively control pain and reduce inflammation; paracetamol can be used if NSAIDs are contraindicated. Patients are advised to perform warm salt-water rinses several times daily and to maintain gentle brushing around the operculum to prevent plaque accumulation [166]. Systemic antibiotics are reserved for moderate-to-severe presentations (e.g., spreading infection, systemic involvement) or when debridement alone is insufficient; in these instances, narrow-spectrum β-lactams and metronidazole are effective [167]. A systematic review by Schmidt *et al.* revealed abundant and unnecessary use of antibiotics for pericoronitis and contrast with evidence-based recommendations of reducing antibiotic use [162]. Even though removal of the inflamed tooth is often necessary, postoperative complications, such as infection, dry-socket, or nerve injury may occasionally occur. Pre-existing pericoronitis sharply increases the risk for postoperative infection [168]. However, removal of the third molars generally improves quality of life in those with minor symptoms of pericoronitis [169] and in those with symptomatic pericoronitis [170]. Removal of third molars is indicated in the presence of symptomatic or asymptomatic infection; if infection or other disease is absent, removal is not indicated [171].

2.4.4 Prevention

Preventive dental care is essential for minimizing the risk of OIs. Regular use of fluoride toothpaste, fluoride varnish, pit-and-fissure sealants, and dietary sugar reduction are effective preventive measures against dental caries and its pulp-related repercussions [172-176]. Managing gingivitis by self- and professionally administered plaque control is the cornerstone of preventing marginal periodontitis [177]. Enhancing overall oral hygiene is also likely to reduce susceptibility to pericoronitis, since oral bacteria have been detected in pericoronal tissues. To lower the local bacterial load, it is important to extend tooth brushing to the area around third molars [178]. In the 20–25-year-old age group, incidence of acute pericoronitis can be reduced by prophylactically extracting mandibular third molars that are partially erupted with an enlarged follicular space, lie close to the occlusal plane, and display either a vertical or distoangular orientation [179, 180].

2.5 Microbiological factors

2.5.1 Microbiome in common dental diseases

The oral microbiome refers to the complex community of bacteria, archaea, fungi and viruses that colonize the various habitats of the mouth, forming structured biofilms on teeth, the tongue, and mucosal surfaces. The oral microbiome plays essential roles in maintaining oral homeostasis and influencing systemic health and disease [181-183]. The oral cavity hosts the most varied bacterial microbiome in the body, with sophisticated physical and chemical signaling systems and approximately 800–1000 distinct species detected in oral microbiological samples [184-186]. The composition of each person's oral bacterial community can influence their risk of developing marginal periodontitis or dental caries; when shifts in this balance coincide with host factors, dysbiosis may trigger disease [187-189]. The bacteria of these communities in the mouth organize into structured biofilms that adhere to the pellicle on hard surfaces like enamel and dental materials and appear as plaque [190-192]. To prevent dysbiosis and subsequent oral pathology, plaque must be routinely removed by mechanical means [193-195]. The formation and development of an oral biofilm is illustrated in Figure 3.

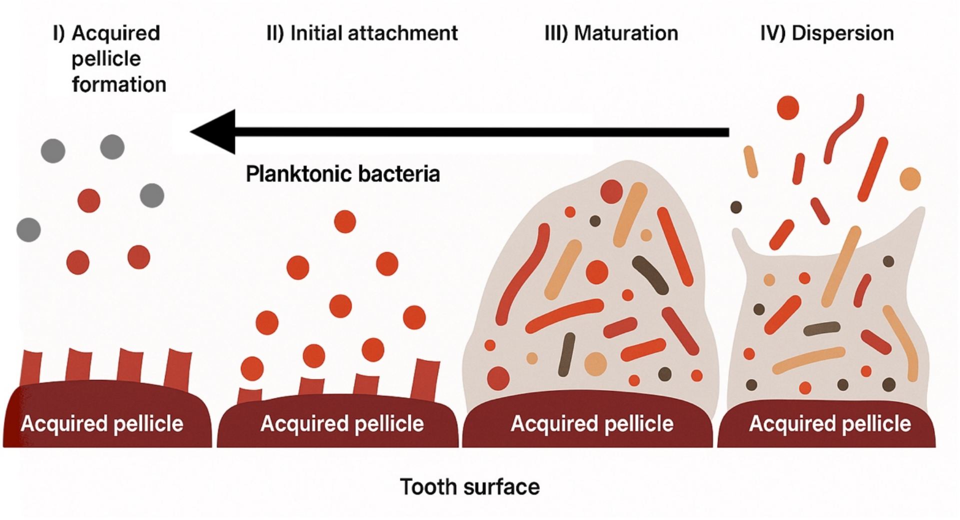

Figure 3 Biofilm formation and development in the oral cavity (figure modified from Abdulkareem *et al.* [196]).

Streptococcus mutans has long been considered the principal driver of dental caries, but numerous other microorganisms also contribute to lesion development and caries is now recognized as a polymicrobial disease [197, 198]. Likewise, AP and marginal periodontitis are mainly caused by multiple microbial species, with anaerobic bacteria predominating as the primary pathogens [129, 199-201]. In primary root-canal infections, *Pseudoramibacter alactolyticus*, *Olsenella uli*, *Fusobacterium* species, *Streptococcus* species, *Porphyromonas endodontalis, Prevotella* species, *Actinomyces* species, *Parvimonas micra*, and *Treponema denticola* are the most frequently or abundantly observed bacterial taxa in the apical canal [201, 202]. In secondary root-canal infections, the most prevalent or abundant bacterial taxa include species of *Streptococcus*, *Enterococcus*, *Fusobacterium*, *Actinomyces*, *Pseudoramibacter*, *Pseudomonas*, and *Propionibacterium* [201, 203]. In marginal periodontitis, the dysbiosis of the subgingival microbiome is often characterized by an increase in pathogenic bacteria of the so called "red complex", specifically *Treponema denticola, Porphyromonas gingivalis*, *Tannerella forsythia* as well as *Fusobacterium nucleatum, Eikenella corrodens*, and *Aggregatibacter actinomycetemcomitans* [196, 204, 205]. The microbial flora associated with pericoronitis is mixed and dominated by anaerobic bacteria, such as in marginal periodontitis, although at lower levels [206-208]. The subgingival pocket microbiota under the third molar operculum increases in richness and converges during the symptomatic phase of pericoronitis and varies by third molar angulation [209].

In general, the human oral microbiome differs between sexes [210]. This is driven by host genetic loci whose effects on bacterial abundances differ between men and women and by lifelong variations in sex-hormone milieus that causally shape the enrichment of specific taxa. Moreover, distinct microbe-metabolite feedback loops, such as sex-specific interactions with trace elements like chromium and selenium, further reinforce divergent ecological niches in male versus female oral cavities. Sex differences in the microbiome of marginal periodontitis, AP, and pericoronitis have not been widely investigated. Thus far, the strongest evidence of sex-based microbiome diversity has been observed in marginal periodontitis. A recent sex-stratified meta-analysis of subgingival plaque from patients with periodontitis revealed clear differences between men and women [211]. Although saliva microbiomes were similar, several key periodontal pathogens were significantly more abundant in female subgingival biofilms than in males. During the progress of periodontitis, significant sex-specific enrichment of phyla in biofilms occurs, with *Firmicutes* more often detected in men [211]. A similar sex-based difference has not been observed in AP [212, 213]. In a mouse model of AP, transcriptomic analysis revealed that ablation of nociceptors led to earlier and greater enrichment of inflammatory and osteolytic gene expression in female than in male mice, revealing distinct, sex-specific mechanisms by which nociceptors modulate periapical lesion development, potentially providing a foundation needed to study sex differences in human AP [214]. There are currently no published data that directly compare the pericoronitis microbiome in men versus women.

2.5.2 Microbiology in OIs

Streptococcus viridans species are frequently observed bacteria in head and neck infections of odontogenic origin; they are commonly polymicrobial [11, 47, 215, 216]. Resistance has been detected to e.g., penicillin, clindamycin, and erythromycin [215, 217, 218]. Common bacterial findings in OIs are presented in Table 3.

Table 3 Typical microbiological findings in studies of odontogenic infections.

Study	Year of publication	Number of patients	Sex with the most infections	The most common bacterial findings
Rega *et al.* [215]	2006	103	Men (54%)	*Viridans streptococci*, *Prevotella*, *Staphylococci*, *Peptostreptococcus*
Al-Qamachi *et al.* [219]	2010	75	NA	*Streptococcus milleri*, mixed anaerobes
Bahl *et al.* [217]	2014	100	Men (55%)	*Viridans streptococci*, *Bacteroides*, *Prevotella*
Fating *et al.* [220]	2014	26	Men (% NA)	α-hemolytic *streptococci*, anaerobic *streptococci*
Plum *et al.* [221]	2018	131	Men (50%)	α-hemolytic *streptococci*, *Streptococcus milleri*, *Prevotella*, coagulase-negative *Staphylococcus*
Sebastian *et al.* [222]	2019	142	NA	*Peptostreptococcus*, *Viridans streptococci*, *Bacteroides*
Böttger *et al.* [223]	2021	50	Men (68%)	*Prevotella*, *Streptococcus*, *Veillonella*
Umeshappa *et al.* [224]	2021	100	Men (76%)	*Staphylococcus aureus*, *Viridans streptococci*, *Peptostreptococcus*
Thol *et al.* [218]	2024	51	Men (53%)	*Fusobacterium*, *Prevotella*, *Parvimonas*, *Porphyromonas*

NA=data not available.

2.5.3 *Streptococcus anginosus* group

Streptococci employ a range of mechanisms to attach to, invade, and colonize host cells or tissues for nutrient acquisition, while also evading defenses by dampening the immune response [225]. *Streptococcus anginosus*, a microaerophilic, catalasenegative, gram-positive member of the *Streptococcus anginosus* group (SAG), can inactivate the antibacterial activity of neutrophil extracellular traps, thereby facilitating severe purulent infections and sheltering other pathogens to promote the development of polymicrobial infections [226]. Members of the SAG, such as *Streptococcus intermedius*, *Streptococcus constellatus*, and *Streptococcus anginosus*, share common traits regarding clinical associations but differ partly in their ability to form abscesses [227]. *Streptococcus anginosus* is as a common finding in odontogenic descending necrotizing mediastinitis, pulmonary infections, and brain abscesses [228-230], while the presence of SAG has also been observed in several other morbidities, such as soft-tissue infections, genitourinary infections, and liver abscesses [231, 232]. Analysis of pediatric brain-abscess cases before and after the COVID-19 pandemic revealed an increasing proportion attributable to SAG pathogens, underscoring their emerging role in serious cranial infections requiring surgical intervention [233]. *Streptococcus anginosus* displays significant genomic heterogeneity that correlates with anatomical site specialization [234]. Table 4 presents the common types of infections associated with SAG.

Table 4 Types of infections associated with the *Streptococcus anginosus* group bacteria and usual sites of origin.

Studies	Species	Common infection types	Usual site(s) of origin
Nisbet & Thomas 2005 [235]; Patel *et al.* 2020 [236]; Pilarczyk-Zurek *et al.* 2025 [226]	*Streptococcus anginosus*	Liver abscess; empyema; bacteremia; intra-abdominal abscess	Normal commensals of the oral cavity, upper respiratory tract, gastrointestinal tract, and genitourinary tract
Claridge *et al.* 2001 [227]	*Streptococcus intermedius*	Deep-seated abscesses (especially brain and liver)	
Xia *et al.* 2021 [237]; Xiao *et al.* 2022 [238];	*Streptococcus constellatus*	Empyema and respiratory-tract infections; brain abscess	

Cases of deep neck-space infection or Lemierre's syndrome caused by *Streptococcus anginosus* have been identified [239-241]. Lemierre's syndrome is a disease that presents with a recent oropharyngeal infection, clinical or radiographic evidence of internal jugular vein thrombosis, and isolation of anaerobic pathogens, potentially of odontogenic origin [242, 243]. In a recent study of odontogenic neck abscesses by Lääveri *et al.*, SAG-positive patients had larger abscesses (36.2 mm vs. 31.7 mm) and a higher prevalence of mediastinal edema 43% vs. 15%) and to require transcervical incisions more often (61% vs. 36%) than SAG-negative patients [244]. Their conclusion underscores the need for early detection of mediastinal edema by magnetic resonance imaging for involvement of SAG in patients with acute neck infections.

2.6 Complications, treatment length, and expenses

2.6.1 Complications

SOIs may lead to local or distant complications via direct or hematogenous dissemination. Prior research has shown that individuals with comorbidities experience infectious complications more frequently than healthy patients [104]. Persons with immunosuppression from medications or illnesses like diabetes are at particular risk [28]. Some studies have reported that elderly patients are more susceptible to complicated deep-neck infections [245, 246]. In addition to male dominance in the incidence of SOIs, a study by Kent *et al.* reported sex differences in clinical characteristics. Men were more likely to present with airway compromise, severe inflammatory response, and requirement for awake fiber-optic intubation on admission [247]. A Chinese study reported male sex as a risk factor for requiring surgical intervention in oral and maxillofacial space infection patients [248]. Other identified factors that predispose to more complicated SOIs include obesity, hypertension, and long-term alcohol and nicotine abuse [6, 28, 118].

In a study by Velhonoja *et al.*, the overall complication rate in deep neck infection patients was 22%, while other SOI studies have reported rates varying between 2–29% [18, 28, 104]. Cervicofacial necrotizing fasciitis is a potentially lethal complication that may originate via direct spread from an SOI. It is a fulminant polymicrobial infection of subcutaneous and fascial planes in the head and neck, with gas formation and extensive tissue necrosis. Another possible direct consequence of a deep OI is descending (necrotizing) mediastinitis, where the infection extends from the retropharyngeal space to the “danger space”. SOIs may additionally involve the orbit or cause cavernous sinus thrombosis. More distant (metastatic) or systemic manifestations of SOIs include brain abscess, meningitis, airway obstruction, mediastinitis, Lemierre’s syndrome, sepsis, and endocarditis [40, 118, 249-256]. Local and distant complications of OIs are illustrated in Figure 4.

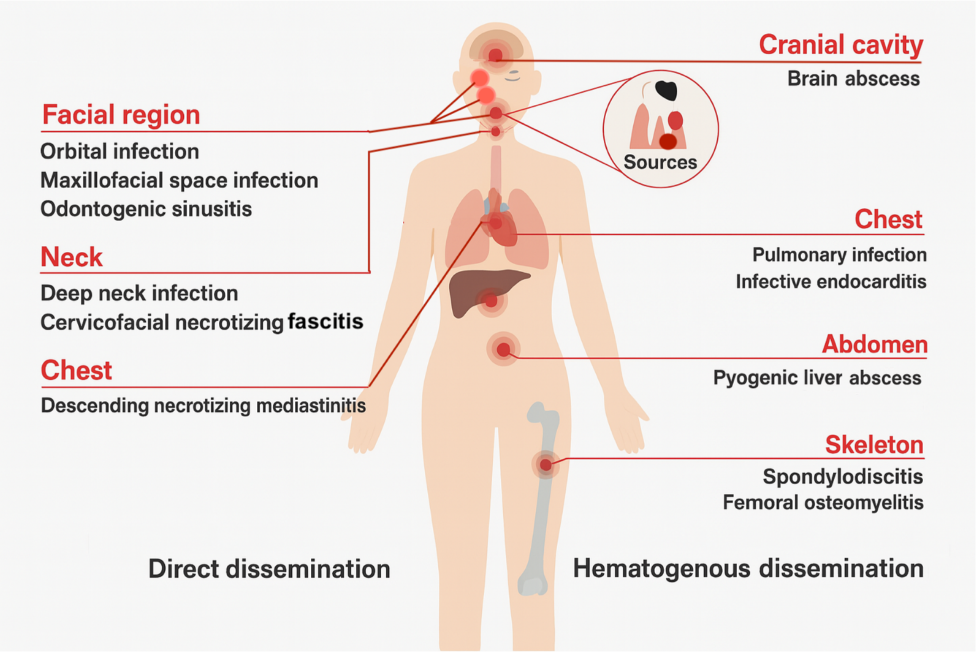

Figure 4 Local (direct dissemination) and distant (hematogenous dissemination) complications of odontogenic infections (figure modified from Lou *et al.* [257]).

The current mortality rate for SOIs is approximately 0.2 per 100 000 person-years. Among adults admitted to an ICU for SOIs, the fatality rate can reach 20–30% [104, 258, 259]. Mediastinitis, *Streptococcus* spp., and low hemoglobin levels are associated with mortality in deep-neck infections [260]. Underlying health conditions also increase the risk for a fatal outcome [104]. Older age and diabetes were identified as specific risk factors for mortality in a Taiwanese study from 1999 on oral and maxillofacial infections, with an overall 0.65% mortality rate [261].

2.6.2 Length of treatment and medical expenses

The length of hospital stay (LOHS) and treatment in an ICU reflect not only the severity of the illness but also the cost of its treatment. The reported mean LOHS for SOIs ranges from 3.9–8.1 days. Identified risk factors for longer hospital stay in SOIs include dysphagia, preadmission antibiotic use, and presence of comorbid conditions, such as deficiency anemias, diabetes, drug abuse, fluid and electrolyte disorders, metastatic cancer, neurologic disorders, psychoses, and weight loss [107, 112, 262, 263]. Moreover, advanced age is associated with prolonged hospital stays in SOIs and other deep-neck infections [10, 246]. Early and sufficient control of the infection reduces the time needed in hospital care [9, 264]. Factors associated with LOHS in SOI and other deep-neck infection patients are shown in Table 5.

Table 5 Factors associated with length of hospital stay in patients with severe odontogenic infections.

Study	Year	Factor	Effect on LOHS
Kim *et al.* [262]	2012	Comorbid conditions	Prolong
Sipahi Calis *et al.* [263]	2015	Dysphagia	Prolongs
Gams *et al.* [112]	2017	Diabetes	Prolongs
Park *et al.* [10]	2019	Diabetes, older age	Prolong
Heim *et al.* [9]	2019	Early removal of odontogenic focus	Reduces
Yew *et al*. [107]	2022	Diabetes	Prolongs
Treviño-Gonzalez *et al.* [264]	2023	Early removal of odontogenic focus	Reduces

LOHS=Length of hospital stay.

Costs in SOIs accrue from multiple interrelated components. Beyond raw cost estimates, patient and disease factors critically influence expenditure. Across diverse healthcare settings, SOIs impose a substantial economic burden. In a U.S. tertiary-care series of 90 patients, Jundt *et al.* reported total hospital costs of $749 382, averaging $17 842 per patient, with a mean length of stay of 4.57 days, including 3.1 days in the ICU. They noted that 83% of their cohort had comorbidities [103]. A study of 327 admissions between 2003 and 2010 found per-case care costs ranging from $1035 to $252 888, and average total hospital costs of $28 841 [265]. In Houston, Gams *et al.* observed among 298 cases from 2010–2015 an average hospitalization cost of $13 058, a mean patient bill of $48 351, and a LOHS of 5.5 days with 45% of patients requiring ICU care [112]. Similarly, a South Australian cohort of 462 deep-space OIs revealed a mean cost of 12 228 Australian dollars per admission, and the study identified high-risk infections with airway compromise, high white blood cell counts, and older age as independent predictors of increased cost [266]. A study by Neal *et al.* revealed that patients with OISS ≥5 incurred significantly higher billed costs than those with lower severity. Male sex and elevated levels of blood glucose and white blood cell count were associated with increased likelihood of OISS ≥5 [16]. Overall, the financial burden of SOIs is primarily driven by infection severity, ICU admission, extended hospital stays, and patient comorbidities.

3 AIMS OF THE STUDY

The general aim of this thesis was to investigate the clinical characteristics of OIs. Of particular interest was to investigate factors predisposing to SOIs in a Finnish health record-based dataset.

The specific aims are:

1. To evaluate demographic and socioeconomic elements in SOIs, with emphasis on sex-related differences (Studies I–IV).
2. To assess predisposing health conditions and behavioral factors, and the role of sex in the most severe OIs requiring treatment in intensive care, and to characterize how infection site anatomy and early physiological markers contribute to the severity and clinical course of SOIs (Studies II–IV).
3. To identify dental diseases and treatment precedent to SOIs (Studies II–IV). Special attention was paid to potentially different patterns in men and women.
4. To clarify the role of *Streptococcus anginosus* in the microbiology of SOIs, especially regarding the role of sex (Studies III and IV).

4 MATERIALS AND METHODS

This thesis examined the characteristics of SOIs within the Helsinki and Uusimaa regions in Finland. It consists of four retrospective cohort sub-studies (I, II, III, and IV). The study cohorts partially overlap. Details of cohort formation are provided in Figure 5. Study I spanned 8 years and 10 months, from January 2012 to October 2020. Studies II and III had 4-year study periods, from January 2015 to December 2018. The study period of Study IV was 5 years, from January 2015 to December 2019.

4.1 Subjects and data registers

The study subjects were patients treated at the oral and maxillofacial emergency unit of Töölö Hospital, Helsinki University Hospital, which provides tertiary care to a catchment area of approximately 1.6 million inhabitants. Medical data of all patients evaluated for suspected or acute infections evaluated in the emergency unit were retrospectively reviewed. Patient data were retrieved from the hospital's electronic patient database. Sub-study I included patients of all ages; sub-studies II–IV included only patients aged ≥18 years.

For Study I, hospital records were combined with the basic data of the FOLK personal data module from Statistics Finland. The target population of the FOLK personal data module is the population permanently living in Finland on the last day of each year. The FOLK Basic data included individual-level information on the following parameters: socioeconomic factors, income level, family relationships, housing quality, living environment, marital status, and country of birth. Patients without available data in the FOLK personal data module were excluded. Reasons for unavailable data were if the patient did not have a Finnish personal identification number or they were deceased before the time of data extraction. Altogether 2838 patient records were included in the study.

The population of Study II included all hospitalized SOI patients in 2015–2018. Among the 335 patients hospitalized for maxillofacial infection, 32 were excluded because their infection focus was unknown or non-odontogenic, yielding a final cohort of 303 patients for analysis. Of those, radiographs of 168 patients were available for further examination in Study III. For Study IV, data from 290 SOI patients with available bacterial samples were investigated. The study designs of Studies I–IV are described in Figure 5.

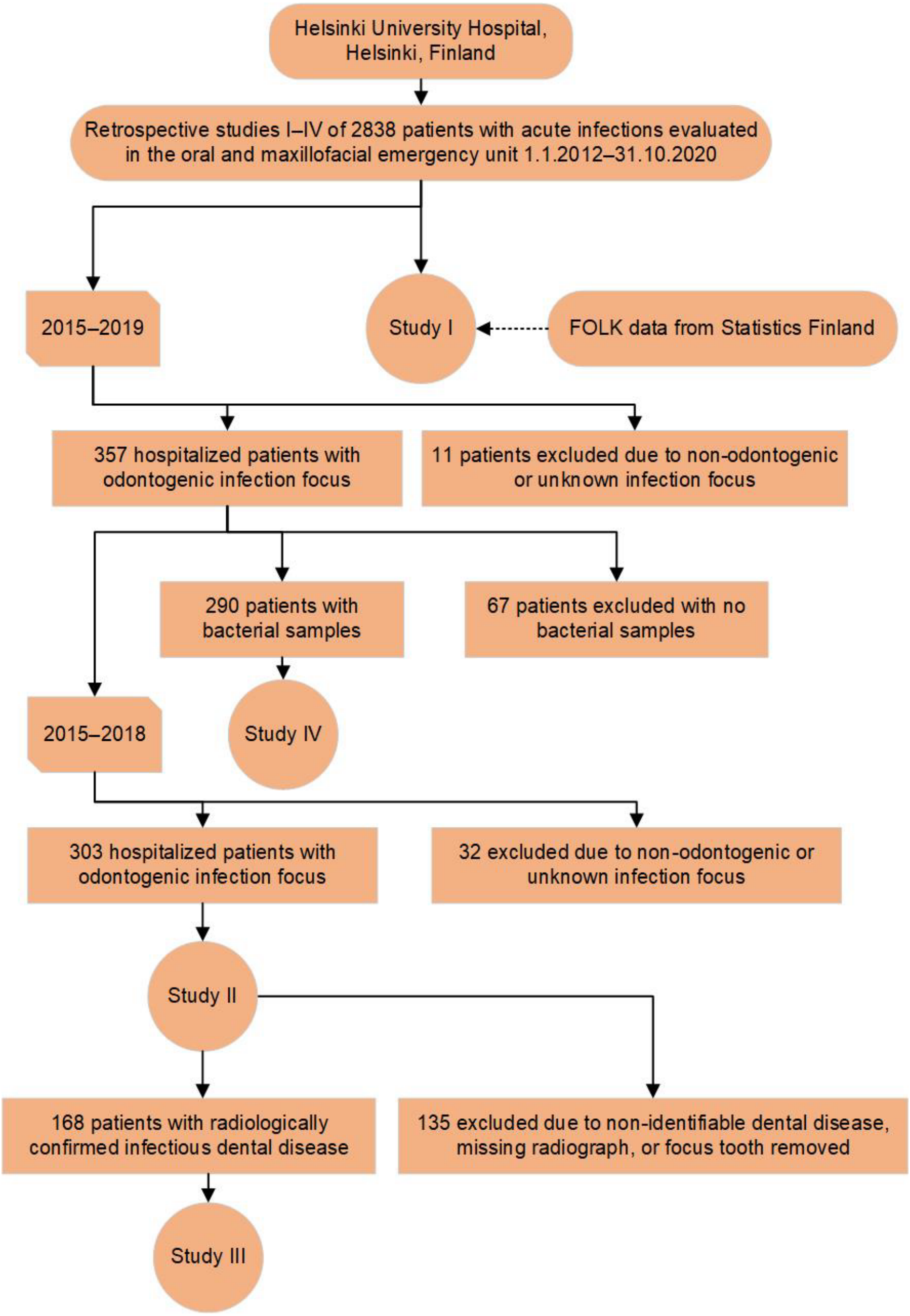

Figure 5 Study designs of original studies I–IV.

4.2 Study variables

The primary outcome was hospitalization due to an SOI in Study I. Predictor variables consisted of sociodemographic factors, namely country of birth, marital status, education level, living arrangement, employment status, and income level. Age and sex were treated as explanatory covariates to adjust for potential confounding.

Study II focused on SOIs with need for ICU treatment as the principal outcome. For ICU patients, length of ICU stay was additionally recorded, while infection-related complications (pneumonia or in-hospital mortality), occurrence of distant infections, or both were secondary outcome measures. Primary predictors included history of a recent dental procedure, defined as any treatment performed during the symptomatic period leading to hospital referral, and prior antibiotic use. Secondary predictors included anatomical focus of infection (maxilla vs. mandible) and specific tooth subgroup (e.g., lower third molar, upper anterior). Clinical and laboratory parameters at admission (body temperature, systolic and diastolic blood pressure, pulse rate, CRP level, and white blood cell count [WBC]) were also evaluated for their association with outcomes. Explanatory variables included sex, age, body mass index (excluded from regression due to missing data), smoking status, excess alcohol consumption (≥12 doses/week for women, ≥23 for men) or regular drug abuse, and history of immunocompromised state (disease, medication, or both).

In Study III, dental infection focus classification was central; radiographically and clinically confirmed diagnoses were grouped by DIDs as AP, marginal periodontitis, combined infection or vertical root fracture, pericoronitis, and root remnant. AP cases were further stratified by RCT status (no RCT, incomplete RCT [presence of intracanal medicament], completed RCT with adequate filling, and completed RCT with inadequate filling [overextension, underfilling >2 mm, untreated canals, or poor root filling quality]). Focus teeth were dichotomized into lower molars versus other teeth. Background variables included sex, age, current smoking, excess alcohol consumption (same dose thresholds as Study II) or regular drug abuse, history of immunosuppressive disease or medication, and symptom duration prior to hospital care. Infection severity outcomes included need for ICU treatment, ICU and total LOHS, and differences in admission laboratory and vital-sign parameters (CRP, WBC count, systolic and diastolic blood pressure, pulse, and body temperature). Microbial culture results from collected samples were also reported.

Study IV examined the role of SAG positivity. Microbiological findings, including SAG and other culture results from routine Helsinki University Hospital Laboratory Services (HUSLAB) reports, were key variables. Pus and blood culture samples were analyzed at HUSLAB using methods accredited under the International Organization for Standardization 9001 and 15189 standards (Finnish

Accreditation Service FINAS, accreditation code T055). The microbiological workflow comprised aerobic and anaerobic culture, bacterial species identification by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry, and antimicrobial susceptibility testing performed according to the clinical breakpoints and procedures of the European Committee on Antimicrobial Susceptibility Testing. Prehospital variables mirrored those in Study III and were age, sex, current smoking, excess alcohol consumption or regular drug abuse, immunosuppressive history, and symptom duration. Infection severity was assessed by ICU admission requirement, CRP level, WBC count, tympanic temperature at admission, ICU, overall LOHS, and occurrence of distant infections or other complications. Multivariable logistic regression models were constructed for ICU admission, LOHS, and CRP level at admission. Finally, types and rates of specific infection complications and distant infections were described.

4.3 Statistical methods

Statistical analyses were conducted using IBM SPSS for Macintosh (versions 25.0–28.0) and Stata MP (version 18.5) for all four studies. Descriptive statistics were reported as frequencies with proportions or means with standard deviations. Categorical variables were examined via Pearson's χ^2 test, with Fisher's exact test employed when expected cell counts were below five. Continuous variables were compared between groups using Student's t-test or nonparametric alternatives (Mann-Whitney U or Kruskal-Wallis H tests), and post-hoc pairwise comparisons for χ^2 and Kruskal-Wallis analyses were performed with Z tests or Dunn's procedure, respectively, applying a Bonferroni correction for multiple testing.

Multivariable modeling employed binomial logistic regression for dichotomous dependent variables; each study selected clinically relevant outcomes (e.g., ICU treatment, length of hospital stay, CRP level, distant infections) as dependent variables, with predictor variables such as age (often categorized into tertiles), sex, smoking status, alcohol or drug use, immunosuppressive conditions or medication, and other study-specific factors (e.g., infection origin, microbial findings). Variables with excessive missing data or multicollinearity (e.g., BMI, education level) were omitted. Generalized linear model with gamma distribution and log-link function was used to analyze LOHS as continuous variable. Across all studies, a two-tailed p-value <0.05 was considered statistically significant.

4.4 Ethical aspects

All sub-studies included in this dissertation were approved by the Internal Review Board of the Head and Neck Center at Helsinki University Central Hospital, Finland

(58/2020). Given the retrospective design, the Board waived the need for informed consent. All studies were conducted in accordance with the Declaration of Helsinki.

5 RESULTS

5.1 Demographic and socioeconomic correlates

Across all sub-studies, men accounted for 54–61% of participants; their mean age was 2–7 years younger than those of women. The difference was statistically significant in the cohorts of Studies I and III. Detailed demographic characteristics are shown in Table 6 (partly previously unpublished data). The overall annual incidence of hospital-treated SOIs in 2012–2020 was 4.9 per 100 000 population.

Table 6 Descriptive demographic characteristics of sub-studies I–IV.

Study	n (%)	Age, mean (SD)	Age, range	P-value (men vs. women)
Study I, all	2838	47 (19.2)	0–100	**0.005**
Men	1532 (54%)	46 (18.3)	0–96	
Women	1306 (46%)	48 (20.1)	2–100	
Study II, all	303	47 (18.2)	18–100	0.102
Men	169 (56%)	45 (15.9)	19–86	
Women	134 (44%)	49 (20.6)	18–100	
Study III, all	168	48 (18.4)	18–100	**0.040**
Men	103 (61%)	45 (15.6)	19–86	
Women	65 (39%)	52 (21.7)	18–100	
Study IV, all	290	47 (17.9)	18–96	0.171
Men	174 (60%)	46 (15.7)	19–87	
Women	116 (40%)	49 (20.6)	18–96	

SD=standard deviation.

Sex and age were not significantly associated with hospitalization in Study I. In Study II, they were not significantly associated with treatment in ICU or with LOHS, although ICU treatment was more common in men (27%) than in women (19%) (Figure 6). In Study III, patients with marginal periodontitis were significantly older (median 65 years, range 49–88 years) and patients with pericoronitis were significantly younger (median 33 years, range 19–73 years) than patients with other DIDs (median 44–54 years, range 18–100 years). In Study IV, age and sex did not differ significantly in patients with and without *Streptococcus anginosus*.

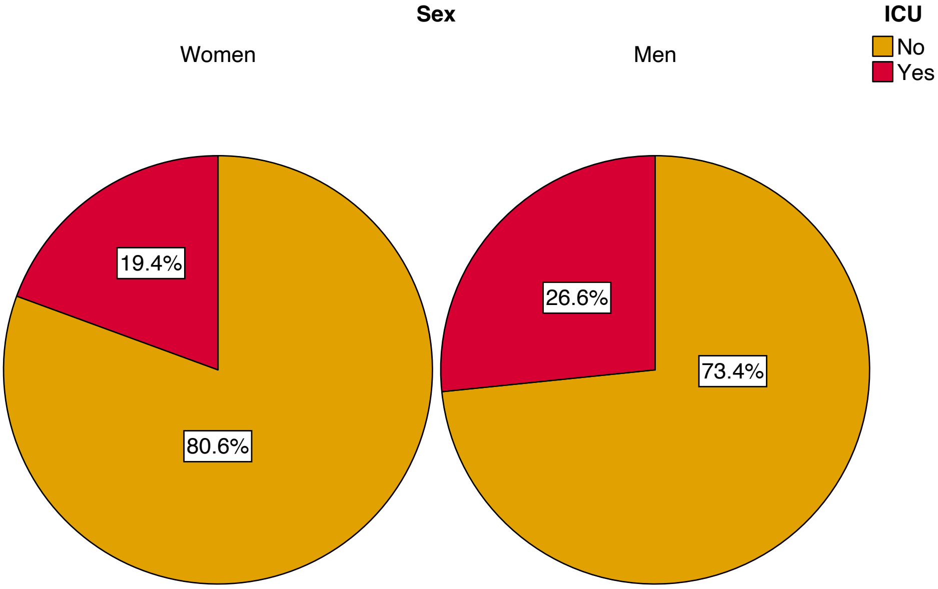

Figure 6 Treatment in intensive care unit (ICU) in men and women in 303 severe odontogenic infection patients.

In Study I, a total of 2838 patient records were analyzed, of which 709 (25%) were from hospitalized patients. The most frequent infection diagnoses were cellulitis and oral abscesses and diseases of the pulp and periapical tissues. The median age of the cohort was 47 years (range 0–100), and 54% were male. In bivariate analyses, hospitalized patients were significantly more likely to be single, divorced, or widowed rather than married ($p<0.001$). Likewise, living in rented accommodation ($p=0.049$), having a lower educational attainment ($p=0.018$), and belonging to a lower income bracket ($p=0.002$) were all associated with hospitalization. No significant differences were observed between hospitalized and non-hospitalized patients for age, sex, country of birth, or employment status. In a binomial logistic regression adjusting for age, sex, and living arrangement, being single, divorced, or widowed (reference: married; odds ratio [OR] 1.406, 95% CI 1.148–1.723, $p=0.001$) and belonging to the lowest income category (reference: highest income; OR 1.418, 95% CI 1.090–1.845, $p=0.009$) were independent predictors of hospitalization (Table 7).

Table 7 Binomial logistic regression predicting the likelihood of hospitalization in 2838 patients with odontogenic infections.

Predictor variable	OR	95% CI for OR	P-value
Age			
year	0.997	0.992–1.002	0.295
Sex, ref. female			
male	1.179	0.984–1.414	0.074
Marital status, ref. married			
single, divorced, or widowed	1.406	1.148–1.723	**0.001**
Living arrangement, ref. own			
rental	1.044	0.856–1.274	0.669
other or unknown	1.202	0.801–1.802	0.374
Income level, ref. highest quartile			
2nd highest quartile	1.146	0.883–1.487	0.304
2nd lowest quartile	1.166	0.894–1.520	0.257
lowest quartile	1.418	1.090–1.845	**0.009**

OR=odds ratio, CI=confidence interval, ref.=reference group.

5.2 Behavioral and health status predictors

5.2.1 Smoking and use of alcohol or drugs

In 303 inpatients with SOIs in Study II, 83 (27%) were current smokers and 27 (9%) had excess alcohol consumption or drug abuse. Smoking prevalence was higher in males than females (33% vs. 21%; p=0.024) as was substance abuse (13% vs. 4%; p=0.005). Neither smoking nor alcohol or drug abuse was significantly associated with ICU admission (smoking: 35% vs. 25 %, p>0.05; alcohol or drug abuse: 13% vs. 8%, p>0.05). The overall mean LOHS was 3.2±3.58 days. Mean LOHS was 3.8±4.27 days and 3.0±3.24 days for smokers and non-smokers; the difference was not statistically significant (p=0.125) (Figure 7, previously unpublished data). However, infection complications or distant infections occurred significantly more often in smokers (p=0.001) and in those with excessive alcohol use or drug abuse (p=0.025); smoking conferred a 3.5-fold independently higher likelihood of such complications (p=0.008) in binomial logistic regression. Substance abuse (excess consumption of alcohol or drug abuse) predicted longer hospital stays in Studies II–III.

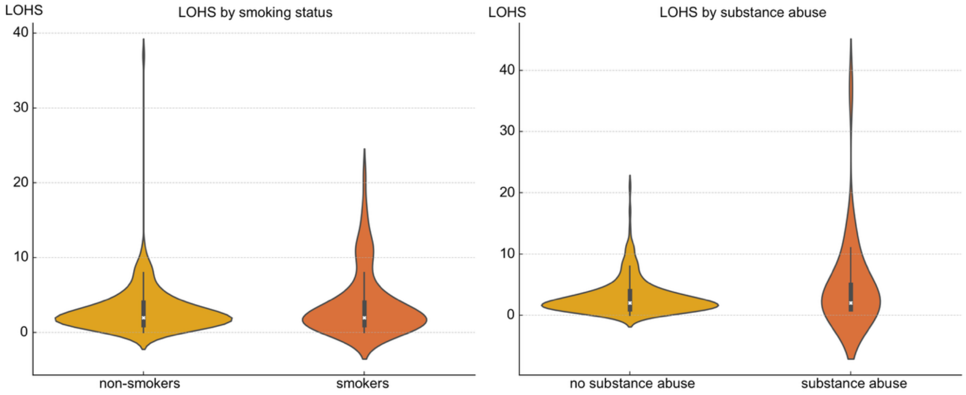

Figure 7 Violin plots illustrating the probability distribution of length of hospital stay (LOHS) in days stratified by smoking and substance abuse in 303 hospitalized patients with odontogenic infections.

Among 168 SOI patients in Study III, 51 (30%) were smokers, with no significant sex difference (25% of women vs. 34% of men, p>0.05). Excess alcohol use or drug abuse was reported in 20 (12%) of the patients, also without a significant sex difference (6% of women vs. 16% of men, p>0.05). Smoking or excess alcohol consumption or drug abuse was not significantly associated with different types of DIDs. In Study IV, smoking and heavy alcohol use or drug abuse (substance abuse) were equally common in patients with and without SAG findings in their OIs, indicating no association between these behavioral factors and SAG carriage in this SOI cohort in bivariate comparisons. However, smoking presented a 2.071-fold increased risk for ICU treatment in binomial logistic regression of this cohort. The distribution of overlapping frequencies of men, smokers, and ICU-treated patients is presented in Figure 8.

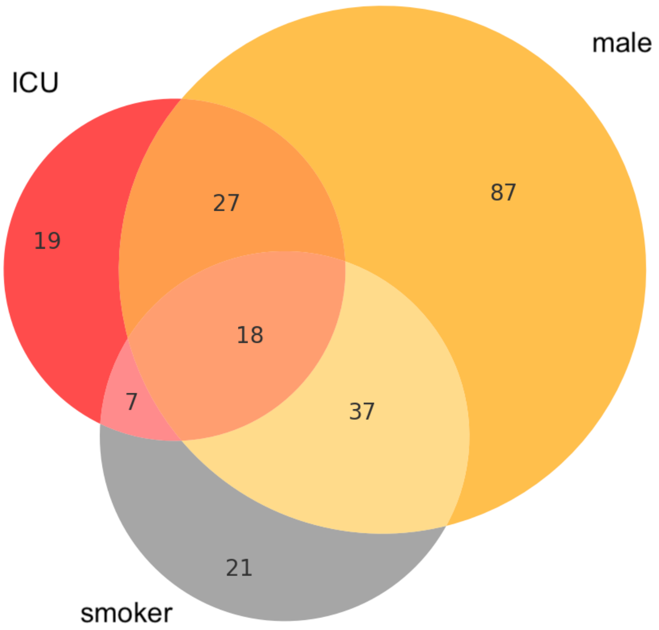

Figure 8 Euler diagram visualizing the relationships and overlaps in frequency between intensive care unit (ICU) treatment, male sex, and smoking among 303 hospitalized patients with odontogenic infections.

5.2.2 General health status

In Study II, 71 patients (23%) required ICU treatment. All ICU admissions were due to airway compromise caused by the deep-seated infection, a decision jointly made by oral and maxillofacial surgeons and anesthesiologists. Throughout hospitalization, options for airway management (conventional intubation, fiberoptic intubation, or tracheostomy) were available. There were no significant differences in body mass index or immunocompromised status between patients treated in the ICU and those who were not. ICU-treated patients had significantly higher levels of body temperature, pulse, CRP, and WBC count at hospital admission. One patient (0.3%) died during hospitalization; this individual had dilated cardiomyopathy, a history of heavy alcohol use, renal dysfunction, and developed pneumonia. In multivariable logistic regression, general health factors did not predict ICU treatment significantly (Table 8, previously unpublished data).

Table 8 Binomial logistic regression model of systemic factors predicting treatment in an intensive care unit in 303 patients with severe odontogenic infection.

Predictor variable	OR	95% CI for OR	P-value
Age			
10-year increment	0.996	0.841–1.180	0.961
Sex, ref. female			
male	1.500	0.836–2.692	0.174
ICC	0.688	0.301–1.573	0.375
Smoking	1.532	0.811–2.891	0.188
Substance abuse	1.420	0.533–3.788	0.483
Site of infection focus, ref. maxilla			
mandible	7.792	1.811–33.513	**0.006**
Preceding local dental treatment, ref. no			
tooth removal	1.585	0.879–2.857	0.126
root canal treatment	0.434	0.118–1.596	0.209
abscess incision only	0.756	0.076–7.562	0.812
tooth removal and abscess incision	2.756	0.185–41.032	0.462

OR=odds ratio, CI=confidence interval, ref.=reference group, ICC=immunologically compromised condition due to a disease or medication.

Complications and associated distant infections of the 303 SOI patients in Study II are presented in Figure 8. In Study III, immunocompromised status varied significantly by dental disease type (p=0.024); immunocompromised status was significantly more common in patients with marginal periodontitis-related SOIs.

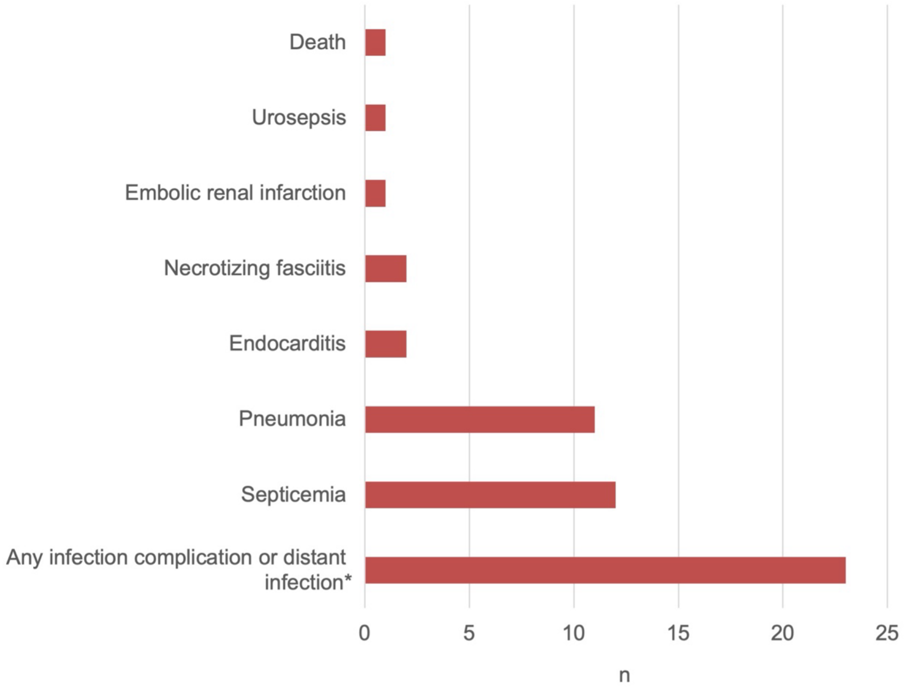

Figure 9 Frequencies of infection complications and distant infections of 303 hospitalized odontogenic infection patients. *4 patients had more than one complication or associated infection.

5.3 Dental disease patterns and treatment

Infections stemming from mandibular teeth were significantly more likely to require ICU care than those from maxillary teeth in Studies II and IV. The lower second molars were the most frequent source of infection. Background variables in Study II are shown in Figure 9. In Study II, after adjusting for relevant covariates, binary logistic regression revealed that mandibular-origin infections had a 7.8-fold increased odds of ICU admission than maxillary-origin infections (p=0.007) (Table 8). In the cohort of Study IV, mandibular infection focus conferred a 5.8-fold increased odds of ICU admission (p=0.021) versus maxillary infection focus. Prior local dental treatment showed no significant associations with ICU admission or OI complications in Study II. Tooth removal before hospitalization was more common in SAG-positive patients (58%) than in SAG-negative patients (42%) in Study IV (p=0.041).

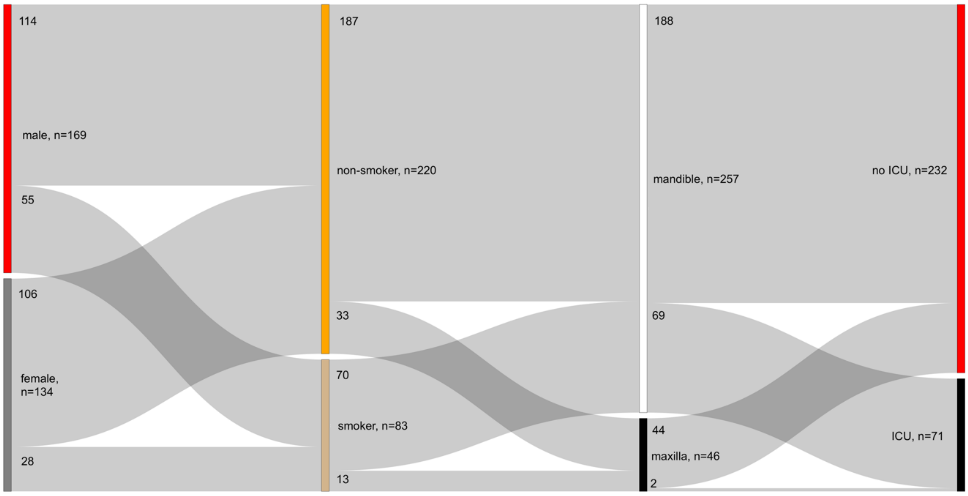

Figure 10 Sankey flow diagram describing sex, smoking status, and site of infection focus relative to intensive care unit (ICU) treatment in 303 patients with severe odontogenic infections.

Study III included 168 patients with confirmed OIs and a clearly identified culprit tooth on imaging. Diagnosis was established by dental panoramic radiography alone in 68 cases, by computed tomography alone in 33 cases, and by both modalities in 67 cases. AP was the most common diagnosis at the focus tooth (113 patients, 67%) and was more frequent in men (75%) than in women (55%). When all other DIDs were pooled together, this difference in the prevalence of AP was statistically significant (p=0.012; previously unpublished data). Among these, 22 had incomplete RCT, 4 had completed but inadequately filled RCTs, and 4 had both completed and adequately filled RCTs. The frequency distribution of DIDs and endodontic treatment status is presented in Figure 11.

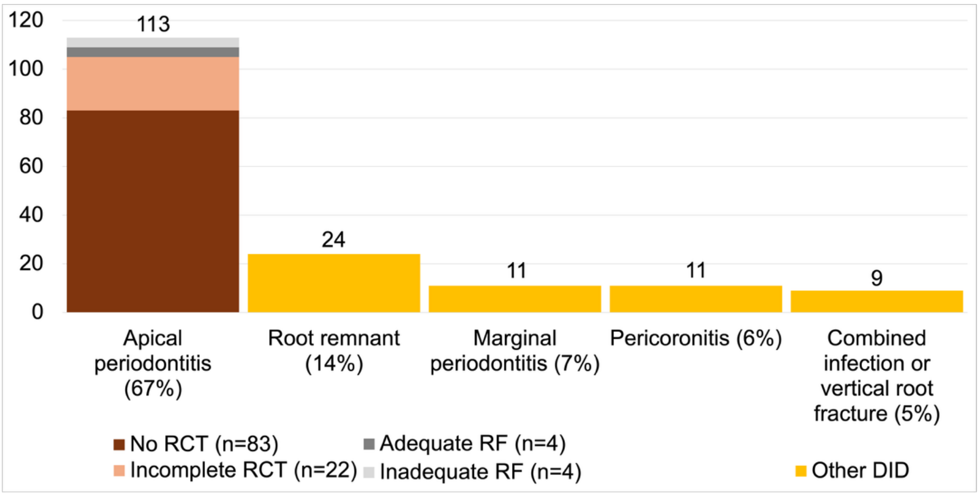

Figure 11 Frequency distribution of dental diseases behind odontogenic infections in 168 hospitalized patients. RCT=root canal treatment, RF=root filling, DID=dental infectious disease.

Lower molars were the predominant source of infection across AP, combined infections, vertical root fractures, and pericoronitis. Marginal periodontitis was the only disease category in which origins other than lower molars were predominant. ICU admission rates, and lengths of hospital or ICU stay did not differ by dental disease type. However, diastolic blood pressure and pulse at admission varied significantly between groups; post-hoc testing revealed a difference in pulse rate only between the AP (median 92, range 52–142) and pericoronitis (median 75, range 58–93) subgroups (p=0.012). Detailed background characteristics are shown in Table 9.

Table 9 Background variables of 168 hospitalized odontogenic infection patients stratified by type of dental infectious disease.

Variable	Apical periodontitis n=113 (67%)	Marginal periodontitis n=11 (7%)	Combined infection or VRF n=9 (5%)	Pericoronitis n=11 (7%)	Root remnant n=24 (14%)	P-value
Age, median (range), years	44 (18–96)	65 (49–88)	54 (35–58)	33 (19–73)	53.5 (22–100)	**<0.001**
Sex, n (%)						0.106
Men	77 (75%)	5 (5%)	5 (5%)	6 (6%)	10 (10%)	
Women	36 (55%)	6 (9%)	4 (6%)	5 (8%)	14 (22%)	
Smoking, n (%)	36 (71%)	5 (10%)	2 (4%)	1 (2%)	7 (14%)	0.412
Substance abuse, n (%)	15 (75%)	0	1 (5%)	0	4 (20%)	0.448
ICC						
All	17 (52%)	6 (18%)	1 (3%)	3 (9%)	6 (18%)	**0.024**
Diabetes	*7 (50%)*	*1 (7%)*	*0*	*1 (7%)*	*5 (36%)*	*0.159*
Symptom duration before hospital admission, median (range), days	3 (0–34)	3 (0–13)	6 (1–13)	3 (1–13)	3 (0–14)	0.457

VRF=vertical root fracture, ICC=immunologically compromised condition due to a disease or medication.

In multivariable logistic regression, SOIs originating from AP were associated with a 9-fold higher likelihood of having a CRP level above the cohort median compared with pericoronitis cases (p=0.043). No significant predictors were identified for ICU admission or LOHS. After pooling other types of DIDs together, AP did not predict ICU treatment or LOHS significantly. Older age (p=0.020) and substance abuse (p=0.019) predicted longer LOHS in a generalized linear model (Table 10, previously unpublished data).

Table 10 Results of binomial logistic regression model predicting the likelihood of treatment in intensive care unit (ICU) and generalized linear model predicting length of hospital stay (LOHS) in 168 patients with severe odontogenic infections.

ICU				
Predictor variable	**OR**	**95% CI for OR**		**P-value**
Age				
year	1.012	0.989–1.036		0.310
Sex, ref. female				
male	1.698	0.701–4.112		0.240
ICC	0.430	0.131–1.406		0.163
Smoking	1.757	0.757–4.077		0.190
Substance abuse	1.764	0.551–5.643		0.339
DID, ref. other				
apical periodontitis	1.211	0.488–3.000		0.680
LOHS				
Predictor variable	**Coeff.**	**95% CI for coeff.**	**Z**	**P-value**
Age				
year	0.011	0.002–0.021	2.32	**0.020**
Sex, ref. female				
male	-0.091	-0.429–0.247	-0.53	0.598
ICC	-0.216	-0.622–0.190	-1.04	0.296
Smoking	0.276	-0.066–0.619	1.58	0.113
Substance abuse	0.581	0.095–1.068	2.34	**0.019**
DID, ref. other				
apical periodontitis	0.138	-0.228–0.505	0.74	0.460

OR=odds ratio, CI=confidence interval, ref.=reference group, ICC=immunologically compromised condition due to disease or medication, DID=dental infectious disease.

5.4 Microbiological etiologies and clinical severity

In Study III, *Streptococcus* species were the most frequently identified bacteria (69%). Other common bacterial findings were anaerobic gram-negative rods (59%) and normal flora of the oral cavity (49%). Of 357 patients with SOIs in Study IV, bacterial cultures were obtained for 290 individuals, who comprised the study cohort. Mixed aerobic and anaerobic flora were detected in 194 patients (67%), while pure aerobic and pure anaerobic growth occurred in 60 (21%) and 55 (19%) cases, respectively. SAG was the single most prevalent pathogen and was present in 49% of patients; SAG was isolated alongside anaerobic organisms in 123 cases (42%). There were no significant differences between men and women. Other frequently isolated organisms included normal oral flora (48%), anaerobic gram-negative rods (47%), *Streptococcus viridans* group, *Prevotella* species, *Parvimonas micra*, and *Fusobacterium nucleatum*. Rare, non-oral commensals were cultured infrequently: β-hemolytic streptococci and *Staphylococcus aureus* (each n=4; 1%), *Klebsiella pneumoniae* and *Enterobacter cloacae* (each n=3; 1%), and *Bacteroides fragilis* group species (n=3; 1%). Mandibular infection foci were significantly more likely than maxillary foci to yield SAG (p=0.012). Bivariate associations between explanatory and infection severity factors are described in Table 11. Nearly all patients (n=289) received antibiotics; 269 (93%) were treated with metronidazole plus a cephalosporin or penicillin, 8 (3%) with clindamycin, and 35 (12%) had their regimen adjusted based on clinical or microbiological findings.

Table 11 Associations between explanatory and infection severity variables and patients (N=290) with and without a positive *Streptococcus anginosus* group (SAG) bacterial sample.

Variable		**Patients with SAG (n=144)**	**Patients without SAG (n=146)**	**P-value**
		n (% of n)	**n (% of n)**	
Age (years)				0.598
	Mean (SD)	46 (19.0)	48 (16.8)	
	Median (range)	43 (18–88)	48.5 (18–96)	
Sex				0.291
	Men (n=174)	82 (47%)	93 (53%)	
	Women (n=116)	62 (53%)	54 (47%)	
Smoking (n=83)		37 (45%)	46 (55%)	0.274
Substance abuse (n=28)		16 (57%)	12 (43%)	0.404
ICC (n=51)		28 (55%)	23 (45%)	0.409
	Diabetes (n=24)	*14 (58%)*	*10 (42%)*	*0.375*
Site of infection				**0.012**
	Mandible (n=256)	134 (52%)	122 (48%)	
	Maxilla (n=34)	10 (29%)	24 (71%)	
Tooth removal before hospital admission (n=104)		60 (58%)	44 (42%)	**0.041**
ICU treatment (n=83)		58 (70%)	25 (30%)	**<0.001**
CRP level at hospital admission (mg/L)				**<0.001**
	Mean (SD)	171 (99.5)	136 (80.5)	
	Median (range)	145.5 (6–565)	120.5 (12–423)	

Variable	**Patients with SAG (n=144)**	**Patients without SAG (n=146)**	**P-value**
	n (% of n)	**n (% of n)**	
WBC count at hospital admission (10^9/L)			**0.001**
Mean (SD)	14 (5.5)	13 (4.3)	
Median (range)	13.55 (1.3–35.9)	12.0 (2.1–32.2)	
Tympanic temperature			0.252
<38°C (n=216)	103 (48%)	113 (52%)	
≥38°C (n=74)	41 (55%)	33 (45%)	
Length of hospital stay (days)*			**<0.001**
Mean (SD)	4.4 (4.62)	2.9 (2.68)	
Median (range)	3 (<1–37)	2 (<1–17)	
Infection complication or distant infection	14 (64%)	8 (36%)	0.172

*Data available for 284 patients.

SD=standard deviation, ICC=immunologically compromised condition due to a disease or medication, ICU=intensive care unit, CRP=C-reactive protein, WBC=white blood cell.

Markers of disease severity were markedly higher in SAG-positive cases. ICU admission rates were greater among SAG patients than non-SAG patients (p<0.001). SAG-positive individuals had elevated CRP levels (p<0.001) and WBC counts (p=0.001) and longer LOHSs (p=0.001). Levels of CRP, WBC, and LOHS are illustrated in Figure 12.

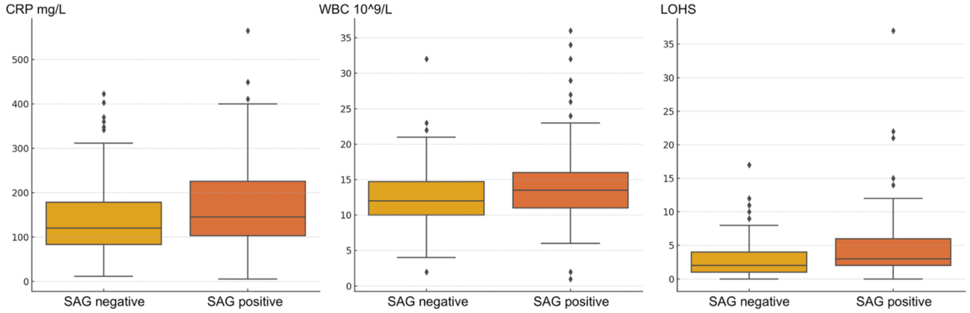

Figure 12 C-reactive protein (CRP) level, white blood cell (WBC) count, and length of hospital stay (LOHS) in days in 290 hospitalized patients with odontogenic infections.

Figure 13 illustrates LOHSs and lengths of ICU stays (LOICUS) in patients with and without SAG findings (previously unpublished data). Distant-site infections or other complications occurred in 22 of 290 patients (8%). Although 14 of these 22 (64%) complications occurred in SAG-positive patients versus 8 (36%)

in SAG-negative patients, this difference was not statistically significant (p>0.05). Among the 125 patients who had blood cultures drawn, 12 developed septicemias; 10 were SAG-positive and 2 were SAG-negative (p=0.042). Additional complications included pneumonia (n=10), endocarditis (n=2), necrotizing fasciitis (n=2), urosepsis (n=1), and embolic renal infarction (n=1), with 8 (62%) occurring in SAG-positive patients (p>0.05). Three deaths were recorded and were all in SAG-positive patients.

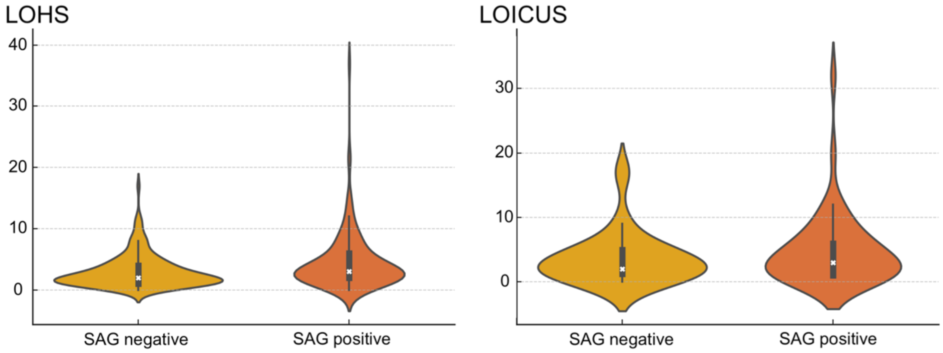

Figure 13 Distributions of lengths of hospital stays (LOHS) and lengths of stays in intensive care unit (LOICUS) in patients with and without *Streptococcus anginosus* group finding in 290 patients with severe odontogenic infection.

In binomial logistic regression, SAG positivity conferred a 3.4-fold increased odds of ICU admission (p<0.001) (Table 12). SAG-positive status was additionally associated with greater odds of prolonged hospitalization (OR 2.3, p<0.001), elevated CRP level above the cohort median (OR 1.9, p=0.010), and WBC counts above median (OR 1.7, p=0.035).

Table 12 Binomial logistic regression of factors predicting treatment in an intensive care unit in 290 hospitalized odontogenic infection patients.

Predictor variable	OR	95% CI for OR	P-value
Age, ref. lowest tertile			
middle tertile	0.822	0.420–1.609	0.568
highest tertile	0.848	0.426–1.687	0.638
Sex, ref. female			
male	1.535	0.843–2.797	0.161
ICC	0.601	0.269–1.344	0.215
Smoking	2.071	1.099–3.904	**0.024**
Substance abuse	1.102	0.420–2.892	0.844

Predictor variable	**OR**	**95% CI for OR**	**P-value**
Site of infection focus, ref. maxilla			
mandible	5.759	1.302–25.481	**0.021**
SAG finding, ref. negative			
positive	3.393	1.907–6.037	**<0.001**

OR=odds ratio, CI=confidence interval, ref.=reference group, ICC=immunologically compromised condition due to a disease or medication, SAG=*Streptococcus anginosus* group.

6 DISCUSSION

This over 8-year, retrospective analysis of OI patients from Finland's largest maxillofacial emergency unit revealed that socioeconomic disadvantage, key clinical parameters, specific dental disease patterns, and SAG microbiology each contribute to the severity and management of SOIs. Our findings confirm and extend previous work by highlighting the independent impact of loneliness and income on hospitalization risk, the central role of AP—particularly in lower molars—in triggering severe infections, and the aggressive and complicated nature of SAG-associated SOIs. Furthermore, this study explored the role of male sex and behavioral health correlates in OIs requiring hospitalization. SOIs pose a risk to the patient's general health and well-being and lead to high costs in expensive specialized healthcare. In this study covering the years 2012–2020, the overall annual incidence of hospital-treated SOIs was 4.9 per 100 000 population. Previously reported incidences from Helsinki University Hospital area were 5.3 per 100 000 per year in 1994–1995 and 7.2 per 100 000 per year in 2004 [17]. These differences may be explained, at least in part, by shifts in hospital admission policies and by progress in outpatient care approaches.

6.1 Sex-related considerations

Men have been reported as over-represented in earlier studies of SOIs (Table 1). In this study, men were likewise over-represented in the sub-study populations compared with women (54–61% vs. 39–46% of the study subjects; Table 6), consistent with earlier findings [8, 17]. In the adjusted binomial logistic regression model, men had a 1.2-fold higher odds of hospitalization than women, although this difference was not statistically significant (p=0.074). Nonetheless, this pattern is compatible with broader observations of sex-related differences in oral health.

Men's generally poorer oral hygiene habits may predispose them to dental decay and related conditions [98, 267]. Among young men, particularly those with lower educational backgrounds, health behaviors also tend to be less supportive of maintaining good oral health [268]. In a Finnish cohort of over 13,000 conscripts, good physical fitness and high self-reported physical activity were strongly associated with lower caries burden, whereas smoking and frequent consumption of energy drinks increased the odds of restorative treatment need [269]. These results illustrate that young Finnish men often display clustered lifestyle patterns, with some combinations promoting oral health and others increasing disease susceptibility. Moderate or poor oral hygiene status is a common observation in SOI patients [119]. Altogether, these factors—rather than any presumed biological susceptibility in men—suggest that a clustering of poorer oral health behaviors, together with lower socioeconomic or educational status, may characterize a subgroup of socially isolated or lonely men who might be in a specific danger zone for less favorable OI outcomes.

Male patients were younger on average and presented AP more frequently. Together with prior findings of poorer oral-health behaviors in men [270, 271], this underlines the need to emphasize self-care and routine dental visits in younger male populations. The objective is twofold, namely, to prevent basic dental diseases from developing and progressing into SOIs, thereby reducing patient morbidity and simultaneously alleviating the economic burden and demand on limited healthcare resources. SOIs may constitute a noteworthy, and potentially partially preventable, health challenge particularly among younger men.

6.2 Determinants related to demographics and socioeconomic position

The present study clarified how demographic and socioeconomic factors shape hospitalization rates among patients with OIs. One of the hypotheses of the study was that lower socioeconomic status would be associated with more severe OIs; this was supported by the data. By examining 8 years of patient records from Finland's largest maxillofacial emergency unit, this study identified key socioeconomic drivers influencing both the management and outcomes of these infections. The mean age of the study population was 47 years, and men accounted for 54–61% of the participants.

Sociodemographic influences on OIs have not been widely examined within European populations. Earlier studies have revealed an association between poorer oral health and loneliness or social isolation [69]. Unmarried men are less likely to seek dental care in response to symptoms, when compared with married men [63]. Marital status was also a predictor of hospitalization in this study; individuals who were single, divorced, or widowed had higher odds of admission than those who were married. This disparity may reflect the social and emotional support typically provided by a stable partnership, which can promote healthier behaviors and more prompt healthcare-seeking. Financial security tied to marriage may also facilitate access to preventive dental services. These observations are consistent with prior findings linking social isolation to greater vulnerability to severe infections [272]. Residence in rental housing was linked to higher hospitalization rates, suggesting that poorer living conditions may contribute to more severe dental infections, perhaps through crowded or unstable environments and weaker social networks. This aligns with Swedish research showing that homelessness, particularly when coupled with substance abuse, increases infection-related mortality [273]. As expected, income and educational levels were closely correlated in this study. Income level was included in the multivariable logistic regression analysis and emerged as a strong independent predictor of OIs requiring hospitalization. This association is likely multifactorial; individuals with lower socioeconomic status may face limited access to dental care, possess less awareness of oral health issues, and lack the social support necessary to seek timely treatment, thereby increasing the risk of infections progressing to more severe stages. Social isolation is also associated with postponed dental visits, further compromising oral health [274].

The Dental Neglect Scale (DNS) provides an objective tool for assessing the theoretical construct of "dental neglect" and exploring its relationship with oral health status [275]. The DNS is a self-reported questionnaire developed to measure the construct of dental neglect, typically in both children and adults. It is designed to assess an individual's attitudes, behaviors, and practices related to oral health care, especially the degree to which a person fails to seek or maintain appropriate dental care despite the availability of services. Higher DNS values are associated with male sex and worse caries experience [276]. A central issue lies in the definition of dental neglect. The DNS does not distinguish between patients who choose to neglect care and those who face systemic or social barriers. The conceptual clarity of dental neglect requires further examination. Accordingly, the definition may need to be revised to incorporate social determinants of health, such as access, socioeconomic status, and education. Nevertheless, the DNS has potential as a screening tool in preventing oral health deterioration and even SOIs.

Lower educational level is associated with poorer oral health status, particularly in older adults [277]. Moreover, a lower maternal level of education is linked to poorer dental health in children [278]. This finding underscores the critical influence of home-based dietary and oral hygiene practices on oral health outcomes later in life. School-based oral health education interventions have a favorable effect on oral health status [279]. Fluoride use is effective in preventing dental caries [174]. A combined strategy that reinforces oral health knowledge within the home environment and implements supportive measures in schools may improve lifelong oral health, particularly when directed toward parents with lower levels of education. This study identified educational attainment as a significant determinant, supporting the hypothesis that lower levels of education are associated with poorer outcomes in OIs, as reflected by higher rates of hospitalization. Individuals with less formal schooling may be less aware of the need for routine dental check-ups and proper hygiene, causing early signs of infection to go unrecognized until hospitalization is required, as theorized previously [280]. Although education could not be included in the multivariable logistic regression of this study due to multicollinearity, its significant bivariate association with hospitalization underlines its potential explanatory role. Additionally, the early prevention of dental diseases and their progression into SOIs could be promoted cost-effectively through health education, the reinforcement of proper oral hygiene practices, targeted interventions for socially or educationally disadvantaged groups, and the provision of accessible primary dental care supported by adequate prophylactic programs.

6.3 Behavioral attributes and health condition indicators

This study sought to characterize the severity of OIs among hospitalized patients, with the expectation that immunocompromised individuals would most frequently require intensive care. Contrary to our hypothesis, underlying disease, sex, and advanced age did not predict the need for ICU admission. Instead, the prototypical SOI patient was previously healthy, lacked any known predisposing conditions, and developed an infection originating from a lower mandibular molar. This suggests that factors beyond age and comorbidity, such as virulence, local anatomy, or perhaps delay in drainage, may override traditional risk dynamics. In addition, the site of infection seems to be a pivotal risk factor. Although half of these SOI patients received outpatient treatment shortly before hospitalization, no clear link emerged between the type of prior local intervention and infection severity.

While the literature suggests that patients with diabetes, HIV, or other immunocompromising illnesses and those with higher body mass index have a greater risk for SOIs and subsequent ICU admission [59, 105, 281, 282], only 20% of our cohort had such comorbidities. Previously healthy patients were as likely to require intensive care, possibly because dental foci in those with known risk factors are detected and treated earlier due to more comprehensive care. As a result, otherwise healthy individuals may be equally vulnerable to life-threatening OIs, which is a risk that warrants broader clinical awareness.

Complications, including distant infections such as septicemia and pneumonia, occurred in 7.6% of patients, with smoking emerging as a significant risk factor. While smoking has generally decreased in Finland in recent past decades, it is still more common in men (23%) compared with women (16%) [283]. Worldwide reports have shown an even greater contrast between the sexes [284]. Compared with the general Finnish population-level numbers, in this study of 303 hospitalized OI patients, the smoking rates were higher (men 33%, women 21%, p=0.024), which may partly reflect underlying risk-profile differences between men and women in this cohort. An overrepresentation of smokers among SOI patients aligns with earlier observations [108]. The rate of septicemia was also consistent with previous findings [118], but overall complication rates were lower than in other series of deep neck infections, where 22% of cases developed severe sequelae like necrotizing fasciitis or mediastinitis [18]. In this study, necrotizing fasciitis occurred in only 0.7% and no cases of mediastinitis were observed; mortality was likewise low (0.3%). These findings highlight that prompt surgical management, including abscess drainage and extraction of the focus tooth, can usually confine OIs to the upper neck.

Previous studies have reported longer hospital stays in elderly patients with deep neck infections [10, 246]. The results of this study support this finding in SOIs; higher age (p=0.046) and substance abuse (p=0.026) independently predicted greater LOHS in a generalized linear model. Excess alcohol use is also associated with more severe OIs in earlier studies [79, 118]. The mechanism of association has been explained by immunosuppression and poor wound healing. On admission, elevated CRP level, leukocytosis, fever, and tachycardia were all significantly associated with ICU transfer, suggesting that routine assessment of these parameters could aid early identification of high-risk OI patients.

6.4 Dental disease and treatment characteristics

This study characterized the dental conditions that led to SOIs and compared how each focus-tooth disease influenced infection presentation and severity. Among hospitalized patients, untreated periapical infections were the most frequent triggers of SOIs. Moreover, AP accounted for over two thirds of all ICU admissions, and those cases exhibited significantly more pronounced clinical signs of infection severity (elevated CRP level and higher diastolic blood pressure and heart rate) upon arrival. However, the ICU admission rates or LOHSs did not differ statistically significantly between SOIs originating from different types of DIDs.

The classic sequence of dental caries leading to root canal infection, followed by AP in the presence of bacteria, has been well-established in earlier studies [138, 285]. In SOIs it often culminates in mandibular molars requiring inpatient care [12]. The microbiological findings of this study, dominated by *Streptococcus* spp., align with recent reports [11], and the anaerobic pathogens characteristic of AP likely explain its aggressive spread from the periapical tissues of lower molars [286].

A recent Swedish study reported a 29-fold higher absolute risk for hospitalization due to an OI for a non-root filled tooth with AP, when compared with a root-filled tooth [287]. Although most periapical infections (73%; 83/113) arose in teeth without prior endodontic treatment, this study also included patients with both incomplete and completed RCTs. Incomplete RCTs predispose to acute infection [128] and shift the microbial profile in the root canal toward facultative anaerobes [288, 289]. In this study, teeth with incomplete RCTs were more common (19%) than teeth with adequate root fillings (7%) in AP cases. Notably, no patient with a properly filled root canal required ICU care and only 1 patient with an inadequate root filling did. This supports the premise that effective endodontic treatment reduces the risk of the most severe OIs, despite challenges in achieving optimal root fill length in molars [290, 291].

Marginal periodontal infections were linked to older age and immunocompromised status but seldom led to critical SOIs; only 1/35 such cases needed ICU support. Likewise, pericoronitis was responsible for approximately 6% of SOIs, which is consistent with earlier reports [292, 293]. Compared with AP cases, pericoronitis was associated with milder infectious presentations (lower CRP level) and did not necessitate ICU transfer. However, post-extraction infections were not evaluated in the study.

Despite guidelines advocating simultaneous tooth removal and abscess incision for acute OIs [9, 294], only 38% of 303 SOI patients had undergone extraction before admission, and just three had combined incision and extraction. This raises questions about the adequacy or timing of dental interventions in preventing severe infection spread. Similarly, although 8.3% had recently undergone endodontic treatment, only 12% of these required ICU care, with no clear association with infection severity.

AP emerged as the most frequent and severe focus-tooth disease. Ensuring high-quality endodontic therapy and early detection of periapical infections should be central goals in dental education and practice to reduce the burden of SOIs.

Anatomically, infections stemming from the second and third lower molars predominated among the most severe cases, reflecting their root position's propensity for deep spread. In general, men have larger mandibular molars with longer roots [295, 296]. While this finding has not yet been confirmed for second and third mandibular molars, it nonetheless suggests an additional pathway by which men may face an increased risk of severe OIs.

6.5 Microbiological aspects

This study evaluated the prevalence of SAG bacterial findings in 290 patients with SOIs and compared the clinical presentation and severity of SAG-positive cases with those caused by other bacteria. Nearly half of all patients harbored SAG, making it the most frequently isolated pathogen. Infections involving SAG were markedly more severe; SAG-positive individuals had a 3-fold increased odds of requiring ICU care (OR 3.4, $p<0.001$) and presented with higher CRP levels and WBC counts and had extended hospital stays. These results emphasize the aggressive, potentially life-threatening nature of SAG-driven OIs and highlight their distinct clinical profile compared with infections from other organisms. According to previous reports, men are overrepresented in SAG infections [297-299]. However, after adjusting for age and infection site, the observed sex difference may reflect healthcare-seeking behavior or exposure patterns, rather than true biological susceptibility. This study found no statistically significant differences between sexes.

Although SAG species normally reside as harmless commensals, they can act as opportunistic pathogens once they breach mucosal barriers and invade sterile tissues or the bloodstream. Previous studies have linked SAG to the most severe OIs, characterized by difficulty swallowing and trismus [300] and have noted its inclination for abscess formation in spreading infections [301]. The findings of this study reinforce the clinical importance of this behavior, even as the full scope of SAG's pathogenic potential remains under investigation [302]. Notably, Ismail et al. (2021) found that among SAG species in pediatric head and neck infections, *S. intermedius* predominated, indicating species-specific tendencies in both site and severity. SAG bacteria employ a multifactorial virulence strategy combining adhesion, immune evasion, tissue invasion, and modulation of host response [303]. Emerging insights into SAG virulence include the discovery of angicin, a bacteriocin that permeabilizes bacterial membranes, inhibits competing species, and may facilitate compartmentalized abscess formation [304, 305]. SAG's acid tolerance further supports chronic inflammation and abscess persistence [306]. Clinically, severe SAG infections can present with high fever, chills, systemic toxemia, airway compromise, and even necrotizing pneumonia [300, 307]. In this study, SAG-positive patients more frequently experienced airway obstruction, exhibited pronounced inflammatory markers, and required longer treatment courses than those with non-SAG SOIs. These features, along with the fact that all three in-hospital fatalities occurred in SAG-positive cases, emphasize the need for rapid recognition and management.

Timely identification of SAG entails recognizing its hallmark signs, namely rapid progression, elevated CRP level and WBC count, fever at admission, and gas pockets on imaging [228]. Surgical teams should maintain a high index of suspicion, employing wide surgical exposures and thorough abscess drainage. Since SAG is typically part of polymicrobial abscesses, complete drainage and eradication of the odontogenic focus are critical; in this study, anaerobes were co-isolated in 85% of SAG patients. Early extraction of the infected tooth can shorten hospital stays compared with delayed removal [9]. According to this study, hospital stays were longer in SAG-positive patients (mean 4.4 days) than those without SAG (mean 2.9 days, $p=0.001$).

Compared with prior reports of deep neck infections [18, 118], the overall complication rate in this study of SOIs was modest (8.3%), with septicemia and pneumonia as the most common. Severe outcomes, such as necrotizing fasciitis and endocarditis, were rare. However, SAG was disproportionately associated with these complications, particularly septicemia, reinforcing its perilous clinical course. This study also revealed that mandibular-origin SOIs were more likely to involve SAG than maxillary cases, reflecting the known predilection of lower-molar infections for severity [13]. Additionally, SAG-positive patients were more likely to have had prior tooth extractions (56% vs. 44%, p=0.041), suggesting that preexisting tissue disruption may facilitate SAG invasion. This phenomenon occurs independently of sex or other sociodemographic characteristics and emphasizes the importance of earlier preventive measures.

While systemic immunity and comorbidities are often considered in SOI risk [18, 104], this study found no link between immunosuppression and SAG positivity, and only 18% of patients were immunocompromised. This supports the view that local factors, such as recent dental procedures, and delayed or inadequate treatment, play a primary role in predisposing to severe SAG infections, rather than shifts in microbial flora due to systemic disease.

Effective management of purulent SOIs demands both surgical drainage and appropriate antimicrobial therapy. In Finland, penicillin has high efficacy against SAG and other *Streptococcus viridans* species with ≤5% resistance, while metronidazole remains reliable for anaerobes [308]. Clindamycin resistance in oral *Streptococcus* species has increased slightly and thus requires monitoring. Current Finnish guidelines recommend penicillin for streptococcal coverage and metronidazole for anaerobes, with cephalosporins or clindamycin reserved for penicillin-allergic patients, and amoxicillin-clavulanate as an alternative when necessary [185].

The findings of this study highlight the importance of early identification of odontogenic SAG infections due to their potentially severe clinical course. Given that SAG organisms are part of the commensal oral microbiota, prevention and timely management of common DIDs are essential to mitigate their progression into SOIs. Furthermore, this highlights the need to strengthen dental health literacy to promote effective oral hygiene practices and regular dental attendance, particularly among socially isolated and socioeconomically disadvantaged populations.

6.6 General considerations

SOIs are influenced by a range of modifiable and non-modifiable factors. Protective factors that reduce the likelihood of developing SOIs include maintaining good oral hygiene, adhering to regular dental check-up schedules, and engaging in sound health behavior practices. Timely and adequate completion of RCTs and prompt and effective management of local dental infections are particularly critical in preventing the escalation of common dental diseases into severe infections. Furthermore, higher levels of dental health literacy and the presence of a supportive social network contribute positively by facilitating preventive care-seeking behavior and adherence to recommended treatments.

In contrast, several risk factors are associated with a heightened risk of severe OIs. Poor oral health, tobacco use, and substance abuse compromise host defenses and increase susceptibility to infection. Social isolation and lower socioeconomic status, including limited education, reduced income, and unstable housing, can impede access to timely dental care, thereby allowing otherwise preventable infections to progress unnoticed. These social determinants underline the complex interplay between behavioral, economic, and environmental influences in the pathogenesis of SOIs.

While male sex has often been reported as a common characteristic among patients with severe infections, its role as a predictive factor remains inconclusive. It is likely that associated behavioral patterns, such as lower utilization of dental services and a higher prevalence of smoking, contribute to this overrepresentation. These factors may play a more significant role than biological sex alone.

Importantly, SOIs are not only detrimental to individual health, leading to pain, functional impairment, and systemic complications, but also impose a significant burden on healthcare systems. Hospitalization, surgical intervention, and prolonged treatment contribute to increased healthcare expenditures, emphasizing the need for targeted prevention strategies and early intervention to reduce both clinical and economic impacts. Factors associated with SOIs are presented in Figure 14.

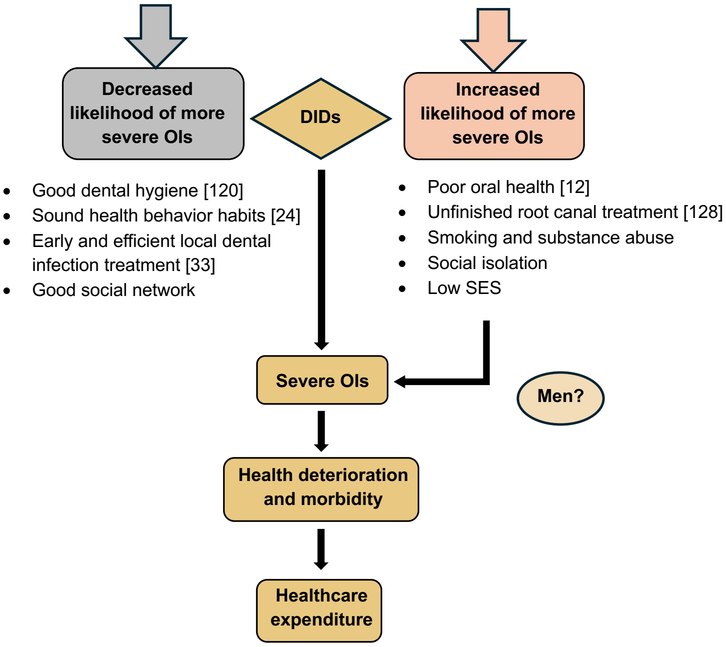

Figure 14 The figure combines the results of this study with previous literature on the pathway of dental infectious diseases (DIDs) into more severe odontogenic infections (OIs). SES=socioeconomic status.

6.7 Limitations

The retrospective design and dependence on existing records may have introduced biases in data completeness and accuracy. Registry-based data are susceptible to variability in documentation practices among clinicians, inconsistencies in the level of detail recorded, and missing information on symptoms, timing, or clinical decision-making. Such factors may lead to misclassification or underestimation of certain variables, particularly behavioral and socioeconomic characteristics that are not routinely captured in clinical notes. Second, excluding education level from the logistic regression due to multicollinearity in Study I restricted our ability to fully assess its influence in comparison with other factors. In Studies II and III, procedural details on tooth removals and other dental treatment prior to hospital admission were not available, limiting our interpretation of the role of earlier treatment decisions in infection progression. In Study IV, the retrospective design also led to the exclusion of some patients because of missing bacterial culture data and because species-level identification via PCR was not routinely performed during the study period. Furthermore, in Studies II–IV, the study population consisted exclusively of hospitalized patients with OIs. As a result, the findings primarily reflect the characteristics of more severe cases and may not fully generalize to milder infections managed in outpatient settings. Including a control group or a broader population-based sample could have improved the generalizability of the results and increased statistical power for detecting associations across the full spectrum of OI severity.

6.8 Prospective developments

The observed overlap between male sex, smoking, and ICU treatment supports the need for targeted preventive efforts, especially in young to middle-aged male populations who may delay seeking dental care. Future research should further elucidate the microbiological and immunological mechanisms driving SOI progression in seemingly low-risk individuals. Prospective studies with more detailed data on confounders and treatment timelines will be essential to fully elucidate the risk factors for SOIs. Given that chronic AP affects over a quarter of adults, further research should delineate which specific dental procedures and delays elevate OI risk.

Future studies incorporating detailed microbiological profiling and precise documentation of dental procedures are essential to improve understanding of how specific DIDs and their treatments, including tooth removals, affect the risk of OIs. Such research is also crucial for optimizing treatment strategies, investigating novel therapies for SAG-associated infections, and developing rapid diagnostic methods for SAG detection.

7 CONCLUSIONS

The findings of this thesis suggest a complex interplay of social, behavioral, dental, and microbiological factors in the development of potentially life-threatening OIs:

1. People with lower income levels or non-married status were more likely to require hospitalization for SOIs, underscoring the need for public health strategies that address these sociodemographic disparities. Men were consistently overrepresented in the study populations, which may reflect underlying behavioral and healthcare-seeking differences rather than biological susceptibility. While systemic health conditions remain relevant, this study reinforces the role of behavioral risk factors, infection site anatomy, and early physiological indicators in SOIs. The observed overlap between male sex, smoking, and ICU treatment supports the need for targeted preventive efforts, especially in young to middle-aged male populations who may delay seeking dental care. Future research should further elucidate the microbiological and immunological mechanisms driving SOI progression in these seemingly low-risk individuals.
2. SOIs often occurred in previously healthy patients. Septicemia and pneumonia were the most common infection complications. Smokers were at a higher risk for more complicated OIs than non-smokers. Excessive use of alcohol or other substance abuse extended the LOHS in SOIs.
3. AP, particularly in teeth with no or incomplete endodontic treatment, was the most frequent dental source of SOIs, emphasizing the need for improved access to timely and definitive dental care. Men developed AP-related SOIs more often than women.
4. SOIs caused by SAG bacteria were associated with more aggressive clinical presentations, reinforcing the importance of early detection, tailored antimicrobial therapy, and adequate surgical management. There appeared to be no significant difference in the occurrence of SAG-related SOIs between men and women.

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