Cost-Utility Analysis of Screening for Periodontitis compared with today's practice in 60 year old individuals in the Norwegian population

Authors:
Celine Møgster
Hanne Stine Bergbråten

Supervisor:
Knut Reidar Wangen

Thesis submitted as part of the Master of Philosophy Degree in Health Economics, Policy and Management

University of Oslo

Faculty of Medicine

Department of Health Management and Health Economics

May 2021

2021

Cost-Utility Analysis of Screening for Periodontitis compared with today's practice in 60 year old individuals in the Norwegian population

Celine Møgster and Hanne Stine Bergbråten

http://www.duo.uio.no/

Trykk: Reprosentralen, Universitetet i Oslo

Abstract

Background: In Norway, dental care services are mostly paid for privately by the individuals themselves. Periodontitis is a gum disease requiring ongoing treatment creating a potential economic burden for the patient. Periodontitis is irreversible, but preventable, and the prevalence is unknown. The disease is the primary cause of tooth loss in the adult population. Regarding screening for periodontitis, there are disagreements on the appropriate starting age and economic evaluations appear to be lacking.

Objective: To assess the cost-effectiveness of screening for periodontitis compared with today's practice in 60 year old individuals, over a lifetime horizon.

Methods: A state transition Markov model was developed to assess changes in costs and quality-adjusted tooth years (QATYs) by a hypothetical screening intervention for periodontitis. There is limited available literature on the progression of periodontal disease, and no available data on the utility associated with the disease. Sub-analyses of 40 and 80 years olds were compared to the main analysis to reflect heterogeneity. Sensitivity analyses were performed to explore and reduce uncertainty, and a value of information (VOI) analysis was conducted to investigate to what extent acquiring additional information would be of value.

Results: Over a lifetime horizon, the incremental cost-effectiveness ratio of the screening intervention was NOK 5 101 per QATY gain, for screening offered from the age of 60. Sensitivity analyses explored uncertainty in several parameters. If the willingness to pay (WTP) threshold was above NOK 40 000, the screening intervention was more likely to be cost-effective than today's practice. The VOI analysis emphasized the need for additional research. The value of acquiring perfect information per individual per year should not exceed NOK 1 050 per QATY gain.

Conclusion: The decision of cost-effectiveness is uncertain, as there is no predetermined WTP threshold for the new intervention. Screening was considered cost-effective for 60 year olds for WTP thresholds above NOK 5 101 per QATY. The results indicated reduced costs by introducing screening from the age of 40 compared with today's practice. The conclusion of this thesis highlights the need for new research in order to reduce the uncertainties of the results.

Acknowledgements

This thesis is written as part of our master's in Health Economics, Policy and Management at the University of Oslo. We have collaborated on all the components of the thesis. All work has been equally divided between the two of us, as a result this has led to rich reflections and discussions. We have both spent the same amount of time and effort on all sections of the thesis. Despite the COVID-19 pandemic, together we have managed to maintain motivation and excitement towards this project.

We would like to thank our supervisor Knut Reidar Wangen for valuable advice and helpful contributions. We are grateful for your time and engagement on this topic.

Special thanks to periodontal specialist Øystein Fardal for constructive feedback on periodontal disease. We would also like to thank the Norwegian Consumer Council and the Norwegian Society of Periodontology for data material. Contributors are not responsible for the results of this thesis. We take full responsibility of any errors or limitations.

Table of Contents

List of tables

List of figures

Abbreviations

CAL	Clinical attachment loss
CBA	Cost-benefit analysis
CEA	Cost-effectiveness analysis
CEAC	Cost-effectiveness acceptability curve
CEAF	Cost-effectiveness acceptability frontier
CPI	Community Periodontal Index
CUA	Cost-utility analysis
EVPI	Expected value of perfect information
EVPPI	Expected value of partial perfect information
HELFO	The Norwegian Health Economics Administration
ICER	Incremental cost-effectiveness ratio
NMB	Net monetary benefit
NOK	Norwegian kroner
OHIP-14	The Oral Health Impact Profile
PSA	Probabilistic sensitivity analysis
QALY	Quality-Adjusted Life Years
QATY	Quality-Adjusted Tooth-years
RR	Relative risk
VOI	Value of information
WHO	World Health Organization
WTP	Willingness to pay

1. Introduction

1.1 Introduction

Periodontal disease is a clinical problem of interest from both a cost-effectiveness perspective and public health care perspective, as it is common, costly, and preventable if detected early. The term periodontal disease is used as a collective term for gingivitis and periodontitis. Periodontitis is a slowly developing, irreversible periodontal disease, caused by bacteria that have been allowed to accumulate on one's teeth and gums (Cafasso, 2017). Prevention and early treatment are both essential in successfully handling this disease. Periodontal disease may be present without the patient experiencing pain or other signs of illness. Often, the patient is not aware of any disease before it is irreversible, and it has resulted in loosening of teeth or even tooth loss (Skjørland et al., 2020). In Norway, the age group 60-69 has the highest treatment prevalence of periodontitis (Fardal et al., 2020b). However, the disease prevalence is unknown. There is no systematic reporting or data collection system regarding dental diseases or the oral health of the Norwegian population.

As of today, there are political interests in including dental care services in the publicly funded Health Insurance Scheme in Norway. Certain groups are financially covered for dental care, however for the majority, dental care services are paid for out-of-pocket, and every patient is responsible for seeking out services themselves. The Norwegian Health Economics Administration (HELFO) covers treatment costs of periodontitis when a diagnosis has been reached. Nonetheless, the treatment costs are lower if periodontal disease is detected at a preventable and less advanced stage.

The approach proposed in this thesis is rather unique, and economic evaluations regarding screening for periodontitis appear to be lacking. In addition, the use of Markov models in dentistry analyses have been limited. To the best of our knowledge, only three previous studies have been identified evaluating the clinical course of periodontitis with the use of Markov models (Faddy et al., 2000; Schätzle et al., 2009; Mdala et al., 2014). In this thesis, it was considered whether it was cost-effective or not to implement a hypothetical screening for periodontitis funded by the public. Better utilization of the resources associated with periodontitis is desirable.

1.2 Research description

The aim of this thesis was to evaluate the cost-effectiveness of a hypothetical screening for periodontitis, in 60 year old individuals, over a lifetime horizon. The intervention was compared with today's practice.

An economic evaluation was carried out, and a state transition Markov model was developed. Sub-analyses were performed on 40 and 80 year olds. Based on costs, health effects, assumed effect of screening, and the probability of transitioning between stages of periodontal disease, it was estimated if introducing screening for certain groups in the population would be cost-effective. Costs are reported in Norwegian kroner (NOK) and health effects in quality-adjusted tooth years (QATYs). 60 year olds are not covered by the publicly financed health scheme, and given their high treatment prevalence, this age group was chosen for the main analysis.

The thesis was conducted based on a health care perspective (Garrison et al., 2018). Only costs and benefits within the dental care sector that are directly related to the screening intervention was included in the model. Given this perspective, costs related to the screening intervention and treatment was included, regardless of whom the payer is. However, patients' productivity cost, i.e. time off work, or time costs associated with treatment were not considered.

A thorough literature review was performed, and there have been few economic evaluations on periodontal disease which can be adapted to a Norwegian setting. The true prevalence and utility related to periodontal disease is unknown for all populations. Due to uncertainty in several input parameters, sensitivity analyses were performed to increase the probability of the analyses yielding realistic results.

2. Background

2.1 Periodontal disease

2.1.1 Overview

Periodontal disease is a set of inflammatory conditions affecting the tissues surrounding the teeth. Gingivitis is a mild form of gum disease that may cause irritation, redness and swelling of the part of the gum surrounding the base of the teeth. Periodontitis is a slowly developing, chronic disease, caused by bacteria that have been allowed to accumulate on one's teeth and gums. In Norway, periodontitis is the most important cause of tooth loss after the age of 45 (Skjørland et al., 2020). Early diagnosis of periodontal disease is a prerequisite for establishing a successful treatment plan. Despite early diagnosis and initiated treatment, there is still a risk of the disease returning, especially with the slightest neglect of optimal oral hygiene (Cafasso, 2017).

An overview of periodontal disease is graphically presented in Figure 1. Healthy refers to a stable case of periodontal health, meaning the absence of inflammation, absence of symptoms and absence of clinical and radiographic bone loss and tooth loss (Brækhus, 2018). Without regular dental visits, symptoms may not be noticed until the disease has reached a stage of severe periodontitis. Gingivitis can be reversed. However, periodontitis is a progressive disease that cannot be reversed once developed (Davis, 2019).

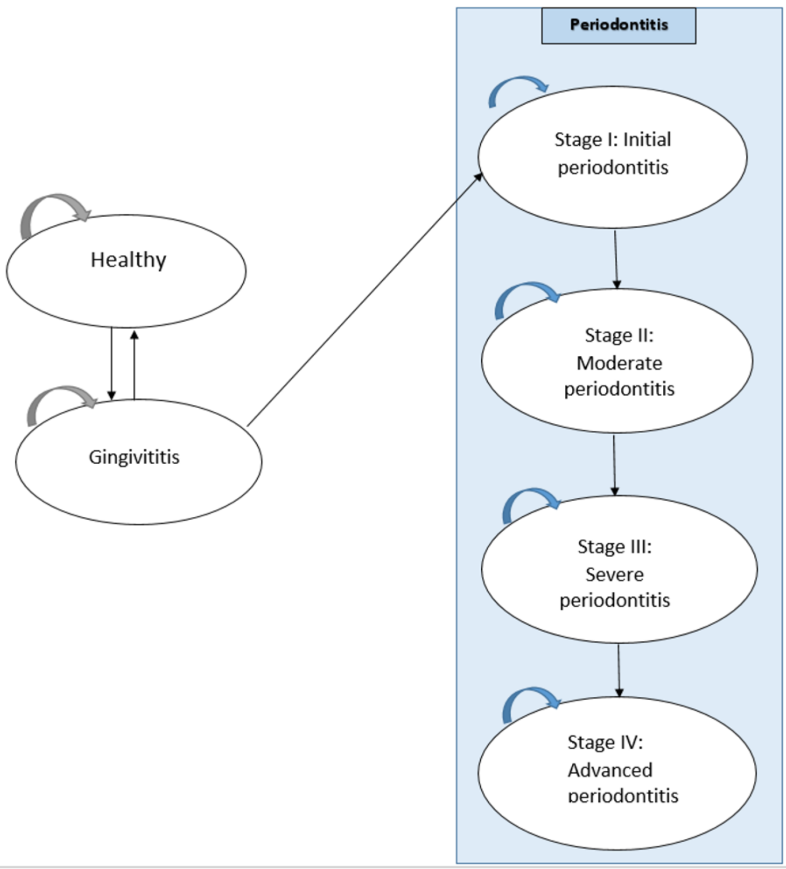

Figure 1: Newest available classification of periodontal disease. Source: Papapanou et al., 2018.

The World Workshop, a cooperative group organized by the American Academy of Periodontology and the European Federation of Periodontology, introduced a new classification system of periodontal diseases in 2018. Using common terminology from the same system of classification allows for more practical and efficient communication between health professionals (Highfield, 2009). Before 2018, forms of periodontitis were classified as either “chronic” or “aggressive”. Chronic periodontitis referred to the most common form of periodontitis, which has a slow rate of progression. With chronic periodontits, there is generally an abundance of plaque and tartar that increases the periodontal destruction. Aggressive periodontitis was indicated by a faster rate of disease progression than chronic periodontitis, and was usually developed at a younger age. Research show that it is likely a genetic component in patients who receive a diagnosis of aggressive periodontitis (Ramachandra et al., 2017). The system of classification from 1999 also includes a section on gingival disease.

However, periodontitis is now grouped under a single category and characterized by a staging and grading system (Papapanou et al., 2018). Dividing disease into stages is commonly done within cancer, but is recently established more in other diseases, as well. Currently, periodontitis is multidimensionally classified according to severity and complexity (Stage I to IV) and progression rate (Grade A to C). Severity is determined by clinical attachment loss (CAL), radiographic bone loss and tooth loss. CAL describes the extent of the periodontal support that has been destroyed around a tooth, usually expressed in millimeters (Fritz, 2013).

Periodontitis is staged from Stage I to Stage IV. Stage I refers to initial periodontitis, and represents the early stages of attachment loss. This stage is borderline between gingivitis and periodontitis. Stage II, moderate periodontitis, is an established form of periodontitis, resulting in characteristic damages to the tooth support. In stages I and II, it is not typical to lose teeth due to the condition. Stage III can be referred to as severe periodontitis with significant damage and potential for additional tooth loss if not treated. Stage IV is the most advanced stage, where the disease has caused significant damages to the periodontal support. It is not uncommon to lose teeth at this stage (Tonetti et al, 2018). Grade A to C indicate the rate of progression, were A represents slow progression and C rapid progression (Papapanou et al., 2018). No relevant studies using the 2018 classification have been identified.

2.1.2 Risk factors

Most studies on periodontitis focus on the effects of a single factor on the prevalence of periodontal disease. Previous research have considered the causal effect from covariates such as smoking, stress, comorbidities, body mass index, medications, and genetics (Coelho et al., 2020; Fardal et al., 2018; Fardal et al., 2020a; Nascimento et al., 2015; Nazir, 2017).

Several factors may increase the risk of periodontal disease. Patient’s self-care is the cornerstone of periodontal health, as bacteria and infections are associated with periodontal disease. Self-care advices regarding oral health are given by a dentist or dental hygienist (Helfo, 2020b). The absence of good oral hygiene increases the risk of developing disease. However, some individuals have a higher risk of developing periodontal disease as development is also associated with genetic components. Fardal et al. (2020a) state in their study that genetics account for 65% of tooth loss due to periodontal disease. In addition, the risk of periodontal disease increases with age (Nazir, 2017). More women than men receive treatment for periodontitis (Fardal et al., 2020b).

Smoking is argued to be one of the most important risk factors of periodontal disease. However, fewer and fewer Norwegians smoke. In 1973, 42% of Norwegians smoked daily, while only 12% reported the same in 2018 (Wettergreen, 2019). People who smoke generally have poorer oral and dental health. As smoking reduces circulation in the oral cavity, and weakens the immune response, smoking is considered to increase the risk of periodontal disease (Brurberg et al., 2008). There is an increased prevalence of periodontal disease among smokers, as well as smoking increases the chance of more severe cases of periodontitis. As smoking rate and the prevalence of periodontal disease is strongly correlated, it can explain the reduction in prevalence of periodontal disease in accordance with the reduction in the severity of smoking the past four decades (Bergstrom, 2014; Fardal et al., 2020b).

It is approximately three times more likely to develop periodontal disease as a diabetic compared with non-diabetics (Mealey & Ocampo, 2007). Several studies support that there is a two-way relationship between periodontitis and diabetes (Casanova et al., 2014; Preshaw & Bissett, 2013). Uncontrolled diabetes contributes to a different concentration in the fluid and saliva that is related to destruction of periodontal ligament, which can lead to tooth loss (Nazir, 2017). Hence, treatment of either disease may be beneficial for individuals with diabetes and periodontitis (Preshaw & Bissett, 2013).

It is further believed that periodontal disease may be connected with other diseases as well, such as cardiovascular disease (CVD), rheumatoid arthritis, osteoporosis, and Alzheimer's disease. It is suggested that these conditions may be improved when patients receive periodontal treatment, and vice versa. Even though an association between periodontitis and another disease is proven, this does not mean there is a direct causal relationship between them (Olsen, 2001).

2.1.3 Treatment of periodontal disease

When left untreated, periodontal disease commonly develops to a more severe stage, starting with gingivitis. However, if treatment is initiated at an early stage, gingivitis may be reversed. Gingivitis usually resolves with longer and more frequent brushing, and flossing of the teeth. The treatment for gingivitis involves a professional cleaning, a so-called scaling, where plaque and tartar are removed. For further treatment and maintenance, the patients are responsible themselves. Patients are recommended to brush their teeth twice daily with an electric toothbrush, floss, and rinse with antiseptic mouthwash (Newman, 2018).

The main treatment for periodontitis is effective oral hygiene, in which the patients perform themselves. Further, a dentist or dental hygienist conduct a professional cleaning, where bacteria and tartar are removed from the surface of the root, in addition to a thorough cleaning of any periodontal pockets. Antibiotics may be prescribed for infections, to prevent overactive enzymes from breaking down tissue after treatment. In some cases, flap surgery may also be recommended for the patient. After completed treatment, the patient should regularly undergo supportive periodontal therapy, often called periodontal maintenance (Teughels et al., 2014). Periodontal maintenance consists of a periodontal evaluation, scaling and root planing where indicated, radiographic review, removal of bacteria, and a review of the patients' plaque control efficacy (Farooqi et al., 2015). This is all directed toward controlling the risk for disease recurrence and tooth loss.

Depending on how severe the patient's periodontitis is, periodontal maintenance should be performed on a regular basis, often at less than 6-month intervals. The course of treatment is very individual, and depends largely on the patient's own efforts. The time interval between each treatment session is extended when the condition is stabilized, and the patient shows good self-effort during the course of treatment (Dentist, personal communication, 10.03.21).

2.1.4 Epidemiology

According to the World Health Organization (2020), periodontal disease is one of the most common oral health conditions, in addition to dental caries. Approximately 10% of the global population will presumably be affected severely by periodontitis. The prevalence of periodontal disease varies among different populations, and the prevalence of the Norwegian population is unknown.

Disease prevalence estimates are influenced by the methodology used, measurement techniques and examination protocols, and are therefore quite challenging to determine (Holtfreter et al., 2015). In Norway, the prevalence of periodontitis and tooth loss have decreased the last 40 years, according to Fardal et al. (2020b). This study stated that only 4.4% of the population was treated for periodontitis in 2013. However, this may not reflect the true prevalence in the Norwegian population, because of the lack of a reporting system regarding dental diseases. Undiagnosed periodontitis was not included in the number of periodontitis patients. In addition, there is no overall, national overview of treatment needs or rehabilitation needs (Lysho & Biehl, 2009).

Further, Holde et al. (2017) have examined the disease prevalence, severity and extent of periodontitis in the adult population in Norway. 1 911 individuals were assessed according to pocket depth, bleeding on probing, and radiographic bone loss in Northern Norway (Troms), where it was found that 49.5% had periodontitis, of which 9.1% was severe periodontitis (Holde et al., 2017). Gingivitis was not considered in this study. This study may indicate a more realistic burden of disease for periodontitis, as relevant covariates (e.g. age, sex, smoking status, education level, and income) were examined.

Treatment prevalence was last recorded in 2013. Nationwide, 4.4% of the population aged 20 years or older were treated for periodontitis in 2013, which corresponded to 166 707 individuals (Fardal et al., 2020b). Note that treatment prevalence and disease prevalence are not necessarily comparable.

The same study also considered treatment prevalence according to county of residence in the 2013 population (Fardal et al., 2020b). Norway still consisted of 19 different counties at that time. Nord-Trøndelag had the lowest percentage, with 2.6% of their population receiving treatment for periodontitis. Several counties were above the nationwide treatment prevalence, such as Oslo, Vest-Agder, Rogaland and Vestfold, which were all above 5%. Oslo had the definite highest proportion of patients in Norway, which partly can be explained by the fact that a higher proportion of the population lives in that region.

2.2 Regulation of Dental Care services in Norway

The dental care service in Norway consists of a public sector that provides services to parts of the population in accordance with the Dental Health Services Act of 1984, and a private sector that offers services to the rest of the population (Ministry of Health and Care Services, 2014). The public services are governed and financed by the counties. However, the private practice has free rights of both establishment and pricing (Ministry of Health and Care Services, 2007). The majority of private services are financed through out-of-pocket payments.

The regulation of dental care services differ from the regulation of other municipal health and care services in Norway. The Dental Health Services Act primarily has a public health and prevention perspective. Dental care services are generally paid for by the consumer themselves. There are some exceptions to this, regulated by law (Dental Health Services Act, 1984, §1-3). The exceptions include children and adolescents from the ages 0-20, groups of elderly, long-term sick and mentally disabled individuals in and outside of care institutions. This legislation also applies to other groups that the county municipality has decided to prioritize, which varies between counties. The expenditures from public dental care services are financed by local taxes and block grants (Grytten et al., 2009).

Currently, there are major political interests in including dental care services in the publicly funded National Insurance Scheme in Norway. Oral conditions can affect the ability to eat, express oneself, and individual’s general well-being. Mainly, the adult, healthy population funds treatment costs themselves. However, some conditions are omitted from this scheme and will, at least partially, be covered by HELFO within the National Insurance Scheme. There are 15 such conditions, including periodontitis

(Helfo, 2021). The patient will receive his or her exemption card (Norwegian: Frikort for helsetjenester) after paying more than NOK 2 460 in total deductibles for health care, which is valid for any time that is left of the calendar year. The price difference between the reimbursement rates decided by the Directorate of Health and the dentists fee must be covered by the patient, regardless of whether they have an exemption card or not. This is in contrast to treatment of other clinical (non-dental) conditions. Further, if an individual is covered by the Public Dental Health Services Act, one cannot additionally receive reimbursement from HELFO.

The regulation of the social security benefit for dental treatment is comprehensive and is used to ensure that patients do not get overtreated and receive benefits they are not entitled to. Therefore, different rates have been introduced. Rate 501 can be used by both dentists and dental hygienists, and it is used for systematic treatment of periodontitis to achieve infection control. When used, there is a list of components that must be included in the treatment, including self-care training, scaling and measures for smoking cessation if appropriate. It should also be explained to the patient how further smoking may affect the development of periodontitis. Use of the rate presupposes a time use of at least 30 minutes, and the rate can be used a maximum of 14 times per calendar year per patient (Helfo, 2020a). To be able to use rate 501, a diagnosis of periodontitis must have been reached beforehand. The ceiling for the maximum number of 501 rates per patient was implemented because systematic abuse of these reimbursement regulations was revealed (Klepp, 2020, p. 969).

2.3 Screening

A screening service aims to detect disease in the seemingly healthy population. The World Health Organization (WHO) has created a list of 10 criteria's for assessing a program before implementing the potential screening service in a population (Norwegian Directorate of Health, 2017). These criteria's include that the disease in question is an overall health problem, that treatment is acceptable, that the disease can be detected and treated early on, and that the cost of finding new cases is economically sound.

There are several ways screening for periodontitis may be performed. One alternative is using community periodontal index (CPI), developed by WHO, to assess the degree of periodontal disease. CPI was created to evaluate the treatment needs in the population (Benigeri et al., 2000). A unique probe is used to record the CPI, which includes bleeding, tartar and pocket depth. The probe also evaluates the clinical attachment loss (CAL). The CPI is reported with a score between 0 and 4. Table 1 contains a more detailed description of each score.

CPI is a rather invasive method of screening that requires well-trained dentists to perform the examination. Although this method is expensive, it is more accurate than other methods suggested in the literature (Tanik & Gul, 2020). A limitation with CPI is its difficulty with differentiating between new disease and already treated stable cases of periodontitis, as both can have attachment loss and reduced bone levels. In these latter cases, it can be assumed that the patient is aware of any previous disease and will inform his or her dentist of this.

Score	Description
Score 0	Healthy periodontal conditions
Score 1	Gingival bleeding
Score 2	Tartar and bleeding (tartar also called calculus)
Score 3	Shallow periodontal pockets, 4-5 mm
Score 4	Deep periodontal pockets, > 6mm.

Table 1: Descriptions of community periodontal index (CPI) scores of periodontal disease. Source: World Health Organization, 2005.

Nomura et al. (2016) proposed using saliva tests for screening, which are cheaper, less invasive, and can be performed by non-specialized dental staff, i.e. oral hygienists or assistants. This test examines lactate dehydrogenase and hemoglobin levels in saliva, by having the patient chew on a gum base for 5 minutes. Nonetheless, the positive predictive value of this saliva test is lower than CPI, 91.7% versus 95.93%, respectively (Tanik & Gul, 2020).

2.4 Today's Practice

Today, dental care services are organized as private provisions. Each patient has a personal responsibility for seeking treatment, and will pay for most services themselves. This does not apply for the predetermined groups described in Chapter 2.2. When a certain amount of time has passed since a patient's last checkup, some dentists send reminders to their patients, but this is not a requirement. Because of free price setting, the prices may therefore vary, and the dentist's price may be higher than the reimbursement rate determined by the Norwegian Directorate of Health.

General dentists perform examinations for intraoral changes in the hard and soft tissues that include mucosal changes, caries control, monitoring of the gingiva and periodontium. They perform scaling to remove calculus and polish to remove plaque. It is also common with re-instruction of the oral hygiene in areas with plaque. The aim of this is to treat and prevent the progression of gingivitis (Øystein Fardal, personal communication, 17.03.21). When this is not sufficient, periodontal treatment is started to prevent progression to severe cases of periodontitis. If that were to happen, the patient is referred to a periodontal specialist for treatment.

With regular visits to dentists, periodontitis should in theory be revealed. 90% of the Norwegian population has reported that they see their dentists at least every second year (Fardal et al., 2020b). For those not consulting their dentists regularly, periodontitis may go unnoticed for some time.

3. Theoretical framework

The theoretical background and terminology of economic evaluation, on which this thesis is based on, is described in this chapter. Further, chapter 4 presents the methods used for the cost-utility analysis.

3.1 Economic Evaluation

Everywhere in society, there is a scarcity of resources, e.g. individuals, equipment, knowledge and money within the health care sector. A prioritization of resources must therefore be made. An economic evaluation will provide a comparison of two or more interventions, in terms of costs and consequences. This is done to ensure that scarce resources are spent in the most efficient way. According to Drummond et al. (2015, p. 4), the basic task of economic evaluations are to identify, measure, value, and compare costs and consequences of the alternatives being considered in the evaluation. It is mainly used to aid decision makers when prioritizing scarce resources within health care.

When doing an economic evaluation, there is no direct answer of what alternative is the best, because both costs and consequences are valued alongside each other. There is a trade-off between the alternatives. The conclusion depends on what amount the provider is willing to pay for the intervention given the health gain it provides (Goodacre & McCabe, 2002). This reflects the concept of opportunity costs, i.e. the benefits forgone when choosing either alternative. The final decision often comes down to being a political question and is rarely done by economists performing the evaluations.

One mainly distinguishes between 3 different types of economic evaluations. These are cost-effectiveness analysis (CEA), cost-utility analysis (CUA), and cost-benefit analysis (CBA). However, the term CEA is occasionally used interchangeably as a common term for all three in the literature (Hunink et al., 2014, p 241). The significant difference between the analyses is the outcome measure used for the effects. In the CEA, health effects is valued in a common measure in both, or all, interventions. This could be life years gained, or disease cases avoided. CUA is relatively similar, yet makes use of a generic measure of health gain, e.g. quality-adjusted life years (QALYs). In a CBA, both costs and effects are valued in monetary terms.

Whilst performing an economic evaluation, a series of decisions and assumptions must be made, such as the choice of study perspective, and what type of analysis is preferable for the current setting. CUA has become the most widely used form of economic evaluation (Drummond et al., 2015, p. 8).

3.2 Cost-Utility Analysis

To determine whether a new diagnostic test, medicine or intervention is cost-effective compared with another alternative, a cost-utility analysis (CUA) may be performed. The comparison is often made between the new intervention and a gold standard, i.e. an intervention that is commonly recognized as the best available option. CUA is a useful tool as it can be used to compare programmes across different health care settings, seeing that it utilizes a generic measure of health gain (Drummond et al. 2015, p. 8). The results of a CUA is typically represented with an incremental cost-effectiveness ratio (ICER), which can be defined as the following (Hunink et al., 2014, p. 244):

Equation 1:

$$\text{ICER} = \frac{\text{Cost of intervention} - \text{cost of comparator}}{\text{Effect of intervention} - \text{effect of comparator}} = \frac{\Delta\text{Cost}}{\Delta\text{Effect}}$$

The cost-effectiveness plane can be used to visually describe the ICERs (Figure 2). The plane is divided into 4 quadrants, yielding different interpretations of the values in it. If the ICER is located in the south-east quadrant, it is said to dominate the comparing alternative, with lower costs and better health effects. The intervention is further said to be dominated if the ICER is located in the north-west quadrant, where the alternative is worse than the comparator on all aspects. In both alternatives, the ICER values would be negative, and the dominated alternative would not be considered. Given a positive ICER, the intervention is either more costly and more effective than its comparator (located in the north-east quadrant), or less costly and less effective than the comparator (located in the south-west quadrant). The question of cost-effectiveness would in these cases depend on the willingness to pay (WTP) threshold for additional health effects (Drummond et al. 2015, p.55).

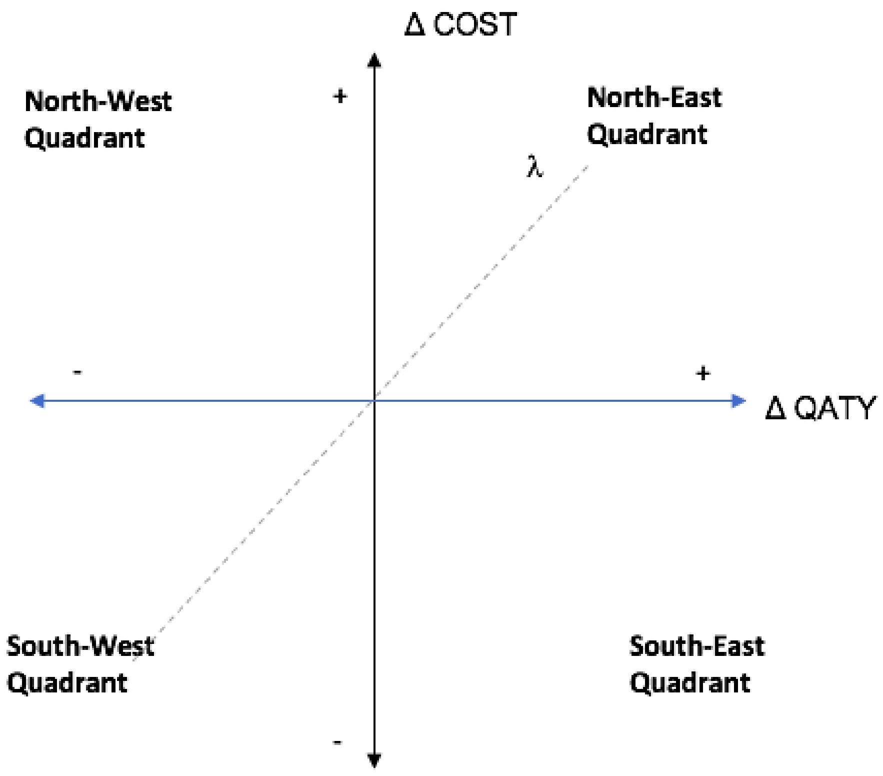

Figure 2: Cost-effectiveness plane with incremental (Δ) effect (QALY/QATY) on the horizontal axis and incremental (Δ) cost on the vertical axis. The dotted line is a hypothesized threshold (λ).

Another way of expressing the cost-effectiveness of an intervention without using ratios is applying net monetary benefit (NMB). A rearrangement of the calculation of the ICER provides us with the equation for NMB (Equation 2). The use presupposes a specified WTP threshold (λ) for the intervention before calculations are performed. The intervention is always considered cost-effective if the incremental NMB is positive (Briggs et al., 2006, p. 129).

Equation 2:

$$NMB = \lambda * \triangle Effect - \triangle Cost$$

As long as the same threshold is used, the analysis of whether an intervention is cost-effective when compared with another alternative will always yield the same answer regardless if you use ICER or NMB (Drummond et al., 2015, p. 300). However, the WTP threshold is not always given or publicly known.

3.3 Perspective

The costs and benefits that are relevant to include in an economic evaluation depends on the study perspective chosen for the analysis. This choice often depends on what type of decision maker is intended to be informed from the specific analysis. Simply explained, the study perspective is the point of view used to determine what costs and benefits to include in the economic evaluation. The different perspectives are patient (individual) perspective, institutional perspective, sectoral (health care) perspective, or societal perspective (Drummond et al., 2015, p. 219).

What perspective is applied to an analysis may change the interpretation of the results, whereas an intervention is cost-effective given one perspective, and may not be cost-effective if another perspective had been chosen for the analysis. Several perspectives may be applied in the same analysis and it should therefore be made explicit and discussed as it may affect the concluding results of the evaluation (Byford & Raftery, 1998). The most commonly used perspectives within CUAs and CEAs are health care perspective and societal perspective.

The healthcare perspective would only consider costs and benefits within the sector that are directly related to the intervention. Costs borne by third-party payers or out-of-pocket payments by patients are thereby included in this perspective (Garrison et al., 2018).

The reasoning for using a societal perspective is that health interventions affect other sectors and areas than just health care. This applies in terms of both costs and benefits (Byford & Raftery, 1998). All relevant costs of implementing a new intervention, drug or treatment should be included in this analysis, regardless of whom the payer is. Ideally, this includes time costs from seeking and receiving care, transportation costs, time lost from work, and current and future effects on productivity (Sanders et al., 2016). This is, however, not always possible to do in practice.

3.4 Health Outcomes

Most often, quality-adjusted life years (QALYs) are used as the outcome measure in economic evaluations. QALYs is a measure for a year of life adjusted for its quality. Perfect health for one year equals 1 QALY (Briggs et al., 2006, p. 4). In theory, one can use QALYs to compare dental health actions with other health care actions. However, whether this works in practice and to what extent the most used questionnaires, as EQ-5D, is suited for use in prioritization in dental care services is open to question (Augestad & Rand, 2018). Further, one can argue that QALYs will be a too insensitive tool for dental health issues, as an individual's QALY-weight will not be significantly affected by certain dental health problems, e.g. periodontitis. The rationale for this is that it usually does not cause much discomfort or pain for the patient.

When evaluating and making decisions within the dental care sector, the outcome measure can be limited to those only focusing on teeth. Several measures are based on QALYs and adjusted to fit oral health programmes specifically. Quality-adjusted Tooth years, QATYs, is one of them. In QATY, the tooth is recognized as the unit of health, where tooth loss generates the lowest score of 0 (Braga et al., 2020). This differs from QALY where the patient’s length and quality of life as a whole is considered.

Fardal and Grytten (2014) state in their study that the main problem by using QALYs in their analysis, is that this measure do not include specific periodontal problems such as “halitosis, bleeding gingiva, swollen painful gingiva, tooth mobility, recession or patient's values or treatment expectations". Further, they argue that often symptoms of periodontal disease are virtually absent, and because of that, it is problematic to calculate the time spent in each health state.

Quality-Adjusted Prosthesis years (QAPY) and Quality-of-tooth-years (QLTY) are other ways of assessing utility and disutility, although these are not widely used in the literature (Augestad & Rand, 2018).

3.5 The Markov model framework

Markov models are commonly used in health economic evaluation to handle decision problems. Markov models consist of a finite number of states. During each cycle of time, an individual must reside in one of the defined states (Briggs et al., 2006, p. 30). Markov models rely on the assumption of memory-less property, which means that the probability of transition depends only on the current health state and not past health states. By that, the individuals in each state are treated as homogeneous. This enables computations with the model that would otherwise be difficult (Drummond et al., 2015, p. 336).

A cohort simulation can be used to evaluate a Markov model. This can be done by taking a cohort of individuals and calculating the distribution of the cohort in each cycle of time. Based on the distribution of the cohort at baseline, i.e. the starting cycle, and the probability of transitioning from one state to another, one can calculate the number of patients in each health state at each cycle. To calculate the expected costs and effects of the cohort, costs and effects are summarized weighted by the proportion of individuals in each state, in each cycle of the model (Briggs et al., 2006, p. 33).

In the way Markov models are organized, all events can only occur at the start or end of a cycle. In reality, events may occur throughout the year. A common solution to correct for this problem without overestimating or underestimating is by half-cycle correction.

3.6 Uncertainty

There is always some uncertainty related to decisions based on expected cost-effectiveness. Thus, decisions rely on a proper examination of the uncertainty. Overall, one can distinguish between different types of uncertainty in modeling: structural uncertainty, stochastic uncertainty, heterogeneity, and parameter uncertainty (Drummond et al., 2015, p. 393).

Structural uncertainty relates to the assumptions and simplifications inherent in the model. Stochastic uncertainty refers to the fact that populations or sub-populations may respond differently to an intervention, both in terms of costs and effects, e.g. as one patient may lose one tooth and the second patient may lose two teeth even though they both undergo the same treatment. This natural variability cannot be reduced by acquiring more evidence on expected or average costs and effects (Drummond et al., 2015, p. 390). On the other hand, heterogeneity relates to differences between patients that can, in part, be explained. For instance, age and sex. This can be considered by sub-group analysis. Parameter uncertainty is the uncertainty related to model input parameters, which may be due to uncertainties in the data, or the calibration process used (Maier & Tolson, 2008).

Deterministic sensitivity analysis and probabilistic sensitivity analysis are methods for managing parameter uncertainty in the model inputs. In reality, these methods do not capture all uncertainty. Value of information (VOI) analysis refers to what one would be willing to give up to acquire better information about the probability distribution governing a given input parameter (Briggs et al., 2012, p. 837).

3.6.1 Deterministic sensitivity analyses

To explore the sensitivity of a model, deterministic sensitivity analyses use manually selected parameters to explore how sensitive the outcome of interest is to changes in parameter values or sets of parameters. This can be explored by several different methods; one-way, to-way, or multi-way sensitivity analyses (Briggs et al., 2012, p. 837).

A one-way sensitivity analyses discover how changes in parameters, one at a time, may change the outcome of interest. It is not recommended to rely on one-way sensitivity analyses alone to represent uncertainty, as not all uncertainty may be captured. Although these analyses are easy to execute and understand, they do not capture potentially important relationships between variables, or tell the likelihood of scenarios (Drummond et al., 2015, p. 394). Multivariable (to-way or multi-way) sensitivity analyses vary the value of two or more input parameters at the same time. Generally, many parameters contain uncertainty, and therefore multivariable sensitivity analysis can get unmanageable (Hunink et al., 2014, p. 368).

3.6.2 Probabilistic sensitivity analyses

Compared to deterministic sensitivity analyses, probabilistic sensitivity analyses (PSA) are considered a better approach as these capture the correlation between the variables and their joint parameter uncertainty on the model outcome. A probabilistic sensitivity analysis reflects uncertainty related to all parameters in the model simultaneously. The input parameters in the model are given a probability distribution, which is usually defined by the expected value and standard error. Monte Carlo simulations can then be performed, preferably as many as possible. This method randomly assigns values to the parameters, based on a range of values the specific parameter is likely to take (Drummond et al., 2015, p. 399).

Graphically, one can present the results from a probabilistic sensitivity analysis in a cost-effectiveness plane, by a cost-effectiveness acceptability curve (CEAC), and a cost-effectiveness acceptability frontier (CEAF). The CEAC describes the probability of an intervention to be cost-effective according to different threshold values. However, in general, it should not be used directly to make decisions. The CEAF describes the probability of cost-effectiveness of the optimal strategy for different threshold values (Drummond et al., 2015, p. 405-406).

3.7 Value of Information Analyses

Important decisions often rely on current available information. One is interested in examining not only the chances that the decision about to be made is wrong, but also to quantify the consequences if the decision is in fact wrong. Value of information analysis (VOI) is a method for valuing the *expected* gain from reducing uncertainty in a decision. One can use the information provided from the simulation of the PSA for conducting a VOI.

A full value of information analysis consists of different measures: Expected Value of Perfect Information (EVPI), Expected Value of Partial Perfect Information (EVPPI), and Expected Value of Sample Information (EVSI). Any additional research on a subject is only justified if the potential benefit exceeds the cost of doing additional research. A value of information analysis is convenient when considering the optimal allocation of research funds (Hunink et al., 2014, p. 381).

3.7.1 Expected Value of Perfect Information (EVPI)

EVPI is the value of eliminating all uncertainty from all parameters in the model. This can be calculated directly based on the output from the PSA simulations. EVPI equals the difference between the net benefit of decision with perfect information, and the net benefit of decisions with current information. In equation 3, (j) represents alternative interventions, where the net benefit (NB) of each intervention depends on uncertain model parameters that may take a range of potential values (*ɵ)*. The optimal decision based on current available information would be the alternative that offers the maximum net benefit. Further data collection costs should not exceed EVPI (Drummond et al., 2015, p. 411).

Equation 3:

$$EVPI = \text{Perfect infomation} - \text{Current information}$$

$$EVPI = E\theta \max_j NB(j, \theta) - \max_j E\theta NB(j, \theta)$$

3.7.2 Expected Value of Partial Perfect Information (EVPPI)

EVPPI is the value of eliminating uncertainty from selected input parameters in the model. As EVPI raises the question of one should collect more evidence, EVPPI raises the question of what evidence one should collect. This is valuable for the decision makers to determine what further research to prioritize.

EVPPI equals the net benefit of decision with perfect information on parameters subtracted by net benefit of decision with current information (Equation 4). θ_1 *and* θ_2 represents unknown parameters in the model. This method is general for non-linear models. As the relationship between model parameters in decision analytic models are non-linear, the EVPPI requires a more computationally extensive simulation with an inner and outer loop. The calculation of EVPPI may therefore be both expensive and cumbersome (Drummond et al., 2015, p. 415).

Equation 4:

EVPPI = Perfect information - Current information of parameters

$$EVPPI_{\theta_1} = E_{\theta_1} \max_j E_{\theta_2|\theta_1} NB(j, \theta_1, \theta_2) - \max_j E_{\theta_2,\theta_1} NB(j, \theta_1, \theta_2)$$

4. Methods

4.1 Overview

The following subchapters present the methods used to carry out the cost-utility analysis presented initially. The analysis was performed on a hypothetical sample of individuals in a Norwegian setting. The program used for the analysis was mainly Microsoft Excel. However, Sheffield Accelerated Value of Information (SAVI) was used to perform the EVPPI analysis. The Norwegian Consumer Council (Norwegian: Forbrukerrådet) has contributed with data on reported prices to hvakostertannlegen.no. The authors have been in contact with one dentist, one periodontal specialist and the Norwegian Society of Periodontology, to get feedback on treatment frequencies and model inputs. The design of the analysis carried out is graphically described in Figure 3.

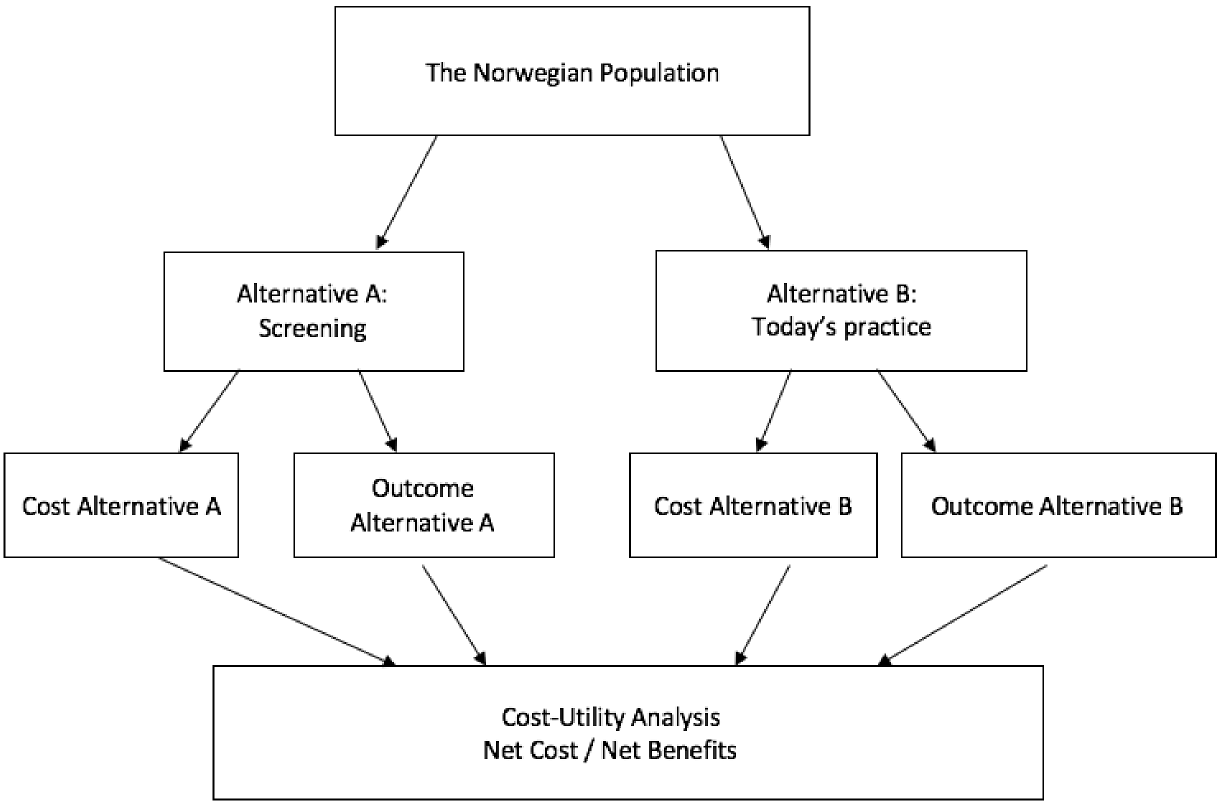

Figure 3: Pathway alternatives for the management of periodontal disease.

4.1.1 Patient population

It is conceivable that screening may be cost-effective for some patient groups, and not the entire Norwegian population. Periodontitis is usually detected after the patient is 35-40 years, while the age group 60-69 has the highest treatment prevalence (Brækhus, 2018; Fardal et al., 2020b). The population of interest chosen for the main analysis was 60 year old individuals. This age group was selected partly because of their high treatment prevalence, and partly because the entire financial burden related to dental services is carried by themselves. It was further conducted sub-analyses of different age groups, 40 and 80 year olds, where it was assumed different effects of screening and a different distribution of individuals at baseline.

4.1.2 Intervention

A screening program for periodontitis is not introduced in any country at this point. In Norway, today's practice for dental check-ups includes examination, which is meant to detect signs of periodontal disease. Unfortunately, this is not always done. In addition, the population is responsible themselves for seeking out services whenever necessary. Therefore, an external quality control, screening of the population, in addition to today's practice, is proposed. This offer will be free of charge for the patient.

The starting point of this analysis is based on screening only being offered to one age group. This population will be offered screening every 5th year, starting at the age of 60. Since there is no registry of periodontitis, all individuals in the specific age group are invited to screening, but it is assumed that those already diagnosed with periodontitis will not attend. Thus, periodontally healthy individuals and individuals with gingivitis, either aware or unaware of disease, would be screened.

As introduced in Chapter 2.3, it is debatable what method is the most valuable to use for screening of periodontal disease. CPI is considered effective as it is assumed that a general dentist can perform the test, and there is no need for a periodontist specialist to perform this examination. In addition, due to free pricing among dentists working in private sector, only dentists working in public sector are chosen to perform the hypothetical screening. If periodontitis is discovered by screening, the patient is referred to a periodontal specialist for treatment. General, private dentists can perform necessary maintenance care. HELFO reimburses a fixed price for periodontal treatment once a diagnosis of periodontitis has been reached, but the remaining cost of the dentist fee must be covered by the patient as a deductible.

4.1.3 Comparator

The comparing alternative for screening is what is referred to as today's practice in Chapter 2.4, where the adult population is responsible for seeking out dental services themselves when needed. There is no active intervention used in this scenario. The patients pay for services out-of-pocket. It is reported that 90% of the population regularly see their dentists, so this scheme may be considered to be working adequately (Fardal et al., 2020b).

4.1.4 Perspective

The thesis was conducted based on a health care perspective, in accordance with Garrison et al. (2018) definition of a health care perspective. All treatment costs and effects are included regardless of whether the state, the provider or patients are paying. Patients' productivity cost, i.e. time off work, and time cost, i.e. travel time and waiting time, are not included in the model. Physicians' time spent on treatment is integrated into the treatment costs. The setting of our thesis is the Norwegian dental care sector, where the majority of private services are financed through out-of-pocket payments. However, HELFO covers treatment costs of periodontitis when a diagnosis has been reached.

4.2 Model Structure

State transition Markov models were constructed for the hypothetical screening program and today's practice. The structure of the state transitions in the Markov model are presented in Figure 4. Three mutually exclusive states have been included in the model. Due to limited available data, all stages of periodontitis is combined into one health state in the Markov model. One can either stay periodontally healthy, or progress to a more severe state. Gingivitis is reversible. Periodontitis cannot be reversed and is therefore an absorbing health state. The cycle length in the model was set to one year. The model structure chosen does not take into account individuals who die throughout the cycles.

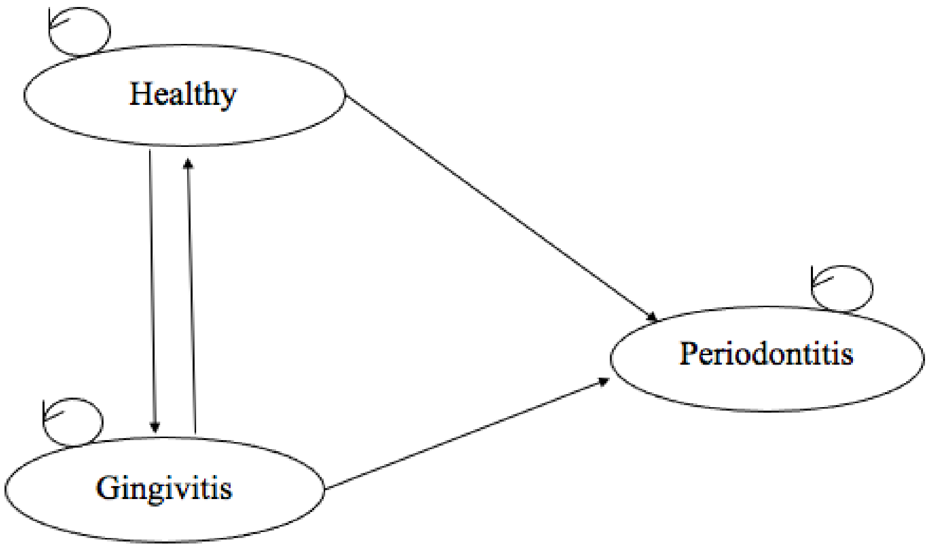

Figure 4: Structure of Markov model.

The prevalence incorporated in the model was based on assumptions, due to lack of data on the prevalence of periodontal disease. There are disagreements among professionals concerning the prevalence of periodontitis in the Norwegian population. In addition, the prevalence of periodontitis in other countries is not necessarily comparable, due to different quality of dental care. The assumptions made on the disease distribution in the main analysis and sub-analyses are presented in Table 2. In the main analysis of 60 year olds, it is assumed that 60% of the population is periodontally healthy at baseline (cycle 0). Further, 30% of the population have gingivitis, and 10% have periodontitis at baseline.

The Markov model was chosen because of its flexibility, and because of the limited available literature on the progression of periodontal disease. Only three studies in the field of periodontal disease have been conducted with the use of Markov models (Faddy et al. 2000; Schätzle et al. 2009; and Mdala et al. 2014).

Analysis	Periodontally healthy	Gingivitis	Periodontitis	Source
40 year olds	90%	7%	3%	Assumption
60 year olds (Main analysis)	60%	30%	10%	Assumption
80 year olds	20%	40%	40%	Assumption

Table 2: Assumption of disease distribution at baseline.

4.3 Model Inputs

4.3.1 Cost estimations

Cost parameters used in the model are presented in Table 3. All costs are reported in Norwegian kroner (NOK). Relevant cost components incorporated in the model were identified partly by a top-down approach based on fee rates (Norwegian: Honorartakst) from the Norwegian Directorate of Health. The cost related to each health state is based on a combination of these fee rates and average prices of treatment from the Norwegian Consumer Council, which are based on reported prices to hvakostertannlegen.no. The prices reported to the latter website are based on a sample of dental clinics in Norway. The cost estimations are based on an external assessment of hypothetical treatment choice and frequencies.

The cost of being periodontally healthy was estimated to be NOK 990 per year, based on the average price of one examination reported to hvakosterlannlegen.no. Examination includes a clinical examination and x-rays. The average price is derived from 1 299 dental clinics in Norway. Thus, it is assumed that a periodontally healthy individual visits the dentist once a year. The yearly cost of gingivitis per year is NOK 2 010 per individual. The price of one examination, one treatment, as well as two simple follow-ups make up the cost of having gingivitis per year. Further, the cost of periodontitis was based on 7 treatments, and 2 simple follow-ups, and was therefore estimated to be NOK 5 520 per year per individual.

If screening detects other diseases beyond gingivitis and periodontitis, neither the cost or health effects of these conditions was considered in the model. 10% of patients with periodontitis need surgical treatment. The cost of surgical treatment is NOK 1 143 per treatment, which includes anesthesia, as well as comprehensive follow-up after the surgery. 2.8% of lost teeth per patient is replaced per year (Fardal et al., 2012). In the main analysis, cost of tooth replacement was set to NOK 20 000, with a range from a lower limit of NOK 13 000 to an upper limit of NOK 27 000 which is taken into account in the PSA. The alternative replacement methods that are included in the joint cost of tooth replacement are bridgework, implant and prosthesis. The cost of bridgework depends on, among other things, how many teeth it will need to replace. The cost of replacement will also vary because of the use of different materials.

The cost of screening consists of a fixed cost and a variable cost. Administrative costs, system costs, equipment, salaries, and rent are included in the fixed cost. The variable cost of screening regards to the actual execution of screening performed by a general dentist. This is an additional cost only applied to periodontally healthy individuals and individuals with gingivitis who are called in for examination. Predetermined rates for treatment costs of periodontitis are reimbursed to the patient by HELFO when a diagnosis of periodontitis has been reached.

The cost parameters were assigned a lognormal distribution, which was considered appropriate as the costs are non-negative and skewed to the right. In the probabilistic sensitivity analysis (PSA) conducted, the values of the different costs are randomly selected between the lower and upper range of values presented in Table 3, for each Monte Carlo simulation. The range of values regarding cost of being healthy, having gingivitis and periodontitis, are based on a range of reported prices from the Norwegian Consumer Council. Further, the range related to variable costs of screening, fixed cost of screening, and cost of surgery are -/+ 50% of the point estimate, as this was considered realistic values. Lower and upper value of tooth replacement was assessed by a periodontal specialist.

Description	**Value in NOK**	**Lower value**	**Upper value**	**LN mean**	**LN SE**
Cost of being periodontally healthy	990	495	1 485	6.898	0.334
Cost of having gingivitis	2 010	1 005	3 015	7.606	0.334
Cost of having periodontitis	5 520	2 760	9 384	8.616	0.372
Variable cost of screening	1 496	748	2 244	7.311	0.334
Fixed cost of screening	1 333	666	1 999	7.195	0.334
Cost of surgery	1 143	572	1 714	7.041	0.334
Joint cost of replacing teeth	20 000	13 000	27 000	9.903	0.222

Table 3: Cost parameters (NOK)

Sources: Norwegian Directorate of Health, the National Consumer Council and periodontal specialist. Lower and upper values indicate the range of values the specific parameter can take in the PSA. Distribution for PSA: Log normal

4.3.2 Outcome measure

The health outcomes are measured in QATYs in this thesis. The utility parameter inputs range from 0 to 1, which are the worst possible oral health and perfect oral health, respectively. A beta distribution was applied for the PSA, as the utilities are far from zero and the inputs are constrained to a range of 0 to 1. The utility values of each state incorporated into the model are presented in Table 4.

Due to lack of data and relevant patient surveys on oral health, the QATY weights were based on assumptions. It is known that periodontal disease rarely has accompanying pain as a result of the diagnosis. This is probably one of the reasons why some people are not aware that they have the disease (Skjørland et al., 2020). However, QATY does not only take into account how the patient values their state of health, but the health of the teeth in full, and also how it affects their ability to function.

Mohd-Doms (2013) article on *Quality-adjusted tooth years as an outcome measure of periodontal treatment* have been identified. However, no directly applicable QATY-values have been identified in the literature that can be adapted to the model of this thesis. Sensitivity analyses were therefore performed to explore how changes in this parameter affected the ICER.

Health state	Mean value	SE	Distribution	Source
Periodontally healthy	0.95	0.038	Beta	Assumption
Gingivitis	0.80	0.032	Beta	Assumption
Periodontitis	0.65	0.026	Beta	Assumption

Table 4: QATY weights

4.3.3 Transition probabilities

Only three previous studies evaluating the clinical course of periodontitis with the use of Markov models have been identified. Transition probabilities based on the classification system of 2018 have not been evaluated in current available research. Faddy et al. (2000), Schätzle et al. (2009), and Mdala et al. (2014) are based on the classification system of 1999.

Transition probabilities from Mdala et al. (2014) have been incorporated into the model, as it was considered most appropriate based on the point in time the study was conducted, and due to the classification system used. In Mdala et al. (2014) study, the age of the population ranges from 26-84, with a median age of 52. The probability of transitioning between periodontally healthy, gingivitis and periodontitis are presented in Table 5. As there are no other available data on transitions, these probabilities are used for the main analysis and sub-analyses in this thesis. The probability of transitioning from periodontitis to either the periodontally healthy state or gingivitis was set to 0, as periodontitis is an absorbing state and this transition is therefore not feasible.

A dirichlet distribution was applied in the PSA. Transition probabilities was estimated to have a standard error of 1%. The dirichlet distribution was determined as the best fit for handling uncertainty in this multinomial data.

Parameter	**Value**	**SE**	**Distribution**	**α**	**β**
Healthy to healthy	0.83	0.008	Dirichlet	1700	348
Healthy to gingivitis	0.12	0.001	Dirichlet	8800	64533
Healthy to periodontitis	0.05	0.001	Dirichlet	9500	180500
Gingivitis to healthy	0.72	0.007	Dirichlet	2800	1089
Gingivitis to gingivitis	0.21	0.002	Dirichlet	7900	29719
Gingivitis to periodontitis	0.07	0.001	Dirichlet	9300	123557

Table 5: Transition probabilities with uncertainty estimates (α, β) from Mdala et al. 2014.

4.3.4 Tooth loss and replacement

Based on Fardal et al. (2004) study on the cost-effectiveness of lifetime treatment of periodontal disease, it was assumed that all individuals had 24 teeth at baseline. The total number of teeth lost due to periodontal reasons was 0.036 teeth per patient per year (Fardal et al., 2004). The rate of tooth loss was assumed constant over time. Of the teeth lost due to periodontal reasons, 2.8% teeth per patient would need to be replaced (Fardal et al., 2012). Teeth behind the premolar are usually not replaced if lost. There is no increased discomfort or pain associated with this, and HELFO does not provide reimbursement for replacing these specific teeth (Helfo, 2020b). The need of replacement given a lifetime perspective is calculated in the model.

4.3.5 Effectiveness of intervention

Relative risk parameters (RR) are used to incorporate the effectiveness of screening into the model. The effect of the hypothetical screening program was not established, and therefore based on assumptions. The assumptions are age-related, where it was assumed a better effect the younger the age group. The risk of developing gingivitis and periodontitis was assumed to be reduced by the screening-intervention. In addition, it was assumed that more individuals will return from having gingivitis to be periodontally healthy. A relative risk below 1 indicates that an event of periodontitis is less likely to occur with the screening intervention compared with today's practice. Relative risks parameters are presented in Table 6, for the main analysis and sub-analyses. In the PSA, a lognormal distribution was used for the relative risk parameters in the models.

Parameter	**Age group**	**Value**	**Distribution**	**Source**
rrScreening_40	40 year olds	0.60	Lognormal	Assumption
rrScreening_60	60 year olds	0.75	Lognormal	Assumption
rrScreening_80	80 year olds	0.90	Lognormal	Assumption

Table 6: Relative treatment effect of screening intervention by age group.

4.3.6 Time perspective

To reflect all relevant differences in costs, events, and outcomes of screening versus today's practice, a lifetime perspective was applied in the analysis. Lifetime was considered to be until the age of 100 years. The sub-analyses are assessed for different lengths of time, given different starting ages.

4.3.7 Discounting

The appropriate value of discounting is debatable. The most common approach in the literature is to discount costs and effects by the same rate. Typically, the discount rate varies between 3-5% per annum (Drummond et al., 2015, p. 245).

In accordance with the Norwegian Directorate of Health (2012) guidelines, both costs and health effects were discounted at 4% in the model. This was done to express that costs and health effects occur at different times. With screening, one will usually not see the effects immediately. The costs occur in present time, while the effect appears way into the future. Further, the discount rates were subject to sensitivity analyses, varied from 1-5% to reflect how discounting of costs or effects influenced the ICER.

4.3.8 Half cycle correction

To take into account that events and transitions may occur in the middle of a cycle, and not just at the beginning or the end, the results of the state transition Markov model were half-cycle corrected. This was done to avoid underestimation or overestimation of the outcomes. The cost of screening was not half-cycle corrected, as this cost occurs at the beginning of the cycle, in comparison to the health benefits and other costs that are spread throughout the cycles.

4.4 Uncertainty

In order to increase the credibility of the results, sensitivity analyses were conducted by testing the model across a wide set of possibilities. One-way sensitivity analyses were conducted on all input parameters in the main analysis. Two-way sensitivity analyses and PSA with 1 000 Monte Carlo simulations were also performed on the same population. Furthermore, a value of information (VOI) analysis was conducted to investigate the value of acquiring additional information. These stages are considered essential to develop decision models useful to inform policy decisions (Briggs et al., 2006, p. 19). SAVI was used to perform the EVPPI analysis (SAVI, 2021). VOI-analysis was only conducted for the main model of 60 year olds.

4.5 Key Assumptions

Several assumptions were made regarding the structure and the included parameters in the state transition Markov model comparing screening with today’s practice in Norway. In summation, the key assumptions are:

- The healthy population in the model was only assumed to be periodontally healthy, i.e. patients may have other dental and oral diseases.
- The intervention of screening was compared with the explained description of today’s practice
- The perspective used for the evaluation of costs and effects was a health care perspective.
- The screening alternative is a hypothetical scenario, and thereby the relative treatment effect (RR) of screening was based on assumptions made by the authors.
- The effects of the intervention are dependent on age, and independent of sex and other covariates, e.g. smoking status.
- Utility values are pure assumptions based on the literature review performed. To the best of our knowledge, QATYs have not been determined in any available research, which is adaptable to the setting of this thesis.

5. Results

5.1 Main Findings

There are significant variations in the results of the analyses, given the model inputs included. It should be emphasized that there is substantial uncertainty in the parameters due to limited available data in this field of research. The deterministic undiscounted and discounted results are presented in Table 7. With only a few exceptions, both costs and effects are higher for the screening intervention compared with today's practice.

	Screening		Today's practice				
Health care perspective	Effect	Costs	Effect	Costs	**△Effect**	**△Costs**	**ICER**
Undiscounted results							
60 year olds (main analysis)	31.06	174 887	30.07	173 798	0.99	1 090	1 100
40 year olds	46.48	264 130	43.81	284 446	2.67	-20 317	-7 600
80 year olds	15.10	95 096	14.99	87 440	0.11	7 656	67 762
Discounted results							
60 year olds (main analysis)	16.18	80 102	15.72	77 750	0.46	2 352	5 101
40 year olds	18.87	85 546	17.90	90 446	0.98	-4 901	-5 014
80 year olds	10.55	64 562	10.48	58 875	0.07	5 687	78 396

Table 7: Results for incremental cost-effectiveness on main analysis and sub-analyses given a health care perspective

In the main analysis of 60 year olds, the incremental effect gained was 0.46 (discounted) over a lifetime perspective with an annual discount rate of 4%. Cost of screening was higher than the cost of today's practice. The discounted total cost of screening was NOK 80 102 versus NOK 77 750 for the comparator. The incremental cost was NOK 2 352. This yielded an ICER of NOK 5 101 per QATY gained.

The sub-analysis conducted on 40 year olds yielded an ICER of NOK -5 014 per QATY gained. As presented in Table 7, the intervention had better effects and lower costs than today's practice in this scenario. The incremental effect was highest in this age group. On the other hand, the sub-analysis of 80 year olds differed substantially from the other analyses, and yielded an ICER of NOK 78 396 per QATY gained. The difference in ICER between the main analysis and 80 year olds was NOK 73 295 per QATY gained, making it less likely for the intervention to be considered cost-effective. The ICER was way higher compared to the analyses created for 40 and 60 year olds.

Given a lifetime perspective of 40 years for the main analysis of 60 year olds, 0.63 teeth needed to be replaced per individual given the screening intervention. For the comparator, 0.72 teeth needed to be replaced per individual. If no intervention was implemented, 90% of the population would be diagnosed with periodontitis after 40 years. The teeth are replaced by either bridgework, implant, or prosthesis. In addition, 10% of people with periodontitis are in need of flap surgery. The ICER takes into account the cost of the different replacement methods and surgery.

5.2 Deterministic Sensitivity Analyses

5.2.1 One-way sensitivity analyses

Results of several one-way sensitivity analyses are presented in a tornado plot in Figure 5. The line represents the ICER result of NOK 5 101 per QATY. Sensitivity analyses were only conducted for the main model. The tornado plot illustrates how a change in one input parameter influences the ICER. The ICER ranges from NOK -25 077 to NOK 40 874 throughout all parameters, given a health care perspective. Changes in ICER values are specified and presented in tables in Appendix 9.1. Lower and upper values from Table 3 correspond to the range of the values varied in the one-way sensitivity analyses (rounded to the closest hundred). Change in utility of being healthy, relative treatment effect, utility of periodontitis, and cost of periodontitis had the greatest impact on the ICER. Utility inputs and the relative treatment effect were both based on assumptions due to lack of data in the literature. Despite uncertainties in the parameters, one-way sensitivity analyses contributed to validate the overall results. Future costs and effects were discounted annually by 4% in the model. When varying the values of the discount rate between 1-5%, the ICERs increased by 64% for the costs from the lowest to the highest (NOK 3 324 vs NOK 5

443) and increased by 105% for the outcomes from the lowest to the highest values (NOK 2 926 vs NOK 6 003).

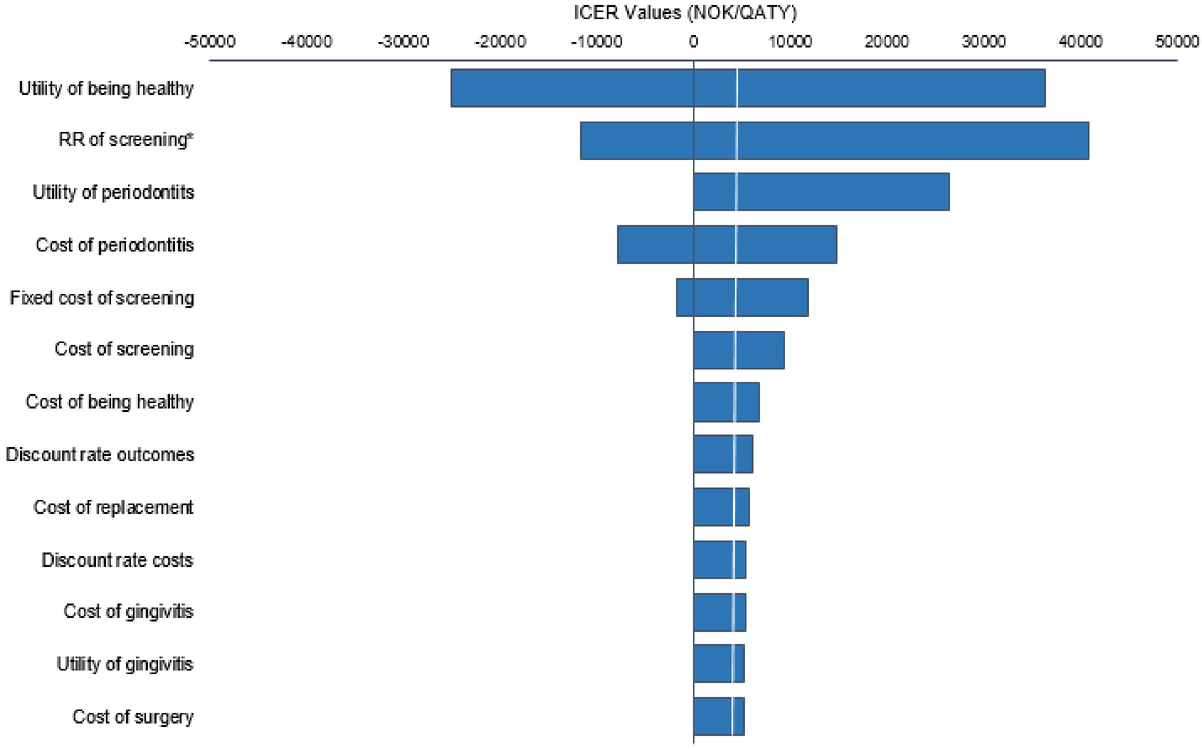

Figure 5: Tornado plot presenting the results of one-way sensitivity analyses for different parameters. The line at 5 101 NOK/QATY represents the ICER in the main deterministic analysis.

*RR: relative treatment effect of screening

An additional graphical presentation of the one-way sensitivity analysis on relative treatment effect (RR) is presented in Figure 6. The ICER varied a lot with a change in relative treatment effect of screening. The ICER decreased in accordance with a lower effect of screening. The ICER turned from a positive value to a negative value around a RR of 0.65 if no other parameters were changed.

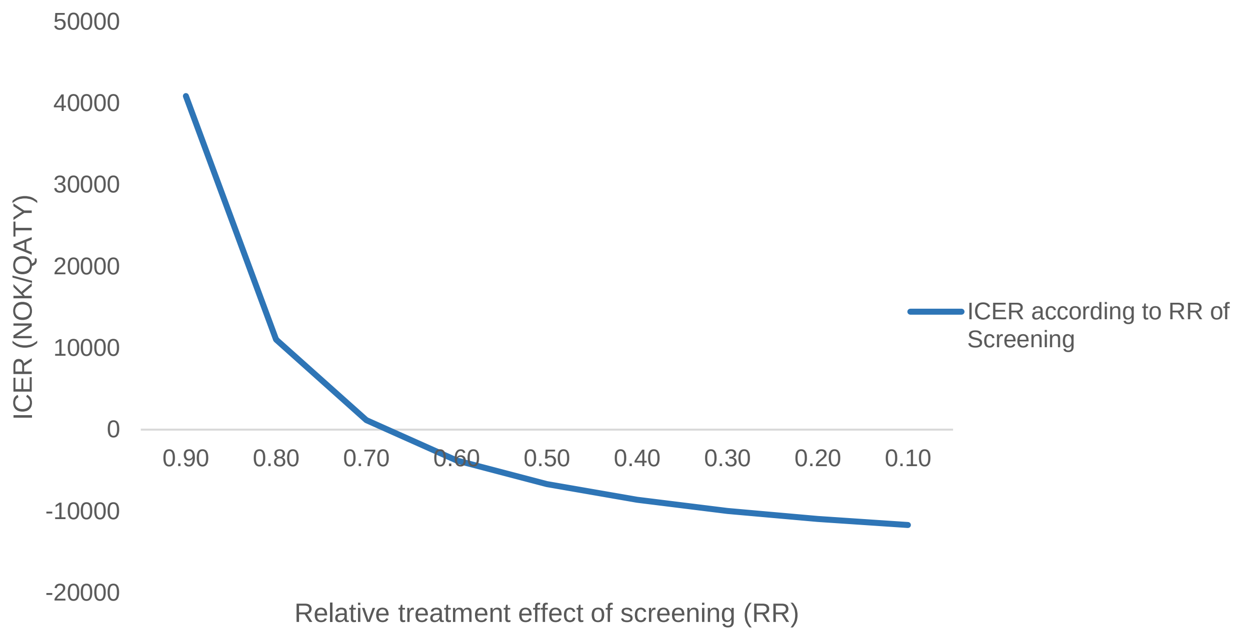

Figure 6: One-way sensitivity analysis of change in ICERs according to change in relative treatment effect of screening (RR).

5.2.2 Two-way sensitivity analyses

Results of the two-way sensitivity analyses are presented in Table 8 and Table 9. Bold numbers present positive ICERs. However, the WTP-threshold is unknown. In the main analysis, the RR of the screening intervention was valued 0.75, the cost of screening was NOK 1 496, and the utility weight of periodontitis was 0.65. Lower values of RR resulted in negative ICERs in both two-way sensitivity analyses. Simultaneously, an increased cost of screening yielded a higher positive ICER. The ICER also increased with a higher utility weight of having periodontitis.

		Relative treatment effect of screening								
		0.9	**0.8**	**0.7**	**0.6**	**0.5**	**0.4**	**0.3**	**0.2**	**0.1**
Cost of screening	**750**	**30 063**	**5 649**	-2 450	-6 468	-8 852	-10 416	-11 512	-12 312	-12 914
	1 000	**33 686**	**7 458**	-1244	-5 563	-8 126	-9 810	-10 990	-11 853	-12 504
	1 250	**37 309**	**9 267**	-39	-4 658	-7 401	-9 204	-10 468	-11 394	-12 094
	1 500	**40 932**	**11 077**	**1 167**	-3 753	-6 676	-8 598	-9 947	-10 936	-11 683
	1 750	**44 555**	**12 886**	**2 373**	-2 848	-5 951	-7 992	-9 425	-10 477	-11 273
	2 000	**48 178**	**14 695**	**3 579**	-1 943	-5 225	-7 386	-8 903	-10 018	-10 863
	2 250	**51 800**	**16 504**	**4 785**	-1 038	-4 500	-6 780	-8 382	-9 559	-10 452

Table 8: Two-way sensitivity analysis on cost of screening and relative risk of screening.

		Relative treatment effect of screening								
		0.9	**0.8**	**0.7**	**0.6**	**0.5**	**0.4**	**0.3**	**0.2**	**0.1**
Utility of periodontitis	**0.1**	**14 682**	**3 976**	**414**	-1 362	-2 423	-3 127	-3 626	-3 997	-4 283
	0.2	**16 618**	**4 500**	**468**	-1 541	-2 741	-3 536	-4 100	-4 519	-4 841
	0.3	**19 142**	**5 182**	**539**	-1 774	-3 155	-4 069	-4 716	-5 197	-5 565
	0.4	**22 571**	**6 109**	**636**	-2 090	-3 715	-4 791	-5 551	-6 114	-6 545
	0.5	**27 496**	**7 439**	**774**	-2 543	-4 519	-5 824	-6 744	-7 424	-7 943
	0.6	**35 170**	**9 510**	**989**	-3 246	-5 765	-7 425	-8 592	-9 450	-10 102
	0.7	**48 786**	**13 178**	**1 368**	-4 488	-7 961	-10 239	-11 833	-12 996	-13 870
	0.8	**79 605**	**21 453**	**2 222**	-7 270	-12 859	-16 492	-19 000	-20 800	-22 124
	0.9	**216 157**	**57 658**	**5 909**	-19 117	-33 425	-42 352	-48 184	-52 067	-54 638

Table 9: Two-way sensitivity analysis on utility weights of periodontitis and relative risk of screening

Additional two-way sensitivity analyses are presented in Appendix 9.2 considering the effect on the ICER based on changes in cost of screening and cost of periodontitis, cost of periodontitis and relative treatment effect of screening (RR), and cost of screening and fixed cost of screening. An increased cost of periodontitis, in combination with increased cost of screening, resulted in a lower ICER. Further, increased fixed and variable cost of screening resulted in higher ICER values. RR had a great impact on the results.

5.3 Probabilistic Sensitivity Analyses

Results from the PSA of the main analysis, with 1 000 Monte Carlo simulations are presented in the cost-effectiveness plane in Figure 7. Mainly, all scatters are located in the north-east quadrant, i.e. both positive incremental costs and positive incremental QATYs. However, it does not necessarily mean that the intervention should be considered cost-effective, as this would depend on the WTP threshold. If the WTP threshold was higher than NOK 5 101 per QATY, the intervention would be considered cost-effective. Correspondingly, if the WTP threshold was below the ICER, it would not be considered cost-effective and the comparator would be the best option.

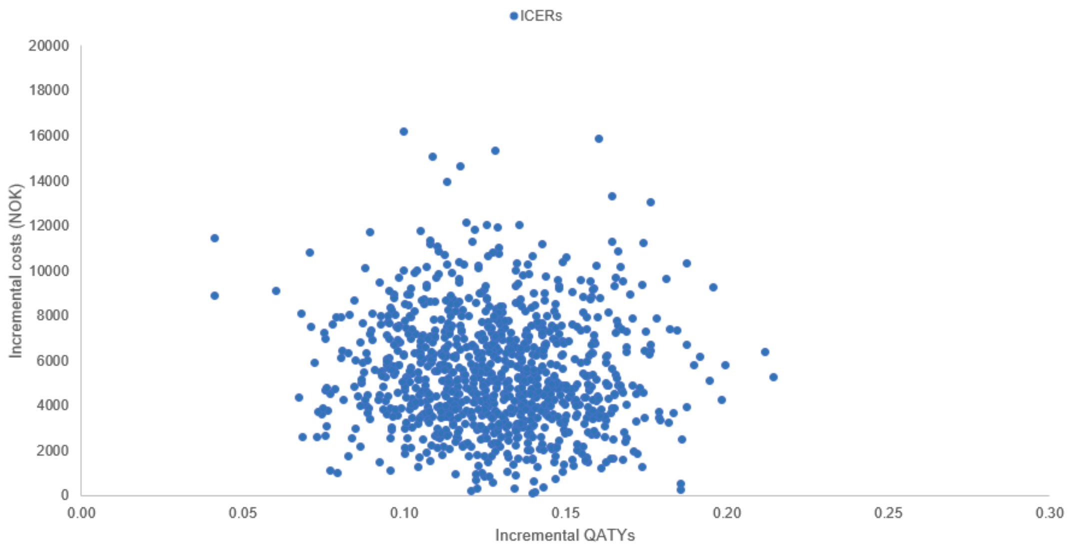

Figure 7: Cost-effectiveness plane of ICERs from PSA. Incremental QATYs on the horizontal axis, and incremental costs on the vertical axis. The WTP threshold per QATY is unknown.

In comparison, given the analysis of 40 year olds, all values would be located in the south-east quadrant. It is thus said that the intervention being evaluated dominates its comparator. Ideally, one should always choose the dominant intervention, as both resources are saved and more health effects are gained.

The results from the PSA are further presented by the cost-effectiveness acceptability curve (CEAC) in Figure 8. The CEAC illustrates where the decision of the optimal intervention changes, which does not necessarily correspond to the ICER value from the deterministic analysis. Today's practice had a higher probability of being cost-effective, compared to the intervention, for WTP thresholds below NOK 40 000 per QATY. Correspondingly, the screening intervention had a higher probability of being cost-effective for thresholds above this value. The cost-effectiveness acceptability frontier (CEAF) is presented in Appendix 9.3. The CEAF describes the optimal alternative at different threshold values.

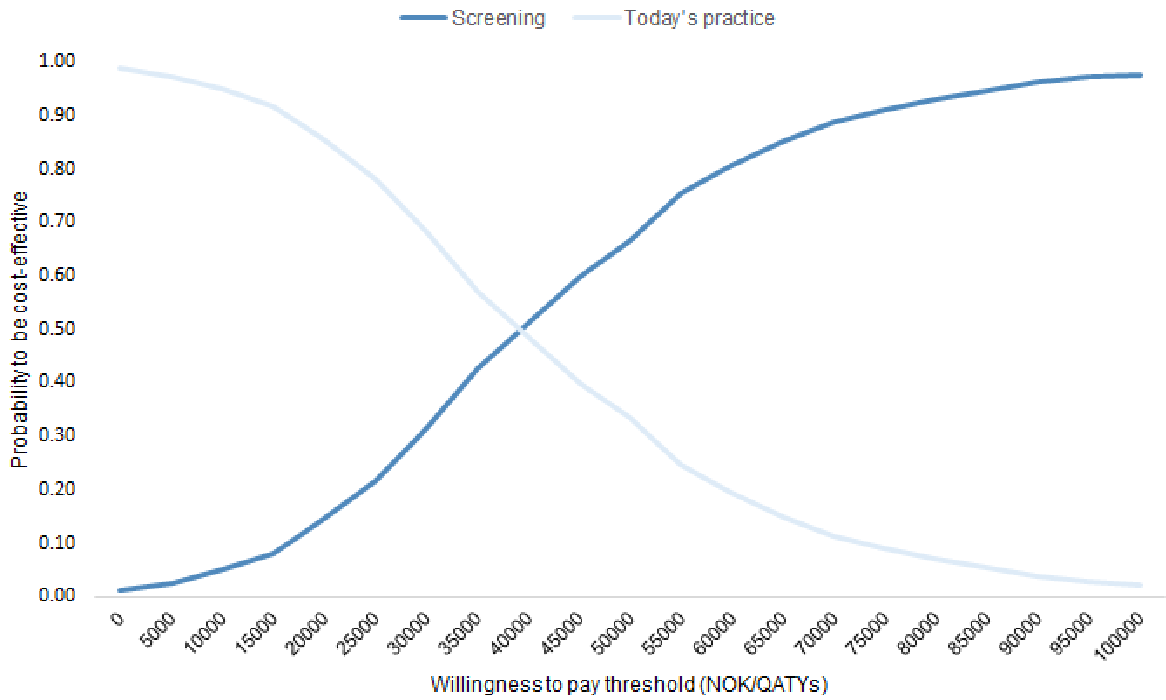

Figure 8: Cost-effectiveness acceptability curve for main model of 60 years olds.

For the sub-analysis of the screening intervention starting at the age of 40, the likelihood of screening to be cost-effective, compared with today's practice, ranged from 17-100% given different threshold values. The intervention had a higher probability of being cost-effective, compared with today's practice, for WTP thresholds above NOK 12 500. The likelihood of today's practice being cost-effective ranged from 0-82%. These wide ranges indicated great uncertainty in regards to the WTP threshold value. The results from the PSA are presented by the CEAC in Figure 9. The CEAF from this analysis is presented in Appendix 9.3.

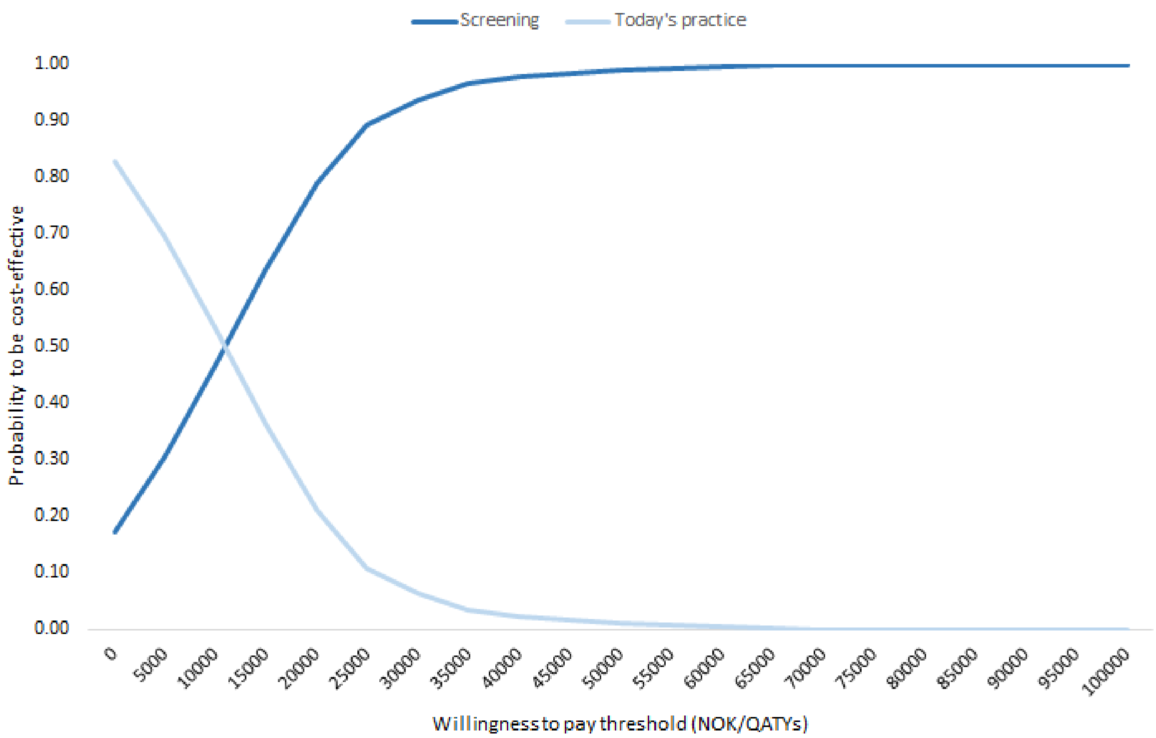

Figure 9: Cost-effectiveness acceptability curve for sub-analysis of 40 year olds.

For the sub-analysis of the screening intervention starting at the age of 80, the results of the PSA are presented by the CEAC in Figure 10. The CEAC is presented in Appendix 9.3. Note that the range of threshold values on the horizontal axis differ for this sub-analysis, as the screening intervention had a higher probability of being cost-effective for WTP thresholds above NOK 200 000.

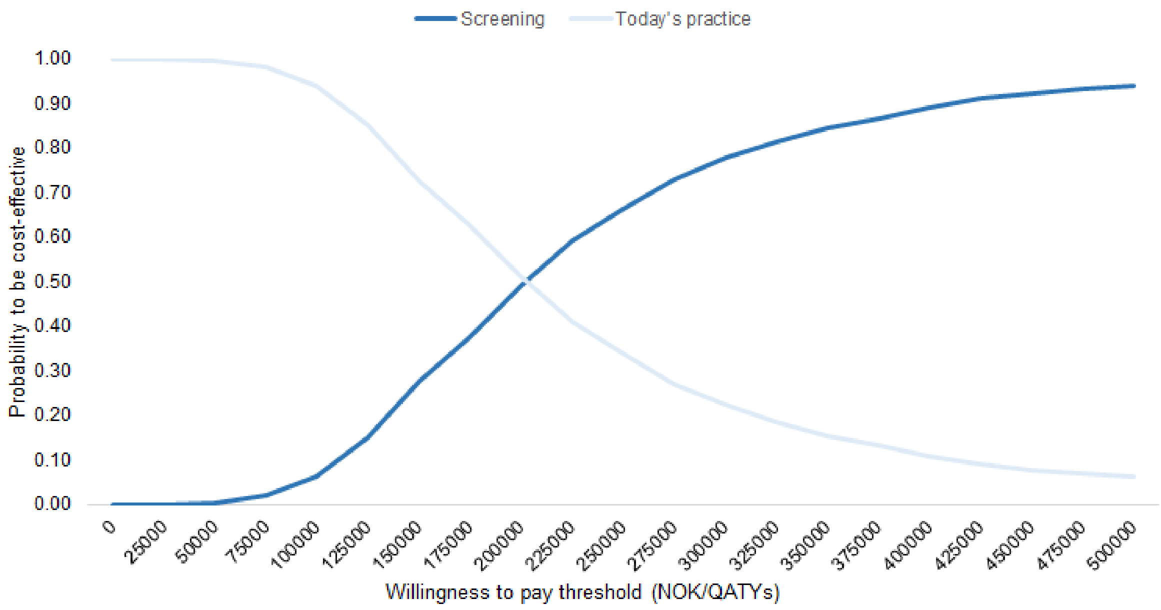

Figure 10: Cost-effectiveness acceptability curve for sub-analysis of 80 year olds.

Based on the analyses performed, it was more likely for the screening alternative to be cost-effective in the 40 year old group given a low WTP threshold per QATY gained. Screening offered to 40 year olds would both yield lower costs and increased effects, compared with today's practice.

5.4 Value of information analysis

5.4.1 Expected value of perfect information

The expected value of perfect information (EVPI) estimation equals the uncertainty from the PSA given a range of threshold values. Figure 11 represents the individual EVPI for the screening intervention versus today's practice. The peaking point of the EVPI was at a threshold value of NOK 40 000, which corresponds to the point of most decision uncertainty as the decision on which alternative to choose was indifferent at this value. A threshold value of NOK 40 000 responded to an EVPI value per individual per year of NOK 1 050 per QATY gain. Value of acquiring perfect information on all parameters should not exceed this amount, as it would not be considered cost-effective use of resources. Only those not already diagnosed with periodontitis will benefit from gaining additional information.

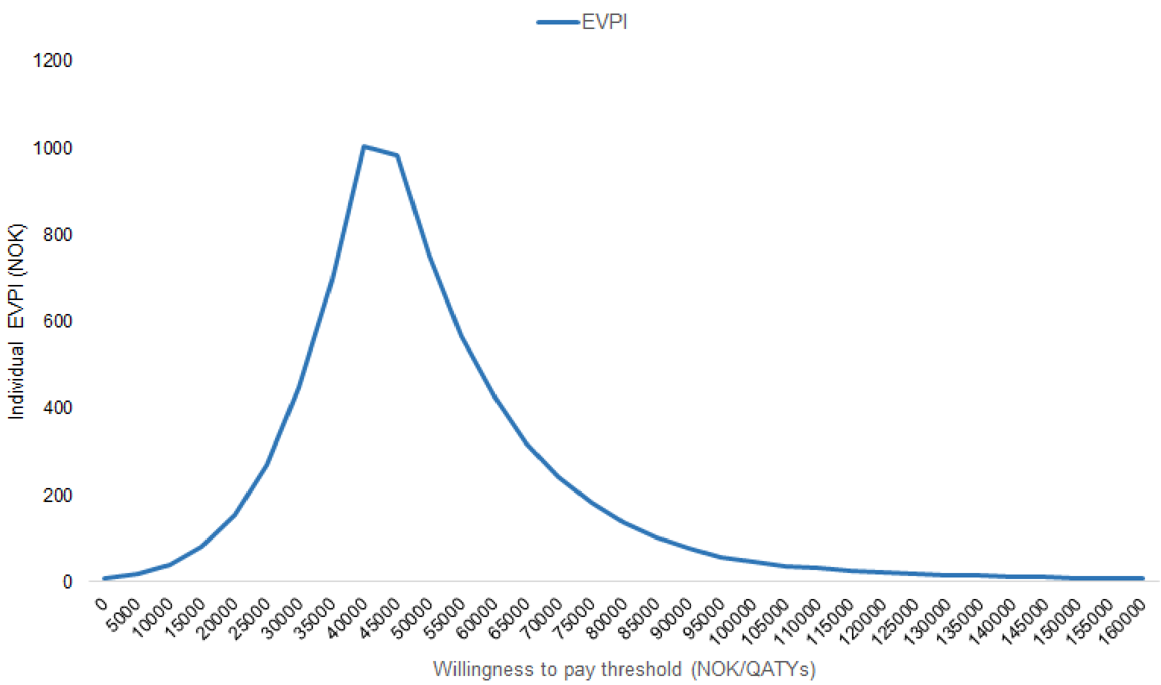

Figure 11: Individual EVPI for screening intervention versus today's practice.

5.4.2 Expected value of partial perfect information

The expected value of partial perfect information (EVPPI) estimation showed which parameters are causing most of the decision uncertainty, and what the potential value was of reducing uncertainty by collecting more data on those parameters. Figure 12 represents the EVPPI per person for single parameters. The VOI analysis indicated that fixed cost of screening, cost of periodontitis and the effectiveness of the intervention were the parameters with the most uncertainty, and were in need of additional research. The value of gaining additional information about the effect of treatment was NOK 233 per individual of the population per year. Given a lifetime horizon of 40 years, the EVPPI equals NOK 9 337 per individual. Further, the results from the VOI analysis indicated that there was no value of acquiring more information on parameters like cost of being healthy, cost of gingivitis, cost of surgery, cost of replacement, and transition probabilities.

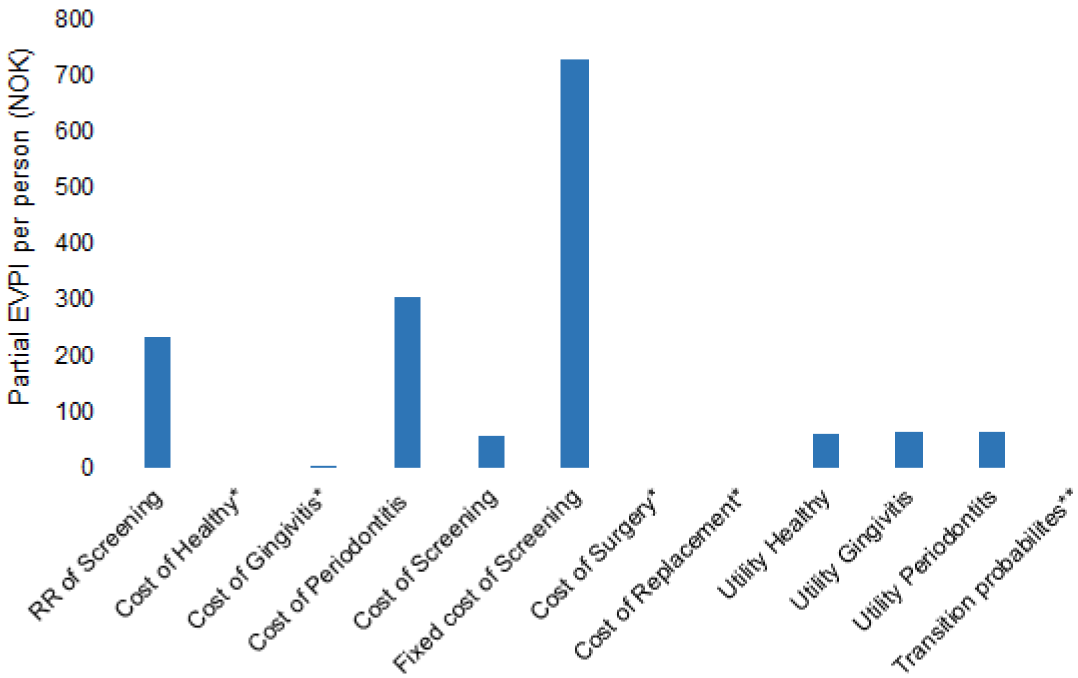

Figure 12: Single parameter EVPPI per person.

*Zero or low value of acquiring additional information

*Transition probabilities are grouped for the sake of graphic presentation

6. Discussion

6.1 Discussion of results

The main findings of this thesis suggested that screening could be cost-effective when offered from the age of 40 or 60. Correspondingly, screening offered from the age of 80 was not likely to be considered cost-effective, given a health care perspective. The sub-analysis of 40 year olds showed that screening dominated the alternative of today's practice, i.e. the intervention was considered cost saving and additional health effects were gained. The lifetime perspective was different between the analyses, as 40 and 60 year olds were evaluated for more years than 80 year olds. The screening costs occur today for all age groups, while the beneficial effects of screening will be seen after several years. However, as the perspective of 80 year olds was shorter, the total effects are not as significant.

Uncertainty explored in deterministic sensitivity analyses established that the ICER was robust to changes in most parameters. Sensitivity analyses were only conducted on the model of 60 year olds. According to the one-way sensitivity analysis, relative treatment effect (RR) was identified as one of the drivers of the ICER. RR of screening could potentially change the conclusion on cost-effectiveness. In addition, the utility of being healthy was shown to substantially influence the ICER. The influence of changes in this parameter alone was likely to yield a negative ICER for utility values below 0.65. One-way sensitivity analyses yielded different effects, with some parameters being more important than others, e.g. changes in discount rate or cost of surgery had limited effect on the final results.

Two-way sensitivity analyses indicated that RR, in accordance with either cost of screening or the utility of periodontitis, yielded negative ICERs at lower values of RR. Combined, these input parameters significantly influenced the ICER. Increased values of RR combined with increased cost of screening, or increased utility of periodontitis, yielded higher ICER values.

As all ICERs from the PSA were located in the north-east quadrant in the cost-effectiveness plane (Figure 7), incremental costs and effects are consistently positive with screening. According to the CEAC, screening was more likely to be cost-effective if the WTP threshold was above NOK 40 000 per QATY. Cost-effectiveness is determined by a trade-off between the alternatives depending on WTP. The initial uncertainty in the parameters was taken into account in the deterministic and probabilistic sensitivity analyses performed.

It was considered appropriate to assess individual EVPI and EVPPI, as the disease prevalence is unknown. The EVPI increased with the WTP threshold as the consequences of decision uncertainty rose. The threshold of NOK 40 000, which was the value at the peaking point in Figure 11, corresponded to the point of most decision uncertainty as the decision on which alternative to choose was indifferent. The EVPI declined to almost 0 for higher threshold values. According to the EVPPI analysis, fixed cost of screening, cost of periodontitis, and relative treatment effect of screening, was of most value of research. All analyses indicated that the effect of screening, in terms of cases detected and avoided, were crucial for the decision of implementation. However, more research should also consider the utility weights of the disease. If EVPI and EVPPI are greater than the expected costs of research, further research might be worthwhile.

6.2 Strengths and Limitations

6.2.1 Cost estimation

Each health state of the Markov model included several cost components. The cost components incorporated in the model were a combination of fee rates from the Norwegian Directorate of Health, and average prices of treatment reported to hvakostertannlegen.no. The prices reported to the latter are based on a sample of dental clinics in Norway. The average price from these clinics was consequently taken into account in the cost of treatments, as the national fee rates for dental treatments alone are not realistic as the actual cost of treatments. Most dentists use a higher fee as they are allowed to charge more than the national tariffs. Thus, the exemption card is not a total exemption from charges, as the individual will have to cover costs exceeding the national tariffs. The top down assessment is considered a strength of the study in accordance with guidelines for economic evaluations in health care. Alternatively, a bottom-up approach, for instance micro costing, could have provided more accurate estimates of the treatment costs.

The model included costs related to detection and treatment of gingivitis and periodontitis. However, costs of other conditions that are detected with screening were not taken into account. Further, teeth that would have been lost due to other conditions than periodontitis, and saved by detection due to the screening program, were not incorporated in the model. Only the cost of tooth loss due to periodontal disease was included in the model. It is unlikely that inclusion would have affected the results to a great extent.

The analysis did not take into account patients' productivity cost, i.e. time off work, or the time costs associated with treatment. However, possible anomalies in cost-effectiveness calculations related to, for instance, differences in earnings, was avoided. To estimate this, the average wage rate after tax could have been incorporated into the model. An alternative could have been to incorporate the productivity loss and time spent into the outcome measure. Technically, this is a potential approach as long as it is not double counted, i.e. counted in both costs and outcomes. However, QATY is not a well-established outcome measure as it varies in how it is measured. As QATYs in this analysis was based on assumptions, productivity cost could have been subsumed in the QATY measure. Further, potential costs of sick leave due to treatment was not considered in the model. It is uncertain how many patients would have been in need of time off work due to treatment.

The fixed cost of screening included administrative costs, system costs, equipment, salaries, and rent. The assessment of the fixed cost of screening was made by comparing other screening programs. As reported from other screening programs, approximately 25% of people summoned for screening do not attend (Sebuødegård et al., 2016). One can assume this also applies for screening for periodontitis. However, this was not included in the model. It was assumed that all patients showed up for screening. Since the prevalence of periodontal disease is unknown, and thereby the disease distribution at baseline was uncertain, it was not desirable to take into account the absence of attendance in the model. Still, attendance will in most cases affect the cost-efficiency, e.g. by influencing the number of disease cases detected. The uncertainty of the fixed cost of screening was valued in sensitivity analyses, and it was concluded, as expected, that the ICER increased in accordance with an increased cost of this cost input.

6.2.2 Outcome measure

The optimal outcome measure of periodontal disease used for economic evaluations are debatable. Fardal and Grytten (2014) used the Visual Analogue Scale (VAS) to measure anxiety and discomfort related to periodontal treatment. Further, they adapted quality-adjusted life years (QALYs) to quality-adjusted tooth years (QATYs) for measuring the outcome. However, these outcome measures were not used in the model after all due to difficulties in the determination of patients QALY or QATY over a period of 21.6 years (Fardal & Grytten, 2014). Also, Mohd-Dom (2013) have tried to develop a simple approach to estimate QATYs. This study calculated QATYs by multiplying utility values, derived from The Oral Health Impact Profile (OHIP-14) index, by tooth life expectancy. The study suggested that this method should be considered in economic evaluation of dental treatments (Mohd-Dom, 2013).

The fact that the QATYs incorporated in the model was fully based on assumptions made by the authors, is considered a major limitation of the results. However, this parameter uncertainty was addressed in the sensitivity analyses. The rationale of the assumptions made in the thesis was based on the fact that periodontitis, in most cases, is not considered to cause significant discomfort for the individual. QATYs take into account the health of the teeth as a whole unit, where the individual's perception of the disease is not the only thing that counts. However, it is difficult to make an assumption on these parameters, partly because the optimal method of determining QATY is not consistent. The most essential challenge is that none of the studies identified, have investigated the QATYs of gingivitis and periodontitis, relatable to the model of this thesis. Further, the QATY values in the analysis are not age-adjusted, as this was considered best given the lack of available data. However, it is likely that the utility of different stages varies between age groups. The results from the VOI-analysis indicated that there was significant value in acquiring additional information on the utility parameters. Future research should strive to determine utility values related to periodontal disease to make it possible to calculate QATYs.

6.2.3 Transition probabilities

Transition probabilities were obtained from the Mdala et al. (2014) study on 162 Swedish and American patients with chronic periodontitis, as these were the only relevant probabilities identified in the literature. Transition probabilities were estimated to have a standard error of 1%. The study reported different transition probabilities for year 1 and 2. The duration of the study was only 2 years. Transition probabilities for year 1 were used in the modelling of this thesis, a decision that could be challenged. A short study duration may yield unstable estimations, as slowly progressive periodontal disease is not captured.

Transition probabilities incorporated in the model take into account the classification system from 1999. Ideally, transition probabilities would have been divided into the health states from Figure 1. However, this has not been assessed in any recent studies. The use of this classification system is considered a simplification inherent in the model, i.e. a structural uncertainty. Using the newest available classification would presumably lead to a more precise and realistic distribution of the patients. Considering this has not been done, more individuals will be placed in the category of periodontitis despite no or few ailments. In stage I and II, the patient may be unaware of the disease occurrence. If data were available on transition probabilities for each stage of periodontitis and gingivitis, it would have been possible to create a model with a more precise classification taking into account the individuals' experience of the disease. Nonetheless, periodontitis is irreversible and hence a progressive disease once first developed.

There are few recent studies conducted on periodontal disease, and it is therefore a chance that the clinical picture may look somewhat different today than it did when Mdala et al. conducted their study in 2014. Without available research, it is problematic to speculate, but periodontal disease may be prevented either less or more often than this study suggested. The transition probabilities were utilized in all models of the thesis, i.e. they are not age dependent, and the same risk of developing disease was used for all individuals over all cycle lengths.

A further assessment that was made was the distribution of patients at baseline, as the true prevalence of periodontal disease of the Norwegian population is unknown. Since transition probabilities were based on assumptions, there is considerable uncertainty associated with the results this have yielded. However, the uncertainty related to the transition probabilities was taken into account in the PSA.

6.2.4 Effectiveness of intervention

Screening for periodontitis has not been tested in any population yet. The effectiveness of the intervention was expected to be different between age groups. Stochastic uncertainty applies as patients who undergo the same treatment regime may experience different disease development, e.g. due to genetics. RR was evaluated in a one-way sensitivity analysis for the main analysis, where there was significant change in the ICER value across different values of RR. EVPPI also showed some value of conducting additional research on RR.

In addition, the relative treatment effect of screening was assumed constant over a lifetime perspective, which may not be a realistic assumption as dental health is determined by several factors that may change throughout life. In addition, the risk of development of periodontitis increases with age.

According to this thesis, the effectiveness of the intervention yielded less tooth loss. Periodontitis is the biggest cause of tooth loss in the adult population. However, despite the number of teeth lost due to periodontitis, the number of teeth that needed to be replaced per individual was low, i.e. 0.63 teeth over a 40 year time horizon. According to today’s classification of periodontal disease, tooth loss rarely occurs in stage I and II of periodontitis, as well as few individuals are assumed to develop stage III or IV.

6.2.5 Discounting

All costs and effects are discounted at 4% in accordance with the Norwegian Directorate of Health guidelines. The choice of the appropriate rate of discounting is not necessarily a straightforward decision and should be reflected on when doing analyses. For instance, the National Institute for Health and Care Excellence (NICE, 2013) suggests discounting both costs and effects at 3.5%, and WHO proposes using a 3% discount rate (Edejer, 2003). It is considered essential to discount screening interventions. This is because with screening, the costs arise in the present while the effect appears in the future.

In the model, it was applied a lifetime perspective to the age of 100. This time perspective was chosen to make sure all relevant costs and effects would be captured over time. In reality, not all individuals would live until the age of 100. Life expectancy in Norway was 83.2 years in 2020 (Statistics Norway, 2021). In the main analysis, the costs and effects were assessed over 40 years. For the stratified analyses with subgroups of 40 and 80 year olds, the time perspective was 60 and 20 years, respectively.

All individuals were included in the model calculations for all cycles, as periodontitis is not a deadly disease. However, the fact that individuals may die of other reasons are not included in the model. This was considered a significant limitation of the model. Given the parameter inputs incorporated in the main analysis of 60 year olds, it was expected that 82% would have periodontitis, 2% would have gingivitis, and 16% would be periodontally healthy after 40 years. Some of these individuals would have died within the time horizon of the analysis, i.e. before the age of 100, and hence not creating further expenditure or gaining health effects. The significance of including death as an outcome would presumably differ between the age groups, where the importance of death is less for 40 and 60 year olds compared to 80 year olds, as the oldest will likely die sooner.

Due to different time perspectives, the value of discounting would affect the age groups differently. The costs are the same as they occur today, but the beneficial effects are lower when the individuals die sooner as the effect of screening does not occur straight away. One-way sensitivity analyses was conducted for the effect of discounting of costs and effects on the ICER. This yielded a relatively small change in the ICER value of this model, but a different effect would be expected for the sub-analyses for 40 and 80 year olds. The incremental effect decreased from 0.99 to 0.46 in the main analysis as a result of discounting.

6.2.6 Perspective

Given a health care perspective, the treatment costs incorporated into the model are estimated based on fee rates from the Norwegian Directorate of Health, rather than reimbursement rates alone, as it does not matter who covers the cost. The fee rate included both the reimbursement rate and the deductible.

A societal perspective is recommended for cost-utility analyses, as this perspective is the broadest and should capture all the welfare gains for the society. However, this thesis does not take into account patients' productivity cost, i.e. time off work, or time costs associated with treatment. Nor societal consequences, e.g. untreated periodontitis leading to other diseases imposing a burden on society was taken into account. The screening program would have entailed more time off work than todays' practice. Time costs related to screening could have been applied to all healthy individuals and individuals with gingivitis in the screening arm. Consequently, the time cost would have been higher for the screening arm. However, more cases of periodontitis would have been avoided. Presumably, inclusion of time costs would have resulted in a higher ICER. As the course of treatment of periodontitis is very individual, and depends largely on the patient's own efforts, the treatment frequency may vary between weekly intervals and up to 6 months. In the combination with an unknown disease prevalence, this makes it difficult to estimate the true total time cost related to treatment of periodontitis.

There is a significant difference between the dental health sector and the health sector in Norway. The perspective applied can not fully take into account the true costs that will be borne by the dental care sector or the patient. The patient would need to pay a deductible of some treatments, e.g. treatment of periodontitis, surgery or replacement of lost teeth. The deductible the patient needs to pay may vary significantly from dentist to dentist, because of free price setting on services or treatments. It is thus unclear how much of the fixed cost is paid by the health care sector and what is paid by the patients. This cost applies to the patient regardless of whether they have an exemption card or not.

Prevention of periodontal disease at an early stage may have a societal benefit by reducing future burden on society. Further, it may be important given a healthcare perspective, as it has the potential of reducing the number of elderly in nursing homes and with home care aides with the need of periodontitis treatment. This group of individuals are already covered by the publicly financed health scheme.

6.3 Model Validation

Several approaches were made to validate the model. Consistent collaboration on model setup and calculations assured the internal validity of the Markov model, due to frequent correcting of each other's work. Debugging was conducted individually, to resolve any bugs in the modelling. However, internal validation could be challenged on the basis that no others have, in depth, considered the technical execution of the model.

To make sure that the model is realistic, it will be necessary to know how many untreated cases of periodontitis there are in the population. It can be argued that the assumed distribution of patients at baseline is incorrect, as there is sufficient funding for dental care services in Norway, leading to individuals seeing their dentist when appropriate, hence preventing periodontitis. In addition, the supply and distribution of dental health professionals are considered excellent, with a ratio of 1:1093 dentists per individual in 2013 (Fardal et al., 2020b). Regardless, disease prevalence in the population is unknown, and literature from other countries was therefore used to estimate the expected prevalence in the Norwegian population for different age groups (Mohd-Dom et al., 2016; Nazir, 2017; Renvert et al., 2013). Even though a substantial part of the model inputs are based on assumptions, several of the estimates have been validated by a periodontal specialist and a general dentist. Feedback from clinicians regarding input parameters included in the model increased face validity.

Despite thorough research completed, no relevant cost-utility analyses were identified for the assessment of cost-effectiveness for a preventive measure for periodontitis or any periodontal disease. Cross-validation and external validation is thus challenging, as there are no results of other models to compare with that address the same issues. The closest comparison identified was Mohd-Dom et al. (2014) assessment of the cost-effectiveness of periodontitis management in a specialist periodontal program, with an ICER of MYR 451 per QALY gained (corresponds to approximately NOK 910 in 2021). Furthermore, no relevant studies have been discovered that state a specific WTP threshold per QATY, a statement that should be known before concluding on cost-effectiveness for an intervention.

6.4 Implications of implementation

6.4.1 Prioritization

It was explained in chapter 2.2 that some groups in the Norwegian population have dental care services covered by the National Health Insurance Scheme, and pay either nothing or just a proportion of the total price out-of-pocket. The basis for this decision may seem incomprehensible for non-clinicians, as no system of collecting and evaluating clinical data on prevalence or incidence, for instance, is used in Norway. Thus, it is uncertain whether treatments funded for the financially covered groups are considered cost-effective, or if other alternatives would be cost-effective to include in the National Health Insurance Scheme as well. Considering the screening intervention, it was chosen to focus on age groups who, on a general basis, pay all expenses related to dental care services themselves.

Consequently, it was assessed what age group should be the starting point for screening, as the overall objective was to prevent disease before development. It is known that the risk of periodontitis increases with age, but no exact value of additional risk has been identified. Both younger and older age groups were considered, and there was a disagreements among clinicians on what age group was the most appropriate to start screening. The Norwegian Society of Periodontology suggested starting screening at 30 years old, but due to lack of available data, e.g. on prevalence and the risk of development of periodontitis was unknown, 60 year olds were used for the main analysis. 60-69 year is the age group with the highest treatment prevalence in 2013 (Fardal et al., 2020b). The decision was supported by clinicians. Due to the disagreements among clinicians, it was decided to compare the chosen age group with 40 and 80 year olds.

Screening was least likely to be cost-effective for the oldest age group considered. Certain groups of elderly are already financially covered for dental care services, through the Dental Health Services Act (1984, §1-3). This applies to those living in nursing homes or receiving home care aid. It can also be discussed whether it is ethically right to stratify within equal groups, i.e. same age group. On the other hand, those in need of additional care aid in everyday life may not be able to take care of their dental health themselves. It is further reported of a potential of improvement regarding dental care at Norwegian nursing homes and in home care. It is therefore considered essential to prevent periodontitis before patients reach hospitalization. A study conducted at several nursing homes in Oslo stated that 44% of the patients have received dental treatment during the last 0-2 years. At the same time, 67% report that they only received treatment when experiencing pain or discomfort. The municipal health service has a clear responsibility for establishing a system that ensures the patient's needs. However, it was pointed out that there is occasional disagreement between nursing staff and patients as to when the patient's last dental examination took place (Haugen & Solheim, 2019).

According to Fardal et al. (2020b), 90% of the Norwegian population over 20 years visit the dentist at least every other year. Despite this, many consider the costs this entails to be too expensive. Among people with low income and unmet needs, 81% considered it too costly to consult a dentist (Ekornrud & Skjøstad, 2017). Parts of the population may therefore choose not to go to the dentists because they cannot afford the costs. This applied especially to individuals in the age group 25-44 years with low income (Svalund, 2005). Accordingly, an offer of a dental health check for periodontitis free of charge may be beneficial to some, because otherwise they would not seek out a dentist. Further, lack of necessary dental treatment can cause consequences later in life.

In the long run, it may be applicable to expand the offer of screening to other age groups. For this to be possible new studies would have to be conducted and the effect of screening would have to be assessed. Considering that there is a significant lack of data on prevalence of periodontitis in the Norwegian population today, it is a possible drawback that there is little basis for comparison. An expansion of screening would have to be a gradual process after the effects have been evaluated over some time.

Available public funds are limited. Therefore, it is important that prioritization considerations regarding public funds are carefully considered. Overall, political objective considerations should follow three criteria for prioritization: the benefit criterion, the severity criterion, and the resource criterion. It is specified that these criterias must be considered together. The more serious a condition is, and the greater the benefit it entails, the higher use of resources can be accepted (Norwegian Directorate of Health, 2019). Severe chronic periodontitis may cause great pain and tooth loss. On the other hand, early stages of gingivitis and periodontitis will not necessarily result in great discomfort or pain for the patient. This influences whether the intervention should be prioritized compared to other interventions, e.g. new interventions regarding stroke. The analysis is based on QATYs, and a rationale for this is that screening for periodontitis may not be a priority issue, but rather an equity issue. The benefit of early prevention is considered substantial. However, the prevalence is uncertain and it is therefore not clear the total benefit for society, compared to the offer of dental health care in Norway today. How much resources to direct to this treatment is thereby up to decision makers to consider.

A separate budget impact analysis has not been conducted. This can be explained by the fact that it would be difficult to determine a total impact of the intervention, given that the costs of dental services are partly covered by patients and partly by the Norwegian government. However, the screening intervention will certainly have an impact on the public budget of the dental health service. Periodontitis is already considered a major expense to the public dental health service. In 2019, NOK 219 million was paid in settlements to private dentists, including specialists, regarding rate 501 for treatment of periodontitis. Correspondingly, NOK 151.1 million was paid to dental hygienists (Helfo, 2020c).

6.4.2 Practical considerations

Several different decisions must be made concerning the implementation of screening. However, there are also some practical considerations involved. For instance, as of today, there is no register for periodontal disease, meaning that all individuals in the chosen age group will receive invitation to screening. It is not possible to omit those already diagnosed with periodontitis. Thus, it can potentially lead to individuals already diagnosed with periodontitis, still attending screening and thereby utilizing this service unnecessarily. A potential solution could be to create a registry for periodontitis, similar to the one used for cancer registration.

It should also be noted that introduction of the proposed screening will lead to some structural changes in how the dental care sector currently functions. As organized today, regular examinations and periodontal treatment for the adult population is carried out by dentists working in the private sector. The proposed screening utilizes general, public dentists, and implementation of screening would probably lead to an increased workload for these dentists. It is less likely that screening for periodontitis only using private, periodontal specialists would be considered cost-effective, as these dentists commonly have a higher fee for examinations and treatment than public dentists do.

Risk factors are not taken into account in the input parameters in the model due to limited data available in the literature, e.g. smoking status. There are several diseases and conditions associated with periodontitis, e.g. rheumatoid arthritis, osteoporosis and CVD. Several of the associated conditions are considered common in the elderly population. Treatment of one condition may affect the results of treatment on another comorbid condition (Holmstrup et al., 2017). This demonstrates a potential need for increased collaboration between general practitioners and dentists going forward, to maximize clinical outcomes. Currently, there are no organized collaboration systems between these sectors.

A potential positive consequence of the introduction of screening is the possibility that general dentists will more easily detect early onset signs of periodontitis. Frequently doing examinations for periodontitis will likely increase the awareness of the disease, potentially preventing several cases of periodontitis. In addition, screening can act as an incentive for patients to maintain recommended oral hygiene and consult with a dentist when necessary, since one is periodically reminded of this.

On the other hand, the screening intervention proposed, can in a sense be interpreted as a claim that dentists do not perform their examinations adequately, i.e. what they have been trained to do during their undergraduate and counting education courses. There have never been publicized concerns that large numbers of dentists are negligent when it comes to discovering and treating periodontal disease. Based on this interpretation of the proposed screening intervention, screening will only be an extra cost on society, and potentially yield an unsustainable treatment frequency. There is thus a risk of overtreatment. Further, an external screening would potentially, for some dentists and patients, feel uncomfortable, as the work ethic is being scrutinized, patients will possibly lose trust in their dentist. In addition, it is conceivable that the intervention will result in an overconsumption of services, as more people will take advantage of the offer, given that this is free of charge.

In this thesis, it has been attempted to combine data from different contexts, which may not be appropriate for all inputs of the model. The different studies are also different in scope. For instance, fewer people smoke today than they did at the turn of the century, likely contributing to an improvement in people's dental health. Since this model is largely based on assumptions due to limited research available, this is not expected to affect the results substantially. In addition, as described, the way periodontal disease is classified differs. The classification system from 1999 divided periodontal disease into either gingival disease, chronic or aggressive periodontitis, while the newest available classification uses a single category for gingivitis and different stages of periodontitis according to severity. No relevant studies have used the latter way of classification. Finally, other practical considerations of implementation beyond those discussed are possible.

7. Conclusions

There are disagreements among professionals regarding what will be the appropriate starting age for screening. The incremental cost-effectiveness ratio of the screening intervention for 60 year olds was NOK 5 101 per QATY gained per year, given a health care perspective. The probability of screening to be cost-effective increased at WTP thresholds above NOK 40 000. However, as the WTP threshold is unknown, the decision of cost-effectiveness is uncertain.

According to this thesis, it will be cost saving to introduce screening from the age of 40. For this group, the screening intervention yielded both lower costs and higher effects compared with today’s practice. This clarifies the benefit of early detection and prevention. It is not considered cost-effective to implement screening for 80 year olds. Screening will not be considered preventive, as almost all elderly have some degree of periodontitis.

The VOI analysis identified the effect of screening, the fixed cost of screening, and the cost of screening as parameters of value of conducting more research. In addition, the utility values are in need of additional research.

The treatment frequency of periodontitis has decreased in Norway for the last decades, but it should still be considered a substantial health concern in the adult population. As periodontitis is expensive to treat, it is beneficial to prevent as many cases as possible with preventive measures, e.g. screening.

As there is a politically expressed desire to include dental care services in the National Health Insurance Scheme, it is especially important to increase the knowledge of periodontal disease to ensure that decisions are made on the right basis. Clinical studies in the field of periodontal disease have been stagnant in a Norwegian setting for some time, and it is therefore not possible to conduct a cost-utility analysis without making assumptions on several parameters included in the model. This thesis should highlight the need for further research providing better evidence to inform decision making if screening for periodontitis would be cost-effective.

8. References

Augestad, L. & Rand, K. (2018). QALYs i kommunale helse- og omsorgssektoren. *Notat til Blankholmutvalget.* Oslo, 03.10.2018.

Benigeri, M., Brodeur, J M., Payette, M., Charbonneau, A., & Ismaı¨l, A I. (2000). Community periodontal index of treatment needs and prevalence of periodontal conditions. *Journal of Clinical Periodontology, 27*(5), 308–312. Available from: https://doi.org/10.1034/j.1600-051x.2000.027005308.x

Bergstrom, J. (2014). Smoking rate and periodontal disease prevalence: 40-year trends in Sweden 1970-2010. *Journal of Clinical Periodontology, 41*, 952–957. Available from: https://doi.org/10.1111/jcpe.12293

Braga, M M., Machado, G M., Rocha, E S., Vigano, M E., Pontes, L R A., & Raggio, D P. (2020). How can we associate an economic evaluation with a clinical trial?. *Brazilian Oral Research*, *34*(2), 1-11. Available from: https://doi.org/10.1590/1807-3107bor-2020.vol34.0076

Briggs, A., Claxton, K. & Sculpher, M. (2006). *Decision Modelling for Health Economic Evaluation*. Oxford: Oxford University Press.

Briggs, A H., Weinstein, M C., Fenwick, E A L., Karnon, J., Sculpher, M J., & Paltiel, A. (2012). Model Parameter Estimation and Uncertainty: A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force-6. *Value in Health, 15*(6), 835-842. Available from: https://doi.org/10.1016/j.jval.2012.04.014

Brurberg, K G., Kornør, H., Landmark, B. (2008). *Effekt av røyking på utfallet av periodontittbehandling* (Rapport Nr 29-2008). Oslo: Nasjonalt kunnskapssenter for helsetjenesten. Available from: https://www.fhi.no/globalassets/dokumenterfiler/rapporter/2009-og-eldre/rapport_0829_effekt-av-royking-pa-utfallet-av-periodontittbehandling.pdf

Brækhus, L A. (2018, 11. august). Tannkjøttsykdom rammer 10-15 prosent - dette bør du vite om periodontitt. *Abc nyheter*. Available from: https://www.abcnyheter.no/helse-og-livsstil/helse/2018/08/24/195426576/tannkjottsykdom-rammer-10-15-prosent-dette-bor-du-vite-om-periodontitt [Accessed 19.01.21].

Byford, S., & Raftery, J. (1998). Perspectives in economic evaluation. *BMJ*, *316*, 1529–1530. Available from: https://doi.org/10.1136/bmj.316.7143.1529

Cafasso, J. (2017). Periodontitis. Available from: https://www.healthline.com/health/periodontitis. [Accessed 05.01.2021]

Casanova, L., Hughes, F., & Preshaw, P. (2014). Diabetes and periodontal disease: a two-way relationship. *The British Dental Journal, 217*(8), 433–437. Available from: https://doi.org/10.1038/sj.bdj.2014.907

Coelho, J M F., Miranda, S S., da Cruz, S S.,Trindade, S C., Passos-Soares, J de S., Cerqueira, E de M., … Gomes-Filho, I S. (2020). Is there association between stress and periodontitis?. *Clinical Oral Investigations* 24, 2285–2294. Available from: https://doi.org/10.1007/s00784-019-03083-9

Davis, Garland K. (2019, 18 September). *How to Reverse Periodontitis.* Available from: https://www.garlanddavisdds.com/reverse-periodontitis

Dental Health Services Act. (1984). *LAW-1983-06-03-54 on dental health services.* Available from: https://lovdata.no/dokument/NL/lov/1983-06-03-54

Drummond, M., Sculpher, M., Claxton, K., Stoddard, G.L,. & Torrance, G. (2015). *Methods for the Economic Evaluation of Health Care Programmes.* Oxford: Oxford University Press

Edejer, T T. (2003) *Making choices in health: WHO guide to cost-effectiveness analysis*. Geneva: World Health Organization

Ekornrud, T. & Skjøstad, O. (2017, 8. september) Personar med låg inntekt går sjeldnare til tannlegen. *Statistics Norway.* Available from: https://www.ssb.no/helse/artikler-og-publikasjoner/personar-med-lag-inntekt-gar-sjeldnare-til-tannlegen

Faddy, M J., Cullinan, M P., Palmer, J E., Westerman, B., & Seymour, G J. (2000). Ante-dependence modelling in a longitudinal study of periodontal disease: the effect of age, gender, and smoking status. *Journal of Periodontology, 71*(3), 454–459. Available from: https://doi.org/10.1902/jop.2000.71.3.454

Fardal, Q., Johannesen, A C., Linden, G J. (2004). Tooth loss during maintenance following periodontal treatment in a periodontal practice in Norway. *Journal of Clinical Periodontology*, *31*(7), 550-555. Available from: https://doi.org/10.1111/j.1600-051X.2004.00519.x

Fardal, Ø., O'Neill, C., Gjermo, P., Fardal, E., Sandvik, L., Hansen, B F., & Linden, G J. (2012). The lifetime direct cost of periodontal treatment: a case study from a Norwegian specialist practice. *Journal of Periodontology*, *83*(12), 1455-1462. Available from: https://doi.org/10.1902/jop.2012.110689

Fardal, Ø., & Grytten, J I. (2014). Applying quality assurance in real time to compliant long-term periodontal maintenance patients utilizing cost- effectiveness and cost utility. *Journal of Clinical Periodontology, 41*(6), 604-611. Available from: https://doi.org/10.1111/jcpe.12252

Fardal, Ø., Grytten, J., Martin, J., Ellingsen, S., Fardal, P., Heasman, P., & Linden, G J. (2018). Adding smoking to the Fardal model of cost- effectiveness for the lifetime treatment of periodontal diseases. *Journal of Periodontology*, *89*(11), 1283-1289. Available from: https://doi.org/10.1002/JPER.17-0467

Fardal, Ø., Skau, I., & Grytten, J. (2020a). Familial tendency as a determinant of tooth loss during long-term periodontal therapy. *Journal of Clinical Periodontology, 47*(2), 213-222. Available from: https://doi.org/10.1111/jcpe.13219

Fardal, Ø., Skau, I., Rongen, G., Heasman, P. & Grytten, J. (2020b). Provision of treatment for periodontitis in Norway in 2013 – a national profile. *International Dental Journal, 70*(4), 266-276. Available from: https://doi.org/10.1111/idj.12565

Farooqi, O A., Wehler, C J., Gibson, G., Jurasic, M M., & Jones, J A. (2015). Appropriate Recall Interval for Periodontal Maintenance: A Systematic Review. *The Journal of Evidence Based Dental Practice, 15*(4), 171-181. Available from: https://doi.org/10.1016/j.jebdp.2015.10.001

Fritz, P C. (2013, 01. October). Clinical Attachment Level - How to Calculate and Interpret this Important Measurement. Available from: https://www.oralhealthgroup.com/features/clinical-attachment-level-how-to-calculate-and-interpret-this-important-measurement/. [Accessed 27.01.2021]

Garrison, L P., Pauly, M V., Wilke, R J., Neumann, P J. (2018). An Overview of Value, Perspective, and Decision Context - A Health Economics Approach: An ISPOR Special Task Force Report [2]. *Value in Health, 21*(2), 124-130. Available from: https://doi.org/10.1016/j.jval.2017.12.006

Goodacre, S & McCabe, C. (2002). Introduction to economic evaluation. *Emergency Medicine Journal 2002, 19*(3), 198-201. Available from: http://dx.doi.org/10.1136/emj.19.3.198

Grytten, J., Holst, D. & Skau, I. (2009). Incentives and remuneration systems in dental services. *International Journal of Health Care Finance and Economics*, *9*, 259–278. Available from: https://doi.org/10.1007/s10754-008-9050-2

Haugen, K & Solheim, T. (2019) Tannforhold hos beboere på alders- og sykehjem i Oslo. *The Norwegian Dental Journal, 129*(11), 998-1005. Available from: https://www.tannlegetidende.no/i/2019/11/m-828

Helfo (2020a). Takst 501 - Systematisk behandling av marginal periodontitt. Regelverk og veiledning for bruk av takst 501. Available from: https://www.helfo.no/regelverk-og-takster/takster/takstveiledning-for-tannlege/takst-501-systematisk-behandling-av-marginal-periodontitt [Accessed 02.02.2021]

Helfo (2020b). 6 Periodontitt. Available from: https://www.helfo.no/regelverk-og-takster/overordnet-regelverk/tilstander-som-kan-gi-rett-til-st%C3%B8nad-til-tannbehandling/tilstand-6

Helfo (2020c). Helserefusjon 2019: Statistikk og nøkkeltall for tannområdet. Available from: https://www.helfo.no/om-helfo/analyse-og-kontrollrapporter-fra-helfo/analyse-og-kontrollrapporter/M%C3%A5ltallsrapport_tannomr%C3%A5det.pdf/_/attachment/inline/e714dc59-5c8f-401c-bf1b-e3095b642f36:001741a61bbf335517ee0af370c34d73166f5c26/M%C3%A5ltallsrapport_tannomr%C3%A5det.pdf

Helfo (2021). Who pays your dental bill? Available from: https://www.helsenorge.no/en/payment-for-health-services/who-pays-your-dental-bill/ [Accessed 19.01.2021]

Highfield, J. (2009). Diagnosis and classification of periodontal disease. *Australian Dental Journal*, *54*(1), 11-26. Available from: https://doi.org/10.1111/j.1834-7819.2009.01140.x

Holde, G E., Oscarson, N., Trovik, T A., Tillberg, A. & Jönsson, B. (2017). Periodontitis Prevalence and Severity in Adults: A Cross- Sectional Study in Norwegian Circumpolar Communities. *Journal of Periodontology, 88*(10), 1012-1022. Available from: https://doi.org/10.1902/jop.2017.170164

Holmstrup, P., Damgaard, C., Olsen, I., Klinge, B., Flyvbjerg, A., Nielsen, C. H., & Hansen, P R. (2017). Comorbidity of periodontal disease: two sides of the same coin? An introduction for the clinician. *Journal of Oral Microbiology, 9*(1), 1332710. Available from: https://doi.org/10.1080/20002297.2017.1332710

Holtfreter, B., Albandar, J M., Dietrich, T., Dye, B A., Eaton, K A., Eke, P I., Papapanou, P N., & Kocher, T. (2015). Standards for reporting chronic periodontitis prevalence and severity in epidemiologic studies – Proposed standards from the Joint EU/USA Periodontal Epidemiology Working Group. *Journal of Clinical Periodontology, 42*, 407–412. Available from: https://doi.org/10.1111/jcpe.12392

Hunink, M., Weinstein, M., Wittenberg, E., Drummond, M., Pliskin, J., Wong, J., & Glasziou, P. (2014). *Decision Making in Health and Medicine: Integrating Evidence and Values* (2nd edition). Cambridge: Cambridge University Press.

Klepp, M. (2020). Helfo-regelverket skal følges, det skal ikke styre din behandling mot overbehandling. *The Norwegian Dental Journal*, *130*, 969. Available from: https://www.tannlegetidende.no/i/2020/11/m-1641

Lyshol, H & Biehl, A. (2009). *Tannhelsestatus i Norge - en oppsummering av eksisterende kunnskap* (Nasjonalt folkehelseinstitutt rapport 2009:5). Available from: https://www.fhi.no/globalassets/dokumenterfiler/rapporter/2009-og-eldre/rapport-20095-pdf-.pdf

Maier, H R., & Tolson B A. (2008). Sensitivity and Uncertainty. *Encyclopedia of Ecology,* 3214-3221. Available from: https://doi.org/10.1016/B978-008045405-4.00230-5

Mdala, I., Olsen, I., Haffajee, A D., Socransky, S S., Thoresen, M., & de Blasio, B F. (2014). Comparing clinical attachment level and pocket depth for predicting periodontal disease progression in healthy sites of patients with chronic periodontitis using multi-state Markov models. *Journal of Clinical Periodontology*, *41*(9), 837–845. Available from: https://doi.org/10.1111/jcpe.12278

Mealey, B L. & Ocampo, G L. (2007). Diabetes mellitus and periodontal disease. *Periodontology 2000, 44*(1), 127-153. Available from: https://doi.org/10.1111/j.1600-0757.2006.00193.x

Ministry of Health and Care Services. (2007). Tilgjengelighet, kompetanse og sosial utjevning - *Framtidas tannhelsetjenester* (Meld. St. nr. 35 (2006-2007)). Available from: https://www.regjeringen.no/no/dokumenter/Stmeld-nr-35-2006-2007-/id475114/?ch=1

Ministry of Health and Care Services. (2014). Tannhelsetjenesten. Available from: https://www.regjeringen.no/no/tema/helse-og-omsorg/helse--og-omsorgstjenester-i-kommunene/innsikt/tannhelse/id115300/ [Accessed 04.02.2021].

Mohd-Dom, T. (2013). Quality-adjusted tooth years (QATY) as an outcome measure of periodontal treatment. *BMC Public Health, 14*(1), 10. Available from: https://doi.org/10.1186/1471-2458-14-S1-P10

Mohd-Dom, T., Wan-Puteh, S., Muhd-Nur, A., Ayob, R., Abdul-Manaf, M., Abdul-Muttalib, K., Aljunid, S M. (2014). Cost-Effectiveness of Periodontitis Management in Public Sector Specialist Periodontal Clinics: A Societal Perspective Research in Malaysia. *Value in Health Regional Issues*, *3*, 117-123. Available from. DOI: 10.1016/j.vhri.2014.04.012

Mohd-Dom, T., Ayob, R., Muttalib, K A., Aljunid, S M. (2016) National Economic Burden Associated with Management of Periodontitis in Malaysia. *International Journal of Dentistry, 2016*, Article ID 1891074. Available from: https://doi.org/10.1155/2016/1891074

Nascimento, G G., Leite, F R., Do, L G., Peres, K G., Correa, M B., Demarco, F F., & Peres, M A. (2015). Is weight gain associated with the incidence of periodontitis? A systematic review and meta-analysis. *Journal of Clinical Periodontology*, *42*(6), 495–505. Available from: https://doi.org/10.1111/jcpe.12417

National Institute for Health and Care Excellence (NICE). (2013). *Guide to the methods of technology appraisal 2013*. Available from: https://www.nice.org.uk/process/pmg9/resources/guide-to-the-methods-of-technology-appraisal-2013-pdf-2007975843781

Nazir, M A. (2017). Prevalence of periodontal disease, its association with systemic diseases and prevention. *International Journal of Health Sciences*, *11*(2), 72–80. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5426403/

Newman, T. (2018, 05. January). Causes and treatment of gingivitis. *Medical News Today.* Available from: https://www.medicalnewstoday.com/articles/241721 [Accessed 28.01.2021].

Nomura, Y., Okada, A., Kakuta, E., Gunji, T., Kajiura, S., & Hanada, N. (2016). A new screening method for periodontitis: an alternative to the community periodontal index. *BMC Oral Health, 16*(1), 1-7. Available from: https://doi.org/10.1186/s12903-016-0216-x

Norwegian Directorate of Health. (2017) *Nasjonalt screeningprogram mot tarmkreft - status og anbefalinger.* Report: Norwegian Directorate of Health.

Norwegian Directorate of Health. (2012). *Økonomisk evaluering av helsetiltak -en veileder.* Oslo: Norwegian Directorate of Health.

Norwegian Directorate of Health. (2019) *Helseøkonomiske og samfunnsøkonomiske analyser*. Oslo: Norwegian Directorate of Health (edited 2020, 07. april) Available from: https://www.helsedirektoratet.no/tema/finansiering/helseokonomiske-analyser

Olsen, I. (2001) Periodontitt og systemiske lidelser. *The Norwegian Dental Journal, 2001,*111. Available from: https://www.tannlegetidende.no/i/2001/8/chap05_0108idp562720

Papapanou, P N., Sanz, M., Buduneli, N., Dietrich, T., Feres, M., Fine, D H., ... Tonetti, M S. (2018). Periodontitis: Consensus report of Workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri- Implant Diseases and Conditions. *Journal of Clinical Periodontology, 45*(20), 162-170. Available from: https://doi.org/10.1111/jcpe.12946

Preshaw, P M., & Bissett, S M. (2013). Periodontitis: Oral Complication of Diabetes. *Endocrinology and Metabolism Clinics of North America, 42(*4), 849-867. Available from: https://doi.org/10.1016/j.ecl.2013.05.012.

Ramachandra, S S., Gupta, V V., Mehta, D S., Gundavarapu, K C., & Luigi, N. (2017). Differential Diagnosis between Chronic versus Aggressive Periodontitis and Staging of Aggressive Periodontitis: A Cross-sectional Study. *Contemporary Clinical Dentistry*, *8*(4), 594-603. Available from: https://doi.org/10.4103/ccd.ccd_623_17

Renvert, S., Persson, R E., Persson, G R. (2013). Tooth Loss and Periodontitis in Older Individuals: Results From the Swedish National Study on Aging and Care. *Journal of Periodontology, 84*(8), 1134-1144. Available from: https://doi.org/10.1902/jop.2012.120378

Sanders, G D., Neumann, P J., Basu, A., Brock, D W., Feeny, D., Krahn, M., … Ganiats, T G. (2016). Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses: second panel on cost-effectiveness in health and medicine. *JAMA*, *316*(10), 1093-1103. Available from: https://doi.org/10.1001/jama.2016.12195

Schätzle, M., Faddy, M J., Cullinan, M P., Seymour, G J., Lang, N P., Bürgin, W., Ånerud, Å., Boysen, H. & Löe, H. (2009). The clinical course of chronic periodontitis: V. Predictive factors in periodontal disease. *Journal of Clinical Periodontology, 36*, 365-371. Available from: https://doi.org/10.1111/j.1600-051X.2009.01391.x

Sebuødegård, S., Sagstad, S. & Hofvind, S. (2016). Oppmøte i Mammografiprogrammet. *Journal of the Norwegian Medical Association, 136*(17), 1448-1451. Available from: https://tidsskriftet.no/2016/09/originalartikkel/oppmote-i-mammografiprogrammet

Skjørland, K K., Espelid, I., & Preus, H R. (2020, 20. april) Periodontitt. Available from: https://sml.snl.no/periodontitt. [Accessed 27.01.2021]

Statistics Norway (2021). 05375: Forventet gjenstående levetid etter kjønn og alder 1986-2020. Dataset available from: https://www.ssb.no/statbank/table/05375/

Svalund, J. (2005) Velferdsstatens siste hull? *Statistics Norway*. Available from: https://www.ssb.no/helse/artikler-og-publikasjoner/velferdsstatens-siste-hull

Tanik, A., & Gul, M. (2020). The validity of the Community Periodontal Index of Treatment Needs (CPITN) in Epidemiological Studies of Periodontal Diseases. *International Dental Research, 10*(2), 44-48. Available from: https://doi.org/10.5577/intdentres.2020.vol10.no2.3

Teughels, W., Dhondt, R., Dekeyser, C., & Quirynen, M,. (2014). Treatment of aggressive periodontitis. *Periodontology 2000*, *65*(1),107-33. Available from: https://doi.org/10.1111/prd.12020

Tonetti, M S., Greenwell, H., & Kornman, K S. (2018). Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. *Journal of Clinical Periodontology, 45*(20), 149–161. Available from: https://doi.org/10.1111/jcpe.12945

University of Sheffield. (2021). SAVI - Sheffield Accelerated Value of Information. Available from: http://savi.shef.ac.uk/SAVI/ . [Accessed 23.04.2021]

Wettergreen, J. (2019). Færre røyker hver dag. *Statistics Norway.* Available from: https://www.ssb.no/helse/artikler-og-publikasjoner/faerre-royker-hver-dag

World Health Organization. (2005, 15 March) Periodontal country profiles. Available from: https://www.who.int/oral_health/databases/niigata/en/ [Accessed 28.02.2021]

World Health Organization. (2020, 25 March). Oral Health. Available from: https://www.who.int/news-room/fact-sheets/detail/oral-health. [Accessed 03.02.2021]

9. Appendix

9.1 One-way sensitivity analyses

Cost of screening	Incremental cost	Incremental QATY	ICER
750	361	0.46	783
1 000	1 028	0.46	2 230
1 250	1 695	0.46	3 677
1 500	2 362	0.46	5 124
1 750	3 029	0.46	6 571
2 000	3 697	0.46	8 018
2 250	4 364	0.46	9 465

Table A.1.1: One-way sensitivity analysis of change in ICER according to cost of screening

Cost of surgery	Incremental cost	Incremental QATY	ICER
500	2 447	0.46	5 309
1 000	2 373	0.46	5 147
1 100	2 358	0.46	5 115
1 200	2 343	0.46	5 083
1 300	2 328	0.46	5 050
1 400	2 313	0.46	5 018
1 500	2 299	0.46	4 986
1 600	2 284	0.46	4 954
1 700	2 269	0.46	4 921

Table A.1.2: One-way sensitivity analysis of change in ICER according to cost of surgery

Cost of periodontitis	Incremental cost	Incremental QATY	ICER
2 500	6 846	0.46	14 851
3 500	5 358	0.46	11 622
4 500	3 870	0.46	8 394
5 500	2 381	0.46	5 166
6 500	893	0.46	1 937
7 500	-595	0.46	-1 291
8 500	-2 083	0.46	-4 519
9 500	-3 572	0.46	-7 748

Table A.1.3: One-way sensitivity analysis of change in ICER according to cost of periodontitis

Utility value	Incremental cost	Incremental QATY	ICER
0.90	2 352	0.09	26 442
0.80	2 352	0.24	9 891
0.70	2 352	0.39	6 083
0.60	2 352	0.54	4 392
0.50	2 352	0.68	3 437
0.40	2 352	0.83	2 823
0.30	2 352	0.98	2 395
0.20	2 352	1.13	2 080
0.10	2 352	1.28	1 838

Table A.1.4: One-way sensitivity analysis of change in ICER according to change in utility of periodontitis

RR	Incremental cost	Incremental QATY	ICER
0.90	6 994	0.17	40 874
0.80	3 973	0.36	11 048
0.70	652	0.57	11 48
0.60	-3 005	0.80	-3 768
0.50	-7 036	1.05	-6 687
0.40	-11 485	1.33	-8 608
0.30	-16 402	1.65	-9 955
0.20	-21 839	2.00	-10 943
0.10	-27 857	2.38	-11 690

Table A.1.5: One-way sensitivity analysis of change in ICER according to change in RR

Utility value	Incremental cost	Incremental QATY	ICER
0.95	2 352	0.46	5 101
0.9	2 352	0.38	6 160
0.8	2 352	0.22	10 534
0.7	2 352	0.06	36 329
0.6	2 352	-0.09	-25 077
0.5	2 352	-0.25	-9 321
0.4	2 352	-0.41	-5 725
0.3	2 352	-0.57	-4 131
0.2	2 352	-0.73	-3 231
0.1	2 352	-0.89	-2 653

Table A.1.6: One-way sensitivity analysis of change in ICER according to change in utility of healthy

Utility value	Incremental cost	Incremental QATY	ICER
0.9	2 352	0.45	5 211
0.8	2 352	0.46	5 101
0.7	2 352	0.47	4 996
0.6	2 352	0.48	4 896
0.5	2 352	0.49	4 799
0.4	2 352	0.50	4 706
0.3	2 352	0.51	4 616
0.2	2 352	0.52	4 530
0.1	2 352	0.53	4 447

Table A.1.7: One-way sensitivity analysis of change in ICER according to change in utility of gingivitis

Discount rate costs	Incremental cost	Incremental QATY	ICER
0.05	2 510	0.46	5 443
0.04	2 352	0.46	5 101
0.03	2 146	0.46	4 654
0.02	1 878	0.46	4 073
0.01	1 533	0.46	3 324

Table A.1.8: One-way sensitivity analysis of change in ICER according to change in discount rate costs

Discount rate outcomes	Incremental cost	Incremental QATY	ICER
0.05	2 352	0.39	6 003
0.04	2 352	0.46	5 101
0.03	2 352	0.55	4 288
0.02	2 352	0.66	3 564
0.01	2 352	0.80	2 926

Table A.1.9: One-way sensitivity analysis of change in ICER according to change in discount rate outcomes

Cost of replacement	Incremental cost	Incremental QATY	ICER
13 000	2 643	0.46	5 734
15 000	2 560	0.46	5 553
17 000	2 477	0.46	5 372
19 000	2 393	0.46	5 192
21 000	2 310	0.46	5 011
23 000	2 227	0.46	4 830
25 000	2 143	0.46	4 649
27 000	2 060	0.46	4 468

Table A.1.10: One-way sensitivity analysis of change in ICER according to cost of replacement

Fixed cost of screening	Incremental cost	Incremental QATY	ICER
650	-827	0.46	-1 794
1 000	802	0.46	1 739
1 350	2 431	0.46	5 273
1 700	4 060	0.46	8 806
2 000	5 456	0.46	11 835

Table A.1.11: One-way sensitivity analysis of change in ICER according to change in fixed cost of screening

Cost of Healthy	Incremental cost	Incremental QATY	ICER
500	1 575	0.46	3 416
750	1 971	0.46	4 276
1 000	2 368	0.46	5 136
1 250	2 764	0.46	5 995
1 500	3 160	0.46	6 855

Table A.1.12: One-way sensitivity analysis of change in ICER according to cost of healthy

Cost of gingivitis	Incremental cost	Incremental QATY	ICER
1 000	2 450	0.46	5 313
1 500	2 401	0.46	5 208
2 000	2 353	0.46	5 103
2 500	2 304	0.46	4 998
3 000	2 256	0.46	4 893

Table A.1.13: One-way sensitivity analysis of change in ICER according to cost of gingivitis

9.2 Additional two-way sensitivity analyses

		Cost of screening						
		750	**1 000**	**1 250**	**1 500**	**1 750**	**2 000**	**2 250**
Cost of periodontitis	**2 500**	**10 533**	**11 980**	**13 427**	**14 874**	**16 321**	**17 768**	**19 215**
	3 500	**7 304**	**8 752**	**10 199**	**11 646**	**13 093**	**14 540**	**15 987**
	4 500	**4 076**	**5 523**	**6 970**	**8 417**	**9 864**	**11 311**	**12 758**
	5 500	**848**	**2 295**	**3 742**	**5 189**	**6 636**	**8 083**	**9 530**
	6 500	-2 381	-933	**514**	**1 961**	**3 408**	**4 855**	**6 302**
	7 500	-5 609	-4 162	-2 715	-1 268	**179**	**1 626**	**3 073**
	8 500	-8 837	-7 390	-5 943	-4 496	-3 049	-1 602	-155
	9 000	-10 451	-9 004	-7 557	-6 110	-4 663	-3 216	-1 769
	9 500	-12 066	-10 618	-9 171	-7 724	-6 277	-4 830	-3 383

Table A.2.1: Two-way sensitivity analysis on cost of periodontitis and cost of screening

		Relative treatment effect of screening								
		0.9	**0.8**	**0.7**	**0.6**	**0.5**	**0.4**	**0.3**	**0.2**	**0.1**
Cost of periodontitis	**2 500**	**50 669**	**20 813**	**10 881**	**5 932**	**2 976**	**1 017**	-371	-1 402	-2 194
	3 500	**47 426**	**17 579**	**7 658**	**2 720**	-224	-2 170	-3 544	-4 561	-5 339
	4 500	**44 182**	**14 346**	**4 435**	-492	-3 424	-5 357	-6 718	-7 720	-8 483
	5 500	**40 939**	**11 112**	**1 212**	-3 703	-6 623	-8 544	-9 892	-10 880	-11 627
	6 500	**37 695**	**7 879**	-2 011	-6 915	-9 823	-11 731	-13 065	-14 039	-14 771
	7 500	**34 451**	**4 645**	-5 233	-10 127	-13 023	-14 918	-16 239	-17 198	-17 915
	8 500	**31 208**	**1 411**	-8 456	-13 338	-16 223	-18 105	-19 412	-20 358	-21 060
	9 000	**29 586**	-205	-10 068	-14 944	-17 822	-19 699	-20 999	-21 937	-22 632
	9 500	**27 964**	-1 822	-11 679	-16 550	-19 422	-21 292	-22 586	-23 517	-24 204

Table A.2.2: Two-way sensitivity analysis on cost of periodontitis and RR of screening

		Fixed cost of screening						
		750	**1 000**	**1 250**	**1 500**	**1 750**	**2 000**	**2 250**
Cost of screening	**750**	-5 103	-2 579	-55	**2 469**	**4 993**	**7 517**	**10 041**
	1 000	-3 656	-1 132	**1 392**	**3 916**	**6 440**	**8 964**	**11 488**
	1 250	-2 209	**315**	**2 839**	**5 363**	**7 887**	**10 411**	**12 935**
	1 500	-761	**1 762**	**4 286**	**6 810**	**9 334**	**11 858**	**14 382**
	1 750	**686**	**3 209**	**5 733**	**8 257**	**10 781**	**13 305**	**15 829**
	2 000	**2 133**	**4 656**	**7 180**	**9 704**	**12 228**	**14 752**	**17 276**
	2 250	**3 580**	**6 104**	**8 627**	**11 151**	**13 675**	**16 199**	**18 723**
	2 500	**5 027**	**7 551**	**10 074**	**12 598**	**15 122**	**17 646**	**20 170**

Table A.2.3: Two-way sensitivity analysis on fixed cost of screening and variable cost of screening

9.3 Cost-effectiveness acceptability frontier

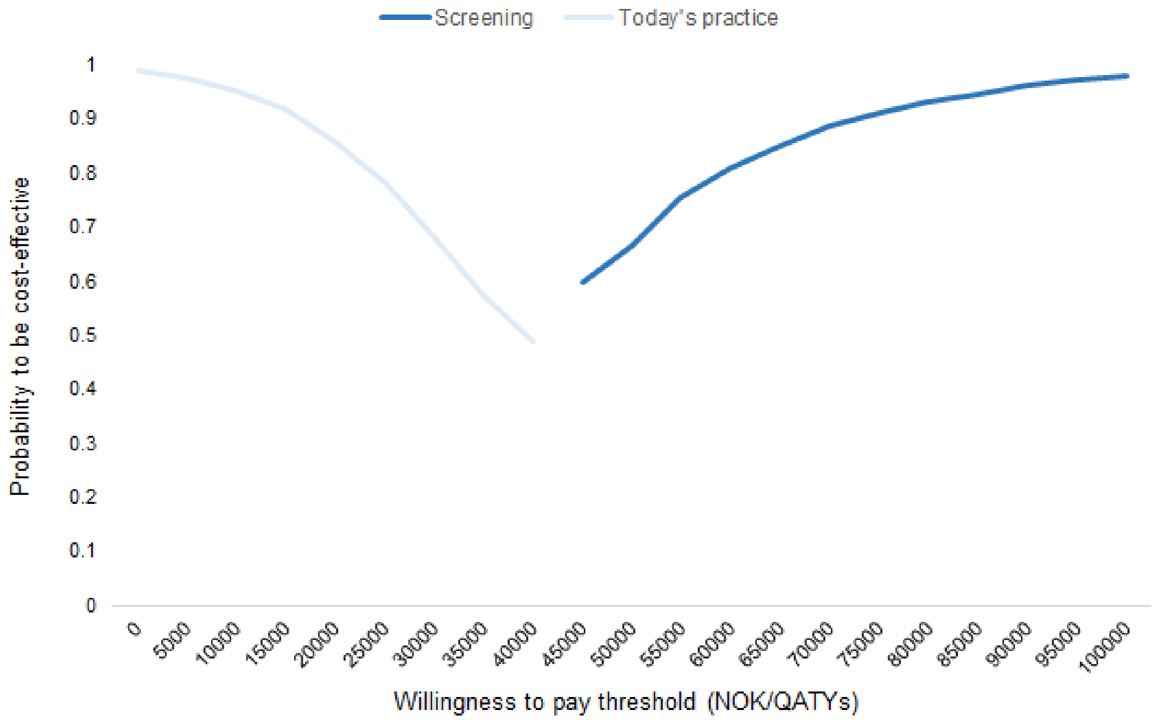

Figure A.3.1: Cost-effectiveness acceptability frontier for main analysis of 60 year olds.

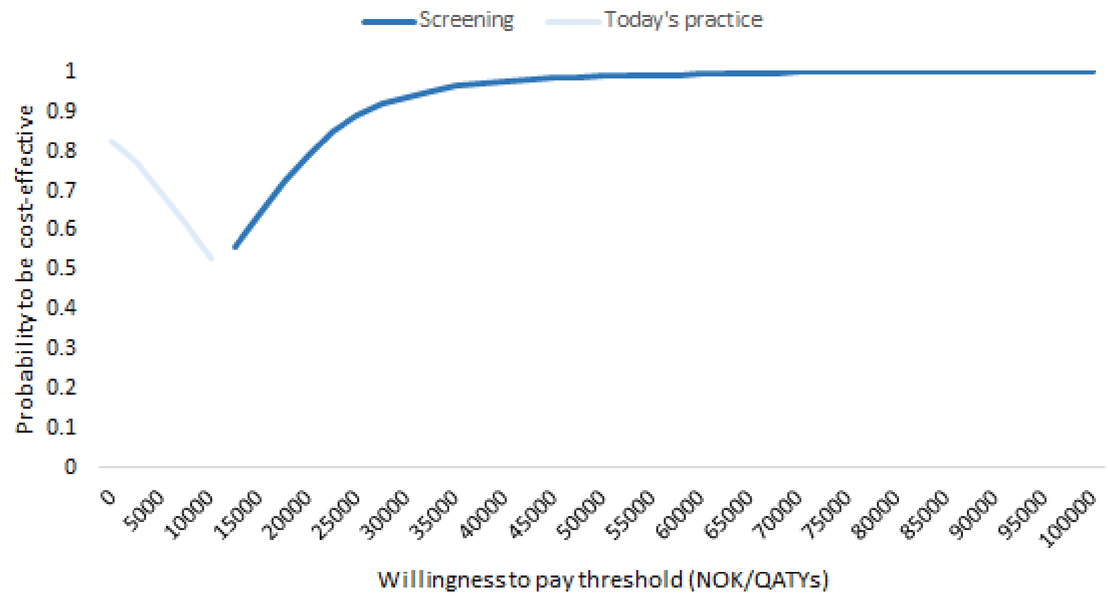

Figure A.3.2: Cost-effectiveness acceptability frontier for sub-analysis of 40 year olds.

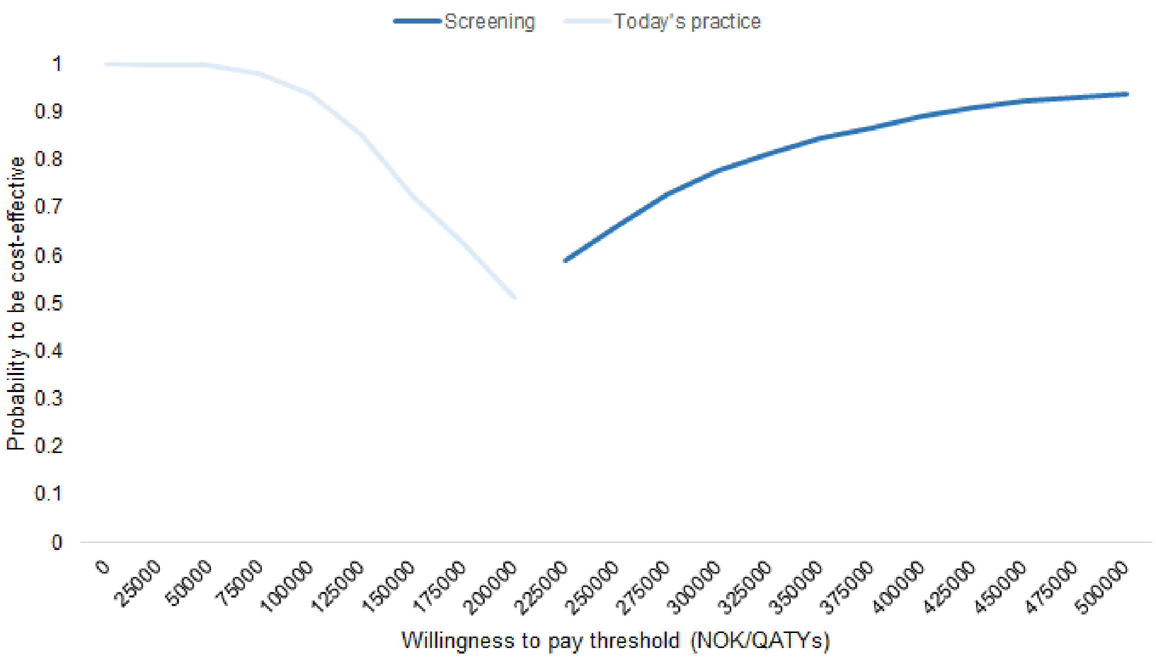

Figure A.3.3: Cost-effectiveness acceptability frontier for sub-analysis of 80 year olds.