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Temporomandibular joint osteoarthritis in older adults:
Frequency of CBCT signs and characteristics

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Contents

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List of papers

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Paper I

Abrahamsson AK, Kristensen M, Arvidsson LZ, Kvien TK, Larheim TA, Haugen IK. **Frequency of temporomandibular joint osteoarthritis and related symptoms in a hand osteoarthritis cohort**. Osteoarthritis Cartilage. 2017 May; 25(5):654-657. doi: 10.1016/j.joca.2016.12.028. Epub 2017 Jan 5. PMID: 28064031.

Paper II

Ottersen MK, Abrahamsson AK, Larheim TA, Arvidsson LZ. **CBCT characteristics and interpretation challenges of temporomandibular joint osteoarthritis in a hand osteoarthritis cohort**. Dentomaxillofac Radiol. 2019 May; 48(4):20180245. doi: 10.1259/dmfr.20180245. Epub 2019 Jan 28. PMID: 30633546; PMCID: PMC6592579.

Paper III

Ottersen MK, Larheim TA, Hove LH, Arvidsson LZ. **Imaging signs of temporomandibular joint osteoarthritis in an urban population of 65-year-olds: A cone beam computed tomography study.** J Oral Rehabil. 2023 Nov;50(11):1194-1201. doi: 10.1111/joor.13547. Epub 2023 Jul 5. PMID: 37356072

List of abbreviations

CBCT	Cone Beam Computed Tomography
CT	Computed Tomography
DSA	Norwegian Radiation and Nuclear Safety Authority
FHI	Norwegian Institute of Public Health (NIPH)
GBD	Global Burden of Disease
FOV	Field Of View
JIA	Juvenile Idiopathic Arthritis
MR	Magnetic resonance
OA	Osteoarthritis
PAN	Panoramic radiography
RDC/TMD	Research Diagnostic Criteria for Temporomandibular Disorder
RA	Rheumatoid Arthritis
TMD	Temporomandibular Dysfunction
TMJ	Temporomandibular Joint
WHO	World Health Organization
TMJ-OA	Temporomandibular Joint Osteoarthritis

1. Introduction and background

1.1. Ageing

1.1.1. Definitions and terminology

In the dictionaries ageing is defined as the process of getting older. However, the exact starting point of old age cannot universally be defined, and the definition of aging is tending to be more fluctuating. According to earlier publications from World Health Organization (WHO) most developed countries accepted the chronological age of 65 years as the definition of elderly or older persons.

WHO defines ageing at a biological level: Ageing results from the impact of the accumulation of a wide variety of molecular and cellular damage over time. This leads to a gradual decrease in physical and mental capacity, a growing risk of disease and ultimately death. These changes are neither linear nor consistent, and they are only loosely associated with a person's age in years. The diversity seen in older age is not random. Beyond biological changes, ageing is often associated with other life transitions such as retirement, relocation to more appropriate housing and the death of friends and partners[1].

A group of researchers proposed cellular and molecular hallmarks of aging in 2013[2]. The nine hallmarks were meant to highlight the underlying causes of age-related dysfunction and assist with research into potential therapeutic interventions. The suggested hallmarks were genomic instability, the telomere attrition (shortening of telomeres), epigenetic alterations and the imbalance between the rates of synthesis and degradation of proteins (loss of proteostasis), dysregulated nutrient sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion and altered intercellular communication. The first four hallmarks were defined by the researchers as "the primary causes of ageing"[2].

National Center to Reframe Aging, led by the Gerontological Society of America is initiated to establish a long-term social change endeavor designed to improve the public's understanding of what aging means and the many ways that older people contribute to our society[3]. Based on the recommendations of The Reframe Aging Initiative, terms like seniors, elderly, aged, aging dependents, old-old, young-old, or similar phrases should be avoided in general and in medical research. This as an attempt to restrict ageism (discrimination against a person because of their age) and to establish a bias-free language[4]. According to the Reframing Aging Journal Manuscript Guidelines, terms like older adults, older persons or older people are recommended for describing people aged 65 and older[5]. Due to these recommendations the term older adults will be used in this thesis.

1.1.2. The ageing population

Globally, the population is ageing, and WHO predicts that, by 2050, the population aged 60 years or more will double, whilst those aged 80 years or more will triple, to reach over 400 million persons[1]. This shift in distribution of the world's population towards older ages is known as population ageing and is leading to an increased number of people living with non-communicable diseases and consequences of injuries. The current demographic and health shifts are contributing to a rapid increase in the number of people experiencing disability or declines in functioning for substantially larger periods of their lives[6].

Figures for Norway from the Global Burden of Disease (GBD) Study in 2015 show that [7]

- 65-year-old men can expect to live for 18.6 years, of which 14.4 years will be healthy life years.
- 65-year-old women can expect to live for 21.5 years, of which 16.7 years will be healthy life years

According to WHO, common conditions in older age include hearing loss, cataracts and refractive errors, back and neck pain and osteoarthritis, chronic obstructive pulmonary

disease, diabetes, depression and dementia. As people age, they are more likely to experience several conditions at the same time[1].

Osteoarthritis is a leading cause of disability and source of societal cost in older adults [8]

1.2. Osteoarthritis

1.2.1. Definition and terminology

Osteoarthritis (OA) is also known as degenerative arthritis, degenerative joint disease, and osteoarthrosis. OA can be defined as a degenerative disorder of synovial joints, primarily affecting articular cartilage and subchondral bone, initiated by deterioration of articular soft tissue cover and exposure of bone. The disease was previously considered non-inflammatory but is now accepted as an inflammatory condition that involves all components of the joint including alterations in the articular cartilage, subchondral bone, ligaments, capsule and synovial membrane, ultimately leading to joint failure [8-10].

1.2.2. Epidemiology

Estimates of prevalence and incidence of OA may vary, depending on the definition of OA, the specific joint(s) being evaluated, as well as on the age categories, countries of origin, and sex distribution of the study population being studied [11-13]. A global disease burden was estimated at nearly 528 million affected persons in 2019[14].

There is a lack of updated data on prevalence and burden of OA in Norway. However, the Ullensaker study is a population study that investigated the prevalence of OA in knee, hip and hand in a general population in Norway and the burden of disease in terms of associations between self-reported OA and health-related variables[15]. A total of 3266 participants aged 24-76 years responded. The presence of OA in hip, knee, and/or hand was obtained in a questionnaire by the question “Have you ever been diagnosed with OA in hip/knee/hand by a medical doctor and/or by x-ray?” The overall prevalence of OA was 12.8 %. A higher prevalence was found among women and older people, people with less than 12 years of education, those out of work, and those overweight. OA was

associated with pain, disability, and poor health status, and frequent use of healthcare providers.

A Norwegian study from 2015 described prevalence estimates of musculoskeletal disorders in the general Norwegian population by using both nationwide health registers and health survey data[16]. This study showed that OA was the most common chronic musculoskeletal disorder reported by women (11.2 %) and second most reported among men (5.46 %). This study also suggests that musculoskeletal disorders in general are highly age and gender dependent and likely to be an increasing public health challenge in Norway in the future.

Population based studies indicate higher prevalence for radiographic OA than for symptomatic OA, and for knee and hand-OA than for hip-OA. Furthermore, knee or hand-OA is more prevalent in women than in men, especially symptomatic OA [13]. In a Swedish population based-study from 2012, with prospectively ascertained data from the Skåne Healthcare Register (SHR) the proportion of people aged ≥45 years with any doctor-diagnosed OA (knee, hip, hand, or other locations except the spine) was almost 27% [17]. According to this study, the proportion of the population aged ≥45 with doctor-diagnosed OA is estimated to increase from 26.6% to 29.5% (any location) by the year 2032. The Swedish study concluded that in 2032, at least an additional 26,000 individuals per 1 million population aged ≥45 years are estimated to have consulted a physician for OA in a peripheral joint compared to 2012. These findings underscore the need to address modifiable risk factors and develop new effective OA treatments [17].

On a global level a systematic analysis of the GBD Study 2017 concerning the burden of OA from 1990-2017 concludes that OA is a major public health challenge[18]. The analysis of GBD 2017 demonstrated a global prevalence estimate of OA, which was higher in women and increased with age. In addition, the number of prevalent cases increased with age and peaked at 60–64 years age for both men and women, then decreasing trends for number of prevalent cases were seen up to the oldest group. In

2017, the global incidence rate was higher in women and increased with age up to the 55–59 years age group. There was no visible difference between the incidence in men and women in any age group. The number of incident cases reached the highest level at the 55–59 years age group, then decreasing trends were seen up to the oldest group[18].

1.2.3. Risk factors

OA has a multifactorial etiology and can be considered the product of an interplay between systemic and local factors. The risk factors of OA can be divided into person-level factors, including increasing age, female gender, obesity diet and genetics. Dominating joint-level factors are joint injury and abnormal loading of the joints[19].

Person-level risk factors

Age: One of the strongest risk factors for OA in all joints. The increase in the prevalence and incidence of OA with age probably is a consequence of cumulative exposure to various risk factors and biologic changes that occur with aging that may make a joint less able to cope with adversity, such as cartilage thinning, weak muscle strength, poor proprioception, and oxidative damage[20]. A review article from 2016 elucidated selected aspects of ageing relevant to OA related to the hallmarks of ageing[21]. One of the main key points in this review is that ageing-associated changes promote development of OA, but ageing and OA are still independent processes[21].

This review also states that an increase in fat mass and related metabolic changes that occur with ageing can result in ageing-related inflammation (so-called 'inflammaging'), a chronic low-grade systemic pro-inflammatory state[21].

Gender: Women are more likely to have OA than men and develop more severe OA than men. At the time of menopause, it has been demonstrated a definite increase of OA in women leading to the hypothesis that hormonal factors may play a role in the development of OA. However, research results of estrogen effect on OA have been conflicting. Other attempts have been done, to explain the difference of both prevalence

and severity of OA between men and women. Differences in cartilage volume, bone strength, alignment, ligament laxity, pregnancy and neuromuscular strength are among the factors that have been suggested [11, 20, 22].

Obesity: Overweight is an important risk factor in the pathophysiology of OA and obesity is a well-documented and high-risk factor for development and progression of OA in the knee [19, 23]. The Framingham Study estimated that weight reduction by 5 kg decreased the risk of developing knee OA by 50 %[24].

Historically, the strong correlation between weight and OA has been associated with excessive joint load and biomechanical effects. However, obesity is also demonstrated to be associated with hand-OA[25]. A Norwegian epidemiological study from 2008 demonstrated that high BMI was significantly associated with knee OA and hand-OA, but not with hip OA [26].

Evidence of the association between development of OA in non-loading joints strengthens the evidence of metabolic and inflammatory systemic effects of obesity, and that OA can be a part of a metabolic disorder [27, 28].

Diet: The risk factors obesity and diet are of course strongly associated, as demonstrated for the relationship between hyperlipidemia and development of OA[12]. A population-based case-control study demonstrated that hyperlipidemia was an independent risk factor for new onset hand-OA[29].

Several dietary factors are suspected to increase the development of OA, including a low level of vitamins. As vitamin C, D and K play a major role in cartilage and bone metabolism, it has been hypothesized that low levels may increase OA risk. Previous studies have been conflicting and further studies are needed to better define the association between OA and these dietary factors[22].

Genetics: Development of OA appears to be associated with genetic factors. However, the genetic association varies from joint to joint. There is strong evidence for the involvement of genetic factors in structural OA of the hand and the spine. On the other

hand, the evidence is inconsistent for genetic impact on OA development for both knee and hip. Studies have demonstrated that genetic susceptibility for the development of OA ranges from 40% to 65% depending on the joint site[19]

Joint-level risk factors

Traumatic joint injury: A major risk factor for OA. The knee is one of the most frequently injured joints[22]. Severe joint-trauma, particularly fracture, cartilage damage, meniscal tear, ligament injury/ instability can result in an increased risk of OA development [30, 31]. A research article from 2017 summarized the prevalence of posttraumatic OA; posttraumatic OA accounts for 20% to 78% of cases of ankle OA, 10% of knee OA, and 2% of hip OA[31].

Abnormal loading of joints: Repetitive joint use is associated with the development of OA[22]. Heavy work and physical activities are risk factors for OA in both hip and knee [8], with physical occupations in e.g. farming and construction industry especially associated with hip OA. The relationship between physical activity and OA is complex, but highly repetitive, intense and high-impact physical activity seems to confer increased risk of developing OA[22]. Several sports (e.g., football, handball, hockey and long-distance running) have been reported as moderately to strongly associated with an increased risk of OA, often with a dose-response dependency [8].

1.2.4. Etiology and pathogenesis

OA is a disease involving all the components of a joint. It can lead to structural alterations in cartilage, subchondral bone, ligaments, capsule, synovium, and adjacent muscles [8].

The pathogenesis of OA is both complex and not fully known. It involves mechanical, inflammatory, and metabolic factors, leading to structural destruction of the joint. Earlier OA was commonly described to be a passive degenerative disease or so-called wear-and-tear disease. Now there is a broad scholarly consensus that OA is an active dynamic alteration of imbalance between repair and destruction of joint tissues [8].

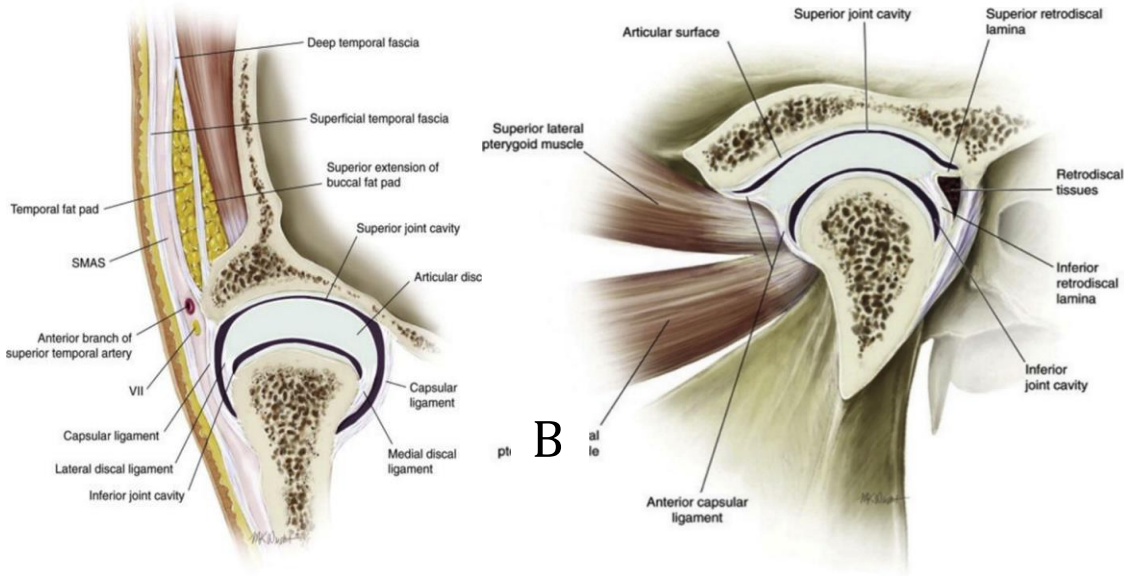
In the initial phase of OA, cartilage composition changes and the cartilage lose its integrity, leading to altered properties and increasing susceptibility to disruption by physical forces.

OA is described as a heterogeneous disease with a wide range of underlying pathways and so can be considered as a syndrome rather than a single disease. Each risk factor might initiate different mechanistic pathways leading to OA. Mediators promoting development of OA in older adults might be different from those in younger adults or in obese individuals. Classification into different mechanistic subgroups has been proposed, based on the specific pathological processes. Suggested subgroups include those with an increased inflammatory component[32], mechanical overload, metabolic alterations, and cell senescence. These mechanistic phenotypes probably overlap, and further validation and research are needed [8].

1.3. The temporomandibular joint

The temporomandibular joint (TMJ) is a complex joint, both anatomically and functionally. Extensive understanding of normal anatomy and clinical features of the

Figure 1: Coronal **(A)** and sagittal **(B)** view of the TMJ
From: C. J. Walker and S. P. R. MacLeod. Atlas of the Oral and Maxillofacial Surgery Clinics 2017 Vol. 25 Issue 1 Pages 11-16; with permission



TMJ is therefore essential for correct and reliable diagnostics in cases of pathological conditions. Compared to other joints in the body, the TMJs are special in more than one way. Although they are two separate joints, they function together as a single unit as they link between the skull and the mandible and are among the most used joints in the human body. Common and to some extent vital activities like speaking, chewing, swallowing and yawning are all based on the function of the TMJs.

The main components in the TMJ are the mandibular component, the temporal component, the articular disc, and the fibrous capsule. The TMJ is a synovial joint, but unlike most synovial joints the articular surfaces in the TMJ are covered by fibrocartilage and not hyaline cartilage[33]. Wadhwa and Kapila summarized the unique characteristics of fibrocartilage compared to hyalin cartilage in the TMJ: The fibrocartilage is better able to withstand sheer forces than hyaline cartilage can, which makes it a superior material for enduring the large amount of occlusal load that is placed on the TMJ. Other advantages of fibrocartilage in the TMJ over hyaline cartilage are that the fibers are tightly packed and are able to withstand the forces of movement; it is less susceptible to the effects of aging; it is less likely to break down over time; and it has a better ability to repair.

Subchondral formation of cortical bone starts during adolescence (12-14 years). A continuous, homogeneous, and compact cortical bony layer is established in young adults by the age of 21-22, indicating full development of the mandibular condyle. The condylar bone develops gradually and is generally fully developed a year earlier in women than in men[34].

Theory regarding anatomy and function of the TMJ is collected from the internationally renowned Sobottas anatomical atlas[35] and comprehensive textbooks concerning the TMJ[33, 36, 37].

1.3.1. Anatomical components of the TMJ

In this chapter the main focus will be on the anatomical components of the TMJ which can be visualized in a CBCT examination, which is, essentially, the bony components. Some of the most important soft tissue components are also mentioned, even though they are not visualized in CBCT. Imaging of the TMJ and the available modalities are reviewed in Chapter 1.4 Imaging of osteoarthritis the temporomandibular joint.

Mandibular component: The mandible (mandibula) is the largest of the facial bones and is composed of the horseshoe-shaped body of mandible (corpus mandibula) with a flat, cranial directed branch (ramus mandibula) on each side. The cranial part of the ramus mandibula divides on both sides into an anterior (processus coronoideus) and a posterior part (processus condylaris). The cranial boundary of the processus condylaris is called the condyle head (caput mandibula) and forms the mandibular component of the TMJ.

Morphology and size of the condyle head varies from person to person. At birth, the condyle head has a rather flat shape. The processus condylaris has the ability for multidirectional growth. That is, growth in several directions. Two periods of increased growth in the TMJ are described: between 5-10 years and between 10-15 years.

In the first three years after birth, a rapid growth of the condyles is seen in both the superior and posterior direction, which results in increased ramus height. The condyle therefore acquires an S-shape which is characteristic at this age This develops into a more cylindrical shape when the teeth are fully developed[38]

Temporal component: The temporal bone (os temporalis) is part of the skull and forms the lower side walls of the skull. The temporal bone is composed of three parts surrounding the external ear opening in the skull (porus actusticus externa): pars petrosa, pars squamosa and pars tympanica. Fossa mandibularis is a concavity in the temporal bone, with space for the condyle head. The anterior boundary of the mandibular fossa is formed by the articular tubercle (tuberculum articulare pars

squamosa). The posterior boundary is formed by the pars tympanica. Cranial delineation in fossa mandibularis is very thin towards the middle cranial fossa (fossa cranii media), which on each side encloses the temporal lobe (lobus temporalis) of the brain (cerebrum).

The articular disc

The articular disc (discus articularis) is made of fibrocartilage. It is located between the condyle head and the mandibular fossa, dividing the joint into an upper and a lower joint cavity (cavitas superior and cavitas inferior). The articular disc is biconcave with a round or oval shape and is composed of an anterior band, thin intermediate zone, and posterior band in the sagittal plane. The articular disc stabilizes the articulating surfaces in the TMJ and acts as a stress absorber and force distributor in the TMJ, during jaw activity.

Medial and lateral parts of the articular disc are attached to the condyle head. The attachment of the disk to the condylar poles, is helping to ensure passive movement of the disc with movement of the condyle. The periphery of the articular disc attaches to the inner surface of articular capsule. The anterior band is also attached to the upper part of the lateral pterygoid muscle. The posterior band is connected to the retro discal tissue.

In closed mouth position, the condyle head is centered in the fossa mandibularis with the articular disk interposed between them. The normal disc is positioned such that the anterior band is in front of the condyle and the junction of the posterior band and bilaminar zone lies immediately above the condylar head near the 12 o'clock position.

The retro-discal tissue

This is the posterior disk attachment and is also known as the bilaminar zone. It divides into an upper (stratum superior) and a lower band (stratum inferior). This part is quite loose which allows the articular disc to move when opening and closing the mouth[36].

The bilaminar zone is highly vascularized and innervated and can play an important role in pain in the TMJ.

Joint capsula

The joint capsule (capsula articularis) encloses the TMJ. It is composed of a thin, fibrous membrane (stratum fibrosum) with an internal lining of synovial membrane (stratum synovium). The synovial membrane consists of a cell-rich connective tissue which is highly vascularized and innervated. The synovial membrane can become inflamed (synovitis). Causes of this can be injury (trauma), inflammation and / or infection.

The upper part of the joint capsule is attached to the mandibular fossa and the lower part is attached to the condylar neck (collum mandibula). As mentioned above, the joint capsule is also attached to the articular disc. The lateral part of the capsule is reinforced by the lateral ligament.

Synovial fluid

The synovial membrane produces a highly viscous joint fluid called synovial fluid. This has several important functions, such as lubrication, stress absorption, preventing friction and transporting nutrients to the articulating surfaces. The synovial fluid contains, among other things, hyaluronic acid and lubricin, which has a lubricating effect on the joint surfaces and facilitates movement of the TMJ. The viscosity of the synovial fluid depends on both the concentration and the molecular weight of hyaluronic acid. Synovitis can lead to increased production and accumulation of synovial fluid (hydrops). This can lead to increased pressure and tension in the joint capsule which in turn can result in swelling and pain. The viscosity and lubricity of the synovial fluid can also be changed by hydrops. Normal synovial fluid is clear, but in inflammatory reactions in the joint (arthritis) it can become unclear.

1.3.2 Chewing muscles

There are several muscles involved in the function and movement of the TMJ, but we have four muscles on each side, which are considered as the chewing muscles: masseter muscle (musculus masseter), temporal muscle (musculus temporalis), lateral pterygoid muscle (musculus pterygoideus lateralis) and medial pterygoid muscle (musculus pterygoideus medialis).

The **lateral pterygoid muscle** is anatomically connected to the TMJ. It is divided into superior part and inferior part. The superior part (musculus pterygoideus lateralis superior) originates from the greater wing (ala major ossis sphenoidalis) of the sphenoid bone (os sphenoidale) and attaches to the joint capsule in the TMJ. The muscle fibers also pass through the joint capsule and attach to the anterior part of the articular disc. The main function is to keep the articular disc stable when the mandible is in motion.

1.3.3 Function and movement

The function and movement of the TMJ is complex and requires the muscles involved to work in a dynamic interaction. The four main chewing muscles are described in chapter 1.3.2. However, the small neck and tongue muscles as well as TMJ related ligaments are also involved. The small neck and tongue muscles as are considered as the accessory masticatory muscles and include: buccinator muscle, suprahyoid muscles (digastric muscle, mylohyoid muscle, and geniohyoid muscle), and infrahyoid muscles (the sternohyoid, sternothyroid, thyrohyoid and omohyoid muscle). The accessory masticatory muscles are especially important in opening of the mouth, in contrast to the masticatory muscles that mainly are involved in closing of the mouth.

Talking, chewing, kissing and yawning are all examples of activities that require movement and function of the TMJ. This dynamic interaction is composed of three basic movements: *hinge movement, sliding movement (translation) and rotation*. During opening of the mouth, the condyle rotates and translates downward and forward;

simultaneously, a hinge-like, rotatory movement occurs with the superior surface of the condyle against the inferior surface of the disc. The extent of normal condylar translation varies considerably. In most individuals, at maximal opening, the condyle moves down and forward to the articular eminence or slightly anterior to it. Reduced condylar translation, in which the condyle has little or no downward and forward movement and does not leave the mandibular fossa, is seen in patients who clinically have a reduced mouth opening. If a superior movement also occurs anterior to the articular eminence, anterior locking or dislocation of the condyle may occur.

1.3 Osteoarthritis in the temporomandibular joint

1.3.1 Definition and nomenclature

OA in the TMJ can be defined as a degenerative disorder involving the joint characterized by deterioration of articular tissue with associated osseous changes in the condyle and/ or articular eminence [39].

The nomenclature of degenerative disorder in the TMJ has not been consistent and has frequently been discussed in the literature for the last decade. The terms osteoarthrosis, osteoarthritis and degenerative joint disease have all been used for the same condition. The term osteoarthritis is well known and used in medical literature as well as in textbooks on TMJ/TMD[37, 40] and multiple papers concerning the topics. The term osteoarthritis was also used in the original Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) edited by Dworkin and LeResche [41]. In 2014 a revised version was published; The Diagnostic Criteria for Temporomandibular Disorders (DC/TMD), by Schiffman et al [39]. In this version, the nomenclature was changed. The former diagnosis of osteoarthritis by the RDC/TMD was now dually coded as degenerative joint disease (DJD) and joint pain (ie, arthralgia). According to DC/TMD osteoarthrosis and osteoarthritis are both subtypes of degenerative joint disease only distinguished by the presence or absence of arthralgia.

In this thesis the term temporomandibular osteoarthritis (TMJ-OA) will be used.

1.3.2 Clinical features and diagnosis

TMJ-OA can appear with a wide range of clinical features, varying from no subjective symptoms to substantial joint pain, dysfunction, dental malocclusion and reduced health-related quality of life [42]. The large variation in symptomatology should be further explored.

Clinically it may be challenging to differentiate TMJ-OA from other TMJ-related conditions. According to the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) the clinical criteria for TMJ-OA is subjective experience of TMJ noises the last 30 days or during exam AND objective detection of crepitus during clinical examination. According to Schiffman et al, the validity of the clinical criteria is low without imaging (sensitivity 0.55 and specificity 0.61) [39].

1.3.3 Epidemiology

The reported prevalence of TMJ-OA varies substantially in the literature. These variations can be explained by differences in research population, inclusion criteria and diagnostic assessment in the epidemiological studies. In a recent systematic review and meta-analysis, the prevalence of TMJ disorders among the general population was evaluated using research diagnostic criteria for temporomandibular disorders (RDC/TMD) and DC/TMD [39, 41]. The review showed that the prevalence of TMJ-OA was 9.8% [43]. It is important to emphasize that this figure was almost exclusively based on clinical studies which have poor sensitivity to detect OA in the TMJ, compared to imaging [39].

As discussed in chapter 1.2.3, both age and gender are considered the strongest risk factors for OA in all joints, which also has been demonstrated for the TMJ [44-46]. According to Alexiou et al., progression and severity of osseous changes in condylar head and mandibular fossa are increasing with age[44]. In older age groups, patients are expected to have more frequent and severe progressive degenerative bony changes due to the development of TMJ-OA, than patients in younger age groups. In symptom-free

individuals, radiographic evidence of OA of the TMJ occurs in 14% to 44%. However, clinical evidence of the disease occurs in only 8% to 16% of the population.

Dos Anjos et al. demonstrated that women have a greater predisposition to degenerative bone changes in the TMJ and that the prevalence of degenerative bone changes increases with age, except for patients over 80 years [45].

Alzahrani et al found that female patients had a higher prevalence and severity of TMJ-OA than male patients. The prevalence and severity of TMJ-OA increased with age, with peaks in the fifth and seventh decades of life[46].

1.3.4 Etiology and pathogenesis

The pathogenesis of TMJ-OA may differ from OA in other joints, as for example knee or hip, which is closely related to the combination of aging, obesity, and overload [47]. However, overload of the TMJ, has been considered one of the main causes for TMJ-OA [48-50] but in most cases TMJ-OA is difficult to attribute to overload or overweight. Therefore, the causes of impaired condylar cartilage in the TMJ remain unclear. Increasing attention has focused on the inflammation and remodeling of subchondral bone, but the pathogenesis of TMJ-OA remains controversial and unclear.

A study found that low condylar bone quality was significantly correlated with TMJ-OA development and that condylar bone mineral density and bone volume fraction can be used together as a potential diagnostic tool for TMJ-OA [51]

TMJ-OA is classified as a low-grade inflammatory arthritic condition, as opposed to rheumatoid arthritis (RA), which is classified as a high-inflammatory condition[52]. Several inflammatory cytokines, including Interleukin (IL)–12, IL-1β, IL-6, and tumor necrosis factor (TNF)–α are increased in the synovial fluid of patients with TMJ-OA [53, 54]

A review by Wang et al from 2015 summarizes the current understanding of mechanisms underlying the pathogenesis of TMJ-OA [42]. The main conclusions regarding pathology of TMJ-OA in this review are:

- Inflammatory cytokines, including IL-1β and TNF-α, mediate the imbalance in the metabolism of articular chondrocytes during the progression of TMJ-OA. Chronic inflammation may deteriorate the adaptive capability of the TMJ.
- Numerous studies have indicated that subchondral bone plays an important role in TMJ-OA pathology.
- The relationships among inflammation, cartilage erosion, and subchondral bone destruction remain unclear. Mechanical sensing of the articular cartilage and subchondral bone may contribute to the understanding of TMJ-OA pathogenesis but associated molecular mechanism and signal pathways are lacking.

A lot of studies have been done in the search of understanding the etiology of TMJ-OA. One study suggests a strong association between condylar bone loss and development of TMJ-OA. The authors suggest that condylar bone mineral density and bone volume fraction can be used together as a potential diagnostic tool for TMJ-OA [51]. Another theory is that the remodeling capacity of TMJ fibrocartilage decreases with age[55]. Therefore, it is possible that, with age, wear and tear of the TMJ will exceed the repair and remodeling capacity of the body, resulting in degeneration.

The association between TMJ-OA and disc displacement has been and still is extensively discussed in the literature [56]. A strong association has been demonstrated both in autopsy studies [57-59] and in clinical studies [60-66]. Therefore, it is widely assumed that disc displacement may be a precursor to TMJ-OA. Some authors have proposed that disc displacement may be a consequence of TMJ-OA rather than its cause[67]. Other studies have indicated no significant association between disc displacement and the onset of TMJ-OA[68].

TMJ-OA may also appear secondary to a number of conditions such as trauma, joint surgery, and inflammatory arthritis, as for example RA and juvenile idiopathic arthritis (JIA) [48, 69].

Several researchers have tried to describe the natural course of disease for TMJ-OA [48, 67, 70]. Three stages of disease have been proposed for TMJ-OA: *early phase*, intermediate *phase,* and *late phase*. The latter is the stage at which there is no degenerative activity, and the joints are said to be stable or in the "burnout phase".

1.3.5 Management

There is a lack of updated evidence-based guidelines on TMJ-OA intervention. The latest Cochrane review "*Interventions for managing osteoarthritis in the temporomandibular joint"* made by de Souza et al was published over a decade ago, in 2012[52]. According to the Cochrane report the management strategies either aim to decrease symptoms, stop progress of the disease, or restore the functions. The management strategies listed in this review are divided into four subgroups: (a) non-invasive, (b) minimally invasive, (c) invasive/surgical modalities and (d) salvage modalities. Details are presented in **Table 1.** Despite the wide range of therapeutic options available, de Souza et al. only included a few trials providing data for comparisons of non-surgical and minimally invasive surgical modalities.

The authors compared sodium hyaluronate with corticosteroids, diclofenac sodium with occlusal splints, and glucosamine sulfate with ibuprofen, and found no important differences when comparing the non-surgical modalities. Although diclofenac sodium (e.g. Voltaren) showed similar benefits when compared with occlusal splints in terms of pain and complications at 3 months. When comparing glucosamine sulfate versus ibuprofen, glucosamine was as effective as ibuprofen in terms of pain, discomfort and jaw movements, according to one of the trials.

Table 1: Therapeutic options in the management of TMJ-OA [52, 71]		
Non-invasive	• Occlusal splint therapy	Stabilization splint, orthotics
	• Medication	NSAIDS, muscle relaxants
	• Physical therapy	Therapeutic exercises, massage, ultrasound, manual therapy
Minimally invasive	• Intra-articular injections	Hyaluronic acid injection, corticosteroid injection
	• Arthroscentesis	
	• Arthroscopic surgery	
Invasive/surgical modalities	• Arthroplasty	Autogenous hemiarthroplasty, alloplastic hemiarthroplasty
	• Osteotomy	
Salvage modalities	• Total joint replacement	Autogenous, alloplastic

Intra-articular injections with sodium hyaluronate appear to be as effective as other modalities. However, TMJ pain seems to be slightly less after 6 months following injections of sodium hyaluronate, as well as TMJ sounds immediately after treatment.

Wang et al. investigated the understanding of the pathogenesis and treatment of TMJ-OA [72]. One of the main conclusions in this review was that most patients with TMJ-OA who have pain are treated effectively with NSAIDs or arthrocentesis. The authors suggested that disease-modifying OA drugs preventing the progression of cartilage degradation and subchondral bone damage should be further explored.

In a more recently published study (2020), Song et al investigated the clinical features of TMJ-OA patients. Longitudinal osseous changes of the TMJ condyle and their interrelationships were analyzed to verify factors and treatment modalities that assist long-term TMJ-OA improvement[68]. Occlusal stabilization splint therapy and nonsteroidal anti-inflammatory drug administration showed a significant effect on improving the prognosis of TMJ-OA.

1.4 Imaging of osteoarthritis in the temporomandibular joint

In a historical perspective conventional/ plain radiography was the only option of choice in imaging of the TMJ. The projections that classically used to be recommended for TMJ imaging were transcranial, transpharyngeal, and transorbital radiographs. None of these projections are currently recommended for TMJ evaluation [73]. Over the last 30 years both the use and perceived value of most of these techniques have been declining, proportional to the development of cross-sectional imaging. Panoramic radiography is the only conventional method to be further discussed in this thesis.

The choice of imaging technique always depends on the specific clinical problem, whether hard or soft tissues will be imaged, radiation dose, cost, availability of the imaging technique, and the amount of diagnostic information provided by the technique. Computed tomography (CT) has been demonstrated as the superior method in imaging of bony changes in TMJ-OA [74]. The last decade it has also been convincingly evidenced that the diagnostic accuracy of CBCT for is comparable with CT[75] . MRI is the modality of choice in imaging of soft tissues of the joint.

Ultrasonography is a modality also used in both diagnostics and treatment of TMJ pathology [37], but will not be further discussed in this thesis.

1.4.1 Panoramic radiography

Panoramic radiography provides an image of the complete mandible and the maxilla, including the bony components of the TMJ. This technique is more available in primary dental care facilities. It is widely used, less expensive and contributes to lower radiation dose.

Panoramic radiography is useful for providing a broad overview of the TMJ and surrounding structures, and for some patients, this could be the only imaging technique required before conservative therapy is initiated. As a result of superimposition by the skull base and zygomatic arch, only larger changes of TMJ-OA may be identified in the condyles, such as extensive erosions and/ or large osteophytes[76]. A disadvantage with

panoramic radiography is therefore that mild osseous changes may be missed. For these reasons, when a detailed assessment of the joint structures is desired, the panoramic view should be supplemented.

In a study comparing panoramic radiography and MRI with CT, about 75 % of CT-assessed OA was not detected with panoramic radiography [74].

It can be concluded that with panoramic imaging we may detect large abnormalities of the mandibular condyles, but minor abnormalities can easily be missed. The shape of the condyle should be considered with caution regarding normalcy versus pathology.

1.4.2 Computed Tomography

Computed Tomography (CT) produces cross-sectional images of the body part of interest. A CT scanner consists of an x-ray tube that emits a finely collimated, fan-shaped x-ray beam directed through a patient to a series of scintillation detectors or ionization chambers. These detectors measure the number of photons that exit the patient. By using advanced image reconstruction mathematics, the information from the CT scanner can be used to construct a cross-sectional image of the patient [33].

CT is an excellent imaging modality to visualize the bone changes/ bone abnormalities that characterize TMJ-OA [77, 78]. Magnetic Resonance Imaging (MRI) has for decades been recommended for examination of the TMJs in TMD patients if imaging is required [79]. This is because MRI is the only method that can visualize both the soft tissues and bone structures. CT is generally accepted as superior to MRI, regarding imaging of the bony parts of the TMJ. The diagnostic validity of CT and MRI in detecting TMJ-OA by has been compared, using the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) by Ahmad et al [74]. The reliability of the radiologists on diagnosing hard tissue status was fair (k=0.47) when using Proton Denisty (PD) MR-images. Reliability was good when diagnosis of hard tissue status was conducted using CT images (k=0.71), almost reaching the threshold for excellent reliability (k=0.75).

CT imaging is capable of some visualization of soft tissues. The articular disc is not adequately visualized with this modality [33].

1.4.3 Cone Beam Computed Tomography

In cone beam computed tomography (CBCT), an X-ray beam in the form of a cone is used to obtain a sequence of several hundred X-rays during a 180- or 360-degree rotation of the tube around patient's head [37]. Image resolution depends on voxel size—the smaller a voxel is, the higher image resolution is obtained. Voxels in CBCT are isotropic, i.e., cubical with all margins equal in contrast to CT where voxels are anisotropic (of different heights depending on the purpose of examination). Voxel size in CBCT varies from 0.05 to 0.4 mm, and its choice is related to the aim of the imaging study [37].

CBCT is increasingly used to assess the TMJ. It is convincingly documented that the diagnostic accuracy of CBCT, with lower radiation dose, is comparable with CT for TMJ diagnostics [80]. CBCT has an acceptable accuracy for diagnosing osseous abnormalities with fairly high sensitivity (in the range 0.7-0.9), although smaller cortical defects might be missed. In most studies, high specificity was also reported. However, it was emphasized that there are differences in image quality depending on imaging protocol and CBCT device.

1.4.4 Magnetic Resonance Imaging

In MRI, short radiofrequency (RF) pulse is used to produce the soft tissue images instead of the other imaging techniques using ionizing radiation. To make an MR image, the patient is first placed inside a large magnet. This magnetic field causes the nuclei of many atoms in the body, particularly hydrogen, to align with the magnetic field. The scanner directs a RF pulse into the patient, causing some hydrogen nuclei to absorb energy. When the RF pulse is turned off, the stored energy is released from the body and detected as a signal in a coil in the scanner. This signal is used to construct the MR image, which basically is a map of the distribution of hydrogen ([81].

MRI has been considered to be the best modality for visualizing soft tissue components of the TMJ and is the only method that directly depicts the position and condition of the disc [82]. The most common protocols used for MR imaging evaluation of the TMJs are

T1-weighted imaging or PD in the closed and open mouth positions, and T2-weighted imaging in the closed and open mouth positions. T1and PD show the structural and positional morphology of the TMJ components. T2-weighted imaging facilitates detection of abnormal fluid, such as in joint effusion or bone marrow edema. Intravenous contrast may be used in suspected inflammatory disorders (such as rheumatic diseases) or in suspected malignancy[83].

1.4.5 Imaging characteristics

As mentioned in 1.4.2 and 1.4.3 both CT and CBCT are excellent imaging modalities to visualize bone abnormalities. Imaging characteristics of TMJ-OA were reported early in the 1980s [77], and CT criteria for the diagnosis were suggested by Koyama et al [78]. Comprehensive and well-defined image criteria for TMJ-OA were given by Ahmad et al [74]. The criteria can be used on panoramic, CT/CBCT and MRI images and the osseous diagnosis is given with imaging signs of deformation due to subcortical cyst, surface erosion, osteophyte, and/or generalized sclerosis. Ahmad et al. defined the imaging signs as follows: osteophyte: marginal hypertrophy with sclerotic borders and exophytic angular formation of osseous tissue arising from the surface; subcortical sclerosis: any increased thickness of cortical plate in load-bearing areas relative to adjacent non load-bearing areas; subcortical cyst: a cavity below the articular surface that deviates from normal marrow pattern; surface erosion: loss of continuity of articular cortex; articular surface flattening: a loss of the rounded contour of the surface; and generalized sclerosis: no clear trabecular orientation with no delineation between the cortical layer and the trabecular bone that extends throughout the condylar head.

TMJ-OA may show productive features (osteophyte formation, sclerosis) or destructive features (erosion, subcortical cyst), in addition to remodelling (flattening). The TMJ-OA may be predominantly bone-productive, bone-destructive or, it may show a combination of both. Additional findings like loose calcified bodies, are, according to Ahmad et al, only a sign of OA when other features of OA are present.

MRI may also show inflammatory features such as effusion and bone marrow abnormalities. In addition, enhancement of the synovial membrane after intravenous

injection of contrast may also be seen, similar to contrast enhancement in joints with RA and related diseases [84, 85]. Osteonecrosis has also been documented in the TMJ with OA[86].

1.1.3 Recommendations for imaging of osteoarthritis in the TMJ

The American Academy of Oral and Maxillofacial Radiology and the American Academy of orofacial pain have recently (2022) published new recommendations for imaging of the TMJ [87]. One of the chapters in this position paper concerns the recommendations for arthritic diseases of the TMJ:

"**CT imaging, preferably CBCT, should be used to evaluate osseous changes in patients with suspected TMJ arthritis. Panoramic radiography has a limited role in establishing arthritic changes".**

It is also emphasized in the position paper, that although both MDCT and CBCT are equivalent for osseous assessments, CBCT exposes the patient to lower amounts of radiation, and thus CBCT is the preferred modality in imaging of TMJ-OA. According to this position paper MRI provides valuable information about the soft tissue components of the TMJ, including the shape, location, and size of the articular disc as well as the presence of fluid effusion. The osseous details are comparatively poor on MRI and current MRI technology cannot fully replace CBCT or MDCT for osseous assessment.

1.1.4 Differential diagnosis

There are various conditions that are similar to TMJ-OA and must be considered as differential diagnoses. As mentioned in chapter 1.3.2. TMJ-OA can appear with a wide range of clinical features. The validity of the clinical criteria, with crepitation/ joint sounds as the only criterion, is low without imaging (sensitivity 0.55 and specificity 0.61) [39]. Thus, clinical diagnostics underestimate the occurrence of OA compared to CT/CBCT diagnostics.

In the first clinical assessment of patients with symptoms from the TMJ, it is important to consider all TMD related conditions. The DC/TMD taxonomic classification for TMDs

is divided into four major groups: TMD, masticatory muscle disorders, headache and assorted structures. Of these the TMD group includes two subtypes of joint pain, three subtypes of joint disorders and seven subtypes of joint disease [88]. Depending on the clinical symptoms and features, the different disorders in **Table 2** should be considered as differential diagnosis.

Table 2 Temporomandibular joint disorders[88]
a. Joint Pain
i. Arthralgia
ii. Arthritis
b. Joint Disorders
i. Disc disorders
1. Disc displacement with reduction
2. Disc displacement with reduction with intermittent locking
3. Disc displacement without reduction with limited opening
4. Disc displacement without reduction without limited opening
ii. Hypomobility disorders other than disc disorders
1. Adhesions/adherence
2. Ankylosis
a. Fibrous
b. Osseous
iii. Hypermobility disorders
1. Dislocations
a. Subluxation
b. Luxation
c. Joint diseases
i. Degenerative joint disease
1. Osteoarthrosis
2. Osteoarthritis
ii. Systemic arthritides
iii. Condylysis/idiopathic condylar resorption
iv. Osteochondritis dissecans
v. Osteonecrosis
vi. Neoplasm
vii. Synovial chondromatosis
d. Fractures
e. Congenital/developmental disorders
i. Aplasia
ii. Hypoplasia
iii. Hyperplasia

As mentioned in Chapter 1.4.5. imaging characteristics of TMJ-OA can have a spectrum of appearances ranging from extensive erosions (bone destructive component) to substantial subchondral sclerosis and osteophyte formation (bone productive component). A more erosive appearance may simulate inflammatory arthritides, such as RA. If bone destruction is prominent with little or no bone proliferation, the diagnosis can be erosive TMJ-OA. Such a condition can hardly be distinguished from RA or other inflammatory arthritides [75].

Psoriatic arthritis and ankylosing spondylitis are both examples of seronegative, systemic arthritides that may affect the TMJs ([33], and sometimes can be difficult to differentiate from TMJ-OA. Psoriatic arthritis occurs in patients with psoriasis of the skin, with inflammatory joint disease occurring in 7% of patients. Ankylosing spondylitis occurs predominantly in males and progresses to spinal fusion. TMJ imaging changes seen in these disorders may be indistinguishable from changes caused by RA, although occasionally a profound sclerotic change is seen in psoriatic arthritis [33]. A more proliferative appearance with extensive osteophyte formation in the TMJ may simulate a benign tumor, such as osteochondroma rather than TMJ-OA [33].

2 General aims and specific research questions

2.3 General aims

The general aims of this thesis were to investigate the prevalence and characteristics of CBCT defined TMJ-OA and related symptoms in older adults.

2.4 Specific research questions

- What is the frequency of CBCT-defined TMJ-OA in a cohort of older adults with hand-OA? (Paper I)
- What is the frequency of self-reported TMJ-related symptoms and clinical findings, and their relationship with CBCT-defined TMJ-OA in this cohort of older adults (Paper I)?
- What are the radiological characteristics of the TMJ-OA in older adults with hand-OA (paper II)?
- What is the prevalence, gender difference and characteristics of imaging signs of TMJ-OA) by means of CBCT in 65-year-old Oslo citizens (paper III)?
- What is the frequency of temporomandibular disorder (TMD) - related symptoms in a population-based sample of 65-year-old Oslo citizens? (paper III)
- Are there any differences in frequencies and radiological characteristics of TMJ-OA between the groups of older adults with hand-OA and the 65-year-old Oslo citizens (comparing results from paper I, II and III)?

3 Material, methods and methodological considerations

3.3 Study design

The results in the current thesis are based on data from two observational studies with cross-sectional study design.

3.4 Study population

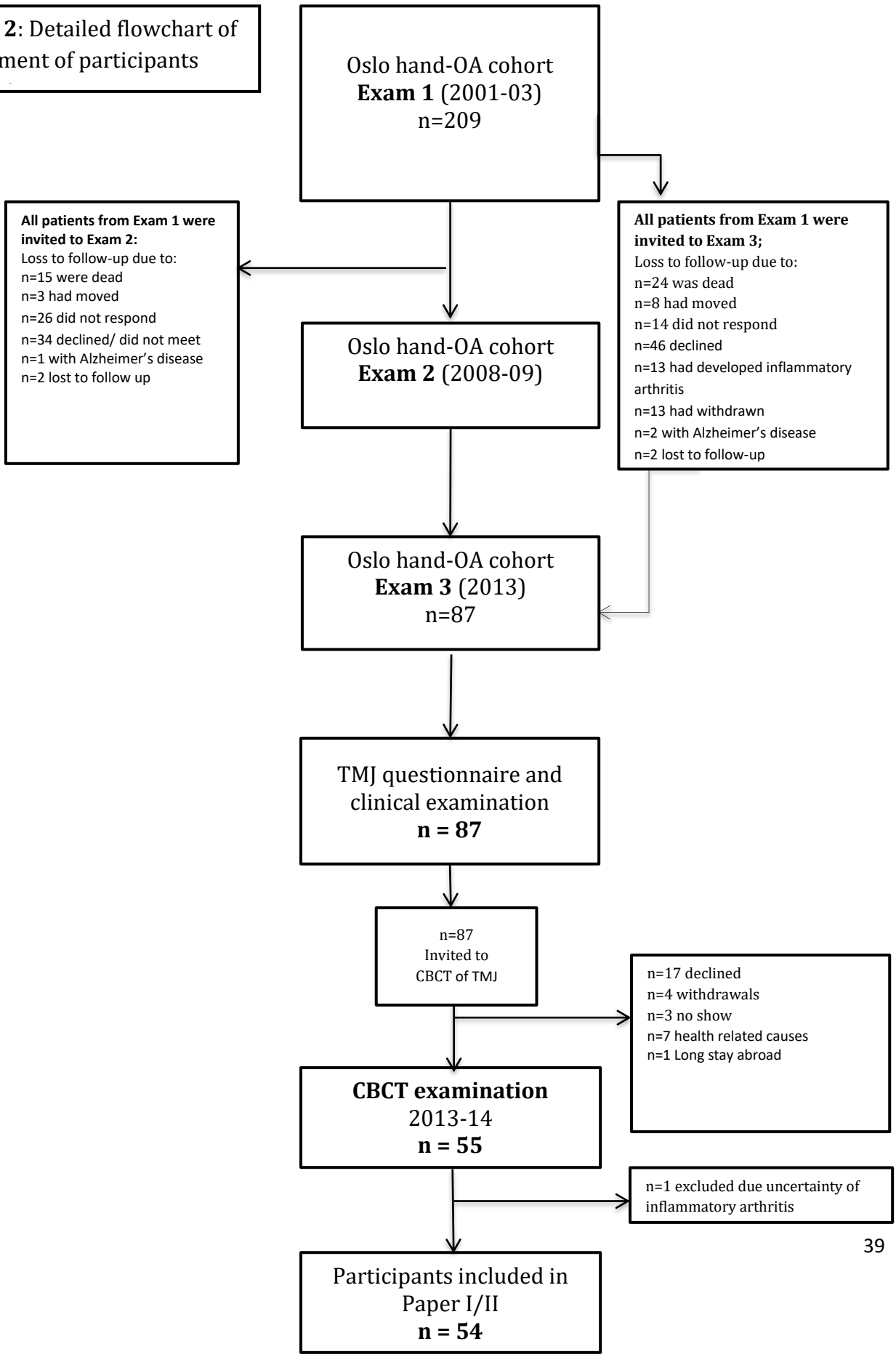
3.4.1 Paper I and II

This project was performed as a collaboration between the Department of Maxillofacial Radiology, Institute of Clinical Dentistry, Faculty of Dentistry, University of Oslo and the Department of Rheumatology, Diakonhjemmet Hospital, Oslo, and the participants were recruited from The Oslo Hand-OA cohort.The Oslo hand-OA cohort was initiated at

Diakonhjemmet Hospital in 2000. The intention of the project was to evaluate health-related quality of life in patients with hand-OA and to study the prediction of long-term outcomes. Patients between 50 and 70 years, who had been examined at the outpatient rheumatology clinic within the previous [89]2 years, were eligible for inclusion in the cohort if they had a diagnosis of hand-OA and no other rheumatic diseases. In total 275 eligible patients with hand-OA were identified, and 209 (76 %) patients consented to participate in the data collection when the Oslo hand-OA cohort was established in 2001.The baseline examinations were performed in 2001-2003. The patients were again contacted in 2008, and 128 of 209 (61%) met for a follow-up examination at Diakonhjemmet Hospital in the period 2008-2009. A second follow-up (10 years) was conducted in 2013, where 87 of 209 (42%) participated. The data collections in the studies of the Oslo Hand-OA cohort included questionnaires and clinical examinations concerning hand-OA as well as imaging (including conventional radiographs, MRI and ultrasonography). Details of patient recruitment and results from the studies of Oslo Hand-OA cohort are published in multiple papers and theses, among others [89-93].

The collaboration started at the follow up of the Oslo Hand-OA cohort in 2013. At this time, we included a questionnaire about facial symptoms and a clinical examination of the TMJs and related muscles. All the patients were in this context invited to participate in the project "Osteoarthritis in the TMJ in patients with hand-OA" at the Department of Maxillofacial Radiology, Faculty of Dentistry. Seventy of the 87 hand-OA patients consented to participate. Among those, 55 were examined and one was excluded due to a diagnosis of inflammatory arthritis. Thus, the resulting population in the project includes 54 hand-OA patients (6males, 48 females) with a mean age of 71.3 (range 61–83) years. This population is included in both Paper I and Paper II. Details of the patient recruitment and dropouts in paper I and paper II are shown in **Figure 2.**

Figure 2: Detailed flowchart of recruitment of participants



3.4.2 Paper III

This study was part of a larger study investigating oral health in 65-yr-old people in Oslo, Norway (the OM65-study). The participants were examined at the Research Clinic of the Institute of Clinical Dentistry, University of Oslo, between 26 February 2019 and 13 December 2019. The target population was 65-yr-old (born in 1954) residents of Oslo, Norway. According to Statistics Norway the total population of 65-yr-olds in Oslo in 2019 were 5413 individuals (2617 men, and 2796 women)[94]. Eligible individuals were randomly selected from the Norwegian tax registry, and invitation letters were sent to 1230 individuals. No later than 2 weeks after sending the invitation letters, the individuals were contacted by telephone and asked if they were interested in participating in the study[95].

The study in Paper III was performed at the Department of Maxillofacial Radiology, as a sub study of the interdisciplinary OM65-study. As a part of the OM65-study, all individuals underwent dental radiological examinations at the Department of Maxillofacial Radiology. During these examinations, a subsample of participants was randomly recruited to the present study, called OM65-TMJ. All participants in OM65-TMJ were recruited independently of TMJ related symptoms and were examined immediately after recruitment.

A total of 159 participants were included in Paper III: (86 (54 %) women, 73 (46 %) men). Among the 169 invited individuals (89 women, 80 men), 10 (6%) rejected or were rejected (three women, 7 men). A detailed flowchart of recruitment and reasons for rejection are shown in **Figure 3**.

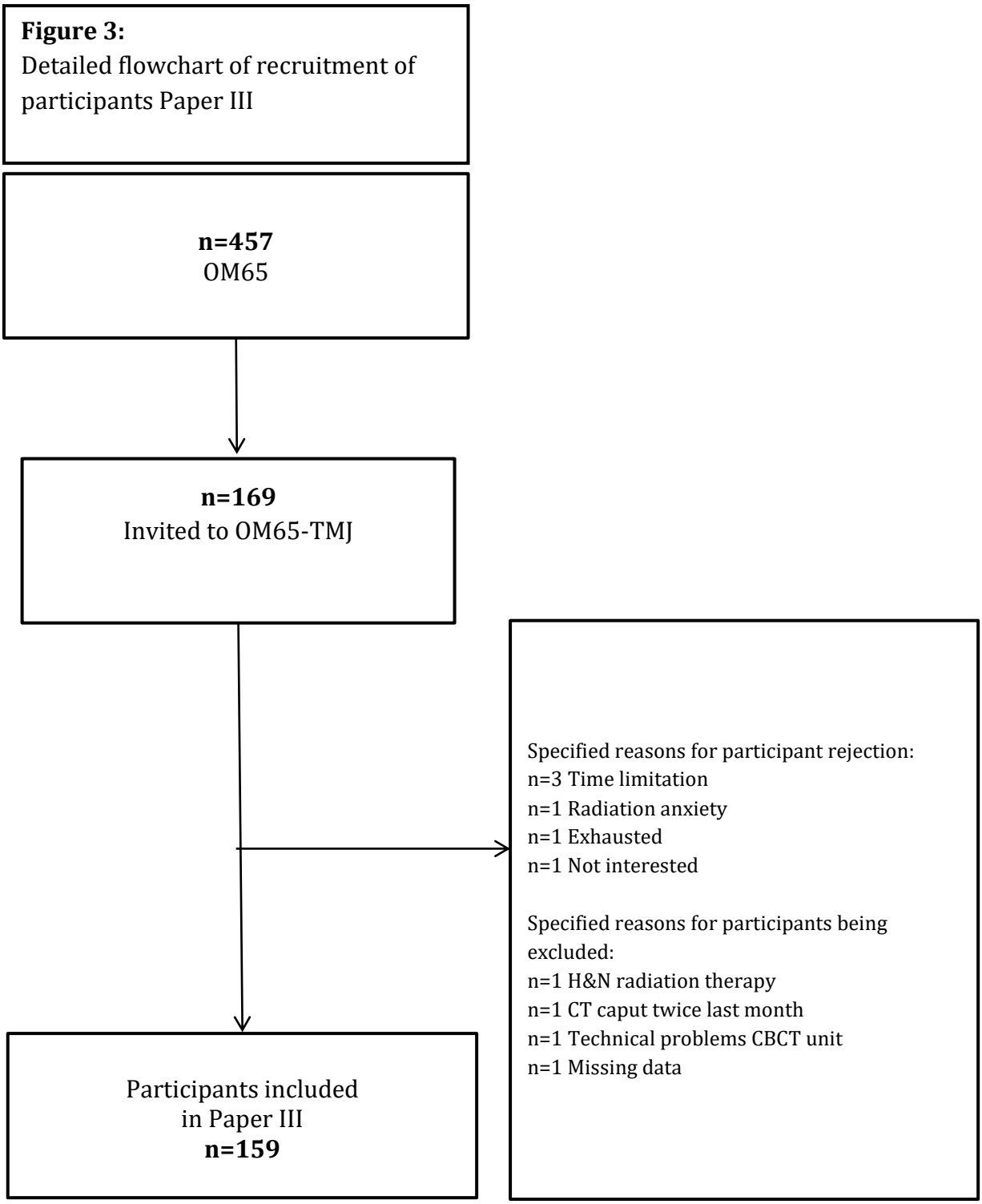


Figure 3:
Detailed flowchart of recruitment of participants Paper III
n=457
OM65
n=169
Invited to OM65-TMJ
Specified reasons for participant rejection:
n=3 Time limitation
n=1 Radiation anxiety
n=1 Exhausted
n=1 Not interested
Specified reasons for participants being excluded:
n=1 H&N radiation therapy
n=1 CT caput twice last month
n=1 Technical problems CBCT unit
n=1 Missing data
Participants included in Paper III
n=159

3.5 Data collection

Data collection for "Osteoarthritis in the TMJ in patients with hand-OA" (Paper I and II) was performed between June 2013 and March 2014. The clinical assessment consisted of a questionnaire and a clinical examination that was included as part of the hand-OA examination protocol at Diakonhjemmet Hospital. This part was performed by fellow PhD-student Anna-Karin Abrahamsson. The radiological assessment was implemented in another session at the Department of Maxillofacial Radiology (Faculty of Dentistry). This part was performed by Margareth Kristensen Ottersen and radiographer Bård Magne Borge. A broad spectrum of variables was collected from the individuals in the Oslo Hand-OA cohort, including demographic and hand-OA related variables. Paper I, II and the present thesis reports TMJ related variables and the most important demographic.

Data collection for "OM65-TMJ" (Paper III) was performed between 23 April 2019 and 13 December 2019. Both clinical and radiological assessment were performed at the Department of Maxillofacial Radiology (Faculty of Dentistry). The clinical assessment was performed with the participant sitting in the CBCT unit as a combination of a face-to-face questionnaire and registration of some clinical parameters. Clinical assessment was performed by Margareth Kristensen Ottersen.

A broad spectrum of variables was collected from the participants in the OM65, including demographic and health related variables. Paper III and the present thesis reports the relevant variables and the most important demographic. All variables used in Paper I, II, II and the present thesis are listed in **Table 3.**

Table 3: Assembled list of the variables used in Paper I, II and II			
	Paper I (n=54)	**Paper II (n=54)**	**Paper III (n=159)**
Demographics			
Age	**x**	**x**	**x**
Sex	**x**	**x**	**x**
Education			
Self-reported outcome measures			
Author developed questionnaire about symptoms	**x**		
TMD Pain screener			**x**
3Q/TMD			**x**
Physical examination-based measures			
Masseter/temporalis muscle pain	**x**		
TMJ pain	**x**		
TMJ noises	**x**		
Maximum unassisted mouth opening	**x**		
CBCT based measures			
Bone change characteristics of TMJ		**x**	**x**
Diagnosis of TMJ-OA	**x**	**x**	**x**
Grading of TMJ-OA		**x**	**x**

3.5.1 Demographical and other background variables

Age, gender and some TMJ/health related parameters were reported in all studies (Paper I, II and III). All participants were asked about previous contact with the healthcare services due to jaw dysfunction and/or facial pain. In the data collection for Paper III smoking habits, profession, self-reported previous diagnosis of joint disease and specific location were registered, but not published. These results and additional self-reported health status and use of medications from participants in both study populations (I/ II, and III) are reported in this thesis.

3.5.2 Self-reported outcome measures

Symptom-questionnaire (paper I)-

The questionnaire about facial symptoms the last 30 days was included in a booklet of different questionnaires that were used in the hand-OA cohort. The patients answered the following questions: the experience of pain (at rest, mouth opening and chewing),

the experience of noise (clicking or crepitus) on jaw movement and previous contact with the healthcare system due to jaw dysfunction and/or facial pain. The first three questions were not side specific and were answered with “yes”, “no” and “no, but earlier in life”. The last question was answered “yes” or “no”. The questionnaire was developed by the authors based on questions from the RDC/TMD Patient History Questionnaire[96] (Appendix 1). The Norwegian translation of DC/TMD was not started at the time of the data collection for paper I and II.

TMD Pain screener (Paper III)

TMD pain screener is a simple, reliable, and valid self-report instrument from the Diagnostic Criteria for Temporomandibular Disorders (DC/ TMD), Axis 1. The TMD pain screener is used to assess the presence of any pain related TMD, to identify potential participants having TMD. Items 1 through 3A constitute the short version of the screening instrument, and items 1 through 3D constitute the long version. Participants answered the long version of a TMD pain screener, which contains six items assessing symptoms of pain related TMDs.

The questionnaire items include duration of pain in the jaw or temple area, presence of pain or stiffness in the jaw on waking, and activities that affect the pain, such as chewing hard food, jaw movements, jaw habits and other jaw activities.

An ***a*** response receives 0 points, a ***b*** response 1 point and a ***c*** response 2 points. The first item has scores of 0-2 (a=0, b=1, c=2), while the remaining items are scored simply as Ta=0, b=1. A sum is computed, and the total score ranges from 0 to 7. Score > 2 is considered to indicate pain related TMD.

A validated translation of the DC/TMD (including the TMD/ pain screener) to Norwegian was completed in 2016. The Norwegian version of the TMD pain screener was used in this study[97] (Appendix 2).

3Q/TMD (Paper III)

All participants in OM65 completed three validated screening questions for temporomandibular disorders (3Q/TMD) [98]. Most participants answered these questions in a questionnaire at home, prior to the clinical/radiological examinations. The 3Q/TMD includes questions on weekly jaw-face-temple pain (Q1), pain on function (Q2) and catching/locking of the jaw (Q3). In Paper III the 3Q/TMD were used to explore any potential TMD related selection bias in the recruitment of participants from OM65 to OM65-TMJ.

3.3.3 Physical examination-based measures

Physical examination-based measures were only used in Paper I. One dentist (AKA) performed the clinical examination according to the Complete specifications (protocol) for RDC/TMD (version: 2013)[99]. The dentist was self-instructed by the English version of the RDC/TMD protocol, which is shown to have almost the same diagnostic reliability as formal RDC/TMD training and calibration[100]. The examination included the following selected items: 1) absence or presence of tenderness upon palpation for musculus masseter, musculus temporalis and the TMJ, 2) TMJ noises (clicking, crepitus) and 3) maximum unassisted mouth opening. All registrations were side specific. Reduced mouth opening was defined as < 40 mm, including vertical overbite. Examination protocol is shown in Appendix 1.

In Paper I DC/TMD was used to define clinical TMJ-OA, which requires presence of crepitus/sounds registered by both examiner and patient. This registration of crepitus was not side specific. Registration of crepitus was also done in the data collection for Paper III, but the results were not published. The results are discussed in this thesis.

3.3.4 CBCT based measures.

Osteoarthritis in the TMJ in patients with hand-OA (Paper I and II)

The CBCT scanning was performed at the Department of Maxillofacial Radiology, Institute of Clinical Dentistry, Faculty of Dentistry, University of Oslo by either resident in maxillofacial radiology (MKO) or radiographer (Bård Magne Borge, BMB). The CBCT

scans were performed from August 2013 until March 2014. See **Table 4**, for detailed imaging protocol for the CBCT scanning.

OM65-TMJ (Paper III)

The CBCT scanning of the participants was performed at the Department of Maxillofacial Radiology, Institute of Clinical Dentistry, Faculty of Dentistry, University of Oslo by specialist maxillofacial radiology (MKO) or radiographer (Alexander Bremnes, AB). The CBCT scans were performed from April 2019 until September 2019. Detailed imaging protocol for the CBCT scanning of Paper I/II and III are shown in **Table 4**.

Table: 4
Protocols for the CBCT scanning of TMJ

	Paper I/II	**Paper III**
CBCT unit	ProMax Mid 3D CBCT (Planmeca Oy, Helsinki, Finland)	3D Accuitomo, XYZ slice Tomograph, (J. Morita)
Tube current	8-10 mA	7-9 mA
Tube voltage	90 kV	85 kV
Rotation	200 ˚	360˚
FOV (Field Of View)	Ø200 mm x 60 mm	Ø140 mm x 50 mm
Voxel size	200 µm	150 µm
Scan time	14 s	17,5 s
Estimated DAP dose	622-785 mGy *cm^2	1430-1840 mGy *cm^2

Interpretation of CBCT images

The CBCT images in all papers (I, II and III) were interpreted in a similar way. They were viewed in axial, oblique sagittal and oblique coronal planes (perpendicular to and

parallel with the long axis of the mandibular condyle) in the multiplanar reformatted view of the software. Observers could adjust the brightness and contrast settings for the best display to mimic the routine diagnostic approach. All images were interpreted separately by two or three maxillofacial radiologists: Paper I and II (TAL, LZA and MKO), Paper III (LZA, MKO).

In both study populations a second image interpretation was made of randomly selected participants after 16 weeks. The re-interpretation was made by the same observers for intra-and inter-observer agreement analysis. The number of randomly selected participants was 15 in Paper I/II and 20 in Paper III. The CBCT examinations for the second interpretation were selected using a random number generator (RNG-Random Number Generator, Intemodino Group s.r.o., App Store

Bone change characteristics of TMJ

The diagnostic criteria described by Ahmad et al [74] were used in the analysis of bone change characteristics. Multislice-CT were by Ahmad et al back in 2009 considered the superior modality for the imaging of bone changes in the TMJ, hence the best imaging method for the diagnostic criteria. Later CBCT has been convincingly demonstrated to have the same diagnostic accuracy as Multislice-CT and is accepted for the use with the diagnostic criteria.

The scoring criteria for CBCT-based assessment of condylar head and fossa/eminence area were used. Each joint was evaluated, and the "worst case" scenario was scored when there were different findings in the different slices. Evaluation of the joints was recorded on a scoring form. Each scoring factor had a Yes/No option. For the condylar head, features to note were hypoplasia or hyperplasia, flattening of the articular surface, subcortical sclerosis or cyst, surface erosion, osteophytes, generalized sclerosis, loose joint bodies, and deviation in form. For the fossa, the criteria included flattening of the articular eminence, subcortical sclerosis, and surface erosion. Definitions of the scoring

criteria are listed in **Table 5**. All features listed in **Table 5** are reported in Paper II. In Paper III only the indeterminate features (articular surface flattening and subcortical sclerosis) and the crucial features (osteophyte, erosion, subcortical cyst and general sclerosis) are reported.

Table 5:
Hard tissue assessment of the TMJ using CBCT images according to Ahmad et al. [74]

Scoring option	Scoring criteria
Condylar head: (score Yes/No for each of the 11 criteria)	**Flattening:** A loss of the rounded contour of the surface.
	Subcortical sclerosis: Any increased thickness of the cortical plate in the load-bearing areas relative to the adjacent non-load-bearing areas.
	Subcortical cyst: A cavity below the articular surface that deviates from normal marrow pattern.
	Cortical erosion: Loss of continuity of articular cortex.
	Osteophyte: Marginal hypertrophy with sclerotic borders and exophytic angular formation of osseous tissue arising from the surface.
	Loose joint body: A well-defined calcified structure(s) that is not continuous with the disc or osseous structures of the joint.
	Deviation in form: Condylar deviation in form is defined as a departure from normal shape, such as concavity in the outline of the cortical plate, and not attributable to flattening, erosive changes, osteophytes, hyper or hypoplasia.
	General sclerosis: No clear trabecular orientation with no delineation between the cortical layer and the trabecular bone that extends throughout the condylar head.
	Bony ankylosis: Continuous osseous structure between the condyle and temporal bone associated with no discernable joint space and no translation of the condyle in the open mouth views.
	Condylar hypoplasia: Condylar morphology is normal, but the size is small from all dimensions
	Condylar hyperplasia: Condylar morphology is normal, but the size is large from all dimensions
Fossa/eminence (score Yes/No for each of the 3 criteria).	**Articular surface flattening:** A loss of the rounded contour of the surface.
	Subcortical sclerosis: Any increased thickness of the cortical plate in the load-bearing areas relative to the adjacent nonload-bearing areas
	Surface erosion: Loss of continuity of cortical margin.

Diagnosis of TMJ

Based on the hard tissue assessment, each TMJ was given a diagnosis based on the criteria by Ahmad et al. The TMJs were categorized as normal, indeterminate, or affected with OA. **Table 6** describes the diagnostic conclusions made, based on the hard tissue assessment by CBCT.

Table 6: Osseous diagnosis for the TMJ from based on CBCT imaging [74] (Scoring options are A, B or C as in table below)	
A **No osteoarthritis**	Normal relative size of the condylar head; and No subcortical sclerosis or articular surface flattening; and No deformation due to subcortical cyst, surface erosion, osteophyte or generalized sclerosis
B **Indeterminate for osteoarthritis**	Normal relative size of the condylar head; and Subcortical sclerosis with/without articular surface flattening; or Articular surface flattening with/without subcortical sclerosis; and No deformation due to subcortical cyst, surface erosion, osteophyte or generalized sclerosis.
C **Osteoarthritis**	Deformation due to subcortical cyst, surface erosion, osteophyte or generalized sclerosis.

Grading of TMJ-OA

The CBCT based TMJ-OA was also graded based on the system proposed by Ahmad and Schiffman[101]: Grade 1 when the joint displayed either a small osteophyte (< 2mm length), or a single small erosion (<2 mm in depth and width), or a single small subcortical cyst (<2 mm in depth and width); Grade 2 when the joint displayed a larger osteophyte (≥ 2mm length), and/or a larger erosion (≥ 2 mm in depth and width),

and/or a larger subcortical cyst (≥ 2 mm in depth and width), and/or two or more imaging signs of Grade 1.

3.4 Statistics

All statistical analyses in all papers and in the present thesis were performed using different versions of IBM SPSS (Statistical Package for Social Services, Chicago, IL, USA). Version 22.0 in Paper I, version 25 in Paper II and version 26 in Paper III.

In Paper I/II we used independent samples t-tests and Chi Square tests, to compare, age, body mass index (BMI), TMJ-related symptoms and clinical examination findings between recruited participants and non-participants and between participants with CBCT-defined TMJ-OA (uni-or bi-lateral) and participants with no/indeterminate for OA. Differences in proportions of TMJ-related symptoms and clinical examination findings in participants with CBCT-defined TMJ-OA vs no/indeterminate for OA were calculated with 95% confidence intervals (CIs). We calculated sensitivity and specificity of the clinical diagnosis using CBCT as reference.

In Paper II and Paper III Kappa statistics analysis was performed to determine consistency of interpreting the CBCT images within and between observers. For the reliability studies, OA ratings were dichotomized as either present (TMJ-OA) or absent (no-TMJ-OA or indeterminate for TMJ-OA). According to Fleiss et al11 κ values of <0.40 are considered to be poor, values from 0.40 to 0.75 to be fair to good, and values >0.75 to be excellent. For interobserver reliability, the agreement was evaluated pairwise, and a mean of these values gave the final κ value. Any disagreement between the observers was discussed until consensus was met and each joint got a final imaging diagnosis.

3.5 Legal and ethical considerations

The studies presented in this thesis are all conducted according to the ethical principles of the Declaration of Helsinki. All participants in Paper I-III gave their written informed consent prior to entering the studies and had the possibility to withdraw their participation at any time throughout the duration of the project. After the CBCT examinations, all participants received short-written feedback about the preliminary findings in the TMJs, but also incidental findings of relevance were noted. If necessary or wanted by the participants, they were offered a CD with their CBCT examinations. In some cases, we found it necessary to make a full radiology report. All participants with findings requiring treatment were informed and encouraged to contact their dentist for further follow-up.

All studies were approved by the Regional Committee of Medical and Health Research Ethics (REC) of south-east Norway; (2011/1411, Paper I/II) and (2018/1383, Paper III). All data were stored, and analyses performed, in the TSD (Service for Sensitive Data, Centre for Information Technology Services, University of Oslo).

Ethical considerations concerning radiation protection:
All studies in this thesis are mainly based on diagnostic imaging leading to ionizing radiation. No exposure to ionizing radiation can be considered completely free of risk; hence, the use of radiation will always be accompanied by a responsibility to ensure appropriate protection.

All use of ionizing radiation in Norway are regulated by the Regulations on Radiation Protection and Use of Radiation (Radiation Protection Regulations, 2017)[102] which is legislated in the Act on Radiation Protection and Use of Radiation (2000)[103]. The purpose of the regulations is to prevent harmful effects of radiation on human health and contribute to the protection of the environment. The national regulations of radiation protection in Norway are to a large extent based on recommendations of the

International Commission on Radiological Protection (ICRP). This is an independent, international organization with volunteer members who are leading scientists and policymakers in the field of radiological protection.

The latest version of ICRP recommendations of radiation protection were published in 2007, known as ICRP Publication 103[104]. The three main principles of the ICRP recommendations are:

The principle of justification: Any decision that alters the radiation exposure situation should do more good than harm. This means that, by introducing a new radiation source, by reducing existing exposure, or by reducing the risk of potential exposure, one should achieve sufficient individual or societal benefit to offset the detriment it causes.

The principle of optimization of protection: the likelihood of incurring exposures, the number of people exposed, and the magnitude of their individual doses should all be kept as low as reasonably achievable, taking into account economic and societal factors. This means that the level of protection should be the best under the prevailing circumstances, maximizing the margin of benefit over harm. In order to avoid severely inequitable outcomes of this optimization procedure, there should be restrictions on the doses or risks to individuals from a particular source (dose or risk constraints and reference levels).

The principle of application of dose limits: The total dose to any individual from regulated sources in planned exposure situations other than medical exposure of patients should not exceed the appropriate limits recommended by the Commission.

The principles of optimization and dose limitation are to a large extent achievable in medical research. On the contrary, the principle of justification can be challenging. The studies in the present thesis are mainly based on radiological examinations of volunteer participants, independent of clinical findings. Are these radiological examinations then justified?

Volunteers make a substantial contribution to medical research. As early as in 1992, ICRP discussed the ethical and procedural aspects of the participation of volunteers in medical research and its justification[105] and states as follows: *Whereas diagnostic or therapeutic irradiation, when competently administered by a qualified physician, carries an actual or potential health benefit to the patient, almost always exceeding the potential detriment, this may not necessarily be so in the case of an exposure for research purposes with volunteers. In the latter situation the potential benefit to society by increase of knowledge, must be weighed against the potential harm to the exposed individual.*

The Declaration of Helsinki[106], and the 2007 ICRP Recommendations[104] require that in such a case exposure to ionizing radiation of individuals participating in research may take place only on a voluntary basis (informed consent).

Section 39 in the Norwegian Radiation Protection Regulations concerns the principle of justification and says: *"The medical use of radiation is justified if the total diagnostic or therapeutic benefits, for the individual and society, is higher than the disadvantages involved with the use of radiation. The benefits and risks connected to alternative methods with the same purpose, involving little or no exposure to ionizing radiation, shall be evaluated".*

Based on both the recommendations of ICRP and the Norwegian Legislation the radiological examinations of the volunteers in the studies presented in this thesis are considered as justified, since the results of the studies will benefit to society by increase of knowledge.

It also has to be emphasized that all claims in Section 39 c) of the Norwegian Radiation Protection Regulations are fulfilled in all studies (I, II and III):

1) All exposure of ionizing radiation in medical research shall be evaluated by a regional ethical committee in order to implement the principle of justification

2) Research protocol for medical research should contain information on the type of radiation, extent of and expected radiation dose.

4 Summaries of results

4.1 Paper I

Frequency of temporomandibular joint osteoarthritis and related symptoms in a hand osteoarthritis cohort

A cross-sectional study was conducted on 54 older adults (mean (range) age 71.3 (61-83) years) from the Oslo hand-OA cohort. The frequencies of TMJ related symptoms, clinical findings and the diagnostic assessment of TMJ-OA were investigated by clinical examination or by CBCT. Results showed that self-reported TMJ symptoms found in and clinical findings were common, found in 24/54 (44%) and 50/54 (93%) respectively. However, only 13% had sought healthcare for TMJ-related issues. The majority (67%) of the individuals was given an imaging diagnosis of TMJ-OA, with one third affected bilaterally. Individuals with an imaging diagnosis of TMJ-OA self-reported more pain at mouth opening and joint sounds than those without. All individuals had normal jaw function capacity except one. Clinical examination demonstrated that registration of crepitus was the only clinical finding more common in individuals with imaging signs of TMJ-OA. Clinical diagnosis of TMJ-OA underestimated the frequency of TMJ-OA (sensitivity 0.42, specificity 0.93). The study revealed that CBCT-defined TMJ-OA was common in patients with hand-OA, suggesting that it could be part of generalized OA. Despite the high burden of TMJ-related symptoms/findings, only a few individuals sought healthcare.

4.2 Paper II

CBCT characteristics and interpretation challenges of temporomandibular joint osteoarthritis in a hand osteoarthritis cohort

In this cross-sectional study CBCT was used to investigate the radiological characteristics of TMJ-OA in 54 older adults (mean (range) age 71.3 (61-83) years) recruited from the Oslo hand-OA cohort.

Imaging signs of TMJ-OA were found in nearly half (49%) of the 108 joints analyzed. Bone productive changes such as osteophyte and sclerosis, in combination with flattening, were the most prominent features. The condylar region showed more frequent imaging signs than the fossa/eminence, with osteophyte formation on the condyle being the most frequent radiological sign of TMJ-OA (72%). The most common combination of imaging signs was osteophyte formation together with flattening of the condyle and fossa/eminence. Large osteophytes (≥ 2 mm) were the main reason for categorizing most (68%) of the OA joints as Grade 2. Erosive findings, such as surface erosion and subcortical cysts, were mostly found in joints categorized as TMJ-OA Grade 1 and were always seen in combination with bone-productive features. However, interpretation challenges, especially those related to subtle radiological findings led to a lower observer agreement, with mean values of 0.67 and 0.62 for inter- and intra-observer agreement, respectively.

The results demonstrated that that imaging signs of TMJ-OA in older adults with hand-OA mostly were characterized by bone productive abnormalities. The radiological features indicated a late-stage TMJ-OA in this population.

4.3 Paper III

Imaging signs of temporomandibular joint osteoarthritis in an urban population of 65-year-olds: a cone beam computed tomography study

Prevalence, gender differences and characteristics of CBCT signs of TMJ-OA were studied cross-sectional among 159 (86 women, 73 men) 65-year-old Oslo citizens. CBCT signs of TMJ-OA were found in 56/159 (35 %) of the participants, with unilateral findings in the majority 36/56 (64 %). We found a significant difference in frequency of TMJ-OA between women 40/86 (47%) and men 16/73 (22 %). On joint level CBCT signs of TMJ-OA were found in 76/318 (24 %). The majority, 46/76 (61%), were categorized as TMJ-OA Grade 2. The most frequent bone changes observed were articular surface flattening, condylar osteophytes, surface erosions, and subcortical sclerosis. Almost all joints with CBCT signs of TMJ-OA had bone productive findings, and CBCT signs of OA were more frequent in the condyle than in the fossa/eminence. There was no significant

difference in pain-related TMD or previous healthcare service contact between participants with and without CBCT signs of TMJ-OA. Participants with and without CBCT signs of TMJ-OA showed no significant difference in TMD-related pain. Twelve participants (8%) had been in contact with health care services due to TMD.

5 General discussion

5.1 Methodological considerations

5.1.3 Study design and participants

All papers in this thesis (Paper, 1, Paper II and Paper III) are based on an observational cross-sectional study design. Cross-sectional studies are primarily used to determine prevalence. The prevalence represents existing cases of a disease and can be seen as a measure of disease status; it is the proportion of people in a population having a disease.

The aim of Paper I and II was to study frequencies/prevalence of TMJ related symptoms and imaging characteristics of TMJ-OA in a sample of older adults with hand-OA. The aim of study III was to study frequencies/prevalence of gender differences and characteristics of CBCT signs of TMJ in 65-year-old Oslo citizens. Hence the observational cross-sectional study design was found to be the most appropriate.

The most important advantage of cross-sectional studies is that in general they are rapid and cost effective to conduct. Cross sectional studies are the best way to determine prevalence and are useful at identifying associations that can then be more rigorously studied using a cohort study or randomized controlled study[107].

Recruitment of participants for Paper I and II were done at follow-up of Oslo Hand-OA cohort at Diakonhjemmet hospital in 2013, where 87 of the original 209 patients participated. All 87 participants were invited to our TMJ study (Paper I/Paper II). For different reasons, 33 (38 %) of the invited patients did not participate in our study, and

a total of 54 patients were finally included in our sample. Of the 33 non-participants 17 declined. Reasons for decline were not asked for because of ethical considerations but were registered if told spontaneously. Seven patients in Oslo Hand-OA declined participation in our study because of health-related issues and seven dropped out because of either withdrawal or no-show. One patient was later rejected from our study sample because of inflammatory joint disease.

The 33 non-participants were significantly older than the participants. The fact that the data collection for our study partly was done during the winter months of 2013-2014 may have biased the participation. Of those spontaneously giving reasons for not to participate, health-related causes and the fear of falling in the slippery, icy streets were the most frequent. Health related issues and fear of going out during the cold Norwegian winter might have been more common in the oldest individuals.
Except for the age difference, we found no other statistically significant differences in symptoms/ clinical examination findings between the participants in our study group compared to the patients in Oslo Hand-OA cohort at follow up in 2013.

In Paper I/II age, gender, and BMI were published for the older adults with hand-OA. Several other variables could have been presented (other joints with OA, other diseases, medication, demographics) which had characterized our sample better. The results of self-reported health status and use of medication (from the questionnaire) were analyzed but never published (Appendix 3).

For scientific results to be generalized, the study population must represent the general population it aims to investigate (external validity). A possible limitation of our study population is the recruitment from a cohort study population, which can be biased due to a non-random sample. The hand-OA cohort at Diakonhjemmet Hospital consisted solely of patients referred to specialist care and may not be representative for patients with hand-OA in general. Due to this, the sample and the target population may differ in significant ways, limiting our ability to generalize our findings.

Our results might also be biased by the overrepresentation of women in the hand-OA cohort. Hand-OA may affect both women and men, but symptomatic hand-OA seems to be more prevalent in women (61). This might explain why more women than men seek medical care and were more likely recruited to the cohort. The incidence of TMJ-OA and TMD are also reported to be more common among women [44, 45]. However, although women were overrepresented, similar proportions of men (4/6, 67%) and women (32/48, 67 %) were found to have TMJ-OA. However, the proportion of men is very small, which increases the margin of error.

The study sample in Paper I and Paper II has some limitations. The sample size is relatively small. A larger sample size and a control group would have strengthened the reliability of the current study results.

The participants for Paper III were recruited from participants in the "OsloMunn65" (OM65). The target population for OM65 was 65-yr-old (born in 1954) residents of Oslo (5413 65-yr-old residents in 2019). A random sample of the target population was drawn from the National Bureau of Statistics Recordings and an invitation letter was sent to1230 individuals. No later than 2 weeks after sending the invitation letters, the individuals were contacted by telephone and asked if they were interested in participating in the study. Of 797 eligible individuals who were reached by phone, 460 individuals accepted the invitation to participate in the main study. The proportion of non-responders (58%) is a potential limitation for the study. As a result of restrictions from the Ethics Committee, it was not permitted to ask potential study participants why they declined to participate.

To explore potential selection bias in the recruitment of OM65 study population, the researchers explored the gender distribution and education level of the study population and compared with the corresponding proportions of the target population (based on register data from Statistics Norway)[95]. They found that the gender

distribution was similar, but the proportion with higher education in the study population was larger than the average in the target population. This may have affected results.

Prior to attending the clinical examination all participants in "OM65" answered a self-administered questionnaire via an electronic link (Nettskjema; University of Oslo).

Participants for OM65-TMJ (Paper III) were recruited directly from the OM65 study population, as the participants underwent dental and panoramic radiographic examinations as a part of the data-collection. During these examinations participants were randomly recruited to the present study, called OM65-TMJ. This process may have some potential limitations. Data-collection for OM65 was performed five days a week, but due to logistical challenges, other clinical activities and staff resources, data-collection for OM65-TMJ was limited to two-three days a week. But all participants from OM65 were invited to OM65-TMJ, those days the recruitment was done. Unfortunately, the data-collection for OM65 started almost 8 weeks before the recruitment for OM65-TMJ, due to delayed approval from the Norwegian Regional Committee for Research Ethics for the OM65-TMJ study. This resulted in a total of 169 individuals invited to OM65-TMJ. During collection days for OM65-TMJ, all present individuals in OM65 were invited, independently of TMD - related symptoms and they were investigated immediately, the same day as recruitment.

A strength of the study population for Paper III is that the participants were of the same age. But the most important strength is that an almost equal number of both genders are included in the population. Previous studies of OA in the TMJ have mainly focused on women [45, 108-110].

The study population in Paper III has some limitations. Compared to the main study, OM-65, population in OM 65-TMJ could have been larger. But as mentioned above, logistical challenges restricted recruitment for OM65-TMJ.

To explore potential selection bias, gender distribution, education level and TMD-related symptoms, the study population for OM65-TMJ was compared with the OM65-study population. The gender distribution was similar, but the proportion of participants with higher education in the OM65-TMJ study population was higher than in the OM65-study population. This may have affected the prevalence estimates; however, the level of education did not show a significant association with the prevalence and grade of OA signs of the TMJs.

In Paper III the age and gender of the participants were published. Previous contact with the healthcare services due to jaw dysfunction and/or facial pain was also published.
Several other demographic and health related variables were registered, both in a self-administered questionnaire in OM65 and by questionnaire-based interview in OM65-TMJ. More variables could have been presented (education, smoking habits, other joints with OA, other diseases, medication) which had characterized our sample better. Demographics, self-reported diseases, and use of medication were analyzed and included in the first submission of Paper III but were not included in the final published version.

Almost 40 % of the participants in OM65-TMJ study population self-reported earlier diagnosis of osteoarthritis in other joints, with hand (20 %), hip (14 %) and knee (12 %) as the most frequently affected joints. OA in two joints or more were self-reported by 11% of the participants. Previously diagnosed rheumatic joint disease was self-reported by 8 % of the participants. Of demographic characteristics it can be mentioned that the

majority of the participants (62 %) reported high education level (college/university level) and that 69 % of the 65-years olds still were active working. This is some lower than corresponding proportions in the target population of 65-year-old Oslo citizens (based on register data from Statistics Norway). Work responsibilities may be a reason for potential participants not responding to or rejecting the invitation to participate in OM65. The most frequent self-reported diseases and demographics of the OM65-TMJ population are listed in Appendix 4.

5.1.4 Assessment of self- reported symptoms and clinical findings

The Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) was published in 1992 and was for almost two decades the most widely employed diagnostic protocol for TMD research [39]. The RDC/TMD were translated to more than 20 languages and the original paper publishing the criteria was one of the most cited in dental research [41]. After identification of some limitations of the system, the RDC/TMD was revised, and the new classification system Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) was developed [39]. DC/TMD were developed to standardize the assessment, diagnosis, and definition of the most common subtypes of TMD. Translated versions of DC/TMD are now available in over 20 languages, which also over the years have been incorporated into both clinical guidelines and national guidelines. The DC/TMD were incorporated in the Norwegian guidelines on temporomandibular dysfunction (TMD) published in 2016, based on the Swedish translation [111]. A validated Norwegian translation of DC/TMD was completed later the same year, available for both clinical use and in research [97].

Data collection for Paper I/Paper II was done in 2013/2014, and assessment of self-reported symptoms and clinical findings were based on the original RDC/TMD protocol (Axis I). This led to some methodological challenges and limitations as the revision and development to DC/TMD were done simultaneously. The RDC/TMD protocol was not yet translated to Norwegian and had not been used in a Norwegian population before. Therefore, the clinical examiner protocol and the questions for self-reported symptoms

in this part of the project were based on the Swedish translation of RDC/TMD. The protocol for assessment of self-reported symptoms and clinical findings in this part of the project were based on a limited selection of questions from the RDC/TMD Patient History Questionnaire and measurements from the RDC/TMD Clinical Examination Form (Appendix 1). Consequently, the results in Paper I cannot be compared to studies based on the full RDC/TMD Axis I protocol. Despite some limitations in the protocol for assessment of self- reported symptoms and clinical findings it is also important to emphasize some strengths. The general directions and specifications for RDC/TMD protocol were strictly followed in those questions and examination items included, hence the results of those can be compared with other studies based on RDC/TMD.

The data collection for OM65-TMJ study was done in 2019. At this time RDC/ TMD were revised and a validated Norwegian version of DC/TMD protocol was available for both research and clinical use. A strict DC/TMD protocol was not implemented in the data collection since imaging characteristics were the main topic of this study. The long version of TMD Pain Screener from the DC/TMD protocol was included to assess TMD-related pain in the population.

All participants in OM65 completed the three validated screening questions for temporomandibular disorders (3Q/TMD) [98]. These questions were implemented in the main questionnaire by another research group, as a part of a TMD study in this interdisciplinary collaborative project. Most participants answered these questions in the online questionnaire at home, prior to the clinical/radiological examinations. Since all participants in OM65 answered these questions, the results were used to explore any potential TMD-related selection bias in the recruitment of participants from OM65 to OM65-TMJ.

The DC/TMD taxonomy classification system differentiates between osteoarthritis and osteoarthrosis in the TMJ, based on the presence or absence of arthralgia. But again;

since the main topic of the study was imaging characteristics, TMJ arthralgia was not assessed, and this differentiation was not made in this study.

5.1.5 CBCT assessment and interpretation

CBCT assessment of the two study populations in this project was done with two different CBCT units from two different manufacturers, which were the available units at the department of Maxillofacial Radiology at the time of data collection.

All participants in the Hand-OA population (Paper I and Paper II) were investigated in the same unit and with the same protocol. And almost all participants were investigated by the same resident (MKO). A few of the CBCT examinations were done by radiographer BMB, but similar protocol was followed for every participant.

Due to the age and health condition of the participants in the Hand-OA population (mean age 71.3 y), they were seated in a stable chair in the CBCT unit, which utilizes a standing position for scanning, but a seating position can be used for patient stability or wheelchair access (Planmeca Pro Max, Mid). In CBCT imaging, movements such as shaking or shivering of the head, for example, because of fear of the ongoing examination or reflections when the C-arm is moving, may occur[112]. This may be more frequent in the older adults. It has further been demonstrated that also artifacts by dental materials are common in older patients, as most of them have had restorative dental treatments with a wide range of materials used[113].

None of the participants in Oslo Hand-OA population were excluded because of movement artefacts in the CBCT examination.

All participants in the OM65-TMJ population (Paper III) were investigated in the same unit (Morita, Accuitomo) and with the same protocol. At this time (2019), this unit was the only CBCT unit available at the Department of Maxillofacial Radiology. Almost all participants were investigated by the same radiographer (AB). A few of the CBCT examinations were done by MKO, but both were well calibrated in the examination

protocol. The Accuitomo, Morita CBCT unit used in this study has a seated position and proper fixation of the patient during scan. None of the participants in the OM65 population were excluded because of movement artefacts in the CBCT examination.

The image quality in the two populations was quite comparable.

All CBCT examinations in both studies populations were quality checked, preliminary investigated and approved by MKO immediately after exposure. In Hand-OA population (Paper II/Paper II) all images were thereafter interpreted separately by three maxillofacial radiologists (MKO, LZA, TAL) with 3–30 years of experience of interpreting TMJ images. The less experienced observer was still a resident in maxillofacial radiology at the time of the observations. There were some discussions in the project group if this large variation in experience could lead to observer bias and a potential limitation in the study. Should the observer with less experience (MKO) be excluded from the interpretation? To minimize this potential observer bias, observers were trained and calibrated in the RDC/TMD protocol before the studies, to make sure all three observers interpreted data in the same way. Even though there was a variability in experience of TMJ imaging at the start of this study, all three observers had similar calibration and experience of the RDC/TMD imaging protocol, as it was new to all three observers, independent of experience. The less experienced observer was finally kept in the study. The reason for doing so is elucidated in 5.2. Statistical considerations.

Due to logistical challenges, CBCT images in OM65-TMJ were assessed by two, but more experienced maxillofacial radiologists (MKO, LZA). Because of the time lapse of almost 7 years between the studies, the observers now had 10 to 20 years of experience of interpreting TMJ images and were even more trained and calibrated in the RDC/TMD protocol.

Several attempts were made in both the studies of the Hand-OA population and in the OM65-TMJ studies, to avoid other potential sources of observer bias in the assessment of

CBCT images. In observational studies, there will always be a risk of so-called observer drift. This can happen if observers depart from the standard procedures in set ways and therefore rate the same events differently over time. In both studies the observers had regular meetings for maintenance of calibration, presentation of results and if disagreement, discussion until consensus was met.

A potential limitation in the CBCT assessment in both studies was that one of the observers (MKO) was present during the CBCT examinations of almost all the participants and also did the quality check, preliminary investigation and approval of the resulting images. In an attempt to avoid this potential source of observer bias, and to blind this observer for clinical information the thorough assessment of the CBCT images was intentionally delayed and performed at least a week after the examination.

5.2 Statistical considerations

Paper I and Paper II are based on observational studies in a relatively small sample size (n=54) which may lead to restricted statistical precision and susceptibility to type II errors. Type II errors occur when the null hypothesis is incorrectly accepted, meaning that research fails to identify a significant difference or effect that actually exists.
A smaller sample size could result in a wider confidence interval (CI) with a larger margin of error. The level of confidence also affects the interval width. A tight CI at ≥ 95 % confidence is statistically ideal. In Paper I the calculated CIs at a confidence level of 95 %, is considerable width, hence the results should be interpreted with caution.

It also has to be emphasized that generalizability of the results in Paper I/Paper II to the general population of hand-OA patients is limited because of the selection process from a non-random sample (described in chapter 5.1.1) and the overrepresentation of women and older patients. Hence, caution should be applied in the interpretation of the results on a population level.

The sample size in Paper III is larger, compared to the sample size used in Paper I and Paper II. Sample size calculations for OM65 were performed in collaboration with a statistician. In order to detect and document oral conditions with a prevalence of 10%, and the possibility for longitudinal follow-up of the participants with a dropout rate of 30% after 5 years, the calculations gave a final sample size estimate of 400 individuals. The final sample size in OM65-TMJ was lower, consisting of 159 individuals which may reduce the statistical power of the results. But compared to other studies on imaging signs of TMJ-OA, in the literature, the sample size in Paper III is quite large.

From a statistical perspective, TMJ studies can lead to some methodological challenges. The two TMJ's are connected to each other and cannot function independently of each other. Data collection including measurements taken from both left and right TMJ within each subject will represent a potential problem. The data is not independent, which is a requirement for tests of statistical significance. In paper I this issue was addressed by analyzing the relationship between symptoms/signs and the presence of imaging signs of TMJ-OA or not, at individual level instead of joint level.

There were some discussions in the project group, if the observer with less experience (MKO) should be avoided to minimize the variability in experience, since one observer had 30 years of experience. However, a closer look at the observer agreement for the imaging assessment in the present study, shows that mean kappa value of inter-observer agreement was 0.67 (range 0.61-0.74) and kappa value for intra-observer agreement was 0.62 (range 0.54-0.66). By removing the least experienced observer, the inter-observer agreement actually would be lower, with a kappa value of 0.61. On the other hand, the intra- observer agreement would have been slightly higher.

In Paper II and Paper III, we presented the imaging characteristics of TMJ-OA at joint level without taking account for intra-individual dependency. In paper II bilateral imaging signs of OA were found in almost half (47%) of the 36 individuals with TMJ-OA. In paper III bilateral imaging signs were found in 36% of the individuals with TMJ-OA.

From a statistical point of view, presentation of characteristics of TMJ-OA at joint level might not represent the most advantageous approach, but this seems to be quite usual in TMJ research in general.

5.3 Discussion of main findings

The general aims of this thesis were to describe the prevalence, gender differences and imaging characteristics of CBCT-defined TMJ-OA in older adults.

In Paper I and Paper II we reported the frequency of CBCT signs of TMJ-OA in hand-OA patients, for the first time. CBCT signs of TMJ-OA were found in as much as two thirds (67%) of the hand-OA patients. Considering the increased susceptibility of patients with hand-OA to develop OA in other joints [114], the frequency of CBCT signs of TMJ-OA in this population was expected to be high. The figure of 67% is somewhat difficult to interpret, due to the challenge in finding comparable studies, and comparison of numbers should be made with caution. However, in a recent CBCT study, Dumbya et al. reported almost similar prevalence of TMJ-OA (66%) in older adults (mean 73 y, range 65-94)[115]. It is noteworthy that the authors used articular surface flattening and subcortical sclerosis as imaging signs decisive for TMJ-OA, which we did not in our studies. By excluding those imaging signs, which according to the criteria of Ahmad et al [74] are indeterminate for the diagnosis, the prevalence found by Dumbuya et al. probably would have been lower. Other studies with different modalities have also shown some similarities to our findings. A CT study of patients with generalized OA and symptomatic TMJs, showed 80% TMJ-OA[116], although the mean age (63 years) was lower compared to the hand-OA patients (71.4 y). In a population-based MRI study of a birth cohort (mean age 74.6 years) the frequency was 70% [117].

However, by using the same diagnostic criteria and methods from Paper I/II in Paper III, we demonstrated a significantly lower frequency (35 %) of CBCT signs of TMJ-OA in a population-based sample of 65-year-old Oslo citizens. In the work with all three papers (I, II and III) it has been challenging to find comparable studies regarding the prevalence of TMJ-OA, because of differences in research population, inclusion criteria and

diagnostic assessment in the existing epidemiological studies. By using the same methods and the most widely accepted diagnostic criteria [74] in our studies, we increased the accuracy of comparison of the results. If we had applied the same criteria as Dumbya et al. in Paper III study, the prevalence of CBCT signs of TMJ-OA would have been 58% instead of 35%. It should be mentioned that the two populations in Paper I/II and Paper III are not quite comparable, regarding sample size, age, gender and distribution. Higher mean age and overrepresentation of women in the hand-OA population can also potentially lead to increased frequency of TMJ-OA. But the significant difference in frequencies between the two populations strengthens our suggestion in Paper I, that TMJ-OA may be a part of generalized OA.

CBCT characteristics of TMJ-OA were discussed in Paper II and Paper III. Even though there was a significant difference in the frequency of the radiological diagnosis of TMJ-OA, the CBCT characteristics of TMJ-OA were quite similar in the two study samples. In agreement with other imaging studies of TMJ-OA in older adults [45, 116, 118], condylar changes were seen more often than temporal bone changes in both the hand-OA patients and the 65-year-old Oslo citizens.

Articular surface flattening and bone productive changes (subcortical sclerosis and osteophyte) were the most frequent imaging signs of TMJ-OA both in the hand-OA patients and in the 65-year-olds. Typically, more than one imaging sign was present, and the combination of articular surface flattening, osteophyte and subcortical sclerosis in the condyle was the most frequent. Since both surface flattening and subcortical sclerosis are considered indeterminate signs of TMJ-OA[74], osteophyte formation was clearly the most frequent imaging sign decisive for OA in both study samples, and with quite similar frequencies, with 72 % in Paper II and 77 % in Paper III. However, there were some differences in the size of the osteophytes between the study samples. In the hand-OA patients, with a mean age of 71.3 y, the osteophytes tended to be larger, and 61 % were ≥ 2 mm. In comparison only 22 % of the osteophytes in the 65-year-olds were ≥

2 mm. This is in agreement with a previous study that showed significant age-related increase in both presence and severity of osteophyte formation in TMJ-OA[44].

Surface erosion was the second most frequent imaging sign, decisive for the radiological diagnosis of TMJ-OA in both study samples, with some similarities and some differences in characteristics and frequencies between the groups. Frequencies of erosions on the condylar head were quite similar in both groups, with 40 % in the hand-OA sample and 55 % in the 65-year-olds. The erosive changes were in general small. Large cortical erosions (≥ 2 mm both in width and depth) on the condylar head were absent in the hand-OA sample and were found in only three TMJs in the 65-year-olds.
On the other hand, we found a higher, but not statistically significant frequency (49 %, 26/53) of cortical erosions in the temporal bone in the hand-OA patients, compared to the 65-years old (43%, 33/76). As in the condylar head, all cortical erosions in the temporal bone were small (< 2 mm both in width and depth) in the hand-OA patients. In the 65-year-olds large cortical erosions in the temporal bone were found in 6 TMJs.

Subcortical cysts were not so frequent and consistently small in size (< 2 mm both in width and depth) in the hand-OA patients; with slightly more cases in the condylar head (15 %, 8/53) compared to the fossa/eminence area. In the 65-year-olds the frequency of subcortical cysts in the condylar head were significantly higher (18/76) but large subcortical cysts were only found in four cases here. Subcortical cysts in the fossa/eminence were small and almost absent in both study samples.
The majority of the participants in both study samples had unilateral imaging signs of TMJ-OA, but there were more bilateral cases in the hand-OA sample (47 % vs. 36 %). There are few comparable studies on the frequency of bilateral TMJ-OA, and the reported range is wide. Most of the studies are performed with other study samples, methods and/or modalities. Due to such differences the frequencies should be compared with caution. In the German population-based MRI study of a birth cohort (mean age 74.6 years), Schmitter et al. found a quite similar frequency of bilateral TMJ-OA (50 %)[117] as we found in the hand-OA sample. A repeated cross-sectional and

longitudinal cohort on radiological findings of TMJ-OA among middle-aged and older women(n=5234) in Sweden showed a low risk of developing OA in both joints[110]. But this study was performed with panoramic radiography, with lower sensitivity and specificity compared to CBCT, and with different diagnostic criteria. However, this study is a valuable and unique epidemiological study of both prevalence and incidence of TMJ OA in different age groups. Bäck et al found a low, but gradual age-related increase in the prevalence of bilateral radiological signs of TMJ-OA. Between the age groups of 62 y and 74 y the authors found a nearly two-fold increase in prevalence of bilateral TMJ-OA. An autopsy study by Åkerman et al from 1984 also indicated that degenerative changes in the TMJ often are bilateral in advanced age[119]. In agreement with others, our studies show that unilateral signs of TMJ-OA are most frequent in older adults, but bilateral findings increase with age.

The frequency of TMJs diagnosed with OA and categorized as Grade 2 were quite similar in the two study samples, but there were still some interesting differences. In the hand-OA sample, only osteophytes were found to be large (≥ 2 mm). All findings of cortical erosions and subcortical cysts in the OA joints were small (< 2 mm both in width and depth). In those joints with small osteophytes, the categorization of TMJ-OA Grade 2 was based on two or more small imaging signs. In the 65-year-olds we found large versions of all imaging signs (osteophytes, cortical erosions, and subcortical cysts), even though large osteophytes were most frequent in this sample too.

Several authors have over the years tried to describe the natural course of osteoarthritis in the temporomandibular joint and staging of the disease has been proposed [67, 120-122]. However, the literature agrees that erosive changes (as cortical erosion and subcortical cysts) represent early or acute stages of the disease and that bone productive changes, and in particular osteophyte formation, represent late stages[120]. Authors have proposed that early stages of the disease, can indicate an unstable TMJ accompanied with bone alternations and potential functional changes[120, 123].

Further, the authors suggest that in the late phase, the body is adapting to repair the joint and osteophytes are developing to stabilize and broaden the surface of the joint, in an attempt to better resist loading forces[120].

The relevance and biology of osteophytes in osteoarthritis have been discussed and reviewed by researchers in rheumatology[124]. The authors states that osteophytes can contribute both to the functional properties of affected joints and to clinically relevant symptoms. Osteophyte formation is highly associated with cartilage damage, but osteophytes can also develop without explicit cartilage damage. These results are leading into the discussion whether osteophytes are a functional adaptation or a pathological phenomenon[124]

Overall, the imaging signs of TMJ-OA found in both our study samples, are mainly characterized by remodeling (articular surface flattening) and bone productive changes, consistently also found in TMJs with bone erosive changes (erosions and subcortical cysts). These radiological findings indicate late stages of the disease in both groups. But as mentioned above, we found some differences between the groups. Findings of significantly larger osteophytes in the hand-OA patients and somewhat more cortical erosions in the 65-year-olds, may indicate a later stage of the disease in the hand-OA patients.

The study sample of 65-year-olds in Paper III included an almost equal number of both genders (86 women, 73 men). The frequency of imaging signs of TMJ-OA was significantly higher in women (40/86, 47 %) compared to men (16/73, 22 %), which is in agreement with studies on OA, both in general and considering the TMJ[44, 125]. The CBCT study of TMJ-OA, by Dumbya et al. also found a significant difference in prevalence between women (73%) and men (56%), with almost the same gender distribution [115]. Although the participants were older (mean 73 years, range 65–94), the higher prevalence may be due to differences in the diagnostic criteria applied, including subcortical sclerosis and articular surface flattening as imaging signs decisive for TMJ

OA. If we had applied the same criteria as Dumbya et al. in Paper III, the prevalence in women would be 69% instead of 47%. Even though there was a significant gender difference in frequency of imaging signs of TMJ-OA in Paper III, the imaging characteristics in the OA group were quite similar between the men and women. Grade 2 TMJ-OA was found in 28/40 (70 %) of the women and in 11/16 (69 %) of the men. Some differences between the genders, but not statistically significant, are worth mentioning: Even though the distribution of grade 2 TMJ-OA were similar between the genders, the frequency of large osteophytes (> 2mm) was higher in women (14/80, 18 %) than men (3/32, 9 %) and the frequency of bilateral imaging findings of TMJ-OA were also somewhat higher in women (16/40, 40 %) than in men (4/16, 25 %). These tendencies agree with studies that have showed higher severity of OA in women compared to men[125].

In Paper I/II the distribution of genders was largely uneven, and studies of gender differences should be performed with caution. But it is noteworthy that exactly the same frequencies of men (4/6, 67%) and women (32/48, 67%) were found to have imaging signs of TMJ-OA in this study sample.

Evaluation of inter- and intra-observer agreement between radiologists was performed both in Paper II and Paper III. The reliability studies showed that the inter and intra-observer agreement in Paper II was fair to good and in Paper III it was good, close to the threshold of excellence (> 0.75)[126] The Kappa values in Paper II was lower than those obtained by Ahmad et al (0.71) and the Kappa values in Paper III (0.75) was slightly higher than the 0.71 based on CT reported by Ahmad et al[74]. Even though all three observers in Paper I/II were introduced to and simultaneously calibrated in the use of the diagnostic criteria developed by Ahmad et al, there was a substantial variation in experience between the observers (2013-2014). Taking this variation into consideration, reliability studies in Paper II also were done without the registrations of the least experienced observer. This resulted in even lower mean Kappa values for inter-observer agreement, with a decrease from 0.67 to 0.61. On the other hand, there was a

slight increase in mean Kappa values for intra observer-agreement from 0.62 to 0.65. Due to these findings, the registrations of the least experienced observer were kept in Paper II.

The rather low Kappa values for observer agreement in Paper II can also be explained by deficient calibration of radiologists in the diagnostic criteria and subsequent interpretation challenges. To some extent, the observers found it difficult to differentiate between pathology and normal anatomy. This was the most common cause of disagreement in the interpretation. The most frequent problem in the interpretation was the differentiation between a subtle beaking of the anterior aspect of the condyle and an osteophyte. In some cases, flattening of the anterior slope and a pointed anterior tip of a condyle could be interpreted as an osteophyte. Assessing the presence of subcortical sclerosis/sclerotic border, which is decisive for an osteophyte according to the diagnostic criteria [74], was the major challenge in those cases. However, in the anterior portion of the condyle, mild sclerosis can in some cases be almost impossible to differentiate from "impression of sclerosis", which may occur due to the close position of the cortical plates[77]. A small (< 1 mm) exophytic angular formation, observed as the only imaging sign decisive for TMJ-OA, should be interpreted with caution as an osteophyte.

Another problem in Paper II, was the interpretation of sclerosis, which may vary considerably from just a slightly thickened cortical plate to a generalized sclerosis. Various degrees of sclerosis are also typical in other joints with OA[127]. We found it particularly challenging to differentiate between subcortical sclerosis, defined as "any increased thickness of the cortical plate", and generalized sclerosis, defined as "no clear trabecular orientation with no delineation between the cortical layer and the trabecular bone that extends throughout the condylar head". Similar challenges have also been addressed by other researchers using the same imaging criteria for TMJ-OA. This differentiation is of great importance, because generalized sclerosis was defined as a decisive imaging sign for OA in the original paper by Ahmad et al. In later

recommendations, published by some of the same authors, generalized sclerosis is removed, without any explanation [101, 128, 129]. This issue is also addressed by Larheim in a Supplementary Commentary following the Recommendations for Imaging of the Temporomandibular Joint by the American Academy of Oral and Maxillofacial Radiology and the American Academy of Orofacial Pain

The observer agreement increased in Paper III. The most obvious explanation for this difference is the five years of gained experience and thorough calibration of the radiologists between the studies for Paper I/II (2013-2014) and Paper III (2019). As mentioned above, all three observers were introduced to and simultaneously calibrated in the use of the diagnostic criteria in the studies for Paper I/II. During the five years between the studies, the two remaining observers used the diagnostic criteria almost on a daily basis, and hence became more experienced and calibrated for the studies in Paper III. Also, the reduction from three to two observers could have affected the agreement between the radiologists.

All the studies showed that it can be a challenge to differentiate between morphologic variations of normalcy and small pathologic changes, in the interpretation of imaging signs of TMJ-OA. In routine clinical practice it is important not to over diagnose the disease. Imaging diagnosis of TMJ-OA should be based on evident abnormalities, that is, frank pathological findings and not on subtle bone changes that may represent a normal anatomic variation or remodeling, which also has been addressed in a review paper[80].

Self-reported TMJ related symptoms were more frequent in the hand-OA patients compared to the 65-year-olds. In Paper I we found that almost half (44%, 24/54) of the hand-OA patients reported at least one TMJ-related symptom. In Paper III (18%, 29/159) of the 65-year-olds reported at least one TMD-related symptom: women 24/86 (28%), men 5/73 (7%). The difference is significant, but the numbers should be compared with caution, because of the methodological differences between the studies;

with the Symptom Questionnaire used in Paper I and the TMD-Pain Screener used in Paper III. In Paper I we also found that self-reported TMJ-related symptoms and clinical examination findings were more common in participants with CBCT-defined TMJ-OA as compared to those with no OA or those indeterminate for OA. Experience of TMJ sounds (crepitus and/or clicking) and pain at mouth opening was self-reported significantly more often in the hand-OA patients with CBCT defined TMJ-OA.

The relatively high frequency of self-reported pain in Paper I is in contrast to most studies, which have shown decrease in TMJ pain with increasing age [130] Additionally, clinical examination of the hand-OA patients in Paper I revealed higher frequencies of objective crepitus and pain than most previous studies of older adults [131, 132]. Crepitus was significantly more frequent in Paper I compared to Paper III, as we registered crepitus in the same number of participants both in the hand-OA patients (15/54, 28 %) and the 65-year-olds (15/159, 9 %,). Overall, the results suggest that both TMJ-OA and related symptoms are more common in hand-OA patients. Despite the high burden of TMJ-related symptoms and clinical findings in Paper I, few of the participants (7/54, 13 %) had sought healthcare. The low frequency of TMD related pain the 65-year-olds is in agreement with the majority of other studies, showing a decrease in self-reported pain with advancing age[133], even though imaging signs of TMJ-OA increase. Even fewer participants (12/159, 8 %) in Paper III reported previous contact with the healthcare services, which also is in agreement with other studies suggesting that older adults are unlikely to seek treatment for TMJ-OA. These results are also in agreement with studies on OA in other joints. Results from the Framingham study on hand-OA suggest that many subjects with symptomatic hand-OA among the older population may not seek medical care[134].

Our clinical investigations (subjective and objective registration of joint sounds/crepitus) underestimated the frequency of TMJ-OA in both study samples, when using CBCT as reference standard. The sensitivity for the clinical diagnosis in Paper I was quite low (0.42) and even lower in Paper III (0.14). Specificity was high with the

same figure in both study samples (0.93). These results support the DC/TMD criteria for degenerative joint disease, which declares a sensitivity of 0.55 and a specificity of 0.61 for the diagnosis without imaging. The criteria conclude that imaging is the reference standard for the diagnosis. The high specificity in both study samples indicates that there were few false positive results in the studies.

In Paper I self-reported TMJ-related symptoms and clinical examination findings were more common in participants with CBCT-defined TMJ-OA as compared to those with no OA or those indeterminate for OA. This was in contrast to the findings in the 65-year-olds, where there was no difference in TMD-related pain between participants with and without CBCT defined TMJ-OA.

5.4 Clinical implications

When TMJ-OA is clinically suspected and the diagnosis needs to be confirmed, imaging and preferably CBCT, should be used for osseous evaluation. Crucial signs for the imaging diagnosis of TMJ-OA are registration of osteophyte, erosion, and/or subchondral cyst. The imaging diagnosis of TMJ-OA should be based on evident and clear abnormalities and then direct the appropriate clinical management of the patient.

This thesis has shown that CBCT defined TMJ-OA is frequently found in older adults and in particular in individuals with hand-OA. Imaging signs of TMJ-OA are more frequent in women compared to men. CBCT signs of TMJ-OA in older adults seems to be mainly characterized by remodeling (articular surface flattening) and bone productive changes (subcortical sclerosis and osteophytes), also in TMJs with signs of bone erosive changes (erosions/subcortical cysts). Despite CBCT signs of TMJ-OA, few older adults seem to seek contact with health care services due to TMD.

Knowledge and experience in treatment of disease in the TMJ seems to be limited among both general practitioners and rheumatologists[135]. The TMJ has earlier been discussed as the forgotten joint[136]. An increasing focus on JIA affecting the TMJ in rheumatology, has to some extent lead to an increasing awareness of the TMJ among

healthcare professionals outside dentistry [137]. In Paper I we suggested that TMJ-OA may be a part of generalized OA and that CBCT defined TMJ-OA and TMJ-related symptoms was common in older adults with hand-OA. Few of them had sought health care. An economical evaluation of the Norwegian health care spending on musculo-and skeletal diseases in Norway in 2016 showed that 43 % of rheumatic patients visit their general practitioners more than six times before they are referred to a rheumatologist[138]. These are high numbers, and the patients sometimes experience symptoms and pain for a very long time, before the final diagnosis is set. The report also showed that both patients and healthcare professionals experienced a lack of interaction and collaboration in the healthcare system, leading to the patients being their own healthcare coordinator. This can be one explanation of why a major part of these patients don't seek health care, when experiencing concomitant symptoms from the TMJ. This combined with findings in this thesis may indicate a room for improvement in interdisciplinary collaboration and interaction between dentists and rheumatologist in treatment of patients with OA.

5.5 Conclusions

- In the hand-OA cohort, CBCT-defined TMJ-OA was found in as many as two thirds (67%) (Paper I). Clinical examination clearly underestimated the diagnosis of TMJ-OA as assessed from CBCT (Paper I)
- The high frequency found in the hand-OA cohort suggests TMJ-OA to be part of generalized OA (Paper I)
- In the hand-OA cohort self-reported TMJ-related symptoms and clinical findings were common. Self-reported pain at mouth opening and joint sounds, in particular crepitus, were significantly more common in individuals with TMJ-OA compared to those without (Paper I)
- In the hand-OA cohort, the imaging findings of TMJ-OA were characterized by bone productive features (osteophyte formation and sclerosis) and flattening, indicating a late stage of OA. Large osteophytes were the main reason that most of the OA joints were categorized with the most severe grade of TMJ-OA.

- Destructive findings (surface erosion and subcortical cysts) were less prominent and always seen in combination with bone-productive features (Paper II)
- About one third of the 159 65-year-old Oslo citizens had CBCT-defined TMJ-OA; almost every second woman and about every fifth man (Paper III)
- Articular surface flattening and bone productive changes were most frequent imaging features in CBCT defined TMJ-OA in 65-year-old Oslo citizens (Paper III)
- Despite a high frequency of CBCT-defined TMJ-OA, TMD-related symptoms were few in 65-year-old Oslo citizens (Paper III).

- Condylar changes of TMJ-OA are more common than changes in the articular eminence and condylar fossa in both study groups.
- Overall, the results suggest that both TMJ-OA and related symptoms are more common in older adults with hand-OA compared to 65-year-old Oslo citizens.
- Imaging findings indicate late stages of TMJ-OA in both groups, but even later stage of the disease in the hand-OA patients.

6 Future perspectives

As mentioned in the introduction the global population is ageing, and by 2050 the population aged 60 years or more will double, whilst those aged 80 years or more will triple, to reach over 400 million persons in the world [1]. This shift in distribution of the world's population is leading to an increased number of people living with non-communicable diseases and consequences of injuries. Prevalence of OA is expected to continue to increase to the year 2050 for all sites of OA leading to a greater health-system burden everywhere. This thesis has demonstrated a high frequency of CBCT related TMJ-OA in older adults, and in particular in older adults with a hand-OA diagnosis. Despite these findings older adults do not seem to apply the same burden on the health care system due to TMJ related symptoms.

This thesis has demonstrated the importance of updated, clear and well-functioning diagnostic criteria for the imaging diagnosis of TMJ-OA, both in research and general practice. The development of RDC/TMD to DC/TMD was an advancement to evidence based diagnostic criteria with greater validity for clinical use, but the image analysis criteria developed by Ahmad et al. has not been updated since 2009. Rapid development in medical research and advancement in the field of imaging enforces continuous update of the diagnostic criteria also in the future.

There have been some major advancements and innovations in bone imaging in the last decade, with the introduction of for example 4-dimentional CT (4D-CT) and Dual-Energy CT (DECT) [139]. But the most significant progress is probably the implementation of Artificial Intelligence (AI) in medical research and diagnostic radiology. A recent study has actually shown that an AI model had equal or better diagnostic performance for CBCT based TMJ-OA compared to human experts [140]. Such results substantiate the question whether AI will replace radiologist in the future.
Even though AI holds great promise in the field of healthcare, including TMJ-OA research, challenges concerning data protection, privacy, ethical considerations, and validation of AI models must be carefully addressed. Ongoing research and collaboration between AI experts, clinicians, and researchers will likely contribute to the development of innovative AI applications in TMJ-OA management in the future.

There is still a lack of longitudinal studies on CBCT defined TMJ-OA. According to the study protocol of OM65-TMJ a 10 years follow up study of the participants is planned and the participants have consented to a reinvestigation with CBCT of the TMJs at the year of 75. This study will hopefully lead to valuable knowledge of the nature of and longitudinal development of TMJ-OA.

7 Errata

Paper III

Page 1, Abstract, Line 11: The word **TMJs** should be replaced by **participants.**
Correction: *CBCT signs of TMJ-OA were unilateral in two-thirds of the ~~TMJs~~* ***participants*** *and…*

Page 4, Figure 1: Flowchart of recruitment. Due to the undersized frame in the published version of Paper III, one participant is missing in the list of participants being excluded from the study. One participant was excluded due to missing data. A total of 10 participants were excluded or rejected participation in the study. A correct version of this flowchart is shown in Figure 2 in this thesis.

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Papers I-III

Appendix

PAPER I

Osteoarthritis and Cartilage 25 (2017) 654–657

Osteoarthritis and Cartilage

Brief Report

Frequency of temporomandibular joint osteoarthritis and related symptoms in a hand osteoarthritis cohort

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Clinical characteristics

SUMMARY

Objective: The prevalence of osteoarthritis (OA) in the temporomandibular joints (TMJs) in hand OA patients is largely unknown. Our aims were to explore (1) The frequency of TMJ-related symptoms and clinical findings; (2) The TMJ OA frequency defined by cone beam computed tomography (CBCT); and (3) The relationship between TMJ-related symptoms/clinical findings and CBCT-defined TMJ OA, in a hand OA cohort.

Methods: We calculated the frequencies of TMJ-related symptoms, clinical findings and diagnosis of TMJ OA by CBCT and clinical examination in 54 patients from the Oslo hand OA cohort (88% women, mean (range) age 71 (61–83) years). Participants with and without CBCT-defined TMJ OA were compared for differences in proportions (95% confidence interval (CI)) of symptoms and clinical findings. Sensitivity and specificity of the clinical TMJ OA diagnosis were calculated using CBCT as reference.

Results: Self-reported symptoms and clinical findings were found in 24 (44%) and 50 (93%) individuals (93%), respectively, whereas 7 (13%) had sought healthcare. Individuals with CBCT-defined TMJ OA (n = 36, 67%) reported statistically significantly more pain at mouth opening (22%, 95% CI 4–40%), clicking (33%, 95% CI 14–52%) and crepitus (25%, 95% CI 4–46%). By clinical examination, only crepitus was more common in TMJ OA (33%, 95% CI 29–77%). Clinical diagnosis demonstrated low sensitivity (0.42) and high specificity (0.93).

Conclusions: CBCT-defined TMJ OA was common in hand OA patients, suggesting that TMJ OA may be part of generalized OA. Few had sought healthcare, despite high burden of TMJ-related symptoms/findings. Clinical examination underestimated TMJ OA frequency.

Introduction

In osteoarthritis (OA) research and patient management, little focus is given to temporomandibular joint (TMJ) OA, although it may lead to substantial joint pain, dysfunction, dental malocclusion and reduced health-related quality of life[1]. Pain and/or dysfunction in the masticatory apparatus represent a public health problem affecting 5–12% of the population[2]. Clinically it may be challenging to differentiate TMJ OA from other TMJ-related conditions, which may occur in combination with OA. The presence of crepitus that clinically defines TMJ OA can be absent, and the clinical definition of TMJ OA is consistently reported to have low sensitivity when using radiological diagnosis as gold standard[2]. Furthermore, radiological findings and TMJ symptoms are poorly correlated[3].

The imaging diagnosis of TMJ OA is most reliably assessed by computed tomography (CT)[4]. The definition is based on evaluation of bony surfaces including erosions, subcortical cysts, osteophytes, and/or sclerosis[4]. Cone beam CT (CBCT), which has lower radiation exposure than CT, is similarly accurate for detecting TMJ OA[3].

Proposed risk factors for TMJ OA are in line with those suggested for other joints; age, sex, genetics, infection/inflammation, congenital and developmental abnormalities[1]. Hand OA is often considered a marker of a generalized susceptibility of OA, leading to

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an increased risk of knee and hip OA[5]. However, the prevalence of TMJ OA in patients with OA in other joints has been explored in few studies only, of which the majority is summarized by Wolf *et al.*[6] Most previous studies show no clear association, but the TMJ OA prevalence is likely underestimated due to insensitive imaging modalities. No previous studies have explored the frequency of TMJ OA by CT or CBCT in hand OA patients.

Hence, our aims were to explore (1) The frequency of self-reported TMJ-related symptoms and clinical examination findings; (2) The frequency of CBCT-defined TMJ OA; and (3) The relationship between TMJ-related symptoms/clinical findings and CBCT-defined TMJ OA, in a hand OA cohort.

Methods

Oslo hand OA cohort

At baseline (2001–03), 209 hand OA patients from the rheumatology outpatient clinic at Diakonhjemmet Hospital were examined. Follow-up examinations were performed in 2008–2009 ($n = 128$) and 2013 ($n = 87$)[7]. Patients with diagnoses of inflammatory joint disease were not invited for participation and excluded if later detected[7]. All examinations were approved by Regional Ethics Committee. Written informed consent was provided by all patients.

In 2013, we included a questionnaire about facial symptoms and a clinical examination of the TMJs and related muscles. Voluntary CBCT examinations of the TMJs were completed by 55/87 non-selected patients, of whom 54 were included in the current study (participants) (Online Supplementary Fig. I).

Clinical assessment of TMJ and related muscles

Eighty-seven patients completed a questionnaire about facial symptoms the last 30 days, including experience of pain (at rest, mouth opening and chewing), jaw locking and noise (clicking or crepitus) on jaw movement ("yes", "no" and "no, but earlier in life"). The questions were not side specific. A question about previous contact with the healthcare system due to jaw dysfunction and/or facial pain was answered ("yes"/"no"). The questionnaire was developed by the authors based on questions from the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) Patient History Questionnaire from the International RDC-TMD Consortium[8].

One dentist (AKA) performed the clinical examination according to the "Complete specifications (protocol) for Diagnostic Criteria for Temporomandibular Disorders (DC/TMD)" (version: 2013)[9] including bilateral assessment of masseter/temporalis muscle pain at palpation, TMJ pain at palpation and TMJ noises (clicking, crepitus) and maximum unassisted mouth opening. Reduced mouth opening was defined as <40 mm, including vertical overbite. The DC-TMD was used to define clinical TMJ OA[2], which requires presence of crepitus registered by both examiner and patient (Online Supplementary Table I).

CBCT of TMJ

CBCT was performed at the Department of Maxillofacial Radiology using a ProMax Mid 3D CBCT unit (Planmeca Oy, Helsinki, Finland) (field of view 200 × 60 mm; voltage 90 kV; tube current 10 mA; spatial resolution 200 μm). Reconstructed images in axial, oblique sagittal and oblique coronal planes were analyzed in Sectra PACS viewer IDS 5 version on 20 inch monitors. The examinations were interpreted by three maxillofacial radiologists (MK, LZA, TAL) with 3–30 years of relevant experience.

The radiologists performed a pre-evaluation of 12 joints and the results were discussed until consensus was met. Each radiologist then interpreted all 54 CBCT examinations independently, blinded to clinical information except age and sex. The TMJs were classified as OA, no OA or indeterminate for OA according to Ahmad *et al.* (Online Supplementary Table II)[4]. After 16 weeks 30 joints were re-evaluated. For reliability analysis, joints registered as indeterminate for OA and no OA were pooled. Average kappa values were calculated and evaluated[10]. Inter-observer disagreement was discussed until consensus was met and each joint got a final imaging diagnosis.

Statistical analysis

Using independent samples *t*-tests and Chi Square tests, we compared, age, body mass index (BMI), TMJ-related symptoms and clinical examination findings between participants and non-participants and between participants with CBCT-defined TMJ OA (uni-or bi-lateral) and participants with no/indeterminate for OA. Differences in proportions of TMJ-related symptoms and clinical examination findings in participants with CBCT-defined TMJ OA vs no/indeterminate for OA were calculated with 95% confidence intervals (CIs). We calculated sensitivity and specificity of the clinical diagnosis using CBCT as reference. Analyses were performed using IBM SPSS version 22.0.

Results

Most participants were women ($n = 48/54$, 88%) and mean (range) age was 71.3 (61.0–83.0) years. Mean (SD) BMI was 27.6 (6.0). The 33 non-participants were slightly older than the participants ($P = 0.04$), with a mean (range) age of 73.9 (64.0–83.0) years. We found no other statistically significant differences in symptoms/clinical examination findings.

Frequency of TMJ-related symptoms and clinical examination findings

Self-reported symptoms were present in 24 individuals (44%, 95% CI 31–57%) with facial pain at rest ($n = 17$, 31%) and joint sounds (clicking/crepitus) (both $n = 15$, 28%) being the most common. Seven (13%) individuals reported previous contact with the healthcare system due to jaw dysfunction and/or facial pain. Clinical TMJ-related examination findings were observed in 50 participants (93%, 95% CI 86–100%) with masticatory muscle pain at palpation ($n = 43$, 80%) and crepitus ($n = 31$, 57%) being most frequent. The mean (range) mouth opening was 51.2 (39–65) mm. One individual (2%) had a reduced mouth opening (39 mm). The criteria for a clinical TMJ OA diagnosis were fulfilled in 22 individuals (41%, 95% CI 28–54%).

Frequency of CBCT-defined TMJ OA

Average kappa values for pairwise inter- and intra-observer agreement for CBCT-defined TMJ OA were 0.67 (range 0.61–0.74) and 0.62 (range 0.54–0.66), respectively, representing substantial reliability.

CBCT-defined TMJ OA was present in 36 participants (67%, 95% CI 54–79%), of whom 17 (31%) had bilateral OA. The 19 (35%) individuals with unilateral TMJ OA, had either no OA ($n = 6$) or were classified as indeterminate for OA ($n = 13$) in the contralateral joint. No TMJ OA was found in 10/54 (18%, 95% CI 8–29%) individuals, whereas 8/54 (15%, 95% CI 5–24%) were categorized as indeterminate for OA ($n = 5$ bilaterally and $n = 3$ unilaterally with no OA in the contralateral joint).

Table I
Self-reported TMJ-related symptoms* in 54 patients with hand OA

	Hand OA patients with TMJ OA† ($n = 36$) *N* (%)	Hand OA patients with no TMJ OA or indeterminate ($n = 18$) *N* (%)	Differences in proportions (95% CI)
Pain‡ at rest	14 (39)	3 (17)	22 (−1, 46)
Pain‡ at mouth opening	10 (28)	1 (6)	**22 (4, 40)**
Pain‡ at chewing	5 (14)	1 (6)	8 (−7, 24)
Experience of locking	3 (14)	0 (0)	8 (−2, 17)
Experience of clicking	14 (39)	1 (6)	**33 (14, 52)**
Experience of crepitus	13 (36)	2 (11)	**25 (4, 46)**

Bold numbers are statistically significant ($P < 0.05$).
* Symptoms in one or both jaw(s) (not side specific) the last 30 days.
† CBCT-defined TMJ OA in one or both joints.
‡ In jaw(s), temple(s) or in front of the ear(s).

Symptoms and clinical examination findings related to CBCT-defined TMJ OA

There were no significant differences in age, sex and BMI in individuals with vs without CBCT-defined TMJ OA (data not shown).

Self-reported TMJ-related symptoms and clinical examination findings were more common in participants with CBCT-defined TMJ OA as compared to no OA or indeterminate for OA (Tables I and II). No statistical significant difference in mouth opening was found across individuals with vs without CBCT-defined TMJ OA (mean (SD) 51.5 (6.1) vs 50.7 (7.1) mm, $P = 0.67$).

The sensitivity for the clinical diagnosis was low (0.42, 95% CI 28–55) using CBCT as reference, whereas the specificity was high (0.93, 95% CI 86–99) (Online Supplementary Table III).

Discussion

For the first time, we report the frequency of TMJ OA by CBCT and clinical examination in hand OA patients, representing a population with increased OA susceptibility. CBCT-defined TMJ OA was more frequent than clinically defined TMJ OA and as much as two-thirds (67%) of the hand OA patients demonstrated CBCT-defined TMJ OA.

Almost half (44%) of the individuals reported at least one TMJ-related symptom, which contrasts the proposed reduction of complaints described in aging populations[11]. We demonstrated much higher frequency than a recent Swedish epidemiological investigation, in which only 12% of the 70-year-old women reported TMJ-related problem(s) on a questionnaire[12]. Additionally, our clinical examination revealed higher frequencies of both crepitus and pain than most previous studies of elderly[11,13–15]. These results suggest that TMJ OA and related symptoms are more common in hand OA patients, but conclusions cannot be made due to the lack of a control group. The higher frequency in our study could also be due to different outcome measures and a different study setting with a dedicated examination of the TMJs, which may have increased the awareness of TMJ-related symptoms. It should be kept in mind that also other conditions may contribute to TMJ-related self-reported symptoms and clinical findings. Several individuals with TMJ OA in the present study may have had concomitant myalgia and/or disc displacement that could contribute to the symptoms.

Table II
TMJ-related clinical examination findings in 54 patients with hand OA

	Hand OA patients with TMJ OA* ($n = 36$) *N* (%)	Hand OA patients with no TMJ OA or indeterminate ($n = 18$) *N* (%)	Differences in proportions (95% CI)
TMJ pain†	11 (31)	4 (22)	8 (−16, 33)
Crepitus	27 (75)	4 (22)	**53 (29, 77)**
Clicking	4 (11)	4 (22)	−11 (−33, 11)
Muscle pain‡	30 (83)	13 (72)	11 (−13, 35)

Bold numbers are statistically significant ($P < 0.05$).
* Individuals with CBCT-defined TMJ OA in one or both joints. In individuals with unilateral disease, we explored whether clinical findings were present in the affected joint. In individuals with bilateral disease, we explored whether clinical findings were present in one or both sides.
† Reported pain at palpation of TMJs (separate assessment of left and right joint).
‡ Reported pain at palpation of one or more muscle sites in temporal and masseter muscles (muscle-zone based) (separate assessment of left and right side).

In addition to crepitus and joint pain, TMJ OA is often associated with impaired jaw function[13]. However, in our study reduced mouth opening was almost absent, consistent with results by Schmitter *et al.*[13] Preserved jaw function may be the reason why few individuals (13%) had contacted the healthcare system because of their symptoms. Furthermore, pain in other joints may overshadow facial symptoms.

Among our hand OA patients, 67% had CBCT-defined TMJ OA. In previous observational studies, the populations and imaging criteria of CT/CBCT-defined TMJ OA have differed leading to large variations in OA frequencies. A population-based study of German birth cohorts demonstrated that 70% had TMJ OA by magnetic resonance imaging (MRI)[13], which is considered as less sensitive than CT/CBCT[4]. The high frequency can partly be explained by higher age (mean 74.6 years) and the fact that most affected individuals had small/moderate alterations such as surface flattening and sclerosis[13], which were interpreted as indeterminate in the present study[2,4].

The clinical examination underestimated the frequency of TMJ OA. Our sensitivity for the clinical diagnosis was low and in line with the DC/TMD[2]. Specificity was higher, but our patient series is too small to draw conclusion on the usefulness of clinical examination as a screening tool for TMJ OA[2]. In clinical care, imaging should always be considered individually based on whether the information will be relevant for the choice of treatment.

Crepitus was the most prominent sign in individuals with CBCT-defined TMJ OA. Frequencies of most TMJ-related clinical findings and self-reported symptoms were much higher in the OA group. However, the frequency of clinical muscle pain at palpation was similar across individuals with vs without TMJ OA, suggesting high frequency of myalgia in the entire study population. Hand OA patients may demonstrate more fibromyalgia-like symptoms[16], and an overlap in TMJ-related pain and muscle tenderness in other parts of the body has been shown[17].

Some study limitations need mentioning. The protocol for the instructions during the clinical examination had a less comprehensive translation procedure than required by the RDC/TMD international, which may result in non-comparability of data/diagnoses with those obtained in other languages. Moreover, the sample size is relatively small and a control group is missing to evaluate our frequency of TMJ OA. Hence, larger studies including a control group are needed. Longitudinal studies are warranted to explore whether hand OA patients are at increased risk of developing TMJ OA. Exploration of the association between TMJ OA and hand OA in a general population could also lead to larger external validity of the findings.

In summary, TMJ OA based on CBCT and clinical examination was common in elderly individuals with hand OA, suggesting that TMJ OA may be part of generalized OA. Individuals with CBCT-defined OA exhibited more TMJ-related clinical findings and self-reported symptoms than those without. Clinical crepitus was the most prominent sign for individuals with TMJ OA, even though the sensitivity of the clinical diagnosis was low. Impaired jaw function

was almost absent. Our results emphasize the importance of assessing TMJ OA and related symptoms in patients with hand OA.

Authors contribution

Study design: AKA, MK, LZA, TKK, IKH, TAL.
Collection and assembly of data: AKA, MK, LZA, IKH, TAL.
Analyses and interpretation of data: AKA, MK, LZA, TAL.
Drafting the article: AKA, MK, LZA, IKH, TAL.
Revising the article critically and final approval: A-K A, MK, LZA, TKK, IKH, TAL.
Statistical analyses: AKA, MK.
Obtaining of funding: IKH.

Conflicts of interest

None.

Role of the funding source

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.joca.2016.12.028.

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PAPER II

PAPER III

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ORIGINAL ARTICLE

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Imaging signs of temporomandibular joint osteoarthritis in an urban population of 65-year-olds: A cone beam computed tomography study

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Abstract

Background: Symptoms of osteoarthritis (OA) in the temporomandibular joint (TMJ) may vary and possible causes should be further explored, such as prevalence and characteristics of imaging features.

Objectives: Investigate prevalence, gender differences and characteristics of imaging signs of TMJ-OA by cone beam computed tomography (CBCT) in a population-based sample of 65-year-old Oslo citizens.

Materials and Methods: 159 (86 women, 73 men) individuals randomly recruited from a cohort of 460 Oslo citizens were examined with CBCT. The TMJs were categorised as with imaging signs of OA, no OA or indeterminate for OA.

Results: CBCT signs of TMJ-OA were found in 35% of the 159 participants: 47% of the women and 22% of the men. CBCT signs of TMJ-OA were unilateral in two-thirds of the TMJs and characterised by articular surface flattening and condylar osteophytes. In almost all joints with bone erosive findings, bone productive findings were also found. Participants with and without CBCT signs of TMJ-OA showed no significant difference in TMD pain screener. Fourteen of the 159 participants (9%) had pain-related TMD and 12 (8%) had been in contact with health care services due to TMD.

Conclusions: CBCT signs of TMJ-OA was common in this study group of 65-year-old Oslo citizens, found in every second woman and every fifth man. Articular surface flattening and bone productive changes, in particular condylar osteophytes, were the most frequent imaging features. Despite the high frequency of CBCT signs of TMJ-OA, few of the participants had pain-related TMD.

KEYWORDS
cone beam computed tomography, DC/TMD, diagnostic imaging, osteoarthritis, radiology, temporomandibular joint

1 | INTRODUCTION

Osteoarthritis (OA) is a major cause of pain and disability in older adults. OA is not simply a process of wear and tear, but rather abnormal remodelling of joint tissues driven by inflammatory mediators within the affected joint. Among the most common risk factors for OA are age, gender and prior joint injury. Despite the multifactorial nature of OA, the pathological changes seen in OA joints have common features that affect the entire joint structure resulting in pain, deformity and loss of function.[1] The changes seen in OA joints

include degradation of the articular cartilage, thickening of the subchondral bone, osteophyte formation, variable degrees of synovial inflammation, degeneration of ligaments and in the knee, the menisci and hypertrophy of the joint capsule. There can also be changes in the periarticular tissues.[1]

OA is the most common joint disease and a leading cause of disability in humans. Hands, knees and hips are the most frequently affected joints,[2,3] but OA can also manifest in the temporomandibular joint (TMJ). Like in other joints, OA in the TMJ is characterised by structural abnormalities and by patient-reported symptoms. TMJ OA can lead to substantial joint pain, dysfunction, dental malocclusion, as well as reduced health-related quality of life.[4] However, TMJ OA may be asymptomatic. Therefore, potential causes for the large variation in symptomatology should be further explored, such as the prevalence and characteristics of imaging features. Studies on the longitudinal development of TMJ OA in the general population may also throw light on this issue. The present cross-sectional study is the baseline examination of a sample drawn from an urban population, planned to be followed with 5- to 10-year intervals.

In the present study we focus on cone beam computed tomography (CBCT) features of TMJ OA. The purpose was to investigate prevalence, imaging characteristics and gender differences of CBCT signs of TMJ OA in a population-based sample of 65-year-old Oslo citizens.

2 | MATERIALS AND METHODS

2.1 | Participants

The present study was performed at the Department of Maxillofacial Radiology, Institute of Clinical Dentistry, University of Oslo as part of the interdisciplinary collaborative project 'OsloMunn65' (OM65) initiated and organised by the Department of Cariology and Gerodontology. The target population was 65-year-old (born in 1954) residents of Oslo (5413 65-year-old residents in 2019). A random sample of the target population was drawn from the National Bureau of Statistics Recordings. Of 797 eligible individuals who were reached by phone, 460 individuals accepted the invitation to participate in the main study (response rate 58%). Details of the recruitment process and drop-outs in 'OM65', have been presented elsewhere.[5]

Prior to attending the clinical examination all participants in 'OM65' answered a self-administered questionnaire via an electronic link (Nettskjema; University of Oslo).

All individuals in the OM65 project underwent dental and panoramic radiographic examinations at the Department of Maxillofacial Radiology. During these examinations participants were randomly recruited to the present study, called OM65-TMJ. Data collection for OM65 was performed 5 days a week, but due to logistical challenges, data collection for OM65-TMJ was limited to two to three days a week, resulting in a total of 169 individuals invited to OM65-TMJ. During collection days for OM65-TMJ, all present individuals in OM65 were invited, independently of TMD-related symptoms and immediately after recruitment. In this paper the recruited individuals to OM65-TMJ will be referred to as participants.

The study was approved by the Regional Committee of Medical and Health Research Ethics (REC) of south-east Norway (2018/1383). The study was conducted in accordance with the World Medical Association Declaration of Helsinki, and all participants signed a written informed consent form prior to study inclusion.

2.2 | Imaging assessment of TMJ

The CBCT examinations were performed from April 2019 until December 2019. All examinations were performed by the same radiographer. The CBCT unit was a 3D Accuitomo, XYZ slice Tomograph, (J. Morita Corp.). Field of view (FOV) was 140 mm × 50 mm. The scans were obtained with 360° rotation at 85 kV and 9 mA. The image acquisition time was 17.5 s. Spatial resolution on CBCT images was set to 150 μm. CBCT images were taken with teeth in occlusion and standardised head position. Reconstructed images were exported in 'Digital Imaging and Communications in Medicine' (DICOM) format files. The images were analysed in Sectra PACS viewer IDS 7 version (Sectra) on an Eizo MX315W (31.1-in., colour, 4096 × 2160) monitor. The images were viewed in axial, oblique sagittal and oblique coronal planes (perpendicular to and parallel with the long axis of the mandibular condyle) in the multiplanar reformatted view of the software. Observers could adjust the brightness and contrast settings for the best display to mimic the routine diagnostic approach. All images were assessed separately by two maxillofacial radiologists (MKO, LZA) with 10–20 years of experience of interpreting TMJ images.

The observers were calibrated before they assessed each joint for CBCT signs of TMJ OA. The observers performed the assessment of CBCT images independently and blinded to clinical information. The diagnostic criteria described by Ahmad et al.[6] were used in the analysis of bone change characteristics, and according to their definitions each TMJ was categorised as with CBCT signs of OA, no OA or indeterminate for OA. Cases of inter-observer disagreement were discussed until consensus was met. A second reading of images of 20 participants was made after 16 weeks by the two observers. Images for second reading were selected using a random number generator (RNG-Random Number Generator, Intemodino Group s.r.o., App Store). Inter-observer variation between the radiologists and intra-observer variation between each radiologist's two readings were identified and assessed by kappa statistic.

CBCT signs of TMJ OA was also graded based on the classification system proposed by Ahmad and Schiffman[7]: Grade 1 when the joint displayed either a single small osteophyte (<2 mm length), or a single small erosion (<2 mm in depth and width), or a single small subcortical cyst (<2 mm in depth and width); Grade 2 when the joint displayed a large osteophyte (≥2 mm length), and/or a large erosion (≥2 mm in depth and width), and/or a large subcortical cyst (≥2 mm in depth and width), and/or two or more imaging signs of Grade 1.

2.3 | Assessment of patient history and pain-related TMD

Self-reported patient history and TMD-related symptoms were registered by one observer (MKO) interviewing the participant. All participants were asked about previous contact with the healthcare services due to jaw dysfunction and/or facial pain.

All participants orally answered the long version of TMD Pain Screener from the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD), Axis I.[8,9] This is a self-report instrument to assess the presence of any pain-related TMD. The long version of the TMD pain screener is a questionnaire containing six questions regarding symptoms of pain-related TMDs, including duration of pain in the jaw or temple area, presence of pain or stiffness in the jaw on waking, and activities that may have an impact on pain, such as chewing hard food, jaw movements, jaw habits and other jaw activities. Based on the participant's response, points are given on each item in the questionnaire. The first item has points from 0 to 2, the remaining items 1. A sum is computed, and the total score ranges from 0 to 7. Score >2 is considered to indicate pain-related TMD.

A validated translation of the DC/TMD (including the TMD pain screener and the clinical criteria for diagnosis of TMJ-OA) to Norwegian was completed in 2019.[10] The Norwegian version was used in the data collection for this study.

All participants in OM65 completed the three validated screening questions for temporomandibular disorders (3Q/TMD).[11] Most participants answered these questions in the online questionnaire at home, prior to the clinical/radiological examinations. The 3Q/TMD includes questions on weekly jaw-face-temple pain (Q1), pain on function (Q2) and catching/locking of the jaw (Q3). In the present study the 3Q/TMD was used to explore any potential TMD-related selection bias in the recruitment of participants from OM65 to OM65-TMJ.

2.4 | Statistical analyses

IBM SPSS version 26.0 (Statistical Package for Social Services) was used for statistical analyses.

Descriptive statistical analyses were performed, and the results are presented in the form of number (*n*) with percentage. All data were stored and analysed in the TSD (Service for Sensitive Data, Centre for Information Technology Services, University of Oslo).

Kappa (κ) statistics analysis was performed to determine consistency within and between observers. For the reliability studies, CBCT signs of TMJ OA were dichotomized as either present (TMJ OA) or absent (no TMJ OA and indeterminate for OA). Kappa values were categorised according to Fleiss et al.[12] Interpretation of values <0.40 were poor, values from 0.40 to 0.75 were fair to good, and values >0.75 were excellent. For inter-observer reliability the agreement was evaluated pairwise, and a mean of these values gave the final kappa value.

3 | RESULTS

A total of 159 participants were included in the present study: 86 women (54%) and 73 men (46%). A detailed flowchart of recruitment with reasons for rejection and exclusion is shown in Figure 1.

Fifty-six (35%) of the 159 participants showed CBCT signs of TMJ OA: 40/86 (47%) women and 16/73 (22%) men (Table 1). The difference between women and men was statistically significant ($p < .05$). The majority, 36/56 (64%), had unilateral findings. Grade 2 signs were found in 28/40 (70%) of the women and in 11/16 (69%) of the men.

Of the 103 participants without CBCT signs of TMJ OA 36 participants had signs indeterminate for TMJ-OA (Table 1), bilaterally ($n = 22$) or unilaterally ($n = 14$).

On joint level 76 (24%) of the 318 joints assessed showed CBCT signs of TMJ OA (Table 1).

Inter- and intra-observer agreement analysis for this assessment showed mean kappa values of 0.75 and 0.75 (range 0.73–0.77), respectively.

Of the 242 joints without CBCT signs of TMJ OA, 70 joints were interpreted as having imaging signs indeterminate for OA: 25 (36%) had articular surface flattening, 18 (26%) subcortical sclerosis and 27 (39%) a combination.

In the 76 joints with CBCT signs of TMJ OA, the most frequent bone changes were articular surface flattening, condylar osteophytes, surface erosions and subcortical sclerosis (Figure 2). The most frequent CBCT sign diagnostic for OA was condylar osteophyte of varying size (Figure 3). Surface erosion, consistently small (<2 mm), was also rather frequent. Almost all these joints had bone productive findings. Only four joints with CBCT signs of TMJ OA were solely erosive, and three of them had small erosions. CBCT signs of OA were clearly more frequent in the condyle than in the fossa/eminence (Figure 2).

Forty-six (61%) of the joints with CBCT signs of OA were categorised as Grade 2 (Table 1). In 23/46 (50%), the categorisation was based on two or more small (<2 mm) findings. In the condyle, large (≥2 mm) osteophytes were found in 17/46 (37%). Large surface erosions and large subcortical cysts were uncommon in the condyle and in the fossa/eminence.

Fourteen of the 159 participants (9%) scored >2 on the TMD pain screener, indicating pain-related TMD. There was a statistically significant difference in proportions of pain-related TMD between women and men in the entire study population; women 12/86 (14%), men 2/73 (3%), but not between those with and those without CBCT signs of TMJ OA, nor between women and men with CBCT signs of TMJ OA.

Twelve of the 159 participants (8%): women 8/86 (9%), men 4/73 (5%) reported previous contact with the healthcare services due to

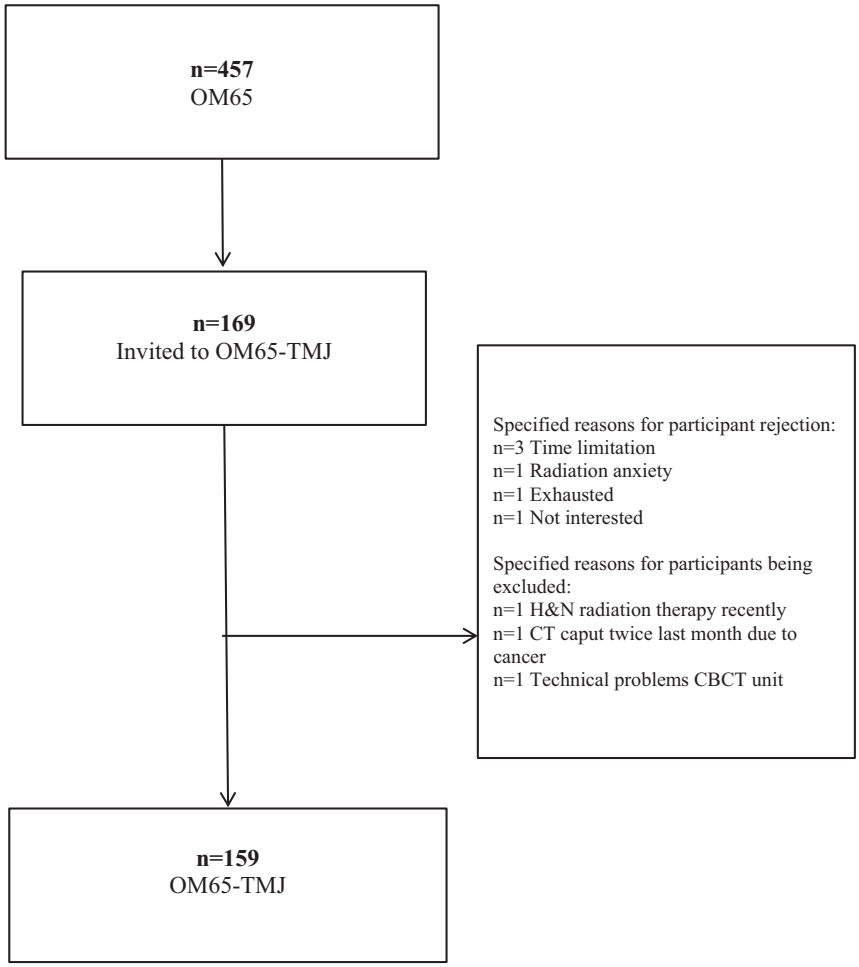

FIGURE 1 Flowchart showing the recruitment of 159 65-year-old Oslo citizens for participation in the OM-65TMJ study. CBCT, cone beam computed tomography; CT, computed tomography; H&N, head and neck; CT, computed tomography; OM65, OsloMunn65; OM65-TMJ, OsloMunn65 temporomandibular joint.

TABLE 1 Frequencies and grading of CBCT signs of OA in the TMJs[a,b] in 159 65-year-old Oslo citizens.

	Participants *n* = 159	Women *n* = 86	Men *n* = 73	Joints *n* = 318	
No TMJ-OA	67 (42%)	27 (31%)	40 (55%)	172 (54%)	
Indeterminate for TMJ-OA	36 (23%)	19 (22%)	17 (23%)	70 (22%)	
TMJ-OA	56 (35%)	40 (47%)	16 (22%)	76 (24%)	
				Grade 1	30 (39%)
				Grade 2	46 (61%)

Abbreviations: CBCT, cone beam computed tomography; OA, osteoarthritis; TMJ, temporomandibular joint.

[a]According to the diagnostic criteria by Ahmad et al.[6]

[b]According to the grading by Ahmad and Schiffman.[7]

jaw dysfunction and/or facial pain. There was no significant difference in proportions between participants with and without CBCT signs of TMJ OA.

4 | DISCUSSION

'Osteoarthritis is a disease of the joint as an organ' stated Loeser et al.[1] The authors concluded that modern definition of OA must include both patient-reported symptoms as well as structural changes within the joint, including not only the remodelling of articular cartilage and neighbouring bone but also the synovial inflammation and damage to ligaments and menisci. Driven by mechanical factors, OA is an active response to injury, rather than a degenerative process.[1]

It is generally accepted that OA is a whole joint low-grade inflammatory disease, this is certainly true for the TMJ as well. As the CBCT features used to define TMJ OA in the present study are limited to the bony structures, we decided to call the condition under investigation CBCT signs of OA. Bony changes in the TMJ may represent different conditions, such as the high-grade

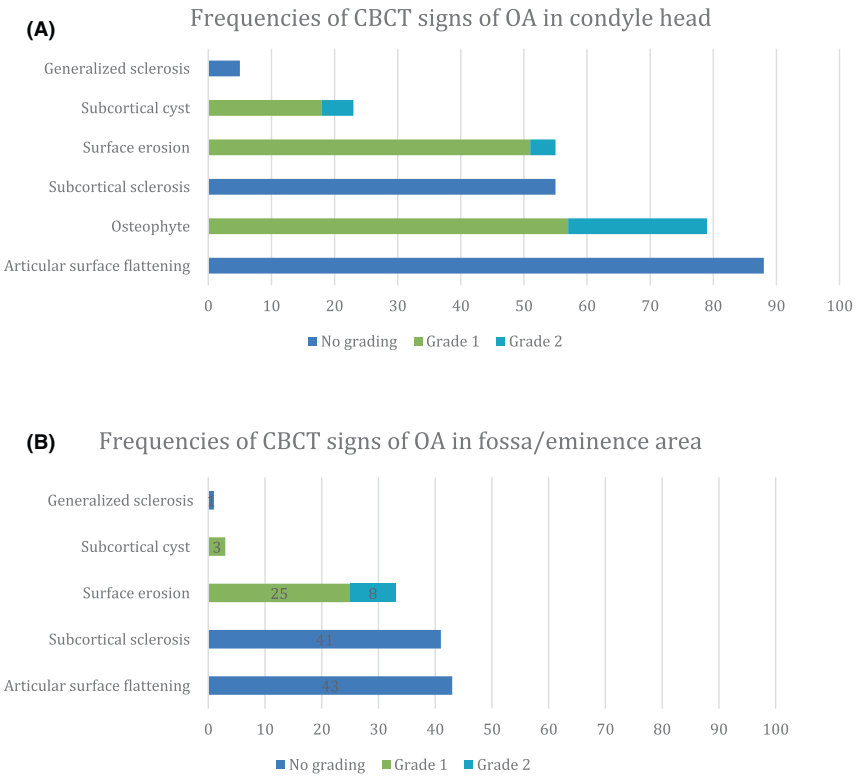

FIGURE 2 (A) The frequencies of the different CBCT signs of OA in the condyle head in 159 65-year-old Oslo citizens. (B) The frequencies of the different CBCT signs of OA in the fossa/eminence area in 159 65-year-old Oslo citizens.

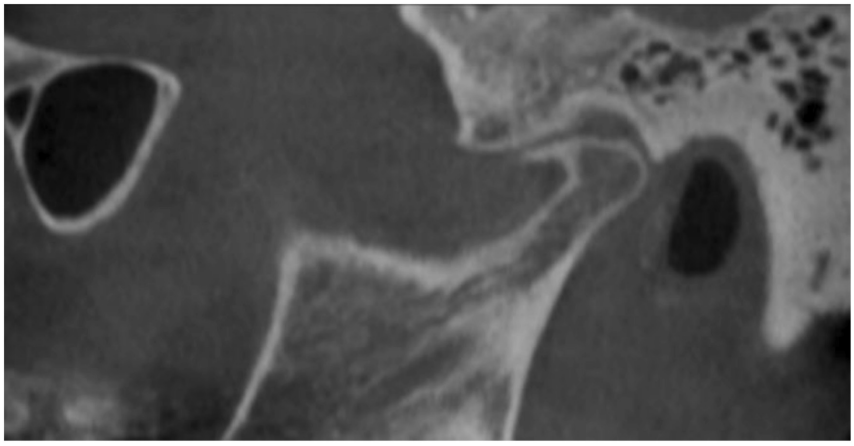

FIGURE 3 Woman, 65 years, with CBCT signs of OA in the TMJ: deformed joint with condylar osteophyte, subcortical sclerosis, flattened condyle and fossa/eminence and no erosion (TMD Pain Score 0).

inflammatory arthritides. In this group rheumatoid arthritis (RA) is the most frequent and may show abnormalities that can mimic OA. However, in the present study the imaging features were characterised by bone production and osteophytes in particular. This is very typical for OA in general, where bone destruction/erosion usually is absent.[13] In contrast, RA is characterised by bone erosions and not bone production/osteophytes.[14] Very few joints in the present study showed pure erosive changes. Therefore, we are convinced that our findings represent TMJ OA. It should be mentioned that in longstanding RA, secondary OA changes may develop.

We used the most widely accepted criteria for diagnosing TMJ OA, the DC/TMD. In these criteria, CT was emphasised as the most superior method for bone evaluation.[6] In studies of CT and CBCT the diagnostic reliability has proved to be high and similar.[15,16] Thus, CBCT with lower radiation exposure was used as the diagnostic method.

CBCT signs of TMJ OA were mainly characterised by remodelling (articular surface flattening) and bone productive changes, consistently found also in TMJs with bone erosive changes. Different imaging signs in the TMJ have been suggested to represent various stages of the disease; erosive changes may indicate early or acute TMJ OA whereas sclerosis, flattening and osteophytes may indicate late changes.[17] In the present study the OA signs were clearly late, approaching end stage disease, similar to the findings seen in our study of elderly patients with hand OA.[18]

In agreement with studies of TMJ OA in ageing adults,[18–20] condylar changes were seen more often than temporal bone changes. Condylar osteophytes of varying size were clearly the most frequent signs. Erosive findings, consistently small, were also rather frequent.

The nature of osteophytes has been discussed in a review by van der Kraan and van der Berg,[21] who found a strong association between osteophyte formation and cartilage damage. However, the same review states that osteophytes may occur without such damage, bringing up the discussion whether osteophytes are a pathological phenomenon or a functional adaptation.

Although the prevalence of CBCT signs of TMJ OA in the present study was more than twice as high in women as in men, the characteristics of findings such as the severity of TMJ OA (percentage of Grade 2 joints) and the high occurrence of unilateral disease appeared quite similar in both genders. About 61% of the joints with CBCT signs of OA were classified as Grade 2. However, only half of the Grade 2 joints showed Grade 2 changes, mostly large (≥2 mm) osteophytes. Those occurred in about one third of the Grade 2 joints, meaning that most showed combinations of two or more small changes (Grade 1).

It can be a challenge to differentiate between morphologic variations of normalcy and small pathologic changes, such as between subtle 'beaking' of the anterior aspect of the condyle and a small osteophyte.[16] In routine clinical practise it is important not to overdiagnose the disease. Imaging diagnosis of TMJ OA should be based on evident abnormalities, that is, frank pathological findings and not on subtle changes[22]

The present sample of participants is truly population based. To the best of our knowledge this is the first study on TMJ OA in an urban population of older individuals of identical age and almost equal numbers of women and men. CBCT signs of TMJ OA proved to be common and the difference between women and men was highly significant.

The inter- (as well as intra-) observer agreement in the present study was good, close to the threshold of excellence (> 0.75).[12] The kappa value of 0.75 was slightly higher than the 0.71 based on CT reported by Ahmad et al.[6] In a previous CBCT study on TMJ OA using the same observers as in the present study, the kappa value was 0.67.[18] We believe the increased observer agreement in the present study could be due to the thorough calibration.

In a recent CBCT study, Dumbya et al. reported a prevalence of 66% TMJ OA in older adults.[23] The percentage of men investigated was similarly high (43%) as compared to the present study, and the prevalence of TMJ OA in women was also higher than in men, 73% versus 56%. As in the present study this difference was significant. Although the participants were older (mean 73 years, range 65–94), the higher prevalence may be due to differences in the diagnostic criteria applied. Dumbya et al. used articular surface flattening and subcortical sclerosis as imaging signs decisive for TMJ OA.[23] In contrast, in the present study these signs were considered indeterminate for TMJ OA.[6]

The use of different diagnostic criteria will surely have an impact on the prevalence. If we had applied the same criteria as Dumbya et al. in the present study, the prevalence of CBCT signs of TMJ OA would be 58% instead of 35%. The prevalence in women would be 69% instead of 47%. These findings are more in line with the frequencies reported by Dumbya et al. and emphasise the importance of using standardised diagnostic criteria in research.

Using CBCT and identical diagnostic criteria, we found a prevalence of 67% TMJ OA in a cohort of patients with hand OA, mostly women.[24] The lower prevalence of CBCT signs of TMJ OA among women in the present study (47%) was expected as hand OA often is considered a marker of a generalised susceptibility to OA.[25] Furthermore, the mean age of the participants in the hand OA study was somewhat higher (mean 71 years, range 61–83) than in the present study.

Most of the participants with CBCT signs of TMJ OA had unilateral findings. This was unexpected as many researchers consider that one TMJ may have an influence on the contralateral joint. From the present study we learned that this is not always the case.

In the present study 8% of the participants had been in contact with the health care services due to TMD and less than 10% scored > 2 on the TMD pain screener. However, the percentage was almost five times higher for women than for men. As there was no significant difference between those with and without CBCT signs of TMJ OA, the origin of pain-related TMD might be non-articular. The discrepancy between symptoms and imaging findings is in accordance with a literature review of TMD in older adults,[26] concluding that self-reported TMJ pain decreases[27] and radiologically assessed TMJ OA increases with age.[19,28] The reasons behind this discrepancy are unknown.[26] Other possible explanations have been suggested,[26] one of them being subjectivity of the interpretation of pain. The majority of elderly patients with TMJ pain describe the pain as mild and it also seems self-limiting.[26] Moreover, as people get older, diseases with more severe symptoms affecting other areas of the body may take precedence. This may result in elderly patients being less aware of TMJ symptoms and refraining from treatment.[24]

A strength of the present population-based study is that the participants were randomly recruited and of the same age. Further, the study included an almost equal number of both genders.

The present study has limitations. Compared to the main study, OM-65, the sample size in OM 65-TMJ could have been larger, but recruitment of participants to OM65-TMJ was restricted by the actual resources for CBCT scanning and coordination at the Department of Maxillofacial Radiology. These resources were available only three out of 5 days a week, even though the participants in the main study OM-65 were recruited for dental examinations all weekdays in the data collection period.

To explore potential selection bias, gender distribution, education level and TMD-related symptoms, the study population was compared with the OM65-study population. The gender distribution was similar, but the proportion of participants with higher education in the present study population was higher than in the OM65-study population. This may have affected the prevalence estimates;

however, the level of education did not show a significant association with the prevalence and grade of OA signs of the TMJs.

Limitations concerning the recruitment of participants to the OM65-study have been discussed elsewhere.[5]

5 | CONCLUSIONS

The present study demonstrated that CBCT signs of TMJ OA were common in an urban population of 65-year-olds, found in every second woman and every fifth man. Articular surface flattening and condylar osteophytes were the most frequent imaging features, seen also in almost all joints with erosions. Despite the high frequency of CBCT signs of TMJ OA, few of the participants had pain-related TMD or had been in contact with health care services due to TMD.

AUTHOR CONTRIBUTIONS

Margareth Kristensen Ottersen was involved in study design, collection and assembly of data, interpretation and statistical analyses of data, drafting the article, revising the article critically and final approval. Tore A. Larheim was involved in study design, drafting the article, revising the article critically and final approval. Lene Hystad Hove was involved in study design, collection and assembly of data, drafting the article, revising the article critically and final approval. Linda Z. Arvidsson was involved in study design, collection and assembly of data, interpretation of data, drafting the article, revising the article critically and final approval.

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CONFLICT OF INTEREST STATEMENT

All authors declare no potential conflicts of interest with respect to the authorship and/or publication of this article.

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/joor.13547.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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APPENDIX (1-6)

Appendix 1

SPØRRESKJEMA «Osteoartritt (OA) i kjeveledd på pasienter med hånd-OA»

Nedenfor finner du spørsmål om kjeveleddsproblemer.
Kryss av for ett alternativ på hvert spørsmål.

Kjeveleddsproblemer *den siste måneden*
Har du opplevd smerte i ansikt, kjeve eller foran øret?

- **Ja**
- **Nei**
- **Nei, men tidligere i livet**

Har du opplevd smerte når du gaper?
For eksempel hvis du spiser en stor bit eller gaper hos tannlegen)

- **Ja**
- **Nei**
- **Nei, men tidligere i livet**

Har du opplevd smerte når du tygger mat?

- **Ja**
- **Nei**
- **Nei, men tidligere i livet**

Har du opplevd at kjeven låser seg, dvs at du ikke kan gape opp?

- **Ja**
- **Nei**
- **Nei, men tidligere i livet**

Andre spørsmål
Har du noen gang tatt kontakt med lege eller tannlege om smerte i kjeven eller problemer med å gape?

- **Ja**
- **Nei**

Har du knase- eller skrapelyd ved gaping eller kjevebevegelse?

- **Ja**
- **Nei**
- **Nei, men tidligere i livet**

Har du klikke- eller kneppelyd ved gaping eller kjevebevegelse?

- **Ja**
- **Nei**
- **Nei, men tidligere i livet**

Har bittet endret seg (tennene flyttet seg) i løpet av de siste 5 årene, dvs biter du annerledes sammen enn tidligere?

- **Ja**
- **Nei**

Appendix 1

UNDERSØKELSESSKJEMA
Kort klinisk kjevefunksjons-undersøkelse utført av: _____

Redusert gapeevne
Er det mulig å gape over de midterste tre fingre (PIP-ledd)?
- ☐ Ja
- ☐ Nei

Kjeveleddslyder (begge sider):
Forekommer det klikking eller krepitasjon (knasing) ved gaping/ kjevebevegelse?

- ☐ Ingen lyd

Klikking
- ☐ Høyre side
- ☐ Venstre side

Krepitasjon
- ☐ Høyre side
- ☐ Venstre side

Smerte ved palpasjon
(bruk pekefinger og langfinger):

Kjeveledd lateralt, ved gap?
- ☐ Høyre
- ☐ Venstre

M. masseter?
- ☐ Høyre
- ☐ Venstre

M. temporalis?
- ☐ Høyre
- ☐ Venstre

Tilbud til pasienten:
Gratis undersøkelse av kjeveledd, inkl. røntgen ved Det odontologiske fakultet ("Tannlegehøyskolen").
Ønsker pasienten det?
- ☐ Ja
- ☐ Nei

Hvis Ja:
Pasientens navn: _____

Mobil: _____

Pasienten blir ringt opp og blir tilbudt en tid som passer han/henne.
Undersøkelsen tar totalt ca. 30 minutter og er som nevnt gratis.
Spørsmål vedrørende undersøkelsen kan besvares av:

Tannlege/ PhD stipendiat
Anna-Karin Abrahamsson, mob tlf: 98815390

Eller:
Professor Tore A Larheim tlf. 22852234 (adm sekr)
Avd for kjeve- og ansiktsradiologi, Institutt for klinisk odontologi,
Universitetet i Oslo

TMD-Smertescreening

1. I løpet av de siste 30 dagene, hvor lenge varte enhver smerte i kjeven eller tinningen på den ene eller andre siden?

    a. Ingen smerte
    b. Smerte kommer og går
    c. Smerte er alltid til stede

2. I løpet av de siste 30 dagene, har du hatt smerte eller stivhet i kjeven din når du våkner?

    a. Nei
    b. Ja

3. I løpet av de siste 30 dagene, førte noen av de følgende aktivitetene til endring av enhver smerte (det vil si, gjorde det bedre eller verre) i kjeven eller tinningen din på den ene eller andre siden?

    A. Tygge hard eller seig mat

    a. Nei
    b. Ja

    B. Gape eller bevege kjeven framover eller til siden

    a. Nei
    b. Ja

    C. Kjevevaner som å holde tenner sammen, presse eller gnisse tenner eller tygge tyggegummi

    a. Nei
    b. Ja

    D. Andre kjeveaktiviteter som snakking, kyssing eller gjesping

    a. Nei
    b. Ja

Appendix 3

Self reported[1] diseases and medications in 54 participants with hand OA (Paper I and II)		
Diseases[2]	n=54	n=54
Blood pressure issues	15	-
Cardiovascular disease (angina, myocardial infarction, other heart failure)	8	-
Lung diseases (asthma, bronchitis, other lung diseases)	10	-
Allergy (hay fever, asthma, eczema)	15	-
Sciatica	3	-
Stroke	2	-
Cancer	4	-
Neurological disease	4	-
Diabetes	6	-
Hypo- or hyperthyroidism	9	-
Mental disorder	3	-
Use of alcohol or other stimulants /drugs/narcotics	1	-
Kidney disorder	3	-
Liver disorder	1	-
Stomach ulcer or other gastric disease	2	-
Blood disorder (anemia or other bleeding disorder)	1	-

Appendix 3

Self reported[1] use of medication in the 54 participants in Paper I and II		
	n=54	n=54
Medications[3, 4]		Previously
Prednisolone	10	3
NSAID	13	25
Coxibs	2	16
Methotrexate*	1	1
Antimalaria*	0	3
Etanercept	0	1
Estrogen*	8	21
Bisphosphonates	3	2
Calcitonin	1	0
Calcium	19	5
D-vitamin	27	7

[1] Results from the Oslo Hand OA cohort questionnaire (2013)
[2] Answered "yes" in the questionnaire on the following medical problem at the (question: "Is the patient's health currently affected by one or more of these medical problems?")
[3] Answered "yes" in the questionnaire on the following medications
[4] No of the participants answered yes for Infliximab, Adalimumab, Rituximab, Abatacept, Auranofin, Sulfasalazine, Myocrisin, Cyclosporine or Leflunomide.
* values were missing for one or two participants
NSAID, Non-steroidal Non-inflammatory Drugs

Appendix 4

Relevant and most frequent self-reported diseases, medications and demographic characteristics of 159 65-year-old Oslo citizens (Paper III)		
		n=159
Previously diagnosed with osteoarthritis[1,2]		63 (40 %)
	Hand	31 (20 %)
	Knee	19 (12 %)
	Hip	22 (14 %)
	TMJ	2 (1 %)
Previously diagnosed with rheumatic joint disease		17 (11 %)
	Polymyalgia rheumatica	4 (3 %)
	Rheumatoid arthritis	3 (2 %)
	Psoriatic arthritis	3 (2 %)
	Gout	2 (1 %)
	Other	5 (3 %)
Education level[3]	Lower education	60 (38 %)
	University/college education	99 (62 %)
Working status[3]	Still working	109 (69 %)
	Not working (retired, disabled)	50 (31 %)
Smoking[3]	Never	68 (43 %)
	Former	69 (43 %)
	Current	22 (14 %)
Most frequent self-reported diseases[3]	High blood pressure	43 (27 %)
	Astma	15 (9 %)
	Osteoporosis	12 (8 %)
	Cardiovascular disease	11 (7 %)
	Diabetes II	8 (5 %)
Most frequent self-reported medications[3]	Blood pressure regulation	34 (21 %)
	Cholesterol regulation	29 (18 %)
	Allergy medication	15 (9%)

[1] Results from the OM65-TMJ Questionnaire (Interview)
[2] Participants were given the option to self-report more than one joint
[3] Results from the OM65 Questionnaire (Online)

Appendix 5
Samtykkeskjema 1

Forespørsel om deltakelse i prosjektet

"Osteoartritt (OA) i kjeveledd på pasienter med hånd-OA"

Bakgrunn og hensikt

I 2013 har du deltatt i prosjektet "Sykdomsforløp ved håndartrose" og gjennomgått ulike undersøkelser på Revmatologisk poliklinikk, Diakonhjemmet Sykehus. I forbindelse med kjeveleddsundersøkelsen som ble utført, ble du spurt om vi kunne få gjøre en røntgenundersøkelse (CT= Computer Tomografi) av dine kjeveledd. Du var positiv, og dette er en skriftlig forespørsel til deg om du fortsatt er interessert i at vi utfører en slik undesøkelse.

Dette prosjektet er en delstudie av prosjektet "Sykdomsforløp ved håndartrose"; vi ønsker å undersøke om personer med hånd-osteoartritt (OA)/artrose også er rammet av kjeveledds-OA.

Studien vil gi en indikasjon på forekomst av kjeveledds-OA hos pasienter med hånd-OA i Oslo området. Vi vil også få svar på hvor store kjeveplager (smerter, funksjonsnedsettelse) en slik tilstand gir, hva slags plager som dominerer (ledd- eller muskelplager), og hvor pålitelig en enkel og rask klinisk undersøkelse er for å kunne påvise kjeveledds-OA, dvs skille et slikt ledd fra et friskt kjeveledd. CT undersøkelsen vil også gi svar på hva slags typiske røntgenfunn vi finner i kjeveledd med OA hos eldre. Selv om en slik undersøkelse er anerkjent som den mest pålitelige røntgenmetoden for å undersøke leddflatene i kjeveledd, er det så vidt vi kjenner til ikke gjennomført større studier av eldre. De aller fleste publiserte studier er utført på pasienter 20 – 40 år, da det er denne aldersgruppen som har mest ansiktssmerter og kjevefunksjonsproblemer, såkalt TMD (TemporoMandibulær Dysfunksjon).

Studien gjennomføres som et samarbeidsprosjekt mellom Revmatologisk avd, Diakonhjemmet Sykehus og Avd. for kjeve- og ansiktsradiologi, Institutt for klinisk odontologi, Det odontologiske fakultet, Universitetet i Oslo (UiO).

Hva innebærer studien?

Hvis du sier ja til å få gjort en CT undersøkelse av dine kjeveledd, betyr det at du vil få en time, som passer deg, på Avd. for kjeve- og ansiktsradiologi, Institutt for klinisk odontologi, UiO, på folkmunne kalt "Tannlegehøyskolen" i Oslo. Vi vil også gjøre en kort klinisk kjeveundersøke som supplement til den undersøkelsen vi foretok på Diakonhjemmet.

Undersøkelsen er gratis for deg og vil ta ca. 45 min.

Mulige fordeler og ulemper

CT undersøkelsen vil gi informasjon om hvorvidt dine kjeveledd er rammet eller ikke rammet av OA. Vi vil gjennomgå undersøkelsen med deg, forklare eventuelle funn og besvare eventuelle spørsmål.

Enhver røntgenundersøkelse innebærer en viss risiko grunnet ioniserende stråling. CT undersøkelsen vi utfører har meget lav risiko. Vi har betydelig erfaring med diagnostikk av kjeveledd på vår avdeling, ikke minst med denne metoden, og vi benytter et svært lite strålefelt og lave eksponeringsverdier (som fører til veldig liten dose; bekreftet av Statens Strålevern).

Appendix 5
Samtykkeskjema 1

Hva skjer med prøvene og informasjonen om deg?

Informasjonen som registreres om deg, skal kun brukes slik som beskrevet i hensikten med studien. Alle opplysninger vil bli behandlet uten navn og fødselsnummer eller andre direkte gjenkjennende opplysninger. En kode knytter deg til dine opplysninger/CT undersøkelsen gjennom en navneliste. Det er kun autorisert personell knyttet til prosjektet som har adgang til navnelisten og kan finne tilbake til deg. Prosjektet forventes å være avsluttet i 2019, og navnelisten vil da bli slettet. Det vil ikke være mulig å identifisere deg i resultatene av studien når disse publiseres. CT undersøkelsen vil arkiveres i en journal, i ditt navn, ved Det odontologiske fakultet, i minst 10 år. Det gjør vi med alle undersøkelser som utføres på vår avdeling.

Frivillig deltakelse

Røntgenundersøkelsen er frivillig og du kan når som helst, og uten å oppgi noen grunn, trekke ditt samtykke. Om du sier ja til CT undersøkelsen, kan du senere trekke tilbake ditt samtykke til at vi får bruke CT funnene i vår forskning. Dette vil ikke få noen konsekvenser for deg.

Dersom du ønsker å få utført en CT undersøkelse, undertegner du samtykke-erklæringen på siste side. Dersom du senere ønsker å trekke denne erklæringen tilbake eller har spørsmål, kan du kontakte Tannlege/ PhD stipendiat Anna-Karin Abrahamsson tlf.: 988 15 390 eller prosjektansvarlig for dette delprosjektet Professor Tore A Larheim tlf.: 22852016.

Ytterligere informasjon om studien finnes i kapittel *A* – *utdypende forklaring av hva studien innebærer.*

Ytterligere informasjon om personvern og forsikring finnes i kapittel B – *Personvern, økonomi og forsikring.*

Samtykkeerklæring følger etter kapittel B

Kapittel A- utdypende forklaring av hva studien innebærer

Kriterier for deltakelse

Pasienter med håndartrose som deltar i prosjektet ”Sykdomsforløp ved håndartrose” ved Diakonhjemmet Sykehus er aktuelle for studien.

Bakgrunnsinformasjon om studien

Osteoartritt, forkortet OA (også kalt osteoartrose, artrose eller slitasjegikt) er den vanligste humane leddsykdommen. Det er også den sykdommen som hyppigst rammer kjeveleddet. Sykdommen kan gi betydelig subjektivt besvær med smerter og redusert funksjon, foruten lyder fra kjeveleddet. Men, sykdommen kan også være asymptomatisk; helt uten symptomer. De fleste pasientene med mye plager (og ”diagnosen” TMD) er som oftest i yngre aldersgrupper, særlig mellom 20 og 40, men kan også være svært unge. Vi er i gang med et eget proskjekt på disse unge pasientene.

På TMD pasienter kan det være meget vanskelig å avgjøre om plagene skyldes selve kjeveleddet eller muskulaturen. Denne studien på eldre vil kunne gi svar på hvor store forandringer man kan ha i kjeveleddene uten å ha subjektive plager og/eller nedsatt funksjon. Dette er viktig kunnskap når vi i vårt daglige kliniske arbeid forsøker å avgjøre de(n) viktigste årsaken(e) til smerter og funksjonsnedsettelse hos pasienter med TMD.

OA er vanlig i den eldre delen av befolkningen, særlig er kne- og hofteledds-OA kjent for mange. Det foreligger imidlertid svært få kjeveleddstudier på eldre og disse er utført med mindre pålitelige røntgenmetoder. Kunnskapen om kjeveledds-OA i denne delen av befolkningen er derfor liten, både hva angår de subjektive plagene og de radiologiske (røntgenologiske) karakteristiska (”endestadiet”). Det er vel kjent at OA i andre ledd kan gi så mye smerter og funksjonsnedsettelse, pga ødelagte leddflater, at det er nødvendig med kirurgiske inngrep, endog kunstige ledd.

Diagnostisering av kjeveledds-OA baseres på anamnese (sykehistorie), klinisk undersøkelse av kjeveledd/tyggemuskulatur, samt supplerende radiologisk undersøkelse basert på den kliniske vurderingen. Det er generelt akseptert at Computer Tomografi (CT), en data-assistert snittbildemetode, er den beste røntgenmetoden for å stille diagnosen OA. Retningslinjene for klinisk undersøkelse av kjeveledd er helt nylig (2013) revidert av en stor gruppe internasjonalt anerkjente TMD forskere. Denne reviderte kliniske undersøkelsen ønsker vi å få testet opp mot CT undersøkelsen for å få mer kunnskap om i hvilken grad dette diagnostiske verktøyet vil kunne avdekke om et individ har kjeveledds-OA. Derfor gjør vi den kliniske tilleggsundersøkelsen samtidig med at vi utfører CT undersøkelsen.

På grunnlag av dette har vi laget en studie der vi ønsker å få svar (indikasjon) på forekomst av kjeveledds-OA hos pasienter med hånd-OA, hva som karakteriserer kjeveledds-OA klinisk og

radiologisk hos eldre («endestadiet»), hva slags funn/observasjoner som dominerer og, i hvilken grad en enkel, klinisk undersøkelse kan skille et kjeveledd med OA fra et friskt kjeveledd. Vi (klinikere og forskere ved Avd for kjeve- og ansiktsradiologi, UiO) inngikk derfor et samarbeid med klinikere, forskere og helsepersonell ved Revmatologisk avd, Diakonhjemmets sykehus om denne delstudien innenfor prosjektet "Sykdomsforløp ved håndartrose", som er en langtidsoppfølging av en kohort med hånd-OA registrert ved sykehuset.

Oversikt over studiebesøk, aktuelle undersøkelser og forventet tidsbruk

Bekrevet ovenfor.

Fordeler og ulemper

Beskrevet ovenfor. Dersom undersøkelsen gir funn som krever behandling, vil dette tas opp med deg og fortrinnsvis gjennomføres på et senere tidspunkt.

Kapittel B – Personvern, økonomi og forsikring

Personvern

Opplysninger som registreres om deg er følgende: Opplysninger om alder, kjønn, resultater fra klinisk- og radiologisk-(CT) undersøkelse. Kliniske opplysninger vil bli nedtegnet i spesielle undersøkelsesskjemaer, og informasjon herfra vil bli lagt inn i en datamaskin for senere forskningsmessig bearbeidelse. Opplysninger vil bli lagret sikkert og kun spesielt autorisert personell vil ha adgang til dem.

Ansvarlige representanter fra forskergruppen ved Avdeling for kjeve- og anskitsradiologi, Det odontologiske faktultet, UiO, og andre forskere tilknyttet prosjektet kan få utlevert studieopplysninger. Alle som får innsyn har taushetsplikt.

Utlevering av materiale og opplysninger til andre

Hvis du sier ja til å gjennomgå CT undersøkelsen, gir du også ditt samtykke til at dine opplysninger utleveres til forskere tilknyttet håndartrose-studien og kjeveledds-studien. Forskningsgruppen ved Avd for kjeve- og ansiktsradiologi, Institutt for klinisk odontologi, UiO arbeider også med forskning på kjeveledd på andre pasientgrupper. Derfor kan noen av de opplysninger som samles inn også brukes i slike forskningsprosjekter. I slike tilfeller vil dataene være anonymisert, dvs at koden som knytter dataene til navnet ditt er fjernet. Hvis du sier ja til å delta i studien, gir du også ditt samtykke til at avidentifiserte opplysninger kan brukes som referensemateriale i andre prosjekter.

Rett til innsyn og sletting av opplysninger om deg og sletting av prøver

Hvis du sier ja til å gjennomgå CT undersøkelsen, har du rett til å få innsyn i hvilke opplysninger som er registrert om deg. Du har videre rett til å få korrigert eventuelle feil i de opplysningene vi har registrert. Dersom du trekker deg fra studien, kan du kreve å få slettet

innsamlede opplysninger, med mindre opplysningene allerede er inngått i analyser eller brukt i vitenskapelige publikasjoner.

Økonomi og sponsors rolle

Studien er finansiert gjennom forskningsmidler fra Det odontologiske fakultet, UiO. Prosjektansvarlig eller andre som arbeider med prosjektet har ingen form for økonomisk vinning knyttet til prosjektet.

Forsikring

Pasienter som deltar i studien er forsikret gjennom Institutt for klinisk odontologis ordinære forsikringsordninger/Norsk pasientskadeerstatning.

Informasjon om utfallet av studien

Resultatene studien vil bli presentert i internasjonale fagtidsskrifter og i en Masteroppgave ved Det odontologiske fakultet, Universitetet i Oslo.

Prosjektansvarlig/Mer informasjon

Hvis du har spørsmål om studien, kan du kontakte Tannlege og PhD stipendiat Anna-Karin Abrahamsson 98815390 eller delprosjektleder Professor Tore A Larheim 22852016.

Samtykke til deltakelse i delstudien:

"Osteoartritt (OA) i kjeveledd på pasienter med hånd-OA"

Jeg (pasientens navn med blokkbokstaver) _____
er villig til å delta i denne studien

Signatur _____ Dato _____
(pasient)

Jeg bekrefter å ha gitt informasjon om studien

Signatur _____ _____ Dato

(rolle i studien)

FORESPØRSEL OM DELTAKELSE I FORSKNINGSPROSJEKT

Utvidet røntgenundersøkelse av tenner og kjeveledd

Dette er en forespørsel til deg som har takket ja til å delta i forskningsprosjektet «Oral helse hos 65 åringer i Oslo» ved Det Odontologiske fakultet ved Universitetet i Oslo, om du vil delta i en understudie med følgende formål:

- Kartlegge på kjeveledd, med hovedfokus på forekomst av artrose
- Kartlegge status på tenner i overkjeven, med hovedfokus på sykdom tilknyttet rotfylte tenner

HVA INNEBÆRER PROSJEKTET?

Hovedprosjektet Oslo 65 innebærer at du vil få en grundig undersøkelse av din orale helse. I denne delen av studien vil vi utføre en utvidet undersøkelse med 3D røntgen av dine kjeveledd og av overkjevens tenner. Undersøkelsen er helt smertefri og vil bli utført av radiograf og tannleger med betydelig kompetanse og vil bli tolket av spesialister i kjeve- og ansiktsradiologi ved det Odontologiske fakultet.

Denne tilleggsundersøkelsen vil ta ca. 15 minutter.

MULIGE FORDELER OG ULEMPER

3D røntgen vil kunne gi deg utvidet informasjon om kjeveleddene dine, med særlig fokus på artroseutvikling. Videre vil du også få informasjon om status på eventuelt rotfylte tenner i overkjeven. Vi vil, om det er ønskelig, gjennomgå undersøkelsen med deg og selvsagt kunne svare på eventuelle spørsmål du måtte ha. For øvrig kan våre funn være grunnlag for ytterligere utredning og eventuelt behandling.

CBCT undersøkelsen du vil få tilbud om vil gi en ekstra stråledose, men denne vurderes til liten og tilsvarer ca. den bakgrunnsstråling man eksponeres for ved en flytur fra Oslo til New York.

FRIVILLIG DELTAKELSE OG MULIGHET FOR Å TREKKE SITT SAMTYKKE

Det er frivillig å delta i prosjektet. Dersom du ønsker å delta, undertegner du samtykkeerklæringen på siste side. Du kan når som helst og uten å oppgi noen grunn trekke ditt samtykke. Dersom du trekker deg fra prosjektet, kan du kreve å få slettet innsamlede opplysninger, med mindre opplysningene allerede er inngått i analyser eller brukt i vitenskapelige publikasjoner. Dersom du senere ønsker å trekke deg eller har spørsmål til prosjektet prosjektansvarlig tannlege/ førsteamanuensis Linda Zamoline Arvidsson (e-mail: l.z.arvidsson@odont.uio.no)

HVA SKJER MED OPPLYSNINGENE OM DEG?

Opplysningene som registreres om deg skal kun brukes slik som beskrevet i hensikten med prosjektet. Du har rett til innsyn i hvilke opplysninger som er registrert om deg og rett til å få korrigert eventuelle feil i de opplysningene som er registrert. Du har også rett til å få innsyn i sikkerhetstiltakene ved behandling av opplysningene.

Personopplysninger og undersøkelser vil registreres i Det Odontologiske fakultets lukkede journalsystem (Salud) og datalagringssystem for røntgenundersøkelser (PACS) og sikres på samme måte som andre pasientrelaterte data ved Det Odontologiske fakultet. Alle andre innsamlede data vil lagres i Tjenester for sensitive data (TSD) ved UiO.

Alle forskningsdata vil bli behandlet uten navn og fødselsnummer eller andre direkte gjenkjennende opplysninger. En kodenøkkel knytter deg til dine opplysninger gjennom hospitalnummer, som vil bli vil bli lagret i TSD.

Prosjektleder har ansvar for den daglige driften av forskningsprosjektet og at opplysninger om deg blir behandlet på en sikker måte. Informasjon om deg vil bli anonymisert eller slettet senest fem år etter prosjektslutt.

FORSIKRING

Pasientene i studien er forsikret gjennom den ordinære forsikringsordningen ved Institutt for klinisk odontologi ved Det Odontologiske fakultet, som har en kollektiv avtale med Norsk Pasientskadeerstatning (NPE)

OPPFØLGINGSPROSJEKT

Det er planlagt en oppfølgingsundersøkelse om 5-10 år hvor du vil bli kontaktet for ny deltagelse. Det er selvfølgelig helt frivillig å være med på denne oppfølgingsstudien.

GODKJENNING

Prosjektet er godkjent av Regional komité for medisinsk og helsefaglig forskningsetikk (REK). Saksnummer hos REK: 2018/1383.

Etter ny personopplysningslov har behandlingsansvarlig universitetet i Oslo og prosjektleder Linda Zamoline Arvidsson et selvstendig ansvar for å sikre at behandlingen av dine opplysninger har et lovlig grunnlag. Dette prosjektet har rettslig grunnlag i EUs personvernforordning kapittel IV, artikkel 25-26 og 28-30.

KONTAKTOPPLYSNINGER

Dersom du har spørsmål til underprosjektet kan du ta kontakt med prosjektansvarlig tannlege/ førsteamanuensis Linda Zamoline Arvidsson (e-mail: l.z.arvidsson@odont.uio.no)

Du kan ta kontakt med institusjonens personvernombud dersom du har spørsmål om behandlingen av dine personopplysninger i prosjektet. (Maren Magnus Voll, e-post: personvernombud@uio.no)

JEG SAMTYKKER TIL Å DELTA I PROSJEKTET OG TIL AT MINE PERSONOPPLYSNINGER BRUKES SLIK DET ER BESKREVET

Sted og dato

Deltakers signatur

Deltakers navn med trykte bokstaver

Jeg bekrefter å ha gitt informasjon om prosjektet

Sted og dato

Signatur

Rolle i prosjektet