UiT
THE ARCTIC
UNIVERSITY
OF NORWAY

Faculty of Health Sciences

The "deep caries" challenge

Prevalence and management of deep carious lesions in Northern Norway

—

Lina Stangvaltaite
A dissertation for the degree of Philosophiae Doctor – October 2015

This thesis is dedicated to the friend of my life, Mathieu, and my other two little fellows, who always share their good energy with me.

"When meditating over a disease, I never think of finding a remedy for it, but, instead, a means of preventing it."

Louis Pasteur, French scientist (1822-1895)

AKNOWLEDGEMENTS

I would like to express my gratitude and appreciation to:

- ❖ My supervisor, Professor Harald M. Eriksen, for introducing me to the scientific world.

- ❖ My supervisor, Professor Eero Kerosuo, for sharing his knowledge and expertise with me during those long, invaluable hours spent discussing my drafts. It was always very fun and extremely useful.

- ❖ My main supervisor, Dr Rita Kundzina, for her generosity and for challenging me.

- ❖ My co-author, Dr Napat Limchaichana Bolstad, for her "sharp eye".

- ❖ The Department leader, Professor Claes-Göran Crossner, for his supportive attitude towards my future.

- ❖ Guri, Inger Anna, Kirsten, Kirsti, Laila and Vibeke, for facilitating all administration-related issues.

- ❖ My senior colleague, Professor Tordis Trovik, for helping to find a light at the end of the tunnel.

- ❖ My senior colleague, Professor Åge Wifstad, for answering my philosophical inquiries.

- ❖ My senior colleague, Professor Hans-Peter Müller, for statistical advice.

- ❖ My senior colleague, Dr Christer Ullbro, for his time and valuable comments.

- ❖ My senior colleague, Professor Raafat El-Gewely, for discussions over a cup of coffee.

- ❖ My senior colleague, Dr Tormod Brenn, for his positive attitude.

- ❖ My senior colleagues, Jorun, Kirsti, and Randi, for trusting me.

- ❖ My research group and its leader, Professor Jan Berghdal, for offering me opportunities and for imparting their knowledge.

- ❖ All the other senior colleagues at the department for creating a cozy and inspiring scientific environment.

- ❖ Professional Standards Editing and Trudy Perdrix-Thoma for great work improving my thesis.

- ❖ Laura and Vibeke, for keeping me in shape.

CONTENTS

LIST OF ABBREVIATIONS

CH, calcium hydroxide

CI, confidence interval

DCL-CC, deep carious lesions and other consequences of caries

DMFT, decayed, missing and filled teeth

DPC, direct pulp capping

GDPs, general dental practitioners

IPC, indirect pulp capping

MTA, mineral trioxide aggregate

OR, odds ratio

PRR, prevalence rate ratio

PDHS, public dental health service

PP, partial pulpotomy

RCT, randomized clinical trial

SWE, stepwise excavation

TCE, total caries excavation

VPT, vital pulp therapy

LIST OF ORIGINAL ARTICLES

This thesis consists of three papers, referred to in the text by the corresponding roman numerals.

I. **Deep carious lesions and other consequences of caries among 18-year-olds at Public Dental Health Service in Northern Norway: a cross-sectional age cohort study**

Stangvaltaite L, Kundzina R, Bolstad NL, Eriksen HM, Kerosuo E.

Acta Odontologica Scandinavica, 2014 [Epub ahead of print print].

II. **Treatment preferences of deep carious lesions in mature teeth: questionnaire study among dentists in Northern Norway**

Stangvaltaite L, Kundzina R, Eriksen HM, Kerosuo E.

Acta Odontologica Scandinavica, 2013; 71: 1532–1537.

Capping carious exposures in adults: a RCT comparing calcium hydroxide and MTA

Kundzina R, Stangvaltaite L, Eriksen HM, Kerosuo E.

In manuscript.

1. ABSTRACT

The overall aim of this doctoral thesis was to increase the understanding and knowledge of the prevalence and management of deep carious lesions. The prevalence of dental caries in Norway was among the highest in the world in the middle of 20th century. Though it has significantly declined, there are indications that the prevalence of caries in Northern Norway is higher than in the rest of the country. A higher prevalence of caries might lead to a higher prevalence of deep carious lesions. *Study I* focused on the prevalence of deep carious lesions and other consequences of caries (DCL-CC) among 18-year-olds enrolled in the Public Dental Health Service in Northern Norway. There were 488 (26%) subjects having at least one molar with DCL-CC. The mean decayed, missing, and filled teeth (DMFT) (SD) score among these 488 subjects was 9.1 (4.6), twice as high as among subjects without DCL-CC (4.5, SD 4.0). The most prevalent modality among untreated deep carious lesions, deep restorations, root canal obturated molars, and molars extracted due to caries were deep restorations, which were observed among 21.5% (n=404) of the age cohort. Root canal obturated molars, molars extracted due to caries, and untreated deep carious lesions were prevalent in 5.1%, 3.6% and 1.6% of this age cohort, respectively. The high prevalence of DCL-CC in Northern Norway is of concern and presents a challenge for dentists, as no treatment guidelines exist for deep carious lesions. *Study II* was a questionnaire study that investigated the preferred treatment methods of general dental practitioners in Northern Norway for deep carious lesions and carious exposures in mature permanent teeth. *Study II* underlined the lack of uniformity in preferred treatment methods among the respondents, and the inconsistency of these methods with those suggested in the current literature. For example, in the absence of symptoms, total caries excavation was favored by a majority of respondents (49%), while in presence of symptoms (indicating reversible pulpitis at most), pulpectomy followed by endodontic treatment was the preferred treatment method for 39% of respondents. Direct pulp capping (DPC), mainly with

calcium hydroxide (CH), was the most preferred treatment method (51%) for carious exposures in the absence of symptoms, although it is still a controversial treatment method for adults. In *Study III*, a promising capping material, mineral trioxide aggregate (MTA), was tested against the gold standard material CH for DPC on carious exposures in adults. After 2-3 years of follow-up, the estimated cumulative survival rate for molars capped with MTA was statistically significantly higher (80%) then for molars capped with CH (46%) (p=0.018). The study is still ongoing, but there are indications that it may provide evidence that will change the established recommendations for the treatment of carious exposures in adults.

2. INTRODUCTION

2.1. Definition of deep carious lesion

Dental caries is one of the most important global oral health burdens and is the most common childhood disease worldwide. It is also the most prevalent oral disease in several Asian and Latin American countries and has a significant impact on quality of life and public health (Petersen, 2003; Beaglehole et al., 2009). Caries is a progressive disease that causes demineralization and destruction of the hard tissues of the teeth. It starts in the enamel as a white spot lesion. If it is not managed, cavitation will develop and will progress into the dentine. Deep carious lesion is a clinical diagnosis that is given when the carious process has penetrated deep into the dentine with possible pulpal exposure (Nygaard-Østby, 1951). Deep carious lesions cause pulpal inflammation (i.e., pulpitis); if not managed, they may result in pulp necrosis and involvement of the periradicular tissues, with possible pain requiring endodontic treatment or extraction (Torneck, 1974; Langeland, 1987).

Deep carious lesions can be detected clinically and/or radiographically. Clinically, according to the contemporary International Caries Detection and Assessment System, (ICDAS) the most severe carious lesion is called "extensive" and is indicated by code 6 (on a scale from 1 to 6) (Pitts, 2004). An extensive carious lesion is both deep and wide, with visible dentine on the cavity walls and at the base; the carious process histologically involves at least half of the tooth surface or may reach the pulp (Ismail et al., 2007). The carious lesion is classified as "active" when it has a yellowish color and a soft, moist consistency. A carious lesion is classified as "inactive" (arrested) when it is heavily pigmented, hard, leathery, and dry (Miller and Massler, 1962; Sarnat and Massler, 1965). Carious dentine consists of two layers: the outer layer, which has been infected by bacteria, has disintegrated, and is not able to remineralize due to the destruction of collagen, and the inner layer, which, although affected by

acids from bacteria (but not by bacteria itself) is able to remineralize, as the collagen texture is still intact (Fusayama, 1979; Fusayama and Terachima, 1972).

Radiographically, deep carious lesions are defined as those close to, but not into the pulp (King et al., 1965). There is no unanimous agreement about the depth that qualifies "a deep carious lesion". Instead, a carious lesion is considered deep when pulpal exposure is anticipated during total caries excavation (Fitzgerald and Heys, 1991; Bjørndal et al., 1997). However, this has been shown to be subjective measurement, as radiographic depth might vary from half into the dentine to reaching the pulp (Bjørndal and Thylstrup, 1998). Radiographically, carious lesions penetrating halfway or more into the dentine (Maltz et al., 2013), into the inner third of the dentine (Ekstrand et al., 1997; Maltz et al., 2011), or into the inner fourth of the dentine have also been assessed as deep (Massler and Pawlak, 1977; Bjørndal, 2010).

2.2. Prevalence of caries in Norway

The prevalence of caries has declined in a majority of industrialized countries during the last decades (Marthaler, 2004). This marked improvement has been extensively documented, particularly among children and adolescents (Marthaler et al., 1996; Petersson and Bratthall, 1996). The prevalence of caries in Nordic countries was among the highest in the world in the 1970s and 1980s, when the DMFT score among 18-year-olds in Norway was 18.4 compared to 4.6 in Hong Kong and the USA and 6.3 in Malaysia (FDI et WHO, 1985). During recent years, the DMFT score among 12-year-olds and 18-year-olds in Norway has declined significantly; in 2011 these scores were 1.1 and 4.3, respectively (von der Fehr, 1982; Haugejorden, 1994; Birkeland et al., 2002; Statistics Norway, 2012)(Fig. 1).

All children in Norway receive free, systematic dental care within the framework of the Norwegian Public Dental Health Service (PDHS) until 18 years of age. Despite this fact, not all children benefit equally from the PDHS. In 1991, 92% of 12-year-olds received treatment through the PDHS, but only 81% of 18-year-olds attended (Norwegian Board of Health, 1992).

The mean individual frequency of cancelled and missed dental appointments among 18-year-olds in 1996 was 4.8% and 11.8%, respectively, and these individuals had a statistically significantly higher mean DMFT score than their peers who did attend their appointments (Skaret et al., 1998).
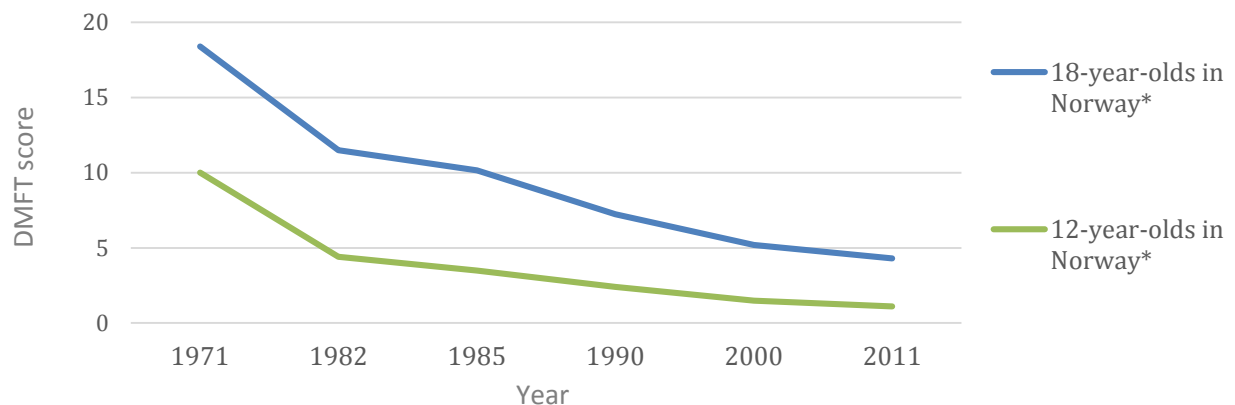
Figure 1. DMFT scores among 12-year-olds and 18-year-olds in Norway, 1971-2011.

*Data for 1971 and 1982 retrieved from FDI et WHO (1985); data for 1985-2011 retrieved from Statistics Norway, 2015.

A similar prevalence of caries was observed in Northern Norway compared to the rest of the country in the late 1970s, but the prevalence of untreated carious lesions was higher in Northern Norway (Helöe et al., 1980). A study performed 2 decades ago reported a mean number of untreated carious lesions reaching the inner half of the dentine in proximal surfaces of 0.11 and 0.02 in Northern and Southern Norway, respectively (Wang and Riordan, 1995). In Northern Norway about one in every five 18-year-olds have a DMFT score higher than 9, which is twice as high as that in Southern Norway (Statistics Norway, 2012). High DMFT score and untreated carious lesions are the main risk factors for deep carious lesions and pulpal involvement, which result in deep restorations, root canal obturations, and extractions (Benzian

et al., 2011; Siqueira Jr., 2012). In 1966, the mean number of permanent teeth extracted due to caries per 100 patients among 6-17-year-olds in Northern Norway was 12 compared to 3 in Southern Norway (von der Fehr and Haugejorden, 1997); however recent data regarding the prevalence of deep carious lesions and other consequences of caries, such as deep restorations, root canal obturations, and extractions, among 18-year-olds in Northern Norway is not available.

2.3. Pulpal status in relation to deep carious lesions

Pulpal status in deep carious lesions varies from almost normal to severe, acute, or chronic pulpitis terminating in necrosis (Massler, 1967; Massler and Pawlak, 1977). The degree of inflammation in the pulp increases with the depth of the carious lesion (Massler and Pawlak, 1977). When a carious lesion approaches within 0.5mm of the pulpal wall of dentine, the amount of pulpal pathosis begins to increase, when the carious process reaches the tertiary dentine, there are irreversible changes that occur in the pulp, such as abscess formation, and a large amount of granulation tissue can be detected (Reeves and Stanley, 1966; Murray et al., 2003). Considerable pulp inflammation has been observed with 0.3 mm of residual dentine, and bacteria in the pulp has been detected with a residual dentine thickness of 0.2 mm or less (Shovelton, 1968). Bacterial invasion in the pulp, acute inflammation with abscess formation, and pulpal necrosis was observed after natural carious exposure (Seltzer et al., 1963a; b; Massler and Pawlak, 1977; Baume and Holz, 1981).

The degree of pulpal inflammation has been shown to depend on the activity of the deep carious lesion. In arrested deep carious lesions, the pulpal status tends to be almost normal, showing sclerosis and repair. In active deep carious lesions, more severe inflammatory process is seen (Massler, 1967). However, active and arrested processes can coexist (Kidd, 2004). The healing potential of the pulp depends on the degree of inflammation and the depth and activity of deep carious lesions might be one of the most important determinants (Bjørndal et al., 2014).

The major challenge in a clinical context is to determine whether pulpitis is reversible or irreversible. Scientific evidence is insufficient to assess the accuracy of the correlation between clinical signs and symptoms of pain and the degree of pulpal inflammation (Seltzer et al., 1963a; b; Reeves and Stanley, 1966; Mejàre et al., 2012). A recent study based on different clinical and histological criteria found a 96.6% correlation between the clinical and histological signs associated with reversible pulpitis and an 84.4% correlation with irreversible pulpitis The authors concluded that in the absence of natural carious exposure, pulpitis is usually reversible (Ricucci et al., 2014b). There is no non-invasive tool available for assessing the degree of pulpal inflammation.

Reversible pulpitis is usually diagnosed in teeth with deep carious lesions that are asymptomatic or have only short-term sharp pain upon thermal or chemical stimulation (Torabinejad and Shabahang, 2009). Irreversible pulpitis, if not asymptomatic, can present with lingering or spontaneous pain (Levin et al., 2009). In irreversible pulpitis the pulp is vital but severely inflamed, with some possible necrosis, which makes healing an unlikely outcome (Levin et al., 2009). Symptoms of pulpitis can be very misleading, as 40%-60% of both reversible and irreversible cases may be asymptomatic (Hasler and Mitchell, 1970; Michaelson and Holland, 2002). "Painless pulpitis" is diagnosed more often among older patients (Michaelson and Holland, 2002). Necrosis of the pulp is diagnosed when vital signs and symptoms are lost (Levin et al., 2009).

2.4. Treatment options for deep carious lesions

There are three treatment options for deep carious lesions with no pain or with mild symptoms that suggest reversible pulpitis at most: i) total caries excavation (TCE); ii) stepwise excavation (SWE); and iii) indirect pulp capping (IPC) (Fig. 2, Table 1). TCE is a procedure during which all infected and affected carious dentine is removed (cited in Jordan and Suzuki, 1971). A procedure is called SWE when a layer of carious dentine is left on the pulpal floor and the

carious lesion is later re-entered in order to perform TCE (Bodecker, 1938; Bjørndal et al., 1997). IPC is a procedure when partial carious tissue excavation and permanent cavity restoration is performed in the same visit (Eidelman et al., 1965; Fitzgerald and Heys, 1991; Maltz et al., 2011; Maltz et al., 2012a).
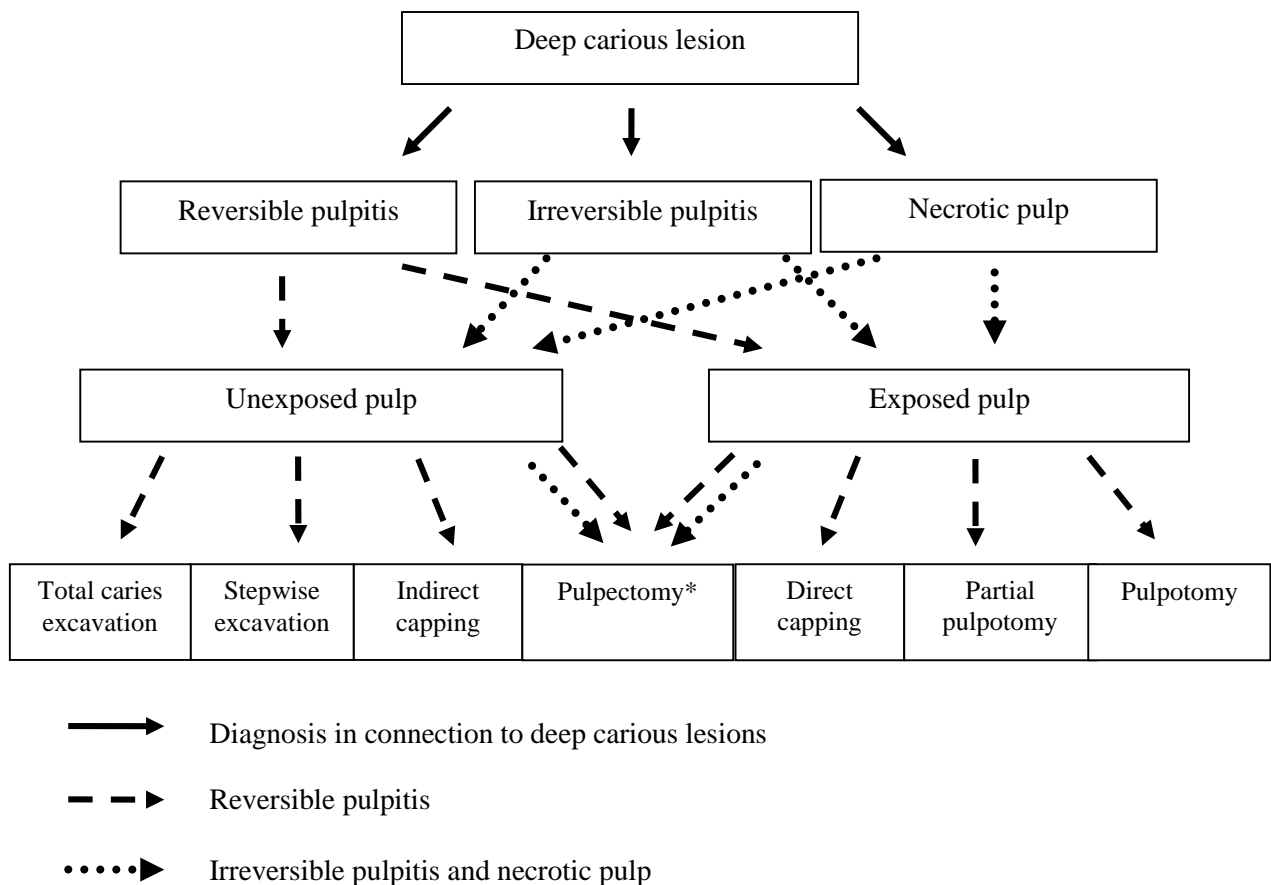
Figure 2. Treatment options for deep carious lesions related to diagnosis and absence/presence of pulpal exposure.

*Pulpectomy in case of reversible and irreversible pulpitis; root canal treatment in case of necrotic pulp.

Total caries excavation

In the early 20th century, G.V. Black suggested the use of TCE (cited in Jordan and Suzuki, 1971). Advocates of TCE argued that it was necessary in order to determine "whether sufficient secondary dentine has been formed to protect the pulp or whether the carious process has

Table 1. Overview of studies on the treatment of deep carious lesions in permanent teeth.

AUTHOR	DESIGN	NUMBER OF TEETH[i], AGE OF SUBJECTS	TREATMENT[ii], MATERIAL(S)	CONTROL, MATERIAL(S)	DEPTH OF LESION, PULPAL STATUS	FOLLOW-UP	MAIN OUTCOMES
Studies investigating SWE and SWE versus TCE							
Jordan & Suzuki, 1971	Pro-spective	n=243 8-37 years	SWE Re-entry 10-12 weeks, CH (Dycal), CH and cresatin, ZOE[iii]	-	Pulpal exposure expected[iv], Reversible pulpitis at most, hypersensitivity and mild pain included	-	Success rate (vital pulp, radiographic and clinic presence of remineralization, absence of exposure): 98% Radiographic signs of remineralization between 10-16 weeks (mean 12)
Leksell et al., 1996	RCT	n=57 treatment n=70 control 6-16 years (mean 10.2)	SWE Re-entry after 8-24 weeks, CH (Calasept)	TCE, CH (Calasept)	Pulpal exposure expected[iv],	1-11 years (mean 3.6)	Pulp exposure: SWE 17.5%, TCE 40% Success rate (normal clinical and radiographic conditions): SWE 82%, TCE 60%
Bjørndal et al., 1997	Pro-spective	n=31, Unknown	SWE Re-entry after 6-12 months, CH containing base material	-	Pulpal exposure expected[iv], 18 lesions >1/3, 13 ≤1/3 into dentine; Reversible pulpitis at most	6-12 months	No exposures Dentine harder, darker, dryer at re-entry, reduction in colony forming units
Bjørndal & Thylstrup, 1998	Pro-spective, multi center	n=94, 11-65 years (median 24)	SWE Re-entry after 2-19 months , CH containing base material	-	1 lesion <1/2, other ≥1/2 into dentine, Reversible pulpitis at most	1 year	Five exposures Dentine harder and darker at re-entry Success rate (vital pulp, absence of subjective symptoms and periapical lesion): 93%
Bjørndal & Larsen, 2000	Pro-spective	n=9 Unknown	SWE Re-entry after 4-6 months, CH containing base material	-	1 lesion <2/3, other ≥2/3 into dentine, Reversible pulpitis at most	4-6 months	No exposures Dentine darker, dryer at re-entry, reduction in colony forming units, dominated not cariogenic flora

Bjørndal et al., 2010	RCT multi-center	n=143 treatment n=149 control ≥ 18 years	SWE Re-entry after 8-12 weeks CH (Dycal)	TCE, CH	≥3/4 into dentine with well-defined radiodense zone, Reversible pulpitis at most, mild-moderate pain included	1 year	Pulp exposure: SWE 17.5%; TCE 28.9% Success rate (unexposed vital pulp and absence of periapical lesion): SWE 74.1%; TCE 62.4%
Corralo & Maltz, 2013	RCT	n=19 CH n=19 GIC n=19 wax, 11-35 years (mean and median 18)	SWE, CH (Dycal), GIC (Vitromolar)	SWE, wax	≥2/3 into dentine, Reversible pulpitis at most	3-4 months	100% vital pulps and absence of periapical lesions On re-entry dentine harder, less cariogenic bacteria, no sig. difference between materials

Studies investigating IPC, IPC versus TCE and IPC versus SWE

Fitzgerald & Heys 1991	Prospective Random selection of material	n=24 IPC CH (Life) n=26 IPC CH (Dycal) n=20 TCE CH (Life) n=23 TCE CH (Dycal) n=20 TCE ZOE[iii], 20-60 years (mean 27)	IPC, CH (Dycal, Life)	TCE, CH (Dycal, Life), ZOE[iii]	Pulpal exposure expected[iv] for IPC and pulpal exposure not expected for TCE, Reversible pulpitis at most	12 months	No sig. difference in symptoms between materials and treatments Sig. decrease in symptoms from pretreatment to six months and from six months to one year in IPC
Maltz et al., 2002	Prospective	n=32, 12-23 years	IPC, CH (Dycal)	-	Pulpal exposure expected[iv], Reversible pulpitis at most	6-7 months	1 exposure during provisional sealing removal, 1 pulpal necrosis, 31 teeth did not present clinical symptoms On re-entry 100% of lesions dry, 80% hard, 17% leathery, 3% soft, reduction in colony forming units
Gruythuysen et al., 2010	Retrospective	Permanent teeth n=34, ≤ 18 years	IPC, Resin-modified glass ionomer	-	Lesion or restoration >2/3 into dentine, pulp exposure expected[iv], Reversible pulpitis at most	3 years	Survival rate (normal clinical and radiographic conditions): 93%
Orhan et al., 2010	RCT	Permanent teeth: n= 19 IPC n=17 SWE n=24 TCE,	IPC, CH (Dycal); SWE	TCE	Pulpal exposure expected[iv], Reversible pulpitis at most	1 year	Pulp exposure for permanent teeth: IPC 5%, SWE 6%, TCE 25% Success rate for permanent teeth (vital not exposed pulp, absence of

		<15 years	Re-entry after 3 months, CH (Dycal)				pain, periapical lesion, sensitivity to percussion and palpation, mobility, fistula and edema): IPC 95%, SWE 94%, TCE 75%
Maltz et al., 2011	Pro-spective	n=31, 12-23 years	IPC, CH (Dycal)	-	≥2/3 into dentine, pulpal exposure expected[iv], Reversible pulpitis at most	1.5 years 3 years 5 years 10 years	Success rates (vital pulp, absence of periapical lesion and sensitivity to percussion): 1.5 years 97%, 3 years 90%, 5 years 82%, 10 years 63%
Maltz et al., 2012	Pro-spective	n=60 TCE n=30 IPC, 12-50 years	IPC, CH (Dycal)	TCE	>2/3 into dentine, pulpal exposure expected[iv], Reversible pulpitis at most	6-7 months for IPC	Reduction in colony forming units after IPC-sealed (after 6-7 months) compared to dentine after TCE (directly)
Maltz et al., 2012	RCT multi-center	n=112 IPC n=101 SWE, 6-53 years (median 14, mean 17)	IPC, CH (Dycal)	SWE Re-entry after median 90 days, CH (Dycal)	≥1/2 into dentine, Reversible pulpitis at most	3 years	2 exposures in SWE group Survival rate (vital not exposed pulp, absence of spontaneous pain, periapical lesion and sensitivity to percussion): IPC 91%, SWE (completed and uncompleted) 69%, SWE completed 88%, SWE uncompleted 13%

---

[i] Analyzed.
[ii] In case of SWE, the interval before re-entry is indicated.
[iii] Zinc oxide eugenol.
[iv] In case of total caries excavation.

penetrated into the pulp" and to establish an appropriate treatment plan (Berk, 1957). The second argument was that TCE was crucial in order to determine the exact outline of the cavity and to provide a well-mineralized dentine base that would ensure a tight seal, as well as the longevity of the restoration (Kroncke, 1970). A Cochrane review found insufficient evidence to conclude whether restorations failed less often after TCE compared with IPC, but data were available for the primary dentition only (Ricketts et al., 2013). The third argument for TCE was that it prevents further cariogenic activity (Kroncke, 1970). However, it has been demonstrated that bacteria still persist in deep carious lesions treated by TCE (Crone, 1968; Shovelton, 1968; Lager et al., 2003). It has also been shown that remaining dentine was more infected after TCE than after IPC covered with a calcium hydroxide (CH) base material and sealed for 6-7 months (Maltz et al., 2012b) (Table 1).

A Cochrane review showed a 49% lower risk of pulpal exposure during SWE compared to TCE for permanent teeth and a 69% lower risk of pulpal exposure in primary and permanent teeth during IPC compared to TCE, but observed no evidence of a differences in the signs and symptoms of pulpal disease (Ricketts et al., 2013). Another systematic review and meta-analysis investigating primary and permanent teeth showed a 69% decreased risk of pulpal exposures and a 42% reduction in pulpal symptoms in teeth treated with SWE and IPC combined compared to teeth treated with TCE, but found a similar risk of restoration failures (Schwendicke et al., 2013a). A randomized clinical trial (RCT) demonstrated a significantly lower 1-year follow-up success rate of TCE (62%) compared to SWE (74%) in adults (Bjørndal et al., 2010) (Table 1)

Stepwise excavation

In the 18th century, Fauchard recommended partial caries excavation in order to avoid pulpal exposure, followed by Tomes in the 19th century (cited in Jordan and Suzuki, 1971). This treatment was based on the theory that a zone of affected dentine laying between the outer

infected layer and the pulp would be able to remineralize (Fusayama and Terachima, 1972; Miyauchi et al., 1978). Fuchsin was suggested as a caries detector dye to discriminate between the two layers (Fusayama, 1979). Other studies have demonstrated that the use of caries detector dye resulted in over-excavation of carious dentine, and concluded that tactile and optical criteria, such as a soft, moist texture, but not color, are satisfactory to detect infected dentine (Kidd et al., 1993a; b; Kidd et al., 1996). Preoperative treatment when most of carious dentine was removed has been advocated in the past (Bodecker, 1938; Kerkhove et al., 1967). The amount of dentine removed during the first step of SWE has decreased during the time (Massler, 1967; Leksell et al., 1996).

The aim of the first step of SWE is to remove superficial parts of infected dentine from the lesion's floor and perform a complete excavation of the peripheral parts of the lesion, thus avoiding pulpal exposure, arresting caries progression, promoting healing of the affected dentine, and stimulating pulpal defense by increasing the dentine barrier (Bjørndal et al., 1997; Bjørndal and Darvann, 1999). After this re-entry is performed, the goal of which is to remove residual demineralized dentine that may be infected and could slowly progress (Bjørndal et al., 1997). However, pulpal exposure may occur during re-entry (Bjørndal and Thylstrup, 1998; Bjørndal et al., 2010; Orhan et al., 2010; Maltz et al., 2012a) (Table 1).

Changes in dentine color (darker), consistency (harder), moisture (dryer), and microflora (less cariogenic) on re-entry indicate arrested caries in deciduous and permanent teeth, irrespective of the material used or the thickness of residual dentine (King et al., 1965; Bjørndal et al., 1997; Bjørndal and Thylstrup, 1998; Bjørndal and Larsen, 2000; Maltz et al., 2002; Corralo and Maltz, 2013) (Table 1). Drastically reduced bacterial counts have been reported under sealed restorations, but they were still present (King et al., 1965; Bjørndal et al., 1997). A Cochrane review concluded that there was insufficient evidence as to whether re-entry was necessary, as studies that did not use re-entry reported no adverse consequences (Ricketts et al.,

2013). A RCT on young permanent teeth with deep carious lesions showed a 94%-95% success rate of both SWE and IPC after 1 year of follow-up (Orhan et al., 2010) (Table 1). Another RCT investigating permanent teeth demonstrated success rates of 69% and 91% for SWE and IPC, respectively, after 3 years of follow-up (Maltz et al., 2012a) (Table 1). Re- entry in SWE seemed to be disadvantageous not only due to the increased risk of pulpal exposure, but also because patients do not show up for their re-entry appointments. Incomplete SWE decreases the success rate of the procedure tremendously (13%) compared to complete SWE (88%) (Maltz et al., 2012a). A systematic review of studies of primary and permanent teeth found a 79% reduced risk of tooth failure after IPC compared to SWE (Schwendicke et al., 2013c).

Indirect pulp capping

Traditional IPC consists of leaving a layer of carious dentine under the permanent restoration to prevent carious exposure (Eidelman et al., 1965; Fitzgerald and Heys, 1991). Before permanent restoration is performed, the carious lesion is treated with a capping material, usually CH, which significantly reduces the number of residual bacteria and arrests the carious process, giving the pulp a chance to recover and produce tertiary dentine (Leung et al., 1980). The disadvantage when using CH is that it might dissolve and thus fail to provide a tight seal (Prosser et al., 1982; Phillips et al., 1984). Caries may progress rapidly if the seal breaks down. A recent RCT investigating primary teeth concluded that IPC with non-resorbing materials, such as mineral trioxide aggregate (MTA) or medical Portland cement, was preferable to CH slurry (Petrou et al., 2014). Another approach is to restore deep carious lesions directly with an adhesive resin system (Falster et al., 2002). One study on carious lesions of moderate depth demonstrated excellent 10-year results in lesions without carious dentine removal but with good sealing (Mertz-Fairhurst et al., 1998). Hermetical restoration prevents nourishment from reaching bacteria, isolating them and leading to either death or dormancy (Oong et al., 2008).

Recently, a less invasive approach to IPC was adopted. It is performed in a similar manner to the first step of SWE, i.e., by removing central parts of the carious lesion superficially and peripheral parts completely (Gruythuysen et al., 2010; Maltz et al., 2011; Maltz et al., 2012a) (Table 1). A systematic review and meta-analysis investigating primary and permanent teeth demonstrated an 80% lower risk of carious exposure during IPC compared to TCE, but concluded that it was too early to make clinical recommendations (Schwendicke et al., 2013a). IPC may also lead to root canal obliteration, which can complicate endodontic treatment if it is needed later on (Woehrlen, 1977).

2.5. Treatment options for carious exposures

During the excavation of deep carious lesions, the barrier of residual dentine may be broken, causing carious exposure that usually occurs under acute, rapidly penetrating carious lesions (Massler, 1967). In this context, the dilemma is whether to preserve tooth vitality or to perform pulpectomy followed by root canal treatment.

Vital pulp therapy

Vital pulp therapy (VPT) refers to three procedures, all of which aim to preserve tooth vitality despite pulpal exposure (Goodis, 2012) (Table 2). The first is direct pulp capping (DPC), a procedure in which exposed pulp is covered with a capping material after the bleeding has been stopped (Haskell et al., 1978; Baume and Holz, 1981; Dammaschke, 2008). The second is called partial pulpotomy (PP), i.e., when part of the coronal pulp adjacent to an exposure is removed and the rest of the pulp is covered with a capping material (Cvek, 1978). Finally, pulpotomy is a procedure where the entire crown pulp is removed from the pulp chamber and the remaining root pulp at the orifices of the root canals is covered with a capping material (Zander, 1939). The first report of VPT in the literature was in 1756, when Philip Pfaff attempted to perform DPC with small pieces of gold (cited in Glass and Zander, 1949). In a laboratory setting under

Table 2. Overview of studies on the treatment of carious exposures in permanent teeth.

AUTHOR	DESIGN	NUMBER OF TEETH[v], AGE OF SUBJECTS	ORIGIN OF EXPOSURE[vi], PULPAL STATUS	TREATMENT, MATERIAL(S)	CONTROL	FOLLOW-UP	RESULTS
Studies investigating DPC in mixed age groups (children and adults)							
Haskell et al., 1978	Retro-spective	n=149, 8-75 years	Carious exposures, Asymptomatic teeth	DPC, CH (powder) Penicillin	-	5-22 years (mean 11.7)	Success rate (vital pulp, absence of symptoms and periapical lesion): 5 years 87.3%, > 5 years 76.5%
Hørsted et al., 1985	Retro-spective	n=80, 10-79 years	Deep carious lesions, carious exposures, No history of pain	DPC CH (Dycal, Pulpdent, slurry)	-	5 years	Success rate (vital pulp, absence of history of pain, periapical lesion and sensitivity to percussion): 78.6%
Barthel et al., 2000	Retro-spective	n=54 5 years n=69 10 years, 10-70 years	Deep carious lesions, carious exposures, No history of pain	DPC CH (Life)	-	5 years 10 years	Success rate (vital pulp, absence of clinical symptoms and periapical lesion): 5 years 37%, 10 years 13%
Bogen et al., 2008	Pro-spective	n=49, 7-45 years (mean 16.6)	Deep carious lesions, carious exposures, Reversible pulpitis at most, moderate-severe pain included	DPC MTA (grey and white MTA, ProRoot)	-	1-9 years (mean 4)	Survival rate (vital pulp, absence of pain and periapical lesion): 97.96%
Mente et al., 2010	Retro-spective	n=59 MTA n=47 CH, 8-78 years (median 40)	Carious exposures, Reversible at most	DPC CH (Hyposal SN)	DPC MTA (grey and white, ProRoot)	1-6.7 year	Success rate (vital pulp, absence of clinical signs and symptoms, periapical lesion and internal root resorption, no loss of function): CH 62%; MTA 80%
Hilton et al., 2013	PBRN[vii] RCT	n=183 MTA n=175 CH, ≥7 years	Carious, traumatic, or mechanical exposures, Reversible at most	DPC MTA (ProRoot)	DPC CH (Life)	Median 12.1 months for CH group and 15.6 months for MTA group	The probability of failure (signs of periapical pathology on radiograph, recommendation for tooth extraction or root canal treatment): CH 31.5%; MTA 19.7%

| Cho et al., 2013 | Retro-spective | n=175 | Carious exposures Reversible pulpitis at most | DPC CH (Dycal) | DPC White MTA (ProRoot) | 1 year 3 years | Survival rate (absence of spontaneous or lingering pain to stimuli, periapical lesion and root canal treatment): 1 year CH 73.9%; MTA 89.9%, 3 years CH 52.5%; MTA 67.4%. |
| Mente et al., 2014 | Retro-spective | n=127 MTA n=49 CH, 7-78 years (median 44) | Carious exposures, Reversible pulpitis at most | DPC CH (Hyposal SN) | DPC MTA (grey and white (ProRoot) | 2-10.25 years (median 3.5) | Success rate (absence of clinical signs and symptoms, PAI <2, absence of pathology on radiograph, root canal treatment, loss of function and extraction): CH 57%; MTA 80% |

Studies investigating DPC in adults

Fitzgerald & Heys 1991	Pro-spective Random selection of material	n=19 CH (Life) n=19 CH (Dycal), 20-60 years	Deep carious lesions, but pulpal exposure not expected, Reversible pulpitis at most	DPC CH (Life)	DPC CH (Dycal)	12 months	No sig. difference in symptoms between materials Sig. increase in symptoms from pretreatment and one week post-treatment and decrease from one week to six months post-treatment
Matsuo et al., 1996	Pro-spective	n=44, 20-69 years (mean 42)	Deep carious lesions, carious exposures, Lingering pain on stimuli and spontaneous pain included	DPC CH (Dycal or Life)	-	≥3 months	Success rates (vital pulp, absence of signs and symptoms of irreversible pulpitis and periapical lesion): 3 months 81.8%
Miles et al., 2010	Retro-spective	n=51, 21-85 years (mean 42)	Carious exposures, Asymptomatic teeth	DPC MTA	-	1-2.5 years	Survival rate (vital pulp, absence of signs and symptoms of irreversible pulpitis and periapical lesion, no endodontic treatment or extraction): 1 year 68%, 2 years 56%

Studies investigating PP in mixed age groups (children and adults)

| Mass & Zilberman, 1993 | Pro-spective | n=35, 7.5-25 years (mean 12.5) | Very deep carious lesions, Recent short duration pain included | PP CH (Calxyl) | - | ≥ 12 months | Success rate (vital pulp, absence of clinical symptoms and pathology on radiograph): 91.4% |
| Mejare & Cvek, | Pro-spective | n=31 no clinical or radiographic symptoms | Deep carious lesions, | PP CH (Calasept) | - | 2-11.7 years | Success rates (vital pulp, absence of clinical symptoms and pathology on |

Study	Design	n[v] / age	Lesion[vi] / pulpal status	Capping material 1	Capping material 2	Follow-up	Outcome
1993		n=6 clinical and/or radiographic symptoms 6-15 years (mean 9)	No pain or temporary pain				radiograph): no symptoms group 93.5%; symptoms group 4 out of 6.
Nosrat & Nosrat 1998	Pro-spective	n=6 10-15, 20-27 years	Large carious lesions, Unknown pulpal status	PP CH (Calasept)	-	14-33 months	Success rate (vital pulp, normal percussion, absence of complains and sensitivity to percussion): 100%
Barrieshi-Nusair & Qudeimat, 2006	Pro-spective	n=31, 7.2-13.1 years (mean 10)	Deep carious lesions, Reversible pulpitis at most	PP Grey MTA (ProRoot)	-	12-26 months	Responsive to vitality testing: 79% Dentinal bridge formation: 64%
Qudeimat et al, 2007	RCT	n=23 CH n=28 MTA, 6.8-13.3 years	Deep carious lesions, Reversible pulpitis at most	PP Grey MTA (ProRoot)	PP CH (Hypocal +Dycal)	2-3.8 years	Success rate (absence of history of pain, swelling, pathology on radiograph and sensitivity to percussion): CH 91%; MTA 93%
Chailertvanitkul et al., 2013	RCT	n=41 MTA n=35 CH, 7-10 years	Deep occlusal carious lesions, Reversible pulpitis at most	PP MTA (ProRoot)	PP CH (Dycal)	2 years	Incidence rate/100 tooth-month (95% CI) (pain, swelling, sensitivity to percussion, periapical or furcation lesion, root resorption or lack of root development in immature tooth): CH 0.11 (0.001–0.60); MTA 0.20 (0.02–0.71)
Studies investigating DPC versus PP in adults							
Bjørndal et al., 2010	RCT, multi-center	n=22 DPC n=29 PP ≥18 years	≥3/4 into dentine with well-defined radiodense zone, Reversible pulpitis at most, mild pain included	DPC CH (Dycal)	PP CH (Dycal)	407-531 days DPC 390-530 days PP	Success rate (vital pulp, absence of unbearable pain and periapical lesion): DPC 31.8%; PP 34.5%

[v] Number of teeth analyzed.
[vi] In case of carious exposure, the depth of the lesion is indicated if given in the original article.
[vii] Practise-based research network

germ-free conditions, surgically-exposed pulps resulted in wound-healing reactions (Kakehashi et al., 1965). Studies have reported healing after surgical exposures and complicated crown fractures when covered with CH (Glass and Zander, 1949; Cvek, 1978). Therefore, VPT was indicated mainly for mechanic and traumatic exposures (Dammaschke, 2008). In the case of carious exposure, the capping material is applied to the pulp that is inflamed and exposed to bacteria in the oral cavity (Massler, 1967; Massler and Pawlak, 1977). In the event of carious exposure the odontoblast layer is lost. The progenitor cells from the pulp are recruited to the pulpal wound and differentiated into odontoblast-like cells. Healing is promoted by the secretion of dentine-like tissue (Smith and Lesot, 2001; Ricucci et al., 2014a). Any capping material should be bactericidal and should initiate the release of signaling molecules necessary for the induction of dentine-like tissue secretion upon interaction with dentine (Graham et al., 2006; Tomson et al., 2007; Ferracane et al., 2010). CH is considered the standard material for VPT because it has a high pH that provides bactericidal activity and stimulates the secretion of dentine-like tissue (Schroder, 1985; Sangwan et al., 2013). However, there are indications that the sealing ability of CH is not optimal; the material might dissolve, causing bacterial leakage and secondary infection (Prosser et al., 1982; Phillips et al., 1984). MTA was introduced more than 2 decades ago for the repair of lateral root perforations and as a root-end filling material (Lee et al., 1993; Torabinejad et al., 1993). Soon it was also suggested for pulp capping (Pitt Ford et al., 1996). The main soluble component of MTA is CH, which dissolves to calcium and hydroxyl ions, but the clinical behavior of MTA and CH differs (Fridland and Rosado, 2005). MTA prevents bacterial leakage better than CH due to its superior sealing ability. Moreover, MTA causes less initial inflammatory response, releases more dentine matrix proteins (TGF-β1, is a key factor in reparative dentinogenesis), raises the expression of proteins involved in dentine-like tissue formation (osteopontin, osteonectin, osteocalcina) in osteoblast-like cells and fibroblasts, and results in faster and higher quality (thicker and fewer tunnel defects)

dentine-like tissue formation (Torabinejad et al., 1995; Téclès et al., 2008; Ferracane et al., 2010; Parirokh and Torabinejad, 2010; Torabinejad and Parirokh, 2010; Laurent et al., 2012).

For young permanent teeth with carious exposures, VPT (in all cases PP) with CH showed excellent results, with success rates of 91%-94% (Mass and Zilberman, 1993; Mejàre and Cvek, 1993; Nosrat and Nosrat, 1998; Qudeimat et al., 2007). No statistically significant difference in the excellent success rate of VPT was observed when MTA and CH were compared in young permanent teeth in two RCTs (Qudeimat et al., 2007; Chailertvanitkul et al., 2013). Thus it was concluded that, in adolescents, VPT with CH works just as well as VPT with MTA.

Direct pulp capping

In mature permanent teeth with carious exposures, DPC may initially produce success rates comparable to those of endodontic treatment (Hørsted et al., 1985; Matsuo et al., 1996), but the procedure has not demonstrated long-term success (Barthel et al., 2000) (Table 2). Indeed, a low success rate (32%) was observed after 1 year of follow-up of carious exposures capped with CH in adults (Bjørndal et al., 2010) (Table 2). A much higher success rate (95%) was achieved when MTA was used as a capping material in permanent teeth with carious exposures both in adolescents and adults (Bogen et al., 2008) (Table 2). DPC with MTA revealed higher success rates (80.3%-80.5%) than DPC with CH (59%-68.5%) (Hilton et al., 2013; Mente et al., 2014) (Table 2). As these studies included pulpal exposures of both

mechanic and traumatic origin, and patients from all age groups, including children, their capability to assess the success rate of DPC over carious exposures in adults is limited (Table 2). So far, there are no RCTs on DPC that compare CH and MTA, and that are restricted to carious exposures in adult patients only. Thus, using VPT instead of pulpectomy followed by root canal treatment in adults is poorly justified.

Partial pulpotomy

PP is an alternative to DPC in carious exposures. Theoretically, it has more advantages and a more predictable outcome than DPC. This is because the introduction of infected dentine chips into the pulp is prevented, superficially inflamed pulp tissue is removed, and space is made for a bacteria-tight seal (Trope et al., 2002; Aguilar and Linsuwanont, 2011). Two follow-up studies showed a 100% success rate after PP with CH for seven mature teeth in young adults (Mass and Zilberman, 1993; Nosrat and Nosrat, 1998), whereas a RCT demonstrated a low success rate for PP (34.5%) and no significant superiority of PP compared to DPC (31.8%) in adults when CH was used as a capping material (Bjørndal et al., 2010).

Pulpotomy

Pulpotomy goes back as far as the work of Codman (1851), and consists of the removal of the entire crown pulp (cited Zander, 1939). Pulpotomy has been recommended in vital, exposed young permanent teeth to promote apexogenesis (Berk, 1957). For adults pulpotomy is used as an emergency treatment (Hasselgren and Reit, 1989). Recently, promising preliminary histological and clinical results have been presented for pulpotomy with MTA as a permanent treatment of deep carious lesions in teeth with signs of reversible and irreversible pulpitis (Barngkgei et al., 2013; Simon et al., 2013).

Pulpectomy (followed by root canal treatment)

If VPT fails, endodontic treatment is the final option. Pulpectomy followed by endodontic treatment is appropriate for carious exposures in mature teeth (Hasselgren, 2008) and is the most predictable treatment methods, although the corresponding long-term success rates vary greatly (60%-100%) (Kojima et al., 2004; Ng et al., 2007; Ng et al., 2010). Endodontic treatment has several disadvantages: i) it is expensive and time-consuming; ii) it increases the probability of tooth fracture due to more coronal destruction (compared with VPT) and loss of

proprioceptive response; and iii) it is impossible to protect against bacterial invasion if vital pulp is lost (Lewis and Smith, 1988).

2.6. The treatment dilemma

Systematic reviews on the treatment of deep carious lesions showed that the level of evidence is currently insufficient for definitive conclusions to be drawn regarding the most effective treatment method, as most of the included studies had only short-term follow-up and a high risk of bias (Bergenholtz et al., 2013; Miyashita et al., 2007). Surveys from the USA, Brazil, Germany, and Sweden, showed no uniform treatment method, further demonstrating the uncertainty regarding the best treatment of deep carious lesions and carious exposures (Oen et al., 2007; Weber et al., 2011; Frisk et al., 2013; Schwendicke et al., 2013b). The majority of the dental practitioners (50%-80%) preferred TCE for the treatment of deep carious lesions in mature teeth in adults; in the case of carious exposure, DPC was preferred by 53%-83%. However, the treatment methods preferred by general dental practitioners (GDPs) in Northern Norway are unknown.

3. AIMS

The aims of this thesis were:

- to document the prevalence of deep carious lesions and other consequences of caries (DCL-CC) among 18-year-olds in Troms County, Northern Norway.

- to analyze the association between DCL-CC and various background factors: gender, urban/rural clinic location, history of medical problems, bitewing examination intervals and DMFT score.

- to investigate the preferred treatment methods and routines for treating deep carious lesions in vital, permanent, mature teeth among GDPs in Northern Norway.

- to disclose factors behind GDPs' preferred treatment methods.

- to investigate whether pulps of molars presenting carious exposure and directly capped with MTA survived longer than pulps directly capped with CH in adult patients.

4. MATERIALS AND METHODS

4.1 Subjects

Study I, cross-sectional age cohort study

The study population sample consisted of all individuals (n=1978) born in 1993 and enrolled in the PDHS in Troms County at the time of the study. The final study sample consisted of 1876 subjects with digital bitewing radiographs in their electronic dental records (Opus Dental software, Opus Systemer AS, Nesbru, Norway); 102 individuals were excluded due to lack of digital bitewing radiographs. The most recent digital bitewing radiographs and dental records of each subject were examined.

Study II, survey

The study sample consisted of all (N=437) GDPs working in Northern Norway (Nordland, Troms, and Finnmark Counties). GDPs' names and home or work addresses were retrieved from the professional registers by the chief dental officers or local dental associations. Questionnaires and invitation letters were sent via mail, and 37 questionnaires were returned due to lack of relevance. Thus the final study sample consisted of 400 GDPs.

Study III, randomized clinical trial

Sample size calculation was based on an estimated 30% difference in the success rates of MTA and CH. The success rate in the CH group was set to 55% after 2 years according to Barthel and colleagues (2000). With a significance level of 5% and a power of 95%, we calculated that 64 subjects were needed in each group. When the drop-out rate of 20% was included, the final goal for recruitment was 160 subjects. Subjects were recruited from three public dental clinics in Northern Norway and one private dental clinic in Lithuania. To be eligible, subjects had to meet strict inclusion criteria: i) caries in first or second permanent molars (only one tooth per subject); ii) presence of proximal caries; iii) age 18-55 years; and iv) non-contributory medical history (including pregnancy). Subjects were excluded if they i) had no pulpal exposure during

treatment; or ii) had bleeding of the exposed pulp that could not be controlled in 10 minutes. In total, 80 subjects were enrolled in the study, 10 of which were excluded due to no pulpal exposure. Thus the total study sample consisted of 70 subjects, who were randomly assigned to either the MTA group (n=33) or the CH group (n=37).

4.2 Methods

Study I, cross-sectional age cohort study

This cross-sectional study was conducted in Troms County during the spring of 2012. We used the most recent digital bitewing radiographs taken before the onset of this study as part of routine dental screening. These radiographs were retrieved from electronic dental records (Opus Dental software, Opus Systemer AS, Nesbru, Norway) and the molar region (except third molars) of each study subject was examined. DCL-CC (deep carious lesions, deep restorations, root canal obturated molars and extractions due to caries) were recorded using tooth as a unit. Deep untreated carious lesions and deep restorations were determined as those reaching the inner ¼ of the dentine (Bjørndal et al., 2010).

Before data collection by the main investigator (LS), calibration was performed in collaboration with a maxillofacial radiologist (NLB) and inter- and intra-observer reliability was calculated. The inter-observer reliability (NLB and LS) rendered a Cohen's kappa value of 0.62 and intra-observer reliability (LS) showed a kappa value of 0.87 (Cohen, 1960). Twenty digital bitewing radiographs showing 34 deep carious lesions and deep restorations at least in the inner half of dentine were selected to for the assessment of reliability.

Study II, survey

The questionnaire study was performed during the autumn of 2011. The multiple-choice questionnaire contained 20 questions and was first written in the English language (Appendix 1). The questionnaire was translated into Norwegian before it was mailed to the subjects.

Variables of interest were: i) preferred treatment methods for deep carious lesions and carious exposures in mature permanent teeth in the absence and presence of symptoms; ii) demographic characteristics of subjects; iii) reasons and factors (options listed) why subjects preferred their chosen treatment method; iv) deep caries treatment routine (instrument and materials used). Content validity was tested by four dental postgraduate students.

The questionnaire was mailed to all subjects along with a personalized invitation letter (Appendix 2) and a coded, pre-paid return envelope. After 8 weeks, an identical set was mailed to non-responders, identified by the code on the envelope. After an additional 8 weeks, five randomly selected non-respondents were contacted by phone to identify the reason for non-response. After a total of 16 weeks the survey was closed.

Study III, randomized clinical trial

In order to assess the long-term survival of pulps after DPC performed with either white ProRoot® MTA (Dentsply, Tulsa Dental, Tulsa, OK, USA) or CH (Dycal®, Dentsply DeTrey GmbH, Konstanz, Germany) over carious exposure, a multicenter, single-blinded RCT was conducted. Balancing randomization was done centrally, at the Department of Clinical Dentistry, UiT the Arctic University of Norway, using an envelope method. Each recruitment clinic served as an allocation unit. Twenty envelopes with block sizes 4-6-4-6 were sent to the participating clinics. Group allocation was not shared with the subjects.

Written informed consent was obtained from each subject (Appendix 3). Paper instructions regarding the study were presented to the GDPs. In order to ensure that DPC was performed in a uniform manner across the clinics, GDPs in Norway met with the main investigator (RK) to demonstrate how DPC should be performed for the study. The GDP in Lithuania met with another author (LS) for this purpose. The results of DPC and the confidential patient number were recorded (Appendix 4) and reported to the main investigator. Follow-up was planned at 1 week and at 6, 12, 24, and 36 months after the procedure, as it has been shown

that at least 21 months of follow-up is necessary for proper outcome assessment (Matsuo et al., 1996). According to the schedule, the recruitment of study subjects was terminated in spring 2013. The primary outcome of the study was survival rate of the capped pulps and the secondary outcome was postoperative pain at 1-week follow-up.

4.3 Statistics

The statistical methods used in the studies are explained in detail in the original articles and summarized in Table 3.

Table 3. Overview of the statistical analyses used in the studies.

	Study I	*Study II*	*Study III*
Statistical program package	IBM SPSS 19	IBM SPSS 21	IBM SPSS 21
Cohen's kappa	+	-	-
Pearson's chi-square test	+	+	+
Mann-Whitney test	+	-	-
Logistic regression analysis	+	+	-
Log-Rank (Mantel-Cox) test	-	-	+

In addition, in *Study I* the variable DMFT score was calculated using mathematical coupling (Walsh and Lee, 1998). In *Study III* the baseline imbalance between groups regarding the depth of carious lesions assessed from radiographs was analyzed by a stratified long-rank test (Altman, 1985).

4.4 Ethical considerations

Study I, cross-sectional age cohort study

This study included data from PDHS dental records and digital bitewing radiographs. The Regional Ethical Committee of Northern Norway considered that the study fell within the

framework of a Quality Assurance Project and that ethical approval was therefore unnecessary (2011/2492/REK nord).

Study II, survey

This study included no patient information. Ethical approval was considered unnecessary by the Regional Ethical Committee of Northern Norway.

***Study III*, randomized clinical trial**

The participation in this RCT was voluntary and written informed consent was obtained from all study subjects. Ethical approval (2010/2112-4) was obtained on 14.09.2010 from the Regional Ethical Committee of Northern Norway. The RCT is registered in ClinicalTrials.gov.

5. MAIN RESULTS

Study I, cross-sectional age cohort study

The outcome in *Study I* was recorded from the most recent digital bitewing radiographs, the majority of which were taken in 2011; for 8.5% of subjects bitewing radiographs were taken in 2010, for 4.4% in 2009, for 1.1% in 2008, and for 0.4% of subjects the most recent digital bitewing radiographs were taken between 2007 and 2005. Among 18-year-olds in Troms County (n=1876) there were 488 (26%) having at least one molar with DCL-CC. The most prevalent modality of DCL-CC was deep restoration; at least one molar with deep restoration was observed among 21.5% (n=404) of the age cohort (Fig. 3). Deep restoration was followed by root canal obturated molars, molars extracted due to caries, and untreated deep carious lesions, which were present in 5.1%, 3.6%, and 1.6% of this age cohort, respectively (Fig. 3).
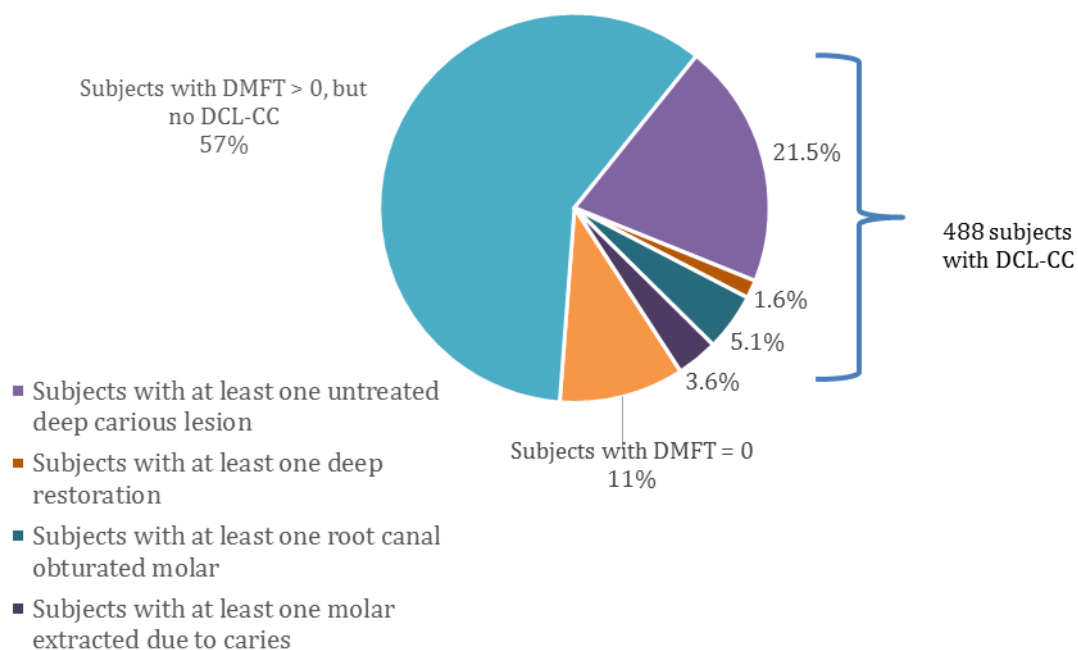
Figure 3. Distribution of 18-year-olds (n=1876) according to DMFT score and presence of DCL-CC in permanent molars.

Of the 15008 molars analyzed, there were 848 (6%) with DCL-CC. The same pattern was observed, with the most prevalent modality of DCL-CC being deep restorations (70%) and the least prevalent modality being untreated deep carious lesions (4%) (Fig 4).

A

94% molars without DCL-CC

6% molars with DCL-CC

B

14%

12%

4%

70%

- Molars with untreated deep carious lesions
- Molars with deep restorations
- Molars with root canal obturation
- Molars extracted due to caries
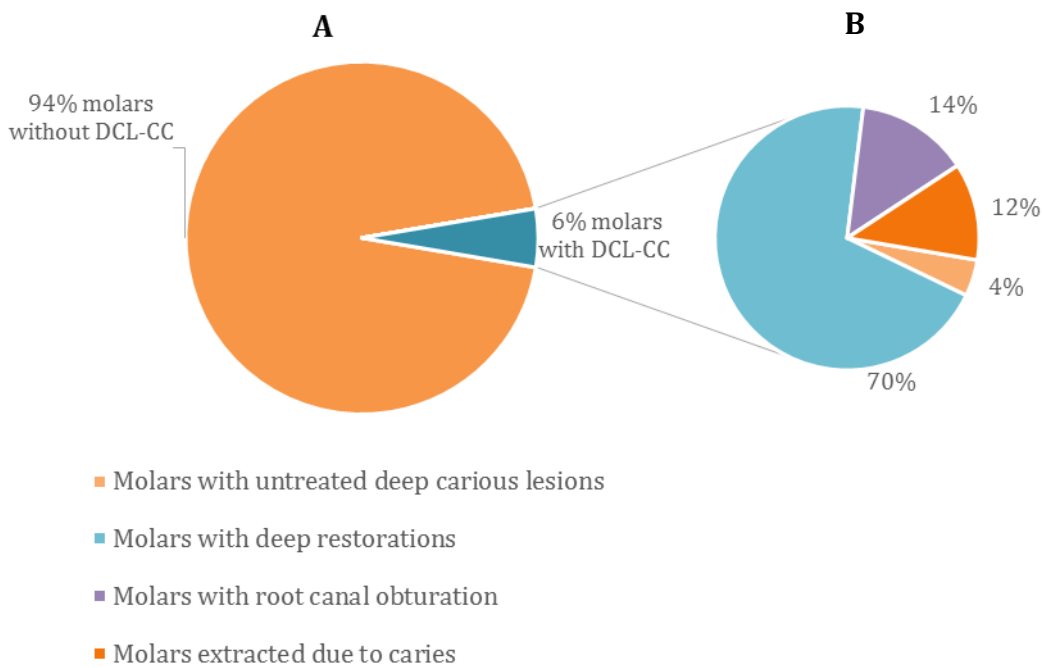
Figure 4. A) Distribution of permanent molars (n=15008) according to the presence/absence of DCL-CC. B) Distribution of 848 molars by modality of DCL-CC: untreated deep carious lesions, deep restorations, root canal obturations, extractions due to caries.

Out of 1876 18-year-olds, there were 206 (11%) with a DMFT score of zero. Four hundred and eighty-eight subjects with DCL-CC had a mean DMFT (SD) score of 9.1 (4.6) and a median DMFT score of 8 (range 1-25), which was more than double the mean DMFT (SD) score of 4.5 (4.0) ($p<0.001$) and median DMFT score of 4 (range 0-21) observed among subjects without DCL-CC. According to the univariable binary logistic regression analysis, DMFT score

was associated with all modalities of DCL-CC (p<0.001). A DMFT score higher than 5 was associated with a self-reported history of medical problems (odds ratio, OR=1.5, CI 1.02-2.09) and with a 6-month decrease in bitewing examination intervals (OR=0.7, CI 0.7-0.8).

Records on recall dates were available for 93 subjects having DCL-CC and recall intervals could be calculated for 83 of them. The mean (SD) length of recall intervals were 16.1 (7.1) months and the median length was 13.35 months (range 5-40 months).

A 1-unit increase in DMFT score was associated with an OR of 1.3, while a 6 month increase in bitewing examination intervals associated with an OR of 1.5 for untreated deep carious lesions (Table 4).

Table 4. OR for having at least one molar with untreated deep carious lesion (versus no DCL-CC) according to background factors retrieved by binary logistic regression.

Independent variable	Crude OR Univariable analysis OR (95% CI), p	Adjusted OR [viii] Multivariable analysis OR (95% CI), p
Female gender (vs male)	0.5 (0.2-1.02), NS	0.5 (0.2-1.2), NS
Rural location of clinic (vs urban)	0.6 (0.2-1.4), NS	0.7 (0.2-1.8), NS
Medical problems (vs healthy)	1.6 (0.5-5.3), NS	1.8 (0.5-6.7), NS
DMFT score[ix] (continuous)	1.2 (1.2-1.3), 0.000[ix]	1.3 (1.2-1.4), 0.000[x]
Bitewing examination interval (every 6 months, continuous)	1.3 (1.004-1.8), 0.047[ix]	1.5 (1.1-2.1), 0.005[ix]
Explained variance Nagelkerke R^2	-	0.202

[viii] Adjusted for all independent variables.
[ix] DMFT score is calculated by mathematical coupling (subtracting the number of molars with DCL-CC from the overall DMFT score).
[x] $p <0.05$.

A 1-unit increase in DMFT score and self-reported history of medical problems was associated with ORs of 1.2 and 3.2, respectively, for extractions due to caries (Table 5). These results are slightly different from those published in *Study I* due to statistical analyses using the mathematical coupling calculation of the DMFT score (Walsh and Lee, 1998). Urban/rural location of the clinic, which represented a socio-economic factor, did not yield a significant association with either DMFT score or DCL-CC.

Table 5. OR for having at least one molar extracted due to caries (versus no DCL-CC) according to background factors retrieved by binary logistic regression. DMFT score represents subtraction of DMFT score from the number of teeth with deep carious lesions.

Independent variable	Crude OR Univariable analysis OR (95% CI), *p*	Adjusted OR[xi] Multivariable analysis OR (95% CI), *p*
Female gender (vs male)	0.8 (0.4-1.3), NS	1.1 (0.6-1.9), NS
Rural location of clinic (vs urban)	1.8 (1.1-2.9), 0.023	1.6 (0.9-2.9), NS
Medical problems (vs healthy)	3.3 (1.7-6.3), 0.000[xii]	3.2 (1.5-6.7), 0.002[xi]
DMFT score[xiii] (continuous)	1.2 (1.1-1.3), 0.000[xi]	1.2 (1.1-1.3), 0.000[xi]
Bitewing examination interval (every 6 months, continuous)	0.6 (0.4-0.9), 0.021[xi]	0.9 (0.6-1.3), NS
Explained variance Nagelkerke R^2	-	0.146

[xi] Adjusted for all independent variables.
[xii] $p < 0.05$.
[xiii] DMFT score is calculated by mathematical coupling (subtracting the number of molars with DCL-CC from the overall DMFT score).

Study II, survey

Two hundred twenty-two of the 400 invited GDPs returned the study questionnaire (response rate of 55.5%). There were 178 respondents after the first mailing round (response rate 44.5%) and 44 after the second mailing round. There was an over-representation of publicly employed GDPs among respondents, otherwise respondents and non-respondents were similar in gender

and in urban/rural location of the clinic. Analysis of early and late respondents showed no differences in background characteristics or preferred treatment methods. Two different scenarios were presented in the questionnaire (presence and absence of symptoms) regarding deep carious lesions and carious exposure in vital, permanent, mature teeth. Different treatment methods were preferred by GDPs in each scenario (Fig. 5). VPT, i.e. TCE (49%) and SWE (45%), was the preferred treatment method for deep carious lesions in the absence of symptoms. Pulpectomy followed by endodontic treatment (39%) and SWE (38%) were almost equally preferred treatment methods for deep carious lesions with symptoms. In cases of carious exposure, the presence of symptoms (indicating reversible pulpitis at most) was statistically significantly associated with pulpectomy followed by root canal treatment as the preferred treatment method ($\chi^2=120$, d.f.=1, $p<.001$). DPC (51%) was the preferred treatment method when symptoms were absent.
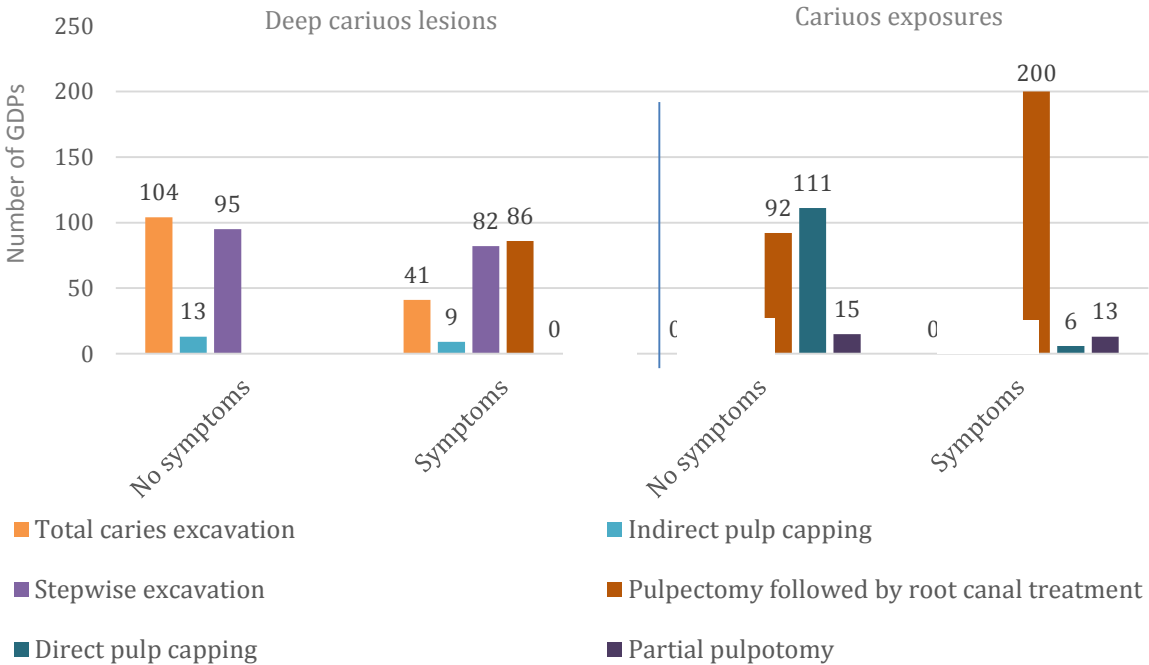
Figure 5. Frequency distribution of preferred treatment methods for deep carious lesions and carious exposures in the presence/absence of symptoms.

The two most frequently chosen patient-related factors were the same ("Final restoration" and "Patient's oral health") regardless of preferred treatment method; "Patient's age" was the second most frequent patient-related factor chosen by GDPs whose preferred treatment method was DPC.

Most of the respondents used CH paste as a capping material when there was no carious exposure (Fig. 6). Around two-thirds of the respondents used CH paste and/or slurry as a capping material for DPC and PP and less than 20% of respondents use rubber-dam while treating carious exposures (Fig. 7).
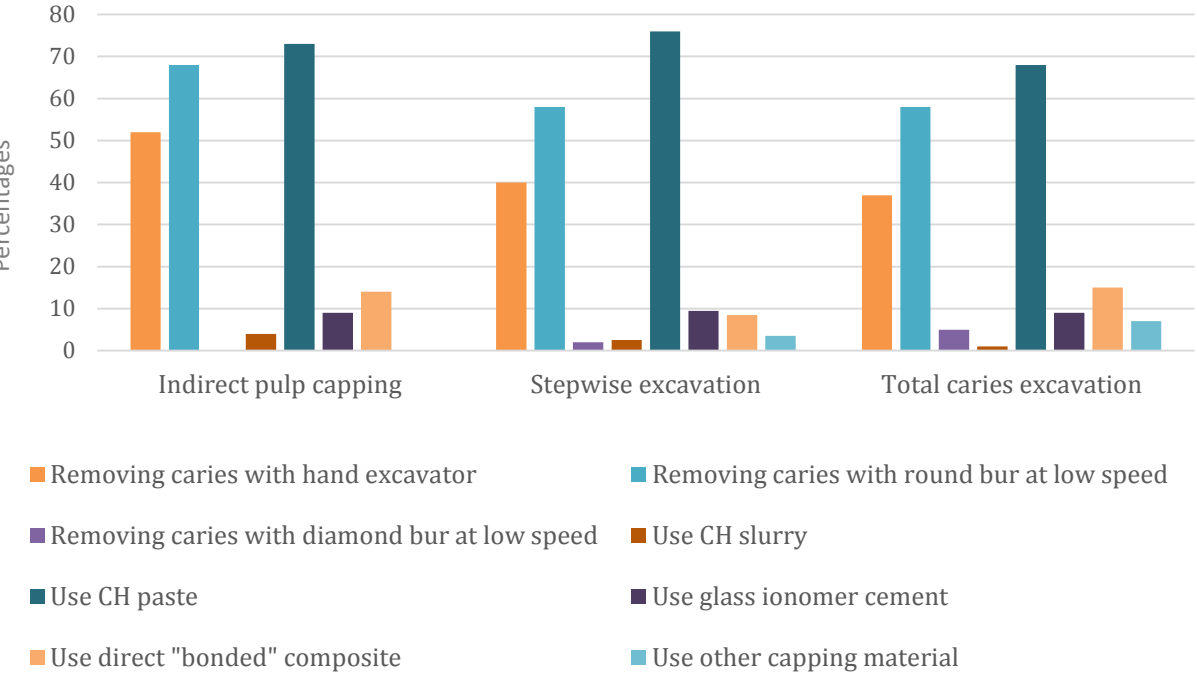
Figure 6. Distribution (%) of treatment routines by preferred treatment method of deep carious lesion.
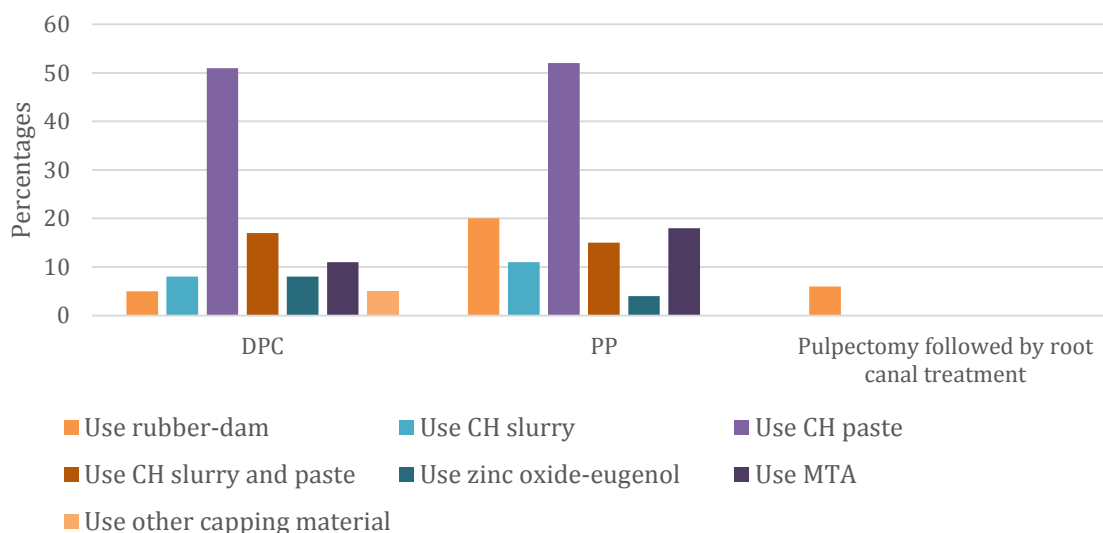
Figure 7. Distribution (%) of treatment routines by preferred treatment method of carious exposures.

In cases with no symptoms and no carious exposure, urban location of clinic was associated with TCE versus IPC and SWE combined (OR=2.2, CI 1.2-4.1) and TCE versus SWE (OR=2.1, CI 1.1-4.1). Graduation from dental school in Norway was associated with a lower OR for TCE versus IPC and SWE (OR=0.5, CI 0.2-0.9) and TCE versus SWE (OR=0.4, CI 0.2-0.9). Models that used TCE and SWE as dependent variables (versus IPC) did not show any statistically significant associations with subjects' background characteristics.

In cases with symptoms but no carious exposure, urban location of clinic was associated with an OR of 2.2 (CI 1.2-4.1) for pulpectomy followed by root canal treatment (versus TCE, SWE and IPC combined. When TCE was used as the dependent variable (versus SWE and IPC individually and combined), no statistically significant association was observed with subjects' background characteristics. The same was true when SWE was compared to IPC.

In cases with carious exposure and symptoms, graduation in Norway and 5 or more years in practice were associated with an OR for pulpectomy followed by root canal that was three times higher than that for DPC and PP combined (OR=3.1, CI 1.1-8.9 and OR=2.8, CI 1.1-7.4, respectively).

Study III, randomized clinical trial

As of January 2015, 80 subjects had been recruited, 10 of whom have been excluded due to lack of carious exposure. In total, 70 subjects were randomly assigned to either the MTA group, (n=33) or to the CH group, (n=37). Subjects in the MTA and CH groups were similar in age, molar number, cavity type, and preoperative pain, but not regarding the depth of the carious lesion, which was assessed from radiographs prior to treatment (Table 6).

Table 6. Baseline characteristics of the subjects and molars included in *Study III* and those excluded due to lack of carious exposure.

Characteristic	MTA group n=33	CH group n=37	Lack of carious exposure n=10
Age at DPC			
18-29 years	19	24	8
30-55 years	14	13	2
Tooth number			
Upper first molar	13	10	3
Upper second molar	7	7	4
Lower first molar	5	14	2
Lower second molar	8	6	1
Cavity type			
Occlusal	2	2	-
MO[xiv]	13	16	4
DO[xv]	11	11	6
MOD[xvi]	7	8	-
Preoperative pain			
Yes	16	18	4
No	17	19	6
Caries depth[xvii]			
2/3 into the dentine	6	5	4
>2/3 into the dentine	15	8	6
Into the pulp	12	24	-

[xiv] Mesial-occlusal
[xv] Distal-occlusal
[xvi] Mesial-occlusal-distal
[xvii] Assessed from the preoperative radiograph.

When the depth carious lesion was dichotomized by pulpal involvement ("into the pulp" and "not into the pulp"), subjects in CH group had a statistically significantly higher number of carious lesions that were "into the pulp" (χ^2=5.672, d.f.=1, p=0.017).

Follow-up periods ranged from 7 to 1173 days in the CH group (median 731 days) and from 4 to 1193 days in the MTA group (median 1092 days). The cumulative survival rate for the capped pulps with MTA was 80%; the rate was 46% for the pulps capped with CH (Fig. 8). This difference was statistically significant according to the log-rank test (χ^2=5.594; d.f.=1; p=0.018). When the data were stratified according to the radiographic appearance before carious tissue excavation, the difference between the materials was not statistically significant when the assessed depth was "into the pulp" (log-rank test, p=0.340) (Fig. 8).

In both groups, the number of subjects with pain decreased 1 week after the procedure compared to baseline, being 16/10 and 18/8 for the MTA and CH groups, respectively. Postoperative pain was not statistically significantly associated with the material either in relieving (χ^2=2.862; d.f.=1; p=0.091) or inducing (χ^2=0.557; d.f.=1; p=0.455) pain. There was no statistically significant difference between preoperative pain and survival rate either in the MTA (χ^2=1.297; d.f.=1; p=0.255) or the CH (χ^2=0.434; d.f.=1; p=0.510) group.
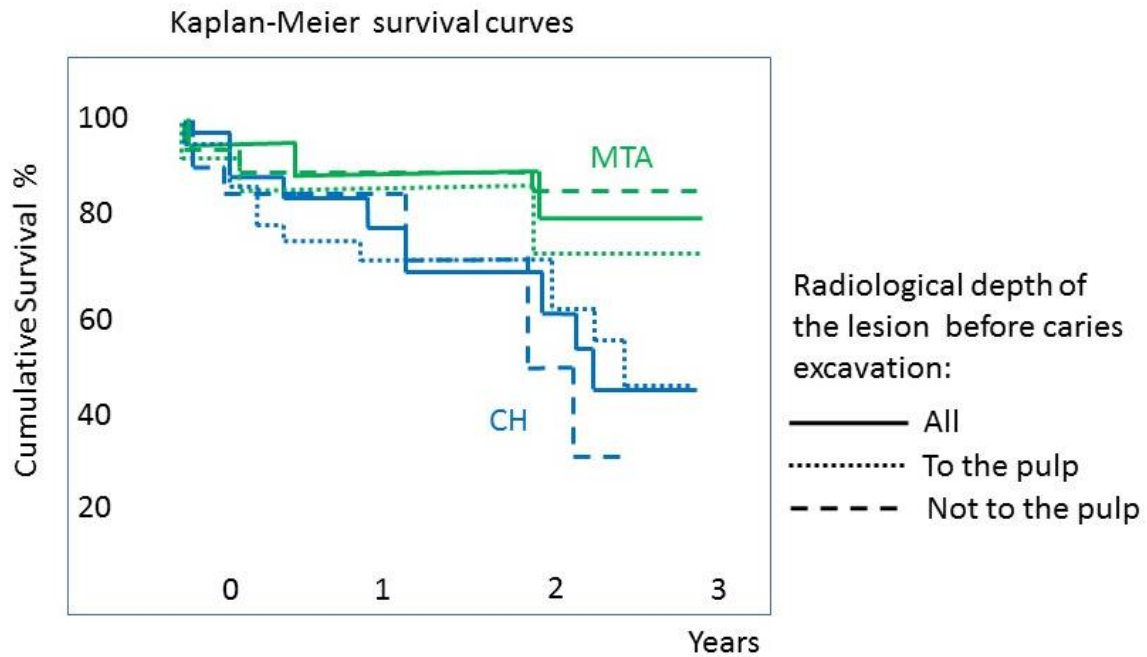
Figure 8. Kaplan-Meier survival curves of molars capped with MTA and CH. Depth of carious lesions were stratified by pulpal involvement (into the pulp and not into the pulp) as assessed from radiographs taken prior to the excavation process. Schematically modified from SPSS curves.

Statistical analysis with log-rank test, p=0.016: MTA group estimated cumulative survival rate 85% vs. the CH group estimated cumulative survival rate 35.5% when the assessed radiographic depth of the lesion was not into the pulp.

Statistical analysis with log-rank test, p=0.340: MTA group estimated cumulative survival rate 71% vs. CH group estimated cumulative survival rate 50.5% when the assessed radiographic depth of the lesion was into the pulp.

6. GENERAL DISCUSSION

6.1 Consideration of methodological aspects

Study design, subjects, internal and external validity

Study I. The target population was well defined: individuals registered at the PHDS in Troms County at the time of data collection and born in 1993, making them 18 years of age at the time of the study. The PDHS is free-of-charge in Norway until the age of 18 years, therefore it was particularly convenient and interesting to study this age cohort, as they are about to leave the PDHS. All individuals who fulfilled inclusion criteria (n=1978) were included in the study except 102 who were excluded due to the lack of a digital bitewing radiograph. The study was conducted at a defined place (Troms County) and time (spring of 2012) and the results were obtained in a cross-sectional study design. According to Bhopal (2008), the function of cross-sectional studies is to measure prevalence and determine associations between disease and related factors.

Inter-observer reliability rendered a Cohen's kappa of 0.62, which is considered substantial, and intra-observer reliability was 0.87, which is considered almost perfect; this reliability gives our study a good background for high validity (Landis and Koch, 1977). In addition, bitewing radiographs been shown to have good reproducibility and validity in epidemiological conditions (da Silva et al., 2011a; 2011b). Furthermore, a systematic review demonstrated a high correlation between radiographic prevalence of carious lesions and clinical and radiographic prevalence combined (Bloemendal et al., 2004).

In *Study I*, the outcome (DCL-CC) was recorded from digital bitewing radiographs. DCL-CC were strictly defined as deep carious lesions and deep restorations in the inner ¼ of dentine, root canal obturations, and extractions due to caries that were confirmed in dental records.

The study period was relatively short – 3 months (March 2012-May 2012). However, the time period covered by the data itself was a bit longer, as 14.4% of the subjects had digital

49

bitewing radiographs that were taken before 2011; this could have introduced mis-measurement (Bhopal, 2008). As our data included prevalent cases, the relative risk of DCL-CC could not be calculated (Szklo and Nieto, 2012). Due to the cross-sectional design of S*tudy I*, reverse causation should be considered when interpreting the associations between background factors and DCL-CC. In addition, cross-sectional studies are prone to confounding (Bray and Parkin, 2014). One way to control for confounding is to use multivariable techniques, and we did this in *Study I* (more in the Statistical analyses section of this doctoral thesis) (Bray and Parkin, 2014).

Study I included 95% of 18-year-olds registered at the PDHS in Troms County. This seems to be representative of the target population, and therefore generalization from the study sample to the source population is strong. However, the interpretation of study results and their generalizability beyond the source population might have some limitations. In Troms County, 85% of 18-year-olds had received dental check-ups in the PDHS in 2011, (Statistics Norway, 2011). The prevalence of caries is higher in Northern Norway compared to the rest of the country and in comparison to other Scandinavian countries, thus our results cannot be generalized to 18-year-olds in all of Norway or in other Scandinavian countries. Cross-sectional studies provide information on the care requirements of the population at a given point of time and are relevant to public health planning (Bray and Parkin, 2014). Our study indicates that the PDHS might eliminate socio-economic differences, which might be interesting for the whole of Norway, Scandinavia, and other countries with a free-of-charge PDHS.

Study II. A structured questionnaire was used to learn the preferred treatment methods of deep carious lesions among GDP working in Northern Norway. A structured questionnaire simplifies the data analysis and contributes to greater uniformity (Abramson, 1990). Content validity, which is a qualitative measurement of validity that shows whether the questions measure what they are intended to measure, was tested by four dental postgraduate students and

was evaluated as strong (Fink, 2014). Internal consistency (like Cronbach's alpha) could not be calculated for this questionnaire due to the type of questions.

We used an invitation letter that included a visual and a written case presentation in the hopes that this would help to predict GDPs' behavior (Appendix 2) (Jones et al., 1990). The age of the patient in the case we presented them was not indicated, but from the radiograph they could see that the root of the first upper premolar was closed and the third lower molar was erupted, indicating a young adult patient.

In order to increase the response rate, we tried to present GDPs with an interesting and relevant topic, we included a short questionnaire with a university logo, a pre-paid return envelope, and a personalized invitation letter. We also resent the questionnaire to non-respondents. However, for practical reasons, we did not record delivery/use registered mail, offer monetary incentives, or contact subjects before sending questionnaires (Edwards et al., 2007; Thorpe et al., 2009).

The final response rate was 55.5%, which is considered sufficient to represent GDPs in Northern Norway (Baruch, 1999). The background characteristics of GDPs who responded directly and those who responded only after a second questionnaire was sent did not differ. However, there was an over-representation of publicly employed GDPs, and this should be taken into consideration when interpreting our results. Self-selection bias might have been introduced, as it is possible that only those who felt confident about the topic answered (Rothman and Greenland, 2014).

Study III. A two-arm parallel group trial design was used to compare the two capping materials. The unit of randomization was 1 tooth per person. According to our sample size calculation, 80 subjects had to be recruited in each of the two arms. Seven dental clinics were initially included in the study, but only four of them finally recruited subjects for this RCT. For practical reasons, the recruitment of the patients did not proceed at the anticipated pace. In order

51

to ensure that the results were reported in a reasonable timeframe, recruitment was terminated in February 2013, even though only 80 of the originally desired 160 subjects had been recruited. As a statistically significant difference was demonstrated between the two materials, the smaller number of subjects did not cause any flaws in the study.

Dentists performing the treatment met with the investigators of the study for calibration before study onset in order to increase inter-observer reliability and to minimize bias (Juni et al., 2001). The probability of bias and confounding was reduced by proper randomization, which was ensured by creating an allocation sequence and concealing that allocation (Altman, 1991; Gluud, 2006). The allocation was concealed from the dentists by means of sealed envelopes, grouped in small blocks in order to keep the balance between groups (Altman and Bland, 1999). The envelope method has been criticized as a code that is easy to break; the block method has been criticized as it allows one to predict what comes next (Hulley et al., 2007). We chose the envelope method for logistic reasons, i.e., centralized on-line allocation was not available. Appropriate randomization allows the same chance for each study subject to be assigned to any group. However, in block randomization each patient has a chance to be allocated within the block and within the clinic, not within the study (Jadad et al., 1996). When blocking is used, the maximum difference between the numbers in the two groups should be half the block size, but 37 and 33 do not fully match half a block of 4-6-4-6, because each clinic had a separate set of envelopes (Altman and Doré, 1990).

Blinding was single, because both materials require different application techniques. The dentists performing the treatment usually examined the outcome and was not blinded, which might have introduced detection bias. Indeed, it has been shown that clinical trials that are not double-blind may have higher success rates, which is be due to bias (Juni et al., 2001). We had a low drop-out rate; only 11% of cases were lost to follow-up, four in the MTA group and four in the CH group. None of the individuals invited refused to take part in this RCT.

RCTs supply the highest grade of evidence (EBM working group, 1992). However, in *Study III* vulnerable groups such the age group older than 55 years, subjects with a contributory medical history and pregnant women, and subjects with periodontitis were not asked to participate, which may limit the generalizability of our study.

Statistical analyses

There has been much discussion on which epidemiological measurement is the most appropriate in cross-sectional studies (Hughes, 1995; Nurminen, 1995). Prevalence rates ratio (PRR) and OR are slightly different measurements and the argument against OR is that confounders might be introduced even if they do not exist (Axelson et al., 1994). Moreover, OR usually shows a stronger association then PRR, since the discrepancies between PRR and OR strongly depend on the prevalence of the exposure and the prevalence of the disease. When the prevalence of disease is very low (<10%), PRR and OR are very similar (Zocchetti et al., 1997). The use of OR in chronic disease might also be appropriate (Zocchetti et al., 1997). For the reasons mentioned above, we decided to calculate OR instead of PRR in *Study I.*

The use of logistic regression analysis was especially appropriate in *Studies I* and *II*, for two reasons: i) the outcomes were dichotomous (presence or absence of DCL-CC and preferred treatment method); and ii) to control for the confounding factors (Bray and Parkin, 2014). In S*tudy I*, multivariable binary logistic regression analysis was used to determine the association between DMFT score and background factors, because the variables DMFT score and bitewing examination interval did not fit the assumptions for a linear multivariable regression analysis. We chose an arbitrary cutoff point of 5 for DMFT score. In *Study I*, models using the outcome untreated deep carious lesions or extractions due to caries obtained acceptable results *(p>0.05)* in the Hosmer-Lemeshow goodness-of-fit test (IBM, 2010). All potential explanatory variables were used as independent variables and were adjusted for each other. DMFT and bitewing examination interval were used as independent continuous variables. DMFT score was

53

calculated using mathematical coupling (subtracting the number of molars with DCL-CC from the overall DMFT score) (Walsh and Lee, 1998). The multivariable binary logistic regression model, which was used to study the association between untreated deep carious lesions and background factors, explained 20% of the variation in the outcome. The other multivariable binary logistic regression model explained 15% of the variation in the outcome.

There are two types of interaction: statistical and biological (Rothman, 2002). Statistical interaction occurs when two independent variables interact to reduce or increase risk. However, as opposed to confounding, interaction association is informative (Rothman, 2002; Bhopal, 2008). In S*tudy I*, statistical interactions were estimated on a multiplicative scale among the independent variables in Table 4 and Table 5 using multivariable binary logistic regression analyses, but none one of them were statistically significant; therefore they were not included in the further analysis.

In *Study II*, the associations between background characteristics and preferred treatment methods were analyzed using multivariable binary logistic regression analyses. In total, eleven models were built for 4 different scenarios. The Hosmer-Lemeshow goodness-of-fit test yielded acceptable results ($p>0.05$) (IBM, 2010) for all models.

Kaplan-Meier survival curves and the log-rank test were performed in *Study III*, comparing the MTA and the CH groups. This test was used in recent studies in which time to outcome was measured with success rates that varied at different time points (Cho et al., 2013; Hilton et al., 2013; Mente et al., 2014). The Kaplan-Meier survival analysis is appropriate when there is just one factor to be studied, like material. Factors other than material may influence the survival rates of teeth with carious exposures treated by VPT. However, due to the limited number of subjects, multivariable Cox regression analysis could not be used in S*tudy III*.

There was some missing data in S*tudy I* due to missing information in the dental records, and in S*tudy II* due to missing information in the questionnaire. These missing data were

ignored in the analyses, as they were not of significant magnitude and influenced sample size on a minor level. No data was missing in *Study III*. Data from patients lost to follow-up was included in the log-rank test due to the nature of the analysis.

6.2 Deep carious lesions and other consequences of caries in Northern Norway

For 2 decades the prevalence of deep carious lesions in Northern Norway was unknown. The findings from *Study I* demonstrated that more than one-quarter of 18-year-olds registered in the PDHS in Troms County at the time of our study had DCL-CC. DCL-CC represents neglected caries, and this high prevalence in a well-educated, wealthy society is of concern.

Firstly, Northern Norway has always reported inferior oral health compared to the rest of the country (Helöe et al., 1980; Wang and Riordan, 1995; von der Fehr and Haugejorden, 1997; Statistics Norway, 2012). In S*tudy I*, our study sample of 18-year-olds already had a higher DMFT score than their counterparts in Southern Norway at 12 years of age (Statistics Norway, 2015). A study among Norwegians over 20 years of age reported that living in Northern Norway was one of the predictive factors for self-perceived inferior oral health (Ekornrud and Jensen, 2010). This situation might have been caused by a lack of GDPs in the PDHS and a high turnover rate of GDPs in Northern Norway (Helse- og omsorgsdepartementet, 2007).

The high prevalence of DCL-CC in Northern Norway might also be due to non-attendance to the PDHS. Indeed, around 80% of 18-year-olds are checked at PDHS yearly, and those who do not have regular check-ups have inferior dental status (Norwegian Board of Health, 1992; Skaret et al., 1998; Statistics Norway, 2015). Long recall intervals might also be among the reasons of high prevalence of DCL-CC. In S*tudy I* very little information regarding recalls could be retrieved, as only a few subjects (19%) with DCL-CC had recall dates in their dental records. However, one would assume that bitewing examination dates reflect recall dates. In *Study I*, longer bitewing examination intervals (every 6 months) were associated with untreated deep carious lesions. It is unclear whether longer recall intervals are associated with

negative outcomes, such as DMFS score increment (Wang et al., 1992; Wang and Riordan, 1995; Riley et al., 2013). It also has been demonstrated that individualized recall intervals did not reduce root canal obturations and extractions due to caries, which leads to questions regarding the general benefit of individualized recall intervals (Flink et al., 2013). The bitewing examination intervals in *Study I* varied between 4 and 72 months and were not in accordance with recall routines in Troms County, which call for intervals of 12 to 24 months. The reason for this difference is unknown.

The importance of caries prevention in Northern Norway has been stressed, and according to a personal communication with the Chief Dental Officer in Troms County, current prevention measures seem to be in accordance with the contemporary literature (Helöe et al., 1980; Ahovuo-Saloranta et al., 201; Weyant et al., 2013). Nevertheless, the high prevalence of both high DMFT score and of DCL-CC underlines the need for improvement in the management of early carious lesions. We did not have information on how long the subjects in our study had been enrolled in the PDHS. Moreover, the nationality of subjects was not recorded in this study, thus the effect of the foreign nationality could not be assessed (Bertea et al., 2007).

Only a small fraction (4%) of DCL-CC were untreated deep carious lesions. This finding reflects the major impact the PDHS has had in Northern Norway, as half a century ago the majority of the DMFT score consisted of the D component (Helöe et al., 1980). *Study I* demonstrated that about every fourth 18-year-old subject had at least one molar affected by DCL-CC. However, due to slightly different methodologies used in other studies (less deep untreated carious lesions and restorations, higher number of teeth analyzed, and different age groups) the prevalence of DCL-CC could not be directly compared to that in the rest of Norway or Scandinavia (Wang and Riordan, 1995; Amarante et al., 1998; Ridell et al., 2003; Hugoson et al., 2005; Ridell et al., 2008; Grytten et al., 2013). Nevertheless, in the light of existing

Scandinavian figures, *Study I* suggested a more severe caries situation in Northern Norway compared to the rest of Norway or Scandinavia.

Subjects with a higher DMFT score seemed to be more prone to DCL-CC; univariate logistic regression analyses showed DMFT score to be associated with all modalities of DCL-CC. A 1-unit increase in DMFT score (calculated using mathematical coupling) was associated with untreated deep carious lesions (adjusted OR=1.3) and extractions due to caries (adjusted OR=1.2) (Tables 4 and 5). This is in line with the study by Benzian and colleagues (2011), who demonstrated a direct link between DMFT score and the number of pulpal involvements and other consequences of untreated caries in mixed dentition.

Self-reported history of medical problems was associated with a DMFT score higher than 5 (adjusted OR=1.5) and extractions due to caries (adjusted OR=3.2). This finding is in line with a study from the USA, in which self-reported systemic diseases (hepatitis, asthma, high blood pressure, stroke, liver disease, and diabetes) were associated with a higher caries experience (Johnston and Vieira, 2014).

In *Study I*, urban/rural clinic location, which is linked with socio-economic status in Norway (Sjolie and Thuen, 2002), was not associated with either DMFT score or DCL-CC. In contrast to our findings, sparsely-populated areas in Norway have been shown to be associated with self-perceived inferior oral health in the adult population when dental service is not free-of-charge (Ekornrud and Jensen, 2010). Our results suggest that free-of-charge PDHS might diminish dental inequality.

6.3 Treatment preferences in Northern Norway

In *Study I*, 18-year-old subjects with DCL-CC had a higher DMFT score than those without DCL-CC. It is therefore reasonable to assume that they belong to a high caries risk group, and an increased risk of restoration failure has been reported in such groups (Demarco et al., 2012; Opdam et al., 2014). The overall median longevity of composite restorations in permanent

molars is limited. (Mjör et al., 2000; Vähänikkilä et al., 2014). When the time comes to replace deep restorations, the pulp is at risk of exposure. Consequently, the high prevalence of untreated/treated deep carious lesions (23%) found in *Study I* among 18-year-olds presents a challenge for further treatment. The lack of a uniform treatment preference was demonstrated in *Study II*, which is in accordance with previous surveys (Oen et al., 2007; Weber et al., 2011; Frisk et al., 2013; Schwendicke et al., 2013b). The absence of a uniform treatment procedure is probably due to the lack of consensus in the literature in this field. The dilemma about whether all caries should be excavated at the first visit is being debated (Ricketts et al., 2013; Schwendicke et al., 2013a). In S*tudy II*, when an adult patient presented with a deep carious lesion but no symptoms, only a half of the GDPs preferred TCE, which is less than the proportion reported in previous surveys from the USA, Brazil, and Germany (Oen et al., 2007; Schwendicke et al., 2013b; Weber et al., 2011). GDPs gave IPC as their least preferred treatment for deep carious lesions in *Study II*, which is in accordance with the above-mentioned surveys. For carious exposure in adults, textbooks and guidelines give pulpectomy as the only treatment method (European Society of Endodontology, 2006; Hasselgren, 2008; Socialstyrelsen, 2011). However, when no symptoms were present, VPT was preferred by more than a half of the GDPs in *Study II*, which is in line with results from the USA, Sweden, and Germany (Frisk et al., 2013; Oen et al., 2007; Schwendicke et al., 2013b). Although the use of VPT is against the recommendations, its use would be more understandable if MTA were the preferred capping material, but about 75% of the GPDs chose CH (as a slurry and/or paste), although both PP and DPC with CH have been shown to yield low success ($< 35\%$) in a recent randomized trial in which both age and origin of exposure were controlled for simultaneously (Bjørndal et al., 2010).

Is it not clear which evidence GDPs follow, and at which point they assume there is enough evidence to adopt a new treatment method, but it is likely they make their decisions

based on a subjective interpretation, with no universally accepted logical rules (Shahar, 1997). Subjective interpretation can be influenced by scientific knowledge (endodontist, cariologist, clinical pragmatic, etc.), clinical experience, and traditions (Bjørndal and Kidd, 2005; Bjørndal, 2008). In S*tudy II,* graduation from a dental school in Norway was associated with the use of conservative treatment options (SWE and IPC) for deep carious lesions, but graduation in Norway and 5 or more years in practice was associated with pulpectomy followed by endodontic treatment in cases of carious exposure accompanied by symptoms. Our finding on the influence of number of years in practice was in line with two other surveys (Weber et al., 2011; Frisk et al., 2013) and might indicate that those with fewer years in practice are avoiding pulpectomy, as root canal treatment might be considered difficult and time consuming. Another possibility is that GDPs with fewer years in practice are more prone to follow recent evidence, but this interpretation is questionable, since CH, not MTA, was still the most preferred material for DPC.

As has been discussed in a previous survey from Brazil, the lack of uniformity in GDPs preferences might be perceived as an "art of dentistry", but this variability may also have a negative impact on the quality of care (Weber et al., 2011). In *Study II*, in the absence of carious exposure but the presence of symptoms, four out of 10 GDPs preferred pulpectomy. There is no substantiation for this in any of the dental literature, as the symptoms were intentionally described to refer to reversible pulpitis at most ("sharp transient pain or sensitivity to hot/cold", (Appendix 1). In such a scenario, SWE or IPC would have an excellent prognosis; even endodontics could not compete (Jordan and Suzuki, 1971; Bjørndal and Thylstrup, 1998; Maltz et al., 2012a). Therefore it is crucial to have guidelines and to follow them. Nevertheless, the present results showed that GDPs' preference was influenced by other factors, such as patient's oral health, final restoration, and patient's age, not just by diagnosis and treatment options, which is in line with an earlier study (Kay and Blinkhorn, 1996).

The goal of *Study II* was to learn about treatment preferences and routines; however studies based on data from self-administered questionnaires should be taken with caution. Indeed, in case of uncertainty, heuristic reasoning (intuitive, automatic, implicit processing) plays an important role in treatment preferences (Hicks and Kluemper, 2011).

6.4 MTA and CH as a direct pulp capping material for carious exposures in adults

CH and MTA perform well, almost flawlessly when it comes to children and adolescents, regardless of the state of the root apex (open/closed). Therefore more focus should be placed on the performance of these materials in adult teeth. There are indications that MTA performs better than CH in adult teeth, but so far no comparative prospective study on adults only has been published to show this (Table 2).

In *Study III,* an imbalance in groups regarding depth of carious lesions assessed from radiographs was detected at baseline. The depth of a carious lesion is one of the most important factors of pulp healing potential (Bjørndal et al., 2014a). However, keeping in mind the two-dimensional presentation of a radiograph, and the fact that in *Study III* dentists performing treatment were not given instructions as to how to evaluate the radiographic depth of the lesion, this measurement might be subjective and not valid. Also, the depth of the lesion might have more influence when choosing between TCE, SWE, and IPC, in which no exposures are involved, but in *Study III* each case that was randomized presented with *de facto* clinical carious exposures, regardless of the depth assessed from radiographs taken prior to the excavation.

The results of *Study III* favored MTA (survival rate of 80%) over CH (survival rate of 46%). This finding is in accordance with other studies, although they are not fully comparable as previous studies included children and adults with a mixed origin of exposures (Cho et al., 2013; Hilton et al., 2013; Mente et al., 2014). CH may not be perceived anymore as a gold standard. In order to assess whether the success rate of DPC with MTA in adults is high enough to warrant the routine use of these methods, it should be compared with that of pulpectomy

followed by root canal treatment. The two most recent meta-analyses on orthograde root canal treatment demonstrated an average survival rate of 83%-86% in teeth that were vital or without an apical lesion (Kojima et al., 2004; Ng et al., 2010). It may be argued that for a GDP, DPC is easier to learn and master compared to the root canal treatment, which is relatively complicated. However, a retrospective study demonstrated an almost 90% success rate of pulpectomy followed by root canal treatment 5 years after the procedure performed by GDPs (Alley et al., 2004).

Study III demonstrated a high survival rate in the MTA group, similar to that reported by Hilton and colleagues (2013), but lower than the rate reported in a prospective study by Bogen and colleagues (2008). However, the study by Bogen and colleagues also comprised children and adolescents, with more than half of the patients being younger than 18 years. Thus the higher success rate in their study could have been anticipated, as study by Qudeimat and colleagues (2007) showed a more than 90% success rate in adolescents after PP with both CH and MTA.

After DPC of carious exposures in adults, S*tudy III* demonstrated a higher estimated survival rate in the CH group, 46% compared to the 31.8% found in a recent Scandinavian multicenter RCT by Bjørndal and colleagues (2010), despite the fact that *Study III* had more than double the follow-up time. Patients with deeper carious lesions (3/4 vs. ≥2/3) were recruited in the latter study and a rubber-dam was placed after *de facto* the carious exposure, which may have a negative impact on their results. *Study II* indicated that less than 20% of the respondents used rubber-dams at all while treating carious exposures. Although one out of the four clinics recruiting patients for S*tudy III* violated protocol by not using a rubber-dam, the survival/failure rate in this clinic was the highest (combining both groups) at 4.4, compared to the average of the rest of the clinics. This calls into question the impact of rubber-dam use in the overall success of DPC, as does a study by de Lourdes Rodrigues Accorinte and colleagues

in which using of rubber-dam showed no difference in pulp healing after DPC with CH in caries-free molars (de Lourdes Rodrigues Accorinte et al., 2006).

In *Study II*, symptoms that indicated reversible pulpitis at most, led to a higher rate of preference for pulpectomy, both in the absence and the presence of carious exposure. This is in contrast with the literature, as reversible inflamed pulp has the potential to heal (Torabinejad and Shabahang, 2009; Ricucci et al., 2014b). In S*tudy III*, the survival rate of molars with preoperative symptoms (indicating reversible pulpitis at most) were not statistically significantly different from the survival rate of molars that did not show any preoperative symptoms. This finding is in accordance with other studies investigating carious exposures (Shovelton et al., 1971; Matsuo et al., 1996) and a systematic review investigating deep carious lesions (Schwendicke et al., 2013c). In contrast, in cases of deep carious lesions without carious exposure, preoperative pain was associated with lower success rates of TCE and SWE (Bjørndal et al., 2010). However, there is no clear association between signs and symptoms of pain and actual pulp status (Mejàre et al., 2012).

In *Study III*, no significant association was detected between the materials and 1 week postoperative pain relief or occurrence. This is in line with a Scandinavian RCT comparing TCE and SWE, which reported no significant difference in postoperative pain relief 1 week after treatment (Bjørndal et al., 2010). In *Study III*, there were fewer molars with postoperative pain after 1 week compared to baseline in both the MTA and CH groups. This is in contrast with an earlier clinical/histological study, also restricted to adults, in which a statistically significant increase in symptoms from baseline to 1 week post-procedure was documented after DPC with CH. But no relation between symptoms and histopathology was found (Fitzgerald and Heys, 1991).

6.5 Future perspectives

Future research perspectives

A high prevalence of 18-year-olds with DCL-CC and who are leaving the free-of-charge PDHS is of concern. Recall dates could only be recorded in a limited number of subjects, and the results from *Study I* were not in line with the recall strategy described by the Chief Dental Officer in Troms County. The effect of recall routines on the prevalence of caries in Troms County is unknown.

There were indications that the PDHS might eliminate dental inequalities related to socio-economic status. Strong socio-economic variables, such as parental education, occupation, and income, should be included in future studies to reveal the impact of PDHS on dental inequalities.

History of medical problems was associated with a higher DMFT score and extractions due to caries, which is in line with other studies (Alavaikko et al., 2011; Anjomshoaa et al., 2009; Johnston and Vieira, 2014; Little, 2002). To avoid temporal bias, studies with a longitudinal design are needed to study the association between contributory medical history and the prevalence of caries.

Knowledge regarding the prognostic factors for successful VPT other than material is still lacking. Previous studies have demonstrated that people in younger age groups have better healing potential due to more blood flow (Cho et al., 2013; Hørsted et al., 1985; Stanley, 1989), while others did not find any such association (Haskell et al., 1978; Matsuo et al., 1996; Barthel et al., 2000; Al-Hiyasat et al., 2006; Mente et al., 2014). The successful outcome of VPT in carious exposures might also depend on: i) the location of the exposure (Benoist et al., 2012; Cho et al., 2013); ii) the integrity of the cavity restoration (Mjör, 2002); and iii) the extent of the lesion (Maltz et al., 2012a). A prospective study using multivariable Cox regression analysis might answer this question.

Clinical recommendations

Targeting caries management to subjects with high DMFT scores in the PDHS might reduce the prevalence of cases with compromised pulps.

Since GDPs in Northern Norway have no uniform strategy for the management of deep carious lesions, often the preferred treatment methods reported were not the best available. Continuous education courses that can inform GDPs about less invasive treatment approaches in cases of carious lesions with reversible pulpitis and could synchronize preferences.

The high success rate of DPC with MTA strengthens the evidence for VPT for carious exposures in adults and might challenge established treatment recommendations.

7. CONCLUDING REMARKS

Study I was the first in 2 decades to assess DCL-CC in Northern Norway. At the age of 18 years, subjects registered in the PDHS in Troms County showed a high prevalence of DCL-CC; more than one-fourth had at least one molar affected. Of those with affected molars, almost one in four had untreated deep carious lesions or deep restorations. Of all molars with DCL-CC, more than a quarter had the most severe modalities: root canal obturations and extractions due to caries. One of the most important goals of the PDHS is the early detection and management of carious lesions in order to prevent DCL-CC. Therefore assessing the prevalence of DCL-CC was an innovative angle by which to address the effectiveness of the free-of-charge PDHS. The overall management of carious lesions should be improved and in cases of untreated deep carious lesions and deep restorations, efforts should be made to maintain pulp vitality.

Our survey on the current preferences and clinical routines for the management of deep carious lesions was the first performed in Northern Norway and showed that there was no uniform treatment method for deep carious lesions in mature, permanent, vital teeth. Moreover, treatment methods that are not in accordance with the current literature were preferred: TCE and pulpectomy followed by root canal treatment were preferred in cases of no carious exposure, while in cases of carious exposure the majority of dentists preferred DPC using mainly CH.

MTA performed significantly better, compared with the gold standard of CH, as a pulp capping material in a unique RCT restricted to adults with carious exposures only. In general, the 80% survival rate in the MTA group could be compared with the success rate of pulpectomy followed by root canal treatment. *Study III* is still ongoing, but already provides evidence that suggests a paradigm shift from pulpectomy followed by root canal treatment to VPT for the treatment of carious exposures in adults.

REFERENCES:

Abramson JH (1990). Constructig a questionnaire. In: Survey methods in community medicine Edinburgh, UK: Churchill Livingstone.

Aguilar P, Linsuwanont P (2011). Vital pulp therapy in vital permanent teeth with cariously exposed pulp: a systematic review. *J Endod* 37(5)*:*581-587.

Ahovuo-Saloranta A, Forss H, Walsh T, Hiiri A, Nordblad A, Mäkelä M *et al.* (2013). Sealants for preventing dental decay in the permanent teeth. *Cochrane Database Syst Rev* 3(CD001830.

Al-Hiyasat AS, Barrieshi-Nusair KM, Al-Omari MA (2006). The radiographic outcomes of direct pulp-capping procedures performed by dental students: a retrospective study. *J Am Dent Assoc* 137(12)*:*1699-1705.

Alavaikko S, Jaakkola MS, Tjäderhane L, Jaakkola JJ (2011). Asthma and caries: a systematic review and meta-analysis. *Am J Epidemiol* 174(6)*:*631-641.

Alley BS, Kitchens GG, Alley LW, Eleazer PD (2004). A comparison of survival of teeth following endodontic treatment performed by general dentists or by specialists. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 98(1)*:*115-118.

Altman DG (1985). Comparability of randomised groups. *J R Stat Soc Series D Statistician* 34(1)*:*125-136.

Altman DG, Doré CJ (1990). Randomisation and baseline comparisons in clinical trials. *Lancet* 335(8682)*:*149-153.

Altman DG (1991). Randomisation. *BMJ (Clinical research ed)* 302(6791)*:*1481-1482.

Altman DG, Bland JM (1999). How to randomise. *BMJ (Clinical research ed)* 319(7211)*:*703-704.

Amarante E, Raadal M, Espelid I (1998). Impact of diagnostic criteria on the prevalence of dental caries in Norwegian children aged 5, 12 and 18 years. *Community Dent Oral Epidemiol* 26(2)*:*87-94.

Anjomshoaa I, Cooper ME, Vieira AR (2009). Caries is associated with asthma and epilepsy. *European journal of dentistry* 3(4)*:*297-303.

Axelson O, Fredriksson M, Ekberg K (1994). Use of the prevalence ratio v the prevalence odds ratio as a measure of risk in cross sectional studies. *Occupational and environmental medicine* 51(8)*:*574.

Barngkgei IH, Halboub ES, Alboni RS (2013). Pulpotomy of symptomatic permanent teeth with carious exposure using mineral trioxide aggregate. *Iranian endodontic journal* 8(2)*:*65-68.

Barrieshi-Nusair KM, Qudeimat MA (2006). A prospective clinical study of mineral trioxide aggregate for partial pulpotomy in cariously exposed permanent teeth. J Endod 32(8):731-735.

Barthel CR, Rosenkranz B, Leuenberg A, Roulet JF (2000). Pulp capping of carious exposures: treatment outcome after 5 and 10 years: a retrospective study. *J Endod* 26(9):525-528.

Baruch Y (1999). Response rate in academic studies - a comparative analysis. *Hum Relat* 52(4):421-438.

Baume LJ, Holz J (1981). Long term clinical assessment of direct pulp capping. *Int Dent J* 31(4):251-260.

Beaglehole R, Benzian H, Crail J, Mackay J (2009). The oral health atlas mapping neglected global health issue Brighton, UK: Myriad Editions.

Benoist FL, Ndiaye FG, Kane AW, Benoist HM, Farge P (2012). Evaluation of mineral trioxide aggregate (MTA) versus calcium hydroxide cement (Dycal®) in the formation of a dentine bridge: a randomised controlled trial. *Int Dent J* 62(1):33-39.

Benzian H, Monse B, Heinrich-Weltzien R, Hobdell M, Mulder J, van Palenstein Helderman W (2011). Untreated severe dental decay: a neglected determinant of low Body Mass Index in 12-year-old Filipino children. *BMC Public Health* 11(1):558.

Bergenholtz G, Axelsson S, Davidson T, Frisk F, Hakeberg M, Kvist T *et al.* (2013). Treatment of pulps in teeth affected by deep caries – a systematic review of the literature. *Singapore Dent J* 34(1):1-12.

Berk H (1957). Preservation of the dental pulp in deep seated cavities. *J Am Dent Assoc* 54(2):226-233.

Bertea PC, Staehelin K, Dratva J, Stutz EZ (2007). Female gender is associated with dental care and dental hygiene, but not with complete dentition in the Swiss adult population. *J Public Health* 15(5):361-367.

Bhopal R (2008). Concepts of epidemiology. Integrating the ideas, theories, principles and methods of epidemiology. 2nd ed. Oxford, United Kingdom: Oxford university press.

Birkeland JM, Haugejorden O, von der Fehr FR (2002). Analyses of the caries decline and incidence among Norwegian adolescents 1985-2000. *Acta Odontol Scand* 60(5):281-289.

Bjørndal L, Larsen T, Thylstrup A (1997). A clinical and microbiological study of deep carious lesions during stepwise excavation using long treatment intervals. *Caries Res* 31(6):411-417.

Bjørndal L, Thylstrup A (1998). A practice-based study on stepwise excavation of deep carious lesions in permanent teeth: a 1-year follow-up study. *Community Dent Oral Epidemiol* 26(2):122-128.

Bjørndal L, Darvann T (1999). A light microscopic study of odontoblastic and non-odontoblastic cells involved in tertiary dentinogenesis in well-defined cavitated carious lesions. *Caries Res* 33(1):50-60.

Bjørndal L, Larsen T (2000). Changes in the cultivable flora in deep carious lesions following a stepwise excavation procedure. *Caries Res* 34(6):502-508.

Bjørndal L, Kidd EA (2005). The treatment of deep dentine caries lesions. *Dent Update* 32(7):402-404, 407-410, 413.

Bjørndal L (2008). The caries process and its effect on the pulp: the science is changing and so is our understanding. *J Endod* 34(7, Supplement):S2-5.

Bjørndal L, Reit C, Bruun G, Markvart M, Kjældgaard M, Nasman P *et al.* (2010). Treatment of deep caries lesions in adults: randomized clinical trials comparing stepwise vs. direct complete excavation, and direct pulp capping vs. partial pulpotomy. *Eur J Oral Sci* 118(3):290-297.

Bjørndal L, Demant S, Dabelsteen S (2014). Depth and activity of carious lesions as indicators for the regenerative potential of dental pulp after intervention. *J Endod* 40(4 Suppl):S76-81.

Bloemendal E, de Vet HCW, Bouter LM (2004). The value of bitewing radiographs in epidemiological caries research: a systematic review of the literature. *J Dent* 32(4):255-264.

Bodecker CF (1938). Histologic evidence of the benefits of temporary fillings and successful pulp capping of deciduous teeth. *J Am Dent Assoc* 25(777-788.

Bogen G, Kim JS, Bakland LK (2008). Direct pulp capping with mineral trioxide aggregate: an observational study. *J Am Dent Assoc* 139(3):305-315.

Bray F, Parkin DM (2014). Descriptive studies. In: Handbook of epidemiology. W Ahrens and P I. editors. New York: Springer Reference, pp. 187-258.

Chailertvanitkul P, Paphangkorakit J, Sooksantisakoonchai N, Pumas N, Pairojamornyoot W, Leela-Apiradee N *et al.* (2013). Randomized control trial comparing calcium hydroxide and mineral trioxide aggregate for partial pulpotomies in cariously exposed pulps of permanent molars. *Int Endod J* 47(9):835-842.

Changing patterns of oral health and implications for oral health manpower: Part I. Report of a Working Group convened jointly by the Federation Dentaire Internationale and the World Health Organisation. (1985). *Int Dent J* 35(3):235-251.

Cho SY, Seo DG, Lee SJ, Lee J, Lee SJ, Jung IY (2013). Prognostic factors for clinical outcomes according to time after direct pulp capping. *J Endod* 39(3):327-331.

Cohen J (1960). A coefficient of agreement for nominal scales. *Educ Psychol Meas* 20(1):37-46.

Corralo DJ, Maltz M (2013). Clinical and ultrastructural effects of different liners/restorative materials on deep carious dentin: a randomized clinical trial. *Caries Res* 47(3):243-250.

Crone FL (1968). Deep dentinal caries from a microbiological point of view. *Int Dent J* 18(3):481-488.

Cvek M (1978). A clinical report on partial pulpotomy and capping with calcium hydroxide in permanent incisors with complicated crown fracture. *J Endod* 4(8)*:*232-237.

da Silva RP, Assaf AV, Pereira SM, Ambrosano GM, Mialhe FL, Pereira AC (2011a). Reproducibility of adjunct techniques for diagnosis of dental caries in an epidemiological situation. *Oral Health Prev Dent* 9(3)*:*251-259.

da Silva RP, Assaf AV, Pereira SM, Mialhe FL, Ambrosano GM, Meneghim Mde C *et al.* (2011b). Validity of caries-detection methods under epidemiological setting. *Am J Dent* 24(6)*:*363-366.

Dammaschke T (2008). The history of direct pulp capping. *Journal of the history of dentistry* 56(1)*:*9-23.

de Lourdes Rodrigues Accorinte M, Reis A, Dourado Loguercio A, Cavalcanti de Araujo V, Muench A (2006). Influence of rubber dam isolation on human pulp responses after capping with calcium hydroxide and an adhesive system. *Quintessence Int* 37(3)*:*205-212.

Demarco FF, Corrêa MB, Cenci MS, Moraes RR, Opdam NJM (2012). Longevity of posterior composite restorations: not only a matter of materials. *Dent Mater* 28(1)*:*87-101.

Edwards PJ, Roberts IG, Clarke MJ, DiGuiseppi C, Wentz R, Kwan I *et al.* (2007). Methods to increase response rates to postal questionnaires. *Cochrane Database Syst Rev* 18(2)*:*MR000008.

Eidelman E, Finn SB, Koulourides T (1965). Remineralization of carious dentin treated with calcium hydroxide. *J Dent Child* 32(4)*:*218-225.

Ekornrud T, Jensen A (2010). Tannhelsetilstand og tannlegetenester. Analysar av regionale og sosiale skilnader i eigenvurdert tannhelse, tannstatus, bruk av tannlegetenester og eigenbetaling hos tannlege. *Statistics Norway* Oslo: Statistisk sentralbyrå(Available online at: https://www.ssb.no/a/publikasjoner/pdf/rapp_201051/rapp_201051.pdf. Last access: 201020.201001.202015.

Ekstrand KR, Ricketts DN, Kidd EA (1997). Reproducibility and accuracy of three methods for assessment of demineralization depth of the occlusal surface: an in vitro examination. Caries Res 31(3):224-231.

European Society of Endodontology (2006). Quality guidelines for endodontic treatment: consensus report of the European Society of Endodontology. *Int Endod J* 39(12)*:*921-930.

Falster CA, Araujo FB, Straffon LH, Nor JE (2002). Indirect pulp treatment: in vivo outcomes of an adhesive resin system vs calcium hydroxide for protection of the dentin-pulp complex. *Pediatric dentistry* 24(3)*:*241-248.

Ferracane JL, Cooper PR, Smith AJ (2010). Can interaction of materials with the dentin-pulp complex contribute to dentin regeneration? *Odontology / the Society of the Nippon Dental University* 98(1)*:*2-14.

Fink A (2014). Epidemiological field work in population-based studies. In: Handbook of epidemiology. W Ahrens and I Pigeot editors. New Your, USA: Springer References, pp. 577-611.

Fitzgerald M, Heys RJ (1991). A clinical and histological evaluation of conservative pulpal therapy in human teeth. *Oper Dent* 16(3):101-112.

Flink H, Tegelberg Å, Arnetz J, Birkhed D (2013). Correlation between perceived experience of caries disease and recorded caries activity among adult patients at a Swedish Public Dental Clinic: a longitudinal study. *Acta Odontol Scand* 71(6):1486-1492.

Fridland M, Rosado R (2005). MTA solubility: a long term study. *J Endod* 31(5):376-379.

Frisk F, Kvist T, Axelsson S, Bergenholtz G, Davidson T, Mejare I *et al.* (2013). Pulp exposures in adults - choice of treatment among Swedish dentists. *Swed Dent J* 37(3):153-160.

Fusayama T, Terachima S (1972). Differentiation of two layers of carious dentin by staining. *J Dent Res* 51(3):866.

Fusayama T (1979). Two layers of carious dentin: diagnosis and treatment. *Oper Dent* 4(2):63-70.

Glass RL, Zander HA (1949). Pulp healing. *J Dent Res* 28(2):97-107.

Gluud LL (2006). Bias in clinical intervention research. *Am J Epidemiol* 163(6):493-501.

Goodis HE, Marshall, S., Franklin, R.T., Marshal Jr, G.W. (2012). Repair of pulpal injury with dental materials. In: Seltzer and Bender`s dental pulp. KM Hargreaves, Goodis, H.E., Franklin R.T., editor. Chicago, IL, USA: Quintessence Publish. Co., Inc.

Graham L, Cooper PR, Cassidy N, Nor JE, Sloan AJ, Smith AJ (2006). The effect of calcium hydroxide on solubilisation of bio-active dentine matrix components. *Biomaterials* 27(14):2865-2873.

group Ew (1992). Evidence-based medicine. A new approach to teaching the practice of medicine. *Jama* 268(17):2420-2425.

Gruythuysen R, van Strijp G, Wu M-K (2010). Long-term survival of indirect pulp treatment performed in primary and permanent teeth with clinically diagnosed deep carious lesions. *J Endod* 36(9):1490-1493.

Grytten J, Holst D, Skau I (2013). Per capita remuneration of dentists and the quality of dental services. *Community Dent Oral Epidemiol* 41(5):395-400.

Haskell EW, Stanley HR, Chellemi J, Stringfellow H (1978). Direct pulp capping treatment: a long-term follow-up. *J Am Dent Assoc* 97(4):607-612.

Hasler J, Mitchell D (1970). Painless pulpitis. *J Am Dent Assoc* 81(3):671-677.

Hasselgren G, Reit C (1989). Emergency pulpotomy: pain relieving effect with and without the use of sedative dressings. *J Endod* 15(6)*:*254-256.

Hasselgren G (2008). Treatment of the exposed pulp-dentin complex. In: Essential endodontology: prevention and treatment of apical periodontitis. D Ørstavik and T Pitt Ford editors. Oxford: Blackwell Munksgaard, pp. 303.

Haugejorden O (1994). Changing time trend in caries prevalence in Norwegian children and adolescents. *Community Dent Oral Epidemiol* 22(4)*:*220-225.

Helse- og omsorgsdepartementet (2007). Tilgjengelighet, kompetanse og sosial utjevning. Framtidas tannhelsetjenester. Stortingsmelding Nr. 35 (2006-2007), . Dagens situasjon Bakgrunn og utviklingstrekk. Oslo, pp. 42-43.

Helöe LA, Haugejorden O, Helöe B (1980). The short-and long-term effects of organized public dental programs. *J Dent Res* DII(59)*:*2253-2258.

Hicks EP, Kluemper GT (2011). Heuristic reasoning and cognitive biases: are they hindrances to judgments and decision making in orthodontics? *Am Journal Orthod Dentofacial Orthop* 139(3)*:*297-304.

Hilton TJ, Ferracane JL, Mancl L, NWP (2013). Comparison of CaOH with MTA for direct pulp capping: a PBRN randomized clinical trial. *J Dent Res* 92(7 suppl)*:*S16-22.

Hughes K (1995). Odds ratios in cross-sectional studies. *Int J Epidemiol* 24(2)*:*463-464, 468.

Hugoson A, Koch G, Gothberg C, Helkimo A, Lundin S, Norderyd O *et al.* (2005). Oral health of individuals aged 3-80 years in Jönköping, Sweden during 30 years (1973-2003). II. Review of clinical and radiographic findings. *Swed Dent J* 29(4)*:*139-155.

Hulley SB, Cummings SR, Browner WS, Grady DG, Newman TB (2007). Designing clinical research. Third ed. Philadelphia, USA: Wolter Kluwe Health Lippincott Williams & Wilkins.

Hume C, Ball K, Salmon J (2006). Development and reliability of a self-report questionnaire to examine children's perceptions of the physical activity environment at home and in the neighbourhood. *International J Behav Nutr Phys Act* 17(3)*:*16.

Hørsted P, Sandergaard B, Thylstrup A, El Attar K, Fejerskov O (1985). A retrospective study of direct pulp capping with calcium hydroxide compounds. *Endod Dent Traumatol* 1(1)*:*29-34.

IBM SPSS Regression 19 manuals (2010). Last accessed: 2014 06 24.

Ismail AI, Sohn W, Tellez M, Amaya A, Sen A, Hasson H *et al.* (2007). The International Caries Detection and Assessment System (ICDAS): an integrated system for measuring dental caries. *Community Dent Oral Epidemiol* 35(3)*:*170-178.

Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ *et al.* (1996). Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Controlled clinical trials* 17(1)*:*1-12.

Johnston L, Vieira AR (2014). Caries experience and overall health status. *Oral Health Prev Dent* 12(2)*:*163-170.

Jones TV, Gerrity MS, Earp J (1990). Written case simulations: do they predict physicians' behavior? *J Clin Epidemiol* 43(8)*:*805-815.

Jordan RE, Suzuki M (1971). Conservative treatment of deep carious lesions. *J Can Dent Assoc (Tor)* 37(9)*:*337-342.

Juni P, Altman DG, Egger M (2001). Systematic reviews in health care: assessing the quality of controlled clinical trials. *BMJ (Clinical research ed)* 323(7303)*:*42-46.

Kakehashi S, Stanley HR, Fitzgerald RJ (1965). The effects of surgical exposures of dental pulps in germ-free and conventional laboratory rats. *Oral Surg Oral Med Oral Pathol* 20(340-349.

Kay EJ, Blinkhorn AS (1996). A qualitative investigation of factors governing dentists' treatment philosophies. *Br Dent J* 180(5)*:*171-176.

Kerkhove BC, Jr., Herman SC, Klein AI, McDonald RE (1967). A clinical and television densitometric evaluation of the indirect pulp capping technique. *J Dent Child* 34(3)*:*192-201.

Kidd EA, Joyston-Bechal S, Beighton D (1993a). The use of a caries detector dye during cavity preparation: a microbiological assessment. *Br Dent J* 174(7)*:*245-248.

Kidd EA, Joyston-Bechal S, Beighton D (1993b). Microbiological validation of assessments of caries activity during cavity preparation. *Caries Res* 27(5)*:*402-408.

Kidd EA, Ricketts DN, Beighton D (1996). Criteria for caries removal at the enamel-dentine junction: a clinical and microbiological study. *Br Dent J* 180(8)*:*287-291.

Kidd EA (2004). How "clean" must a cavity be before restoration? *Caries Res* 38(3)*:*305-313.

King JB, Jr., Crawford JJ, Lindahl RL (1965). Indirect pulp capping: a bacteriologic study of deep carious dentine in human teeth. *Oral Surg Oral Med Oral Pathol* 20(5)*:*663-669.

Kojima K, Inamoto K, Nagamatsu K, Hara A, Nakata K, Morita I *et al.* (2004). Success rate of endodontic treatment of teeth with vital and nonvital pulps. A meta-analysis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 97(1)*:*95-99.

Kroncke A (1970). Treatment of deep carious lesions. *Int Dent J* 20(2)*:*338-343.

Lager A, Thornqvist E, Ericson D (2003). Cultivatable bacteria in dentine after caries excavation using rose-bur or carisolv. *Caries Res* 37(3)*:*206-211.

Landis JR, Koch GG (1977). The measurement of observer agreement for categorical data. *Biometrics* 33(1)*:*159-174.

Langeland K (1987). Tissue response to dental caries. *Endod Dent Traumatol* 3(4)*:*149 171.

Laurent P, Camps J, About I (2012). Biodentine(TM) induces TGF-beta1 release from human pulp cells and early dental pulp mineralization. *Int Endod J* 45(5):439-448.

Lee SJ, Monsef M, Torabinejad M (1993). Sealing ability of a mineral trioxide aggregate for repair of lateral root perforations. *J Endod* 19(11):541-544.

Leksell E, Ridell K, cvek M, Mejare I (1996). Pulp exposure after stepwise versus direct complete excavation of deep carious lesions in young posterior permanent teeth. *Endod Dent Traumatol* 12(4):192-196.

Leung RL, Loesche WJ, Charbeneau GT (1980). Effect of Dycal on bacteria in deep carious lesions. *J Am Dent Assoc* 100(2):193-197.

Levin LG, Law AS, Holland GR, Abbott PV, Roda RS (2009). Identify and define all diagnostic terms for pulpal health and disease states. *J Endod* 35(12):1645-1657.

Lewis R, Smith BG (1988). A clinical survey of failed post retained crowns. *Br Dent J* 165(3):95-97.

Little JW (2002). Eating disorders: dental implications. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 93(2):138-143.

Maltz M, de Oliveira EF, Fontanella V, Bianchi R (2002). A clinical, microbiologic, and radiographic study of deep caries lesions after incomplete caries removal. *Quintessence Int* 33(2):151-159.

Maltz M, Alves LS, Jardim JJ, Moura Mdos S, de Oliveira EF (2011). Incomplete caries removal in deep lesions: a 10-year prospective study. *Am J Dent* 24(4):211-214.

Maltz M, Garcia R, Jardim JJ, de Paula LM, Yamaguti PM, Moura MS *et al.* (2012a). Randomized trial of partial vs. stepwise caries removal: 3-year follow-up. *J Dent Res* 91(11):1026-1031.

Maltz M, Henz SL, de Oliveira EF, Jardim JJ (2012b). Conventional caries removal and sealed caries in permanent teeth: a microbiological evaluation. *J Dent* 40(9):776-782.

Maltz M, Jardim JJ, Mestrinho HD, Yamaguti PM, Podestá K, Moura MS *et al.* (2013). Partial removal of carious dentine: a multicenter randomized controlled trial and 18-month follow-up results. *Caries Res* 47(2):103-109.

Marthaler T, O'Mullane D, Vrbic V (1996). The prevalence of dental caries in Europe 1990-1995. ORCA Saturday afternoon symposium 1995. *Caries Res* 30(4):237-255.

Marthaler TM (2004). Changes in Dental Caries 1953–2003. *Caries Res* 38(3):173-181.

Mass E, Zilberman U (1993). Clinical and radiographic evaluation of partial pulpotomy in carious exposure of permanent molars. *Pediatric dentistry* 15(4):257-259.

Massler M (1967). Pulpal reactions to dental caries. *Int Dent J* 17(2):441-460.

Massler M, Pawlak J (1977). The affected and infected pulp. *Oral Surg Oral Med Oral Pathol* 43(6):929-947.

Matsuo T, Nakanishi T, Shimizu H, Ebisu S (1996). A clinical study of direct pulp capping applied to carious-exposed pulps. *J Endod* 22(10):551-556.

Mejàre I, Cvek M (1993). Partial pulpotomy in young permanent teeth with deep carious lesions. *Endod Dent Traumatol* 9(6):238-242.

Mejàre IA, Axelsson S, Davidson T, Frisk F, Hakeberg M, Kvist T *et al.* (2012). Diagnosis of the condition of the dental pulp: a systematic review. *Int Endod J* 45(7):597-613.

Mente J, Geletneky B, Ohle M, Koch MJ, Friedrich Ding PG, Wolff D et al. (2010). Mineral Trioxide Aggregate or Calcium Hydroxide Direct Pulp Capping: An Analysis of the Clinical Treatment Outcome. Journal of Endodontics 36(5):806-813.

Mente J, Hufnagel S, Leo M, Michel A, Gehrig H, Panagidis D *et al.* (2014). Treatment outcome of mineral trioxide aggregate or calcium hydroxide direct pulp capping: long-term results. *J Endod* 40(11):1746-1751.

Mertz-Fairhurst EJ, Curtis JWJ, Ergle JW, Rueggeberg FA, Adair SM (1998). Ultraconservative and cariostatic sealed restorations: results at year 10. *J Am Dent Assoc* 129(1):55-66.

Michaelson PL, Holland GR (2002). Is pulpitis painful? *Int Endod J* 35(10):829-832.

Miles JP, Gluskin AH, Chambers D, Peters OA (2010). Pulp capping with mineral trioxide aggregate (MTA): a retrospective analysis of carious pulp exposures treated by undergraduate dental students. Oper Dent 35(1):20-28.

Miller WA, Massler M (1962). Permeability and staining of active and arrested lesions in dentine. *Br Dent J* 1962(187-197.

Miyashita H, Worthington HV, Qualtrough A, Plasschaert A (2007). Pulp management for caries in adults: maintaining pulp vitality. *Cochrane Database Syst Rev* 18(2):CD004484.

Miyauchi H, Iwaku M, Fusayama T (1978). Physiological recalcification of carious dentin. *The Bulletin of Tokyo Medical and Dental University* 25(3):169-179.

Mjör IA, Dahl JE, Moorhead JE (2000). Age of restorations at replacement in permanent teeth in general dental practice. *Acta Odontol Scand* 58(3):97-101.

Mjör IA (2002). Pulp-dentin biology in restorative dentistry. Part 7: The exposed pulp. *Quintessence Int* 33(2):113-135.

Murray PE, Smith AJ, Windsor LJ, Mjör IA (2003). Remaining dentine thickness and human pulp responses. *Int Endod J* 36(1):33-43.

Ng YL, Mann V, Rahbaran S, Lewsey J, Gulabivala K (2007). Outcome of primary root canal treatment: systematic review of the literature – Part 1. Effects of study characteristics on probability of success. *Int Endod J* 40(12):921-939.

Ng YL, Mann V, Gulabivala K (2010). Tooth survival following non-surgical root canal treatment: a systematic review of the literature. *Int Endod J* 43(3):171-189.

Norwegian Board of Health (1992). Tannhelsetjenesten i Norge. Annual report 1991. In: Norwegian Board of Health editor. Oslo.

Nosrat IV, Nosrat CA (1998). Reparative hard tissue formation following calcium hydroxide application after partial pulpotomy in cariously exposed pulps of permanent teeth. *International Endodontic Journal* 31(3):221-226.

Nurminen M (1995). To use or not to use the odds ratio in epidemiologic analyses? *European journal of epidemiology* 11(4):365-371.

Nygaard-Østby B (1951). Deep caries. *Nor Tannlaegeforen Tid* 61(3):96 - 105.

Oen KT, Thompson VP, Vena D, Caufield PW, Curro F, Dasanayake A *et al.* (2007). Attitudes and expectations of treating deep caries: A PEARL Network survey. *Gen Dent* 55 (3):197-203.

Oong EM, Griffin SO, Kohn WG, Gooch BF, Caufield PW (2008). The effect of dental sealants on bacteria levels in caries lesions: a review of the evidence. *J Am Dent Assoc* 139(3):271-278.

Opdam NJ, van de Sande FH, Bronkhorst E, Cenci MS, Bottenberg P, Pallesen U *et al.* (2014). Longevity of posterior composite restorations: a systematic review and meta-analysis. *J Dent Res* 93(10):943-949.

Orhan AI, Oz FT, Orhan K (2010). Pulp exposure occurrence and outcomes after 1- or 2-visit indirect pulp therapy vs complete caries removal in primary and permanent molars. *Pediatric dentistry* 32(4):347-355.

Parirokh M, Torabinejad M (2010). Mineral trioxide aggregate: a comprehensive literature review—part I: chemical, physical, and antibacterial properties. *J Endod* 36(1):16-27.

Petersen PE (2003). The World Oral Health Report 2003: continuous improvement of oral health in the 21st century--the approach of the WHO Global Oral Health Programme. *Community Dent Oral Epidemiol* 31 Suppl 1(3-23.

Petersson GH, Bratthall D (1996). The caries decline: a review of reviews. *Eur J Oral Sci* 104(4 (Pt 2)):436-443.

Petrou M, Alhamoui F, Welk A, Altarabulsi M, Alkilzy M, H. Splieth C (2014). A randomized clinical trial on the use of medical Portland cement, MTA and calcium hydroxide in indirect pulp treatment. *Clin Oral Investig* 18(5):1383-1389.

Phillips RW, Crim G, Swartz ML, Clark HE (1984). Resistance of calcium hydroxide preparations to solubility in phosphoric acid. *The Journal of prosthetic dentistry* 52(3):358-360.

Pitt Ford TR, Torabinejad M, Abedi HR, Bakland LK, Kariyawasam SP (1996). Using mineral trioxide aggregate as a pulp-capping material. *J Am Dent Assoc* 127(10)*:*1491-1494.

Pitts N (2004). "ICDAS"--an international system for caries detection and assessment being developed to facilitate caries epidemiology, research and appropriate clinical management. *Community Dent Health* 21(3)*:*193-198.

Prosser HJ, Groffman DM, Wilson AD (1982). The effect of composition on the erosion properties of calcium hydroxide cements. *J Dent Res* 61(12)*:*1431-1435.

Qudeimat MA, Barrieshi-Nusair KM, Owais AI (2007). Calcium hydroxide vs mineral trioxide aggregates for partial pulpotomy of permanent molars with deep caries. *Eur Arch Paediatr Dent* 8(2)*:*99-104.

Reeves R, Stanley HR (1966). The relationship of bacterial penetration and pulpal pathosis in carious teeth. *Oral Surg Oral Med Oral Pathol* 22(1)*:*59-65.

Ricketts D, Lamont T, Innes NP, Kidd E, Clarkson JE (2013). Operative caries management in adults and children. *Cochrane Database Syst Rev* 3(Cd003808.

Ricucci D, Loghin S, Lin LM, Spångberg LSW, Tay FR (2014a). Is hard tissue formation in the dental pulp after the death of the primary odontoblasts a regenerative or a reparative process? *J Dent* 42(9)*:*1156-1170.

Ricucci D, Loghin S, Siqueira Jr JF (2014b). Correlation between clinical and histologic pulp diagnoses. *J Endod* 40(12)*:*1932-1939.

Ridell K, Sundin B, Matsson L (2003). Endodontic treatment during childhood and adolescence. A survey of 19-year-olds living in the city of Malmö, Sweden. *Swed Dent J* 27(2)*:*83-89.

Riley P, Worthington HV, Clarkson JE, Beirne PV (2013). Recall intervals for oral health in primary care patients. Cochrane Database Syst Rev 12 (CD004346).

Ridell K, Olsson H, Mejàre I (2008). Unrestored dentin caries and deep dentin restorations in Swedish adolescents. *Caries Res* 42(3)*:*164-170.

Rothman KJ (2002). Epidemiology: an introduction New York, USA: Oxford University Press.

Rothman KJ, Greenland S (2014). Basic concepts. In: Handbook of epidemiology. W Ahrens and I Pigeot editors. New York, USA: Springer Reference, pp. 75-122.

Sangwan P, Sangwan A, Duhan J, Rohilla A (2013). Tertiary dentinogenesis with calcium hydroxide: a review of proposed mechanisms. *Int Endod J* 46(1)*:*3-19.

Sarnat H, Massler M (1965). Microstructure of active and arrested dentinal caries. *J Dent Res* 44(6)*:*1389-1401.

Schroder U (1985). Effects of calcium hydroxide-containing pulp-capping agents on pulp cell migration, proliferation, and differentiation. *J Dent Res* 64 Spec No(541-548.

Schwendicke F, Dörfer CE, Paris S (2013a). Incomplete caries removal: a systematic review and meta-analysis. *J Dent Res* 92(4):306-314.

Schwendicke F, Meyer-Lueckel H, Dörfer C, Paris S (2013b). Attitudes and behaviour regarding deep dentin caries removal: a survey among German dentists. *Caries Res* 47(6):566-573.

Schwendicke F, Meyer-Lueckel H, Dörfer C, Paris S (2013c). Failure of incompletely excavated teeth—a systematic review. *J Dent* 41(7):569-580.

Seltzer S, Bender IB, Ziontz M (1963a). The dynamics of pulp inflammation: correlations between diagnostic data and actual histologic findings in the pulp. *Oral Surg Oral Med Oral Pathol* 16(7):846-871.

Seltzer S, Bender IB, Ziontz M (1963b). The dynamics of pulp inflammation: correlations between diagnostic data and actual histologic findings in the pulp. *Oral Surg Oral Med Oral Pathol* 16(969-977.

Shahar E (1997). A Popperian perspective of the term 'evidence-based medicine'. *J Evaluation Clinical Pract* 3(2):109-116.

Shovelton DS (1968). A study of deep carious dentine. *Int Dent J* 18(2):392-405.

Shovelton DS, Friend LA, Kirk EE, Rowe AH (1971). The efficacy of pulp capping materials. A comparative trial. *Br Dent J* 130(9):385-391.

Simon S, Perard M, Zanini M, Smith AJ, Charpentier E, Djole SX *et al.* (2013). Should pulp chamber pulpotomy be seen as a permanent treatment? Some preliminary thoughts. *Int Endod J* 46(1):79-87.

Siqueira Jr. JF (2012). Pulpal infection including caries. In: Seltzer and Bender`s Dental Pulp. KM Hargreaves, Goodis, H.E., Franklin R.T., editor. Chicago, IL, USA: Quintessence Publish. Co., Inc., pp. 227–245.

Sjolie AN, Thuen F (2002). School journeys and leisure activities in rural and urban adolescents in Norway. *Health Promot Int* 17(1):21-30.

Skaret E, Raadal M, Kvale G, Berg E (1998). Missed and cancelled appointments among 12-18-year-olds in the Norwegian Public Dental Service. *Eur J Oral Sci* 106(6):1006-1012.

Smith AJ, Lesot H (2001). Induction and regulation of crown dentinogenesis: embryonic events as a template for dental tissue repair? *Critical reviews in oral biology and medicine : an official publication of the American Association of Oral Biologists* 12(5):425-437.

Socialstyrelsen (2011). Nationella riktlinjer för vuxentandvård 2011-stöd för styrning och ledning Västerås: Edita Västra Aros.

Stanley HR (1989). Pulp capping: conserving the dental pulp—can it be done? Is it worth it? *Oral Surg Oral Med Oral Pathol* 68(5)*:*628-639.

Statistics Norway (2012). Over 2,9 milliardar til tannhelse i Noreg. Oslo: Statistisk sentralbyrå.

Statistics Norway (2015). Statistikkbanken Tannhelsetenesta. . Available online at https://wwwssbno/statistikkbanken/selectvarval/Defineasp?subjectcode=&ProductId=&Main Table=TannstatEtAlder&nvl=&PLanguage=0&nyTmpVar=true&CMSSubjectArea=helse&K ortNavnWeb=tannhelse&StatVariant=&checked=true Last accessed 20150114. Oslo: Statistisk sentralbyrå.

Szklo M, Nieto FJ (2012). Epidemiology: beyond the basics. 3rd ed. MA, USA: Jones & Bartlett Learning.

Téclès O, Laurent P, Aubut V, About I (2008). Human tooth culture: a study model for reparative dentinogenesis and direct pulp capping materials biocompatibility. *J Biomed Mater Res B Appl Biomater* 85(1)*:*180-187.

Thorpe C, Ryan B, McLean S, Burt A, Stewart M, Brown J *et al.* (2009). How to obtain excellent response rates when surveying physicians. *Fam Pract* 26(1)*:*65-68.

Tomson PL, Grover LM, Lumley PJ, Sloan AJ, Smith AJ, Cooper PR (2007). Dissolution of bio-active dentine matrix components by mineral trioxide aggregate. *J Dent* 35(8)*:*636-642.

Torabinejad M, Watson TF, Pitt Ford TR (1993). Sealing ability of a mineral trioxide aggregate when used as a root end filling material. *J Endod* 19(12)*:*591-595.

Torabinejad M, Rastegar AF, Kettering JD, Pitt Ford TR (1995). Bacterial leakage of mineral trioxide aggregate as a root-end filling material. *J Endod* 21(3)*:*109-112.

Torabinejad M, Shabahang S (2009). Pulp and periapical pathosis. In: Endodontics: principles and practices. M Torabinejad and R Walton editors. Missouri: Saunders Elsevier, pp. 54.

Torabinejad M, Parirokh M (2010). Mineral trioxide aggregate: a comprehensive literature review--part II: leakage and biocompatibility investigations. *J Endod* 36(2)*:*190-202.

Torneck CD (1974). Changes in the fine structure of the dental pulp in human caries pulpitis. *J Oral Pathol* 3(2)*:*83-99.

Trope M, McDougal R, Levin L, May KN, Swift EJ (2002). Capping the inflamed pulp under different clinical conditions. *J Esthet Restor Dent* 14(6)*:*349-357.

von der Fehr FR (1982). Evidence of decreasing caries prevalence in Norway. *J Dent Res* 61(Sp)*:*1331-1335.

von der Fehr FR, Haugejorden O (1997). The start of caries decline and related fluoride use in Norway. *Eur J Oral Sci* 105(1)*:*21-26.

Vähänikkilä H, Käkilehto T, Pihlaja J, Päkkilä J, Tjäderhane L, Suni J *et al.* (2014). A data-based study on survival of permanent molar restorations in adolescents. *Acta Odontol Scand* 72(5)*:*380-385.

Walsh TS, Lee A (1998). Mathematical coupling in medical research: lessons from studies of oxygen kinetics. *Br J Anaesth* 81(2)*:*118-120.

Wang N, Marstrander P, Holst D, Ovrum L, Dahle T (1992). Extending recall intervals--effect on resource consumption and dental health. *Community Dent Oral Epidemiol* 20(3)*:*122-124.

Wang NJ, Riordan PJ (1995). Recall intervals, dental hygienists and quality in child dental care. *Community Dent Oral Epidemiol* 23(1)*:*8-14.

Weber CM, Alves LS, Maltz M (2011). Treatment decisions for deep carious lesions in the Public Health Service in Southern Brazil. *J Public Health Dent* 71(4)*:*265-270.

Weyant RJ, Tracy SL, Anselmo T, Beltrán-Aguilar ED, Donly KJ, Frese WA *et al.* (2013). Topical fluoride for caries prevention: executive summary of the updated clinical recommendations and supporting systematic review. *J Am Dent Assoc* 144(11)*:*1279-1291.

Working Group by FDI and WHO (1985). Changing patterns of oral health and implications for oral health manpower: part I. *Int Dent J* 35(3)*:*235-251.

Zander HA (1939). Reaction of the pulp to calcium hydroxide. *J Dent Res* 18(4)*:*373-379.

Zocchetti C, Consonni D, Bertazzi P (1997). Relationship between prevalence rate ratios and odds ratios in cross-sectional studies. *Int J Epidem* 26(1)*:*220-223.

APPENDICES

Questionnaire

Treatment preferences of deep carious lesions in vital, permanent teeth with closed apex.

Please, follow the present guidelines:

- Use blue ballpoint pen
- Mark your answer(s) with an ☐ X
- If you want to change your answer, you can shade the box.

Questionnaire

Demographic information

1. Gender

Female   ☐

Male   ☐

2. Where have you graduated from

Oslo   ☐

Bergen   ☐

Tromsø   ☐

Other university/dental school

3. Present practice

Public   ☐

Private   ☐

Both   ☐

4. Year of practice

< 5 years   ☐

5 – 10 years   ☐

≥ 10 years   ☐

5. In which area is your practice

Rural   ☐

Urban   ☐

Choice of treatment

6. When deep carious lesion is detected, in which of the following situations do you usually consider pulpectomy and root canal filling (RF) as your primary choice of treatment

7.

No symptoms – no subjective complaints or history of pain	☐
Symptoms – sharp transient pain or sensitivity to hot/cold	☐
I usually choose other treatment than RF	☐

*If in question 6 in **both** alternatives you have marked "RF", please, go to question 10, if not – proceed with question 7*

8. In which of the following situations when deep carious lesion is present do you provide total (TOTAL) or partial caries excavation (PARTIAL)

	TOTAL	PARTIAL
No symptoms	☐	☐
Symptoms	☐	☐

*If in question 7 in **both** alternatives you have marked "TOTAL", please, go to question 10, if not – proceed with question 8*

9. If you perform PARTIAL caries removal, how much of soft dentine do you leave

Just to protect eventual pulp exposure	☐
Remove totally from the lateral walls, leave at the bottom	☐
Remove just superficial layer	☐

10. If you perform PARTIAL caries removal, do you include a second visit (stepwise excavation) before placing a permanent restoration

Yes	☐
After 6 weeks – 3 months	☐
After 3 – 6 months	☐
Longer than 6 months	☐
No	☐

11. What is your treatment choice of the following situations in case of carious pulp exposure after caries removal

Direct pulp capping (DPC)

Partial pulpotomy (PP)

Pulpectomy and root canal filling (RF)

	DPC	PP	RF
No symptoms	☐	☐	☐
Symptoms	☐	☐	☐

12. My main reasons for performing the chosen treatment options (questions 5,7,8,9,10) are (mark three most relevant options):

Easy to operate, familiar	☐
Brings good results	☐
Has a biological proof	☐
Recommended by colleagues	☐
Recommended in clinical courses	☐
It is recommended in textbooks	☐
It is recommended by recently published studies	☐
Other	☐

13. Which are the main factors your treatment option depends on (mark the three most relevant options)

Patient's general health	☐
Patient's age	☐
Patient's attitude and priority	☐
Type of tooth (front/premolar/molar)	☐
Further restoration of the tooth	☐
Patient's oral health	☐
Duration of the total treatment	☐
Other	☐

Treatment procedure

14. Do you use rubber dam for the treatment of deep carious lesion

Yes ☐

No ☐

15. Do you use dye solution (caries indicator) during excavation

Yes ☐

No ☐

16. What instruments do you use when excavating deep carious lesion

Sharp spoon shaped hand excavator ☐

Large sharp round bur at a low speed   ☐

Diamond bur at a low speed   ☐

Other   ☐

17. Do you use an antimicrobial agent before a liner or bonding agent is applied

Yes   ☐

No   ☐

18. Which material do you usually use as a first layer on the pulpal wall under permanent restoration in the absence of exposure

Calcium hydroxide slurry (powder + water)   ☐

Calcium hydroxide commercial liner (Dycal, Life etc.)   ☐

Glass ionomer cement   ☐

None, directly bonded composite resin   ☐

Other   ☐

19. Which material do you usually use as a first layer on the exposed pulp

Calcium hydroxide slurry (powder + water)☐   ☐

Calcium hydroxide commercial liner (Dycal Life etc.)   ☐

Combination of both previously mentioned   ☐

Zinc oxide eugenol   ☐

MTA   ☐

Other   ☐

20. Are you satisfied with the results of your treatment of deep carious lesions

Yes   ☐

Partly, I need to improve   ☐

No, I am not satisfied   ☐

21. Do you provide follow up after treatment of deep carious lesions

Yes   ☐

No   ☐

Invitation letter

**Dear Name Surname, we invite you to participate in a survey**

Treatment preferences of carious lesions in vital, permanent teeth with closed apexes

The investigation

The present investigation is a part of a PhD-project at The Institute of Clinical Dentistry (IKO) in Tromsø (Norway). The present survey is intended to give relevant information about clinical routines regarding treatment of carious lesions among dentists in Northern Norway. The present investigation is anonymous, no names will be linked to the answers.

Example case

Here you see bitewing and clinical picture of a carious lesion at distal surface of the tooth 14.
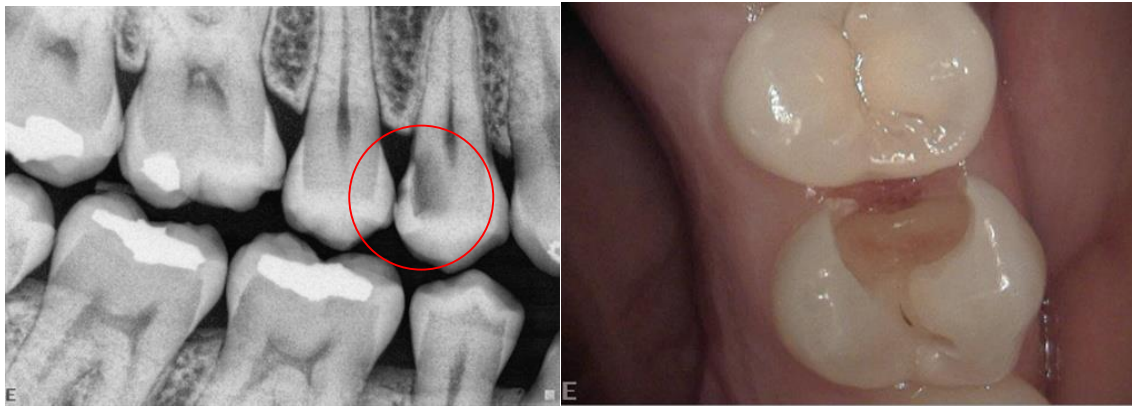
You will find enclosed questionnaire asking about preferred treatment methods and materials of cases like this.

Definitions

Total caries excavation: Removal of all infected and affected carious dentine.

Partial caries excavation: Removal of all or part of infected (soft) dentine leaving affected dentine at the deepest part of the cavity.

Direct pulp capping: An exposed pulp is covered with capping material.

Partial pulpotomy: Part of the coronal pulp adjacent to an exposure is removed and the rest part is covered with a capping material.

Pulpectomy: Total removal of vital pulp tissue and root canal filling.

We hope that you are able and willing to participate in the present survey. Please, fill in the questionnaire and put it in prepared stamped envelope, which is enclosed. The results will

increase our knowledge of caries treatment in general practice and give an appropriate background for estimating prognosis of various treatment options used.

If you are willing, you will be personally informed about survey's results, as soon as they are ready.

Contact us if you are in doubt about something.
Lina Stangvaltaite: 77649132, lina.stangvaltaite@uit.no
Rita Kundzina: 77649118
Harald M Eriksen: 77649103
Eero Kerosuo: 77649128

THANK YOU FOR YOUR COOPERATION!

Written informed consent

Request for participation in the research
"Clinical pulp capping" (Treatment of very deep holes in teeth).

Background and purpose
This is a question for you to participate in a dental examination on the treatment of very deep holes in the teeth. Such holes (caries attack) that reach into the nerve of the tooth can be painful and is a treatment challenge. One is presented with options to cover the wound with a special type of insulating cement before making a normal filling or root canal treatment the tooth. The first option is easy and affordable, while a root canal can be technically demanding and expensive. It is therefore important to find good and safe guidelines for selecting the best and safest option in such situations.

What does the study?
The method involves sårdekning of an exposed nerve in the tooth has been known and taught in more than 50 years. Materials and criteria have varied over time and the results have been uncertain. Over the past few years has developed a new material (Mineral trioxide Aggregate, MTA), which shows promising properties. The material is tested in experimental models and in normal clinic without having found adverse side effects. What is lacking, however, controlled clinical trials comparing the results of treatment with a traditional cement with the new material. MTA is as the name says a mineral oxides without medical additives.
You are invited to participate in a survey in which a process suitable teeth either traditionally or with the new material for a random distribution. The teeth will be followed up with

examinations after 6, 12, 24 and 36 months by an experienced dentist who does not know which of the two treatment options that are used. If you experience pain or discomfort with the treatment during the study period, there will of course be taken care of.

Advantages and disadvantages
The advantages for you as a participant is competent treatment for well gjennomarbeidete guidelines, close monitoring of the outcome of treatment and rapid access to treatment for any complications. As responsible for the study, we expect no disadvantages over the elapsed time for annual inspections.

What happens to your information (privacy)?
All personal information about you especially related to the survey will be used only in this context and will be deleted at the end of the study. Only authorized personnel involved in the project that has access to the name lists and other information related to the study. It will not be possible to identify the results of the study when they are published, but you will be informed of the results.

Right of access
It recorded only regular journal information in connection with the study and the right of access to follow patients' right to access their own records.

Voluntary participation
It is voluntary to participate in the study. If you do not want to join the tooth to be treated by the commonly used guidelines at the clinic. If you wish to participate in the draw you consent to the statement on the last page. If you now agree to participate, you can later withdraw your consent without affecting your other treatment. The study is in accordance with normal, necessary dental treatment and will therefore not be given special compensation for

participating.

Economy
The study is funded by research grants available from the Department of Clinical Dentistry, University of Tromsø and the dental health resource center for northern Norway. There will also be applied for research funding from independent external research funds. There are no ties to commercial companies.

Insurance
In that study represents the normal, necessary dental treatment, the participants are insured through existing patient and insurance responsibilities.

Further information
Detailed information can be found in the project description that is available to participants if desired. 1. Professor Rita Kundzina
Main Responsible
E-mail: rita.kundzina @ uit.no, phone: 77 64 91 18

Consent Statement:
I have received and read the written information about the study, "Clinical pulp capping" and is willing to participate in the survey.
Date: _____
Signature: _____
Block Letters: _____

Baseline

1. |_|_|_|_|_|_|_| Patient's OPUS number

2. |_|_|.|_|_|.|_|_|_|_| Patient's birthday

3. _____   Clinic

4. |_|_|.|_|_|.|_|_|_|_| Date of capping procedure

5. _____   Operator

6. |_|_| Tooth number

7. |_| Cavity type

    - 1=MO   2=DO   3=MOD

8. |_| Pre-operative pain history

    - 1=No   2=Yes, but indicating not more severe condition than reversible pulpitis

9. |_| Medical status at baseline

    - 1=Non-contributory

    - 2=Use of antibiotics during the last year, but not during the last 3 weeks

10. |_| Caries depth at baseline

    - 1=Reaching inner 1/3, but not deeper

    - 2=Clearly beyound the inner 1/3 limit, but not into pulp

    - 3=Into the pulp

11. |_| Periapical status at baseline

    - 1=Normal, apex closed

12. |_| Periodontal status

    - 1=Normal

    - 2=Deepened pocket but NOT > 4 mm

13. |_| Vitality at baseline

    - 1=Response to cold or EPT

14. |_| Written consent obtained

    - 1=Yes, signed

15. |_| Pulpal exposure

    - 1=Yes

    - 2=No

16. |_| Hemostasis

    - 1=Yes

- 2=No

17. |_|_| Clinic allocation number (1-20)

18. |_| Allocated material
    - 1=Dycal
    - 2=MTA ProRoot grey

Second visit (1 week)

19. |_|_|.|_|_|.|_|_|_|_| Date at final restoration

20. |_| Pain during the first week and/or at second visit (1 week)
    -1=No

    -2=Yes, but during the 3 first days only and not indicating more severe than reversible pulpitis

    -3=Yes, occasionally during the entire week, but not at present. But not indicating more severe than reversible pulpitis.

    -4=Yes, pain at present, but not not indicating more severe than reversible pulpitis

    -5=Yes, severe pain earlier or at present indicating irreversible pulpitis

6 months

1. |_|_|_|_|_|_|_| Patient's OPUS number

21. |_|_|.|_|_|.|_|_|_|_| Date of 6 months examination

22. |_| Pain at 6 months or during the followed period

    -1=No

    -2=Yes, but not indicating more severe than reversible pulpitis

    -3=Yes, indicating irreversible pulpitis or more severe

23. |_| Vitality at 6 months

    - 1=Response to cold or EPT

    - 2=Lingering

    - 3=No response on either method

24. |_| Periapical status at 6 months

    - 1=No lesion

    - 2=Widening PDL

    - 3=Lesion

,

12 months

1. |_|_|_|_|_|_|_|_| Patient's OPUS number

25. |_|_|.|_|_|.|_|_|_|_| Date of 12 months examination

26. |_| Pain at 12 months or during the followed period

    -1=No

    -2=Yes, but not indicating more severe than reversible pulpitis

    -3=Yes, indicating irreversible pulpitis or more severe

27. |_| Vitality at 12 months

    - 1=Response to cold or EPT

    - 2=Lingering

    - 3=No response on either method

28. |_| Periapical status at 12 months

    - 1=No lesion

        - 2=Widening PDL

        - 3=Lesion

24 months

1. |_|_|_|_|_|_| Patient's OPUS number

29. |_|_|.|_|_|.|_|_|_|_| Date of 24 months examination

30. |_| Pain at 24 months or during the followed period

   -1=No

   -2=Yes, but not indicating more severe than reversible pulpitis

   -3=Yes, indicating irreversible pulpitis or more severe

31. |_| Vitality at 24 months

   - 1=Response to cold or EPT

   - 2=Lingering

   - 3=No response on either method

32. |_| Periapical status at 24 months

   - 1=No lesion

      - 2=Widening PDL

      - 3=Lesion

36 months

1. |_|_|_|_|_|_| Patient's OPUS number

33. |_|_|.|_|_|.|_|_|_|_| Date of 36 months examination

34. |_| Pain at 36 months or during the followed period

    -1=No

    -2=Yes, but not indicating more severe than reversible pulpitis

    -3=Yes, indicating irreversible pulpitis or more severe

35. |_| Vitality at 36 months

    - 1=Response to cold or EPT

    - 2=Lingering

    - 3=No response on either method

36. |_| Periapical status at 36 months

    - 1=No lesion

        - 2=Widening PDL

        - 3=Lesion

37. |_|_|.|_|_|.|_|_|_|_| Date of exclusion

ORIGINAL ARTICLES I-III