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der Universitätsmedizin der Ernst-Moritz-Arndt-Universität Greifswald

Prevalence of Molar-Incisor-Hypomineralisation (MIH) among German school children at four cities in Germany: an epidemiological study

Inaugural - Dissertation

zur

Erlangung des akademischen

Grades

Doktor der Zahnmedizin (Dr. med. dent.)

der

Universitätsmedizin

der

Ernst-Moritz-Arndt-Universität Greifswald

2012

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geb. am: 17.07.1985

in: Athen/ Griechenland

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Tag der Disputation: 08. Mai 2013

“Ο βίος βραχὺς, ἡ δὲ τέχνη μακρὴ, ὁ δὲ καιρὸς ὀξὺς, ἡ δὲ πεῖρα σφαλερὴ, ἡ δὲ κρίσις χαλεπή. ”

Ιπποκράτης (460- 370 π. Χ.)

“Life is short, (the) art long, opportunity fleeting, experience misleading, (the) judgment difficult.”

Hippocrates (460- 370 BC)

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List of Abbreviation

DAJ	Deutsche Arbeitsgemeinschaft für Jugendzahnpflege
DDE	Developmental Defects of Enamel Index
DMFT	Demarcated Missing Filled Teeth (permanent dentition)
Dmft	demarcated missing filled teeth (primary dentition)
EAPD	European Academy of Paediatric Dentistry
EDI	Enamel Defect Index
Kappa/K	Cochran's Kappa value
mDDE	moderate Developmental Defects of Enamel Index
MIH	Molar-Incisor-Hypomineralisation
MH	Molar-Hypomineralisation
MP	Marina Petrou
N	Number
P	p-value
SGB V	Sozialgesetzbuch Fünftes Buch
SPSS	Statistical Package for Social Science
Yrs	Years
WHO	World Health Organization

1. Introduction

Since the late 1970s examiners had been using different descriptions for molars with demarcated opacities (white, yellow, brown) and enamel breakdown such as: cheese molars, non-endemic mottling of enamel, idiopathic enamel opacities, non-fluoride enamel opacities, idiopathic enamel hypomineralisation, enamel opacities, internal enamel hypoplasia, opaque spots, non-fluoride hypomineralisation and hypomineralised permanent first molars (Koch et al., 1987; Weerheijm, 2003). The term “Molar-Incisor-Hypomineralisation” (MIH) was proposed for the first time by Weerheijm et al. (2001a) in order to describe specific developmental defects of dental enamel affecting first permanent molars as well as permanent incisors.

Various diagnostic criteria for MIH had been reported in the literature, constituting studies discussing MIH prevalences unreliable in terms of representativeness. Furthermore, due to that variety, reported prevalences of the condition could hardly be considered fit for comparison (Jälevik et al., 2010).

It took until the EAPD (European Academy of Paediatric Dentistry) seminar 2003 for this problem to be addressed and new criteria of MIH to be established (Weerheijm et al., 2003). In 2009 in the EAPD interim seminar and workshop concerning MIH the “Best Clinical Guidance for Clinicians Dealing with Children Presenting with MIH” has been suggested (Lygidakis et al., 2010).

The prevalence of MIH seems to differ considerably among countries (2.4- 40.2 %) and so do the criteria and the consistency of the study-samples (Jälevik, 2010). With respect to this diagnostic variation the prevalence of MIH according to epidemiological studies of some European countries appears to have increased (Chawla et al., 2008a). This tendency seems to appear also in Germany among three local studies (Dresden: 5.6 %, Gießen: 5.9 % and Munich: 14.7 %) which were conducted using different criteria (Dietrich et al., 2003; Preusser et al., 2007; Heitmüller et al., 2012).

Hypomineralisation defects can also appear in primary teeth (Jälevik et al., 2000). Additionally Elfrink et al. (2008; 2010) suggested the term “Deciduous Molar Hypomineralisation” for the hypomineralisation of second primary molars. Recent studies (Elfrink et al., 2012; Ghanim et al., 2012) focused on the relationship between MIH and hypomineralisation of second primary molars. A connection of these defects could lead to a predictor for MIH and thus an earlier prevention for the permanent dentition (Elfrink et al., 2012).

The aim of this study is primarily to determine a representative prevalence of MIH in Germany conducting examinations according to the EAPD criteria in different parts of the country (East: Greifswald, North: Hamburg, South: Heidelberg, West: Düsseldorf) and secondly to compare the findings with those of previous studies. An analysis of MIH characteristics and its connection with hypomineralisation of second primary molars as well as caries experience is also going to be discussed.

1.1 Definition of Molar-Incisor-Hypomineralisation (MIH)

"Molar-Incisor-Hypomineralisation" (MIH) is the terminology used to describe the clinical picture of a hypomineralisation of systematic origin of one or more of the four permanent first molars, as well as any associated and affected incisors (Weerheijm et al., 2003). When the hypomineralisation affects only one to four first permanent molars the term “Molar-Hypomineralisation” (MH) is often preferred (Chawla et al., 2008a).

The clinical presentation of MIH varies considerably, not alone in different patients, but also among the teeth of the same affected individuals (Fig. 1- 6). The affected teeth according to the EAPD criteria may present with demarcated opacities, post-eruptive enamel breakdown, and atypical restorations. Furthermore MIH teeth may even fail to erupt (Weerheijm et al., 2003; Lygidakis et al., 2010).

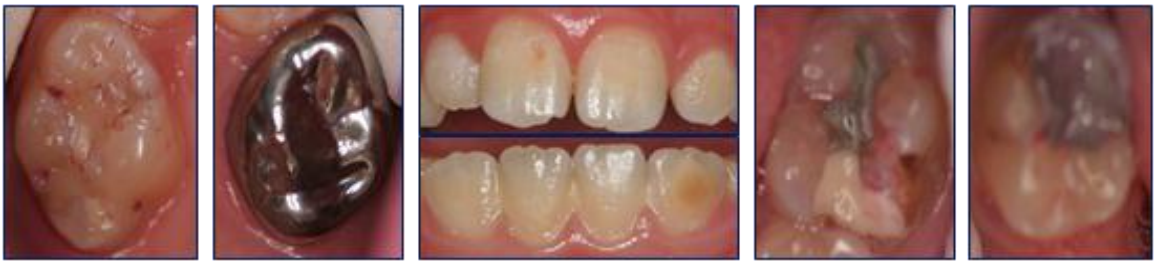


Fig. 1- 6: Female patient with various MIH defects and restorations among index teeth (first permanent molars, upper and lower incisors)

The defects described as MIH can sometimes also be noticed on second primary molars (Fig. 7), second permanent molars (Fig. 8), tips of permanent canines (Weerheijm et al., 2003; Lygidakis et al., 2010) and premolars (Fig. 9; Heitmüller et al., 2012) without clear indications of having a comparable cause (Jasulaityte et al., 2007). Meanwhile Elfrink et al. (2012) support that second primary molars' hypomineralisation could be a clinical predictor for MIH. The association of hypomineralisation of the two dentitions was also found in the study of Ghanim et al., (2012).

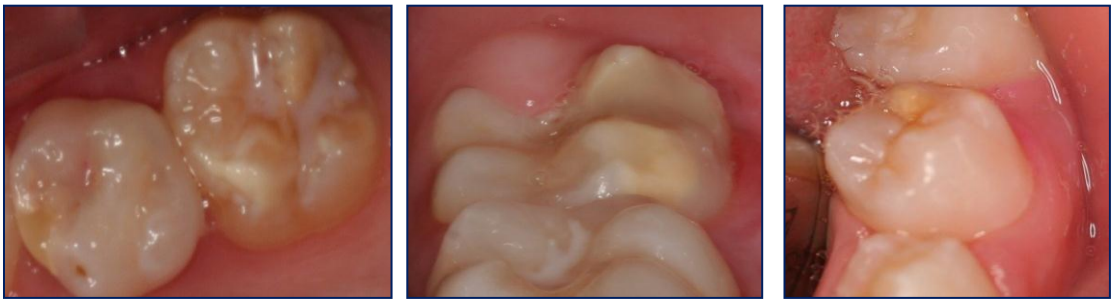


Fig 7: Demarcated opacities in the first permanent molar (26) and in the borders of the restoration in the second primary molar (65)

Fig 8: Demarcated opacities and atypical restoration in the second permanent molar (37)

Fig. 9: Demarcated opacities in the second premolar (35)

1.2 Clinical characteristics of MIH

MIH is defined as a qualitative defect of enamel. The opacities of hypomineralised teeth are localized and demarcated. Masticatory forces may lead to a post-eruptive enamel breakdown of one or more affected surfaces, soon after eruption, which presents with irregular sharp boundaries (Chawla et al., 2008a; Weerheijm, 2003).

The clinical presentation of the hypomineralised index teeth among children with MIH is investigated in several studies. Nevertheless, it seems that there is a variability of characteristics.

The presence of MIH is equally distributed between genders (Behrendt et al., 2004; Calderara et al., 2005; Fteita et al., 2006; Martinez Gomez et al., 2012; Jälevik et al 2001; Jasulaityte et al., 2007; Leppäniemi et al., 2001; Muratbegovic et al., 2007; Preusser et al., 2007). There are though studies showing that more females than males present with MIH (Chawla et al., 2008a; Cho et al., 2008; Dietrich et al., 2003; Lygidakis et al., 2008a).

The mean number of affected teeth differs between the studies from 2.4 to 5.7 (Calderara et al., 2005; Cho et al., 2008; Ghanim et al., 2011; Jälevik et al., 2001; Jasulaityte et al., 2003; Lygidakis et al., 2008a; Muratbegovic et al., 2007; Wogelius et al., 2008). The mean number of affected first permanent molars per child varies from 1.5 to 3.16 (Chawla et al., 2008a-b; Lygidakis et al., 2008a; Muratbegovic et al., 2007; Wogelius et al., 2008), whereas the mean number of affected incisors among children with MIH was found 2.2 by Lygidakis et al. (2008a). In general, the condition affects more molars than incisors (Lygidakis et al., 2008a; Preusser et al., 2007; Willmott et al., 2008). The number of affected molars per child differs among the studies (Dietrich et al., 2003; Muratbegovic et al., 2007; Parikh et al., 2012; Preusser et al., 2007)

The number of affected teeth as well as the presence of MIH versus MH is positively correlated with the severity grad of the MIH defects in most of the studies (Chawla et al., 2008b; Ghanim et al., 2011; Jasulaityte et al., 2007;

Leppäniemi et al., 2001; Willmott et al., 2008). Severity grad is scored among the studies according to different criteria (chapter 1.4).

The index teeth in the maxilla were found to be more affected than those in the mandible (Martinez Gomez et al., 2012; Leppäniemi et al., 2001; Lygidakis et al., 2008a; Parikh et al., 2012; Preusser et al., 2007). On the other hand, there are also studies indicating the opposite (Jälevik et al., 2001) or even no difference between the jaws (Chawla et al., 2008a). The most affected tooth was found by Ghanim et al. (2011), Martinez Gomez et al. (2012) and Lygidakis et al. (2008a) to be the upper right molar and by Behrendt et al. (2004) and Parikh et al. (2012) the mandibular right first permanent molar. When Parikh et al. (2012) in their study compared the number of hypomineralised teeth appearing in the right and left side of the patient's mouth, the right side revealed a statistically significant greater number of hypomineralised teeth. Nevertheless, similar studies by Preusser et al. (2003) and Leppäniemi et al. (2001) found no statistically significant differences.

The presence of MH instead of MIH varies from 7.6- 77.4 % (Cho et al., 2008; Jasulaityte et al., 2007; Lygidakis et al., 2008a; Muratbegovic et al., 2007; Parikh et al., 2012; Wogelius et al., 2008). In the study of Munich/Germany 5.1 % of the study group show a combination of hypomineralisation in permanent and primary dentition, whereas 2.7 % of MIH cases presented with the same finding (Mach, 2009).

The most common hypomineralised surface found in molars is the occlusal and as far as incisors is concerned, the buccal. (da Costa-Silva et al., 2011; Muratbegovic et al., 2007; Preusser et al., 2007) Furthermore, the most common enamel defects among MIH teeth are demarcated opacities (Ghanim et al., 2011; Wogelius et al., 2008).

The characteristics of the hypomineralised second primary molars seem to follow the same variations as the hypomineralised first permanent molars, as found in the studies of Ghanim et al. (2012) and Elfrink et al. (2008).

1.3 Aetiology of MIH

To understand how the MIH lesions develop, the formation of enamel on teeth “amelogenesis” has to be primarily discussed.

1.3.1 Amelogenesis

The strictly genetically controlled procedure of amelogenesis is mainly divided into three stages. This delicate procedure is very sensitive to environmental parameters. The first stage or “secretory stage” starts with the formation of the cusp tips’ enamel and ends with the disposition of the full thickness of enamel. Disturbances at this stage lead to hypoplastic enamel. The enamel matrix degradation with massive mineralization appears in the “transition stage”. The final mineralization of enamel is performed during the third stage of amelogenesis which is called “maturation stage”. Disturbances in these stages lead to hypomaturated or hypomineralised enamel (Alaluusua, 2010). In MIH molars the thickness of enamel is comparable to the unaffected molars (Farah et al., 2010; Jälevik et al., 2005) but its mineral density is reduced by almost 20% (Farah et al., 2010). It seems to be “looser and less well organized” (Jälevik et al., 2005). Jälevik et al. (2005) also describe that the clinically well districted borders of the defect were mostly recognizable during the scanning electron micrograph analysis.

There is an overlap among the hypomineralisation periods of permanent first molars, permanent incisors and second primary molars (Tab. 1 and Tab. 2). Therefore, a shared cause of the hypomineralisation defects in both dentitions is suggested (Elfrink et al., 2012). The lower mineral content of hypomineralised second primary molars was found by the study group of Elfrink (2012). According to this paper, yellow opacities had 30% lower mineral density, whereas white ones were similar to white spot lesions.

Table 1: Development of second primary molars during pregnancy (utero) and months/years of life

Tooth	Begin of calcification	Completed crown	Eruption
second primary molar	18 weeks in utero	11 months	2- 2 ½ year

(Schroeder, 1987)

Table 2: Development of first permanent molars and incisors during pregnancy (utero) and months/years of life

	Begin of calcification		Completed crown		Eruption	
Tooth	**Maxilla**	**Mandibula**	**Maxilla**	**Mandibula**	**Maxilla**	**Mandibula**
central incisor	3 months	3 months	4 ½ year	3 ½ year	7 ¼ year	6 ¼ year
lateral incisor	11 months	3 months	5 ½ year	4 year	8 year	7 ½ year
first perm. molar	32 weeks in utero	32 weeks in utero	4 ½ year	3 ¾ year	6 ¼ year	6 year

(Weerheijm, 2003)

1.3.2 Factors related with the aetiology of MIH

Despite the increasing research on the aetiology of MIH insufficient evidence still exists. Different parameters which can affect the development of teeth and cause MIH defects are over the years thoroughly investigated. Furthermore, the contribution of more than one factor has been recently suggested (Chawla et al., 2008a-b; Lygidakis et al., 2010). The previous lack of distinction between

hypomineralisation and hypoplasia may be a further parameter of this insufficiency (Crombie et al., 2009).

Genetics

As recorded by Bailleul-Forestier et al. (2008) “the genes involved in enamel (AMELX, ENAM, MMP20, KLK4) and dentin (DSPP) structures are highly specific for tooth.” Although according to experiments in rats there is a connection between fluorosis and genetics, there is no clear evidence to support this claim for MIH (Lygidakis et al., 2010).

Pre- peri- and post-natal periods

Medical problems during the prenatal period are more common among mothers whose children developed MIH than those that did not (Lygidakis et al., 2008b; Souza et al., 2012). The medical conditions during the perinatal period (e.g. prolonged delivery, premature birth) seem common among many children with MIH (Dietrich et al., 2003; Lygidakis et al., 2008b). In the study of Lygidakis et al. (2008b) this fact was statistically significant. Hypoxia related to birth and hypercalcaemia are also discussed as potential aetiological factors (Alaluusua, 2010). Postnatal medical problems such as respiratory problems, asthma, otitis media, childhood illnesses, chickenpox, high fever up to the fourth year of life are related to MIH (Alaluusua, 2010; Chawla et al., 2008a; Crombie et al., 2009; Lygidakis et al., 2010; Willmott et al., 2008).

Antibiotics

Studies relate MIH to the use of antibiotics, especially amoxicillin and erythromycin, during the first years of life. However, it is difficult to determine the use of antibiotics as an isolated aetiological factor, due to fact that there is a frequent co-existence of antibiotics use with the presence of high fever and childhood illness (Alaluusua, 2010; Lygidakis et al., 2010).

Environmental toxicants

There are studies proving the influence of high levels of dioxins or polychlorinated biphenyls (PCBs) in the prevalence of MIH (Alaluusua, 2010). On the other hand, in studies of Laisi et al. (2008) and Kusku et al. (2009) no relationship was found.

Breast feeding

Alaluusua et al. (1996a-b) brought forward an association of prolonged duration of breast feeding and MIH. These studies suggested also a possible influence of environmental contaminants (e.g. dioxin) in breast milk. However, the children with and without enamel defects in the Jälevik (2001) study had the same breast feeding history.

Fluorides

The majority of the studies have reported that fluoride is not clearly associated with the MIH aetiology (Crombie et al., 2009). On the other hand, Balmer et al., (2012) found a significant decrease of MIH defects in areas with supply of fluoridated in addition to those with non-fluoride water supply. As possible explanation, the investigators suggested that there is remineralisation caused by long-term exposure to optimum levels of fluoride and it probably leads to change in teeth clinical appearance.

Conditions in medically compromised populations

According to the critical review of Crombie et al. (2009), the prevalence of dental defects is significantly higher in medically compromised populations, probably because of the high prevalence of chronic medical conditions (e.g. coeliac disease) and/or their treatment.

No otherwise reported aetiological factor

There are MIH cases with no related reported medical history, indicating the potential implication of other systemic, environmental or genetic etiological factors (Lygidakis et al., 2008b).

1.4 Differential diagnosis of MIH

The classification of the different enamel defects is determined by their clinical characteristics (Alaluusua et al., 2001), which may present as very similar, regardless of their aetiology (Chawla et al., 2008a).

A differential diagnosis of MIH (Fig. 10) includes hereditary enamel development disorders such as amelogenesis imperfecta (Alaluusua et al., 2001) and enamel disorders with a known cause such as trauma in primary dentition (Alaluusua et al., 2001; Fig. 11), fluorosis (Fig. 12), white spot lesions and hypoplasia (Fig.13) (Chawla et al., 2008a).

The histologic differences among hypomineralised enamel, early caries lesions, different types of amelogenesis imperfecta and fluorotic enamel are stressed in the study of Jälevik et al. (2005). Since such an examination could not be realistic in everyday clinical practice, only the aetiological and clinical parameters of differentiation are stressed in the following chapters (chapter 1.4.1, 1.4.2).

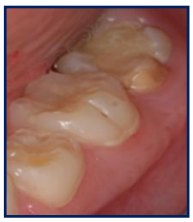


Fig.10: Initial caries in primary molars (74, 75) and MIH permanent molar (36)

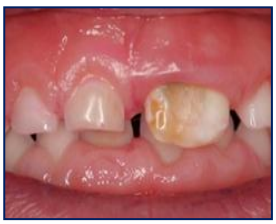


Fig. 11: Enamel defect in an upper incisor (21) due to trauma in the primary dentition

Fig. 12: Dental fluorosis (teeth: 12-22)

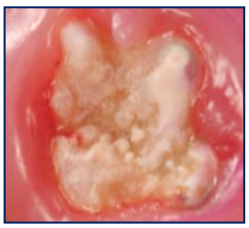


Fig. 13: A hypoplastic first permanent molar (26) with hypomaturation after surgical exposure of its occlusal surface

1.4.1 Differential diagnosis of MIH and genetically determined enamel disorders

Amelogenesis imperfecta

“Amelogenesis imperfecta” is a genetically determined defect present in all permanent teeth of the patient (Aldred et al., 2003), contrary to MIH, whose origin is independent of genetic factors (Lygidakis et al., 2010) and its clinical

appearance differs even among the affected index teeth (first permanent molars, incisors) of the same patient (Weerheijm et al., 2003; Lygidakis et al., 2010). In this case the differential diagnosis seems to be “a matter of definition” as Weerheijm (2004) claimed.

Syndromes

Syndromes (Alaluusua et al., 2001; Bailleul-Forestier et al., 2008) and some medical diseases e.g. nephrocalcinosis (Martelli-Junior et al., 2011) are also related to enamel anomalies but not to MIH defects.

Other dental hart tissue defects

Dentinogenesis imperfecta and dentin dysplasia are also genetically determined defects, which can also affect the appearance of enamel (Alaluusua et al., 2001). Their deferential diagnosis from MIH is based on the same principles as in the case of amelogenesis imperfecta.

1.4.2 Differential diagnosis of MIH and other enamel defects caused during enamel development

Hypoplasia

Hypoplasia is a quantitative defect. Hypoplastic teeth have a reduced enamel thickness and the borders of the normal enamel are mostly smooth (Chawla et al., 2008a; Weerheijm, 2003). This appearance contrasts with the characteristic qualitative defects of hypomineralisation (Chawla et al., 2008a; Weerheijm, 2003; details in chapter 1.2).

Dental fluorosis

In case of fluorosis the defects of the enamel may present as diffuse opacities (opaque and white, brown and pitted) or in more severe cases enamel may fracture (Chawla et al., 2008a). The cause of fluorosis is consumption of high fluoride levels during the affected teeth’s developmental stage (Abanto Alvarez et al., 2009). Diffused opacities caused from fluoride are different to the demarcated

opacities caused from hypomineralisation (Chawla et al., 2008a; Weerheijm et al., 2003).

Caries (cavitated and non-cavitated)

Unlike enamel developmental disorders, caries is a demineralisation phenomenon and the metabolic activity in the biofilm is its driving force (Kidd, 2004). Therefore, early caries lesions, the so called “white spots”, differ from the white demarcated opacities of MIH because of their location in the tooth and aetiology (Chawla et al., 2008a). Caries experience of a study-sample is an important factor, because caries can mask the hypomineralised lesions (Willmott et al., 2008).

Tetracycline defects

Administration of tetracycline may cause discoloration (yellow, gray, brown) of both dentitions because of its incorporation into tissues that are calcifying at that time (Sánchez et al., 2004). In this case the aetiological factor is well determined and the discolorations of the teeth are related to duration, dosage and type of tetracycline preparation (Alaluusua et al., 2001).

Other localized defects

Traumatic injury as well as a prolonged periapical inflammation process of a primary tooth (Alaluusua et al., 2001) could affect the delicate developmental procedure of permanent successor.

1.5 Previous and recent indices of MIH

Different diagnostic criteria have been used in the epidemiological studies of MIH worldwide (Tab. 4).

Chronologically in 1982 the first index for Developmental Defects of Enamel (DDE index) was published in order to differentiate hypoplasia from demarcated and diffuse opacities. Defects less than 1mm were not recorded (Jälevik, 2010).

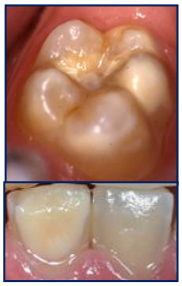
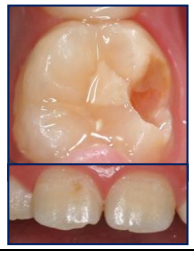
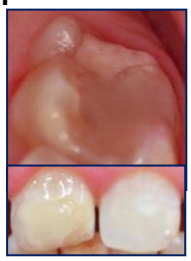
Koch et al. (1987) presented in their study a modified DDE index describing the enamel defects according to their colour and substance changes. The colour changes were noted as white, yellow and brown and the surface changes as roughly abraded and disintegrated. Atypical restorations were also included. Defects involving less than “one third of area of a tooth unit” were not recorded.

In 1992 the DDE index was modified into a simpler form: the “mDDE” index (Jälevik, 2010; Alaluusua et al., 1996a-b). This index recorded enamel defects in first permanent molars excluding defects related to dental fluorosis, heritable defects and defects caused by general health problems. The defects were categorized into three severity grades with respect to their clinical characteristics. Three working teams from the same country (Finland) used criteria comparable to those (Alaluusua et al., 1996a) in three publications (Alaluusua et al., 1996a; Alaluusua et al., 1996b; Leppäniemi et al., 2001). In 2001, the “Enamel Defect Index” (EDI) was introduced. Nevertheless, EDI had the disadvantage of scoring demarcated together with diffuse opacities (Weerheijm et al., 2003).

In 2003, EAPD established criteria for diagnosing MIH (Tab. 1) in order to avoid the problems of previous indices. According to the EAPD recommendations for the clinical assessment of MIH, the examinations should be performed at eight year- old children, on wet teeth after brushing. All first permanent molars and incisors have to be examined for the presence of MIH (Weerheijm et al., 2003).

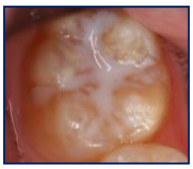
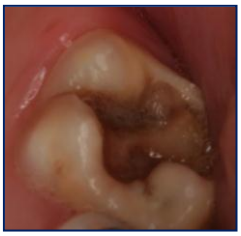
The EAPD (2010) clinical guidance manuscript recommends that “defects less than 1mm are not to be recorded”. Extracted teeth should be recorded as MIH, but only if these were diagnosed with MIH as stated in the dental records of the patient or in the case that the other first permanent molars have evidence of MIH. The hypersensitivity of MIH teeth should also be assessed. It can range after external stimuli from mild to spontaneous (Lygidakis et al., 2010). In the same manuscript the criteria of MIH severity are also presented (Tab. 2).

Table 1: Clinical appearance, and definition of MIH criteria according the EAPD criteria (2003)

Criteria and clinical appearance of MIH	Definition of MIH-criteria
Demarcated opacity 	➢ translucency of enamel: • variable in degree • normal thickness • smooth surface • colour: white, yellow or brown
Post-eruptive enamel breakdown 	➢ loss of initially formed surface enamel after tooth eruption; a demarcated opacity may have pre-existed
Atypical restoration 	➢ molars: “The size and shape of the restoration are not conforming to the temporary caries picture” (Weerheijm et al., 2003). In most cases the restorations extend to the palatal or buccal surfaces and at the borders a demarcated opacity may be present. ➢ incisors: any buccal restorations not related to trauma
Extracted molar due to MIH	It should be related to the clinical characteristics of the other index teeth.
Unerupted	➢ index teeth that have not yet erupted

(Weerheijm et al., 2003)

Table 2: Definition of the MIH-severity-index according the EAPD criteria (2010)

Severity grad of MIH	Definition
mild 	• demarcated enamel opacities without enamel breakdown • occasional sensitivity to external stimuli (e.g. air) but not brushing • mild aesthetic concerns on discoloration of incisors
severe 	• demarcated enamel opacities with breakdown • caries • persistent/spontaneous hypersensitivity affecting function (e.g. brushing) • strong aesthetic concerns that may have socio-psychological impact

(Lygidakis et al., 2010)

There is great variability among the MIH severity criteria used in international studies (da Costa-Silva et al., 2011; Calderara et al., 2005; Leppäniemi et al., 2001; Preusser et al., 2007), a fact which creates problems concerning the comparison of the results (Parikh et al., 2012). Meanwhile demarcated opacities are found to be the most frequent form of MIH in international studies (Jasulaityte et al., 2007; Muratbegovic et al., 2008; Ghanim et al., 2011; Heitmüller et al., 2012; Soviero et al., 2009). A recent Indian cross-sectional study, which used the EAPD criteria (Lygidakis et al., 2010) found that 77.7% of 546 MIH teeth presented mild enamel defects (Parikh et al., 2012).

1.6 Epidemiology of MIH

Previous studies of MIH have reported a prevalence of 2.4- 40.2 % (Jälevik, 2010) depending on the country and the age of the patients (Jasulaityte et al.,

2008). In Europe, this prevalence is between 5.9 and 14.3 % (Lygidakis, 2010), whereas Germany, as described in previous studies by Dietrich et al. (2003) and Preusser et al. (2007), has a MIH prevalence of 5.6 % and 5.9 %, respectively. In a more recent study, following the EAPD criteria, Heitmüller et al. (2012) found that MIH in Munich/Germany was present in 14.7 % of the study sample (n= 693) whereas another 21.8 % presented hypomineralisation on other permanent teeth than first permanent molars and incisors. The prevalence of hypomineralised second primary molars was found to vary between 2.7 and 9 % at child level (Elfrink et al., 2008; Elfrink et al., 2012; Ghanim et al., 2012; Mach, 2009).

A problem that arises from the previous diagnostic classifications used in epidemiological MIH studies is that the actual prevalence of defected teeth may not have been correctly recorded (Lygidakis et al., 2008) or may even have been underestimated (Willmott et al., 2008). Although, the EAPD guidelines (Lygidakis et al., 2010) suggest that the size of the MIH study sample should be representative for the whole population of a country, representative data exist only in few cases. Clear examples of this situation can be evident in the cross sectional studies conducted in Bosnia Herzegovina, Jordan and the Netherlands (Muratbegovic et al., 2007; Jasulaityte et al., 2008; Weerheijm et al., 2001b; Zawaideh et al., 2011). The epidemiological studies for MIH are summarized in the following Table (Tab. 4).

Table 4: Summary of epidemiological studies for MIH

Country	City/ Region	N	Criteria/ Indices	Prevalence	Reference
Argentina	Buenos Aires	1098	not reported	15.9 %	Biondi et al., 2011
Australia/UK	Sydney/Leeds	25/25	mDDE	40 %/44 %	Balmer et al., 2005
Australia	Westaustralien	511	mDDE	22 %	Arrow, 2008
Bosnia-Herzegowina	Sarajevo, Benjaluka, Tuzla, Visoko, Govazde,Vitez, Siroki Brijeg, Sanki, Mostor	560 (40/city)	EAPD 2003, (Defects≥ 2mm)	12.3 %	Muratbegovic et al., 2007
Brazil	Bothelos	918	EAPD 2003, (Defects≥ 1mm)	19.8 %	da Costa-Silva et al., 2010
Brazil	Rio de Janeiro	249	EAPD 2003	40.2 %	Soviero et al., 2009
Bulgaria	Plovdiv	2970 (age cohorts)	EAPD 2003	2.4 %-7.8 %, Ø3.6 %	Kukleva et al., 2008
Denmark	Støvring, Nibe	647	EAPD 2003	37.5 %	Wogelius et al., 2008

Table 4: Summary of epidemiological studies for MIH; continued

Country	City/ Region	N	Criteria/ Indices	Prevalence	Reference
England*	North England	3233	mDDE	15.9 %	Balmer et al., 2012
Finland	Helsinki	102	Alaluusua et al.,1996a	17 %	Alaluusua et al 1996a
Finland	Helsinki	97	Alaluusua et al., 1996a	25 %	Alaluusua et al., 1996b
Finland	Helsinki	488	Alaluusua et al., 1996	19.3 %	Leppäniemi et al., 2001
Finland	Kotka, Anjalankoski	1030	DDE (1992)	14.2 %, 5.6 %	Hölttä et al., 2001
Germany	Dresden	2408	mDDE	2.4 %-11 % Ø5.6 %	Dietrich et al., 2003
Germany	Gießen	1002	Koch et al., 1987	5.9 %	Preusser et al., 2007
Germany	Munich	693	EAPD 2003 (Defects≥ 1mm)	14.7 %	Heitmüller et al., 2012
Greece	Athens	3518	EAPD 2003	10.2 %	Lygidakis et al., 2008
China	Hong Kong	2635	EAPD 2003	2.8 %	Cho et al., 2008
India	Gandhinagar's Region	1366	EAPD 2003	9.2 %	Parikh et al., 2012
Iraq	Mosul	823	EAPD 2003	18.6 %	Ghanim et al., 2011
Italy	Lissone	227	mDDE, MIH Criteria 2001 (Defects≥ 2mm)	13.7 %	Calderara et al., 2005
Jordan	Amman, Irdid, Al-Karak	3241	EAPD 2003	17.6 %	Zawaideh et al., 2011
Kenya	Matungulu, Kangundo (Machakos' Regionen)	3591	Demarcated opacities, post-eruptive defects, extensive restorations	13.7 %	Kemoli et al., 2008
Libya	Benghazi	378	mDDE, MIH Criteria 2001 (Defekte≥ 2mm)	2.9 %	Fteita et al., 2006
Lithuania	Kaunas	1277	EAPD 2003	9.7 %	Jasulaityte et al., 2007
The Netherlands	Alphen aan de Rijn, Gouda, Breda, Den Bosch	497	mDDE	9.7 %	Weerheijm et al., 2001b
The Netherlands	Alphen aan de Rijn, Gouda, Breda, Den Bosch	442	MIH Criteria 2001	14.3 %	Jasulaityte et al., 2008
New Zealand	Wainuiomata	522	mDDE	14.9 %	Mahoney et al., 2009
New Zealand	Wellington/ Wellington and Wainuiomata	235/756	mDDE	18.8 %/ 15.7 %	Mahoney et al., 2011
Spain	Barcelona	505	EAPD 2003	17.85 %	Martinez Gómez et al., 2012
Sweden	Jönköping's Region	2252	colour and surface changes; Fluorosis and hypomin. of known origin excluded (Defects ≥ 1/3 of tooth's surface)	3.6 %- 15.4 %	Koch et al., 1987
Sweden	Kallered, Mölndal	519	mDDE (Defects≥ 2mm)	18.4 %	Jälevik et al., 2001
Turkey	Kocaeli/Canakkale	109/44	EAPD 2003	9.1 %/9.2 %	Kuscu et al., 2009
Turkey	Istanbul	147	EAPD 2003	14.9 %	Kusku et al., 2008
UK	Leeds	307	mDDE	14.6 %	Zagdwon et al., 2002

1.7 Clinical considerations and treatment options regarding hypomineralised teeth

1.7.1 Clinical considerations

The relationship between MIH severity and the colour of enamel opacities has been evaluated in various studies (da Costa-Silva et al., 2011; Farah et al., 2010; Jälevik and Noren, 2000). According to these studies yellow and brown (Fig. 14) enamel opacities run a higher risk of presenting with increasing severity of MIH and they are more porous than opacities lighter in colour.

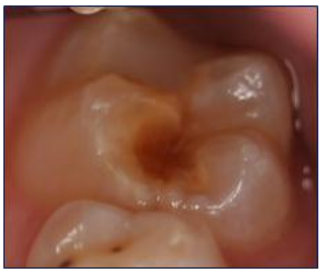


Fig 14: Brown demarcated opacity in the occlusal surface of first permanent molar (16)

The difficulty of risk prediction of post-eruptive enamel breakdown (da Costa-Silva et al., 2011) and the recognition of risk factors in the post-eruptive time of MIH teeth (Leppäniemi et al., 2001) is imperative for the treatment plan of a patient.

The enamel disintegration leads to unprotected dentin (Lygidakis et al., 2010). The combination of MIH teeth's fragility and the fact that children tend to avoid brushing the sensitive MIH teeth, favors rapid caries development, which can mask the original cause of the problem (Leppäniemi et al., 2001; Weerheijm, 2003; Weerheijm, 2004). According to some epidemiological studies, older children tend to have more severe forms of MIH (da Costa-Silva et al., 2011; da Costa-Silva et al., 2010; Leppäniemi et al., 2001; Lygidakis et al., 2008). Macroscopically, teeth with demarcated opacities may have enamel breakdown (da Costa-Silva et al., 2011; Wogelius et al., 2008). Furthermore, according to Jälevik et al. (2002) by the age of nine, children with MIH require ten times more dental therapy than children without MIH and on average each defective tooth needs twice the amount of treatment. Statistically significantly higher DMFT

values in children with than without MIH were observed in the studies of Preusser et al. (2007) and Behrendt et al. (2004). In the Behrendt et al. (2004) study, it was also found a statistically significantly higher caries experience in the primary dentition in the MIH group. On the other hand, the DMFT difference between the two groups was not significant in the Dietrich et al. (2003) study, whereas Heitmüller et al. (2012) found no relationship between the presence of MIH and caries among 10-year old children.

The MIH teeth can be very sensitive to air, cold, warm or even mechanical stimuli (e.g. tooth brushing) and therefore they require a robust local analgesia before treatment (Fayle, 2003; Weerheijm, 2003). Difficulties during the anesthesia may occur because of probable chronic inflammation of the pulp (Lygidakis, 2010).

Dental fear, anxiety and behavioral management problems are common among children with severe hypomineralisation. Possible aetiological parameters are the experience of pain and discomfort related to MIH and previous unpleasant dental treatment sessions (Jälevik and Klingberg, 2002). Functional limitations (e.g. eating, cleaning mouth) also have an impact in the quality of life of children with enamel defects (Castro et al., 2011; Vargas-Ferreira et al., 2011). In severe cases of MIH, aesthetic concerns (Fig. 15- 17) may have a socio-psychological impact (Lygidakis et al., 2010).

Prevention from the early stage of eruption may reduce the necessity of future restorative treatment (Lygidakis et al., 2010). Although it is not yet scientifically confirmed, regular fluoride applications may reduce hypersensitivity and enhance remineralisation of teeth's hypomineralised areas (Fayle, 2003; Lygidakis, 2010).

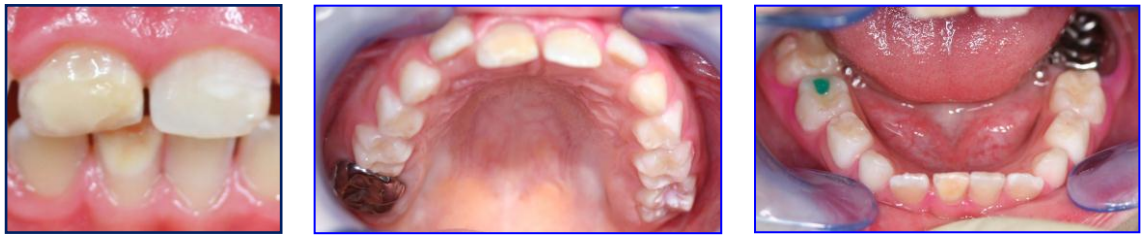


Fig. 15- 17: Post-operative appearance of an 8-year old patient's teeth affected with MIH; aesthetic improvement of the anterior central incisor (11), stainless steel crowns in molars 16 and 36, sealant in molar 26 and glass ionomer atypical restoration in molar 46.

1.7.2 Treatment approaches

Treatment approaches for MIH affected teeth vary according to their severity grade. They include prevention, fissure sealants (Fig. 7), glass ionomer cement (Fig. 18 and Fig. 19) or composite resin restorations, preformed metal crowns (Fig. 20) for posterior teeth and microabrasion, as well as “bleach and seal” technique for anterior teeth. Cast restorations are recommended for MIH teeth in late post-eruptive stages. Extractions are also proposed after taking orthodontic aspects into consideration. Unfortunately, for MIH patients, ideal treatment options may not be possible and, therefore, alternative treatment approaches may be needed. Although each of the cavity design options (removal of all defective or only the porous enamel) has its advantages and disadvantages, amalgam restorations (Fig. 21) in MIH cases should be avoided (Lygidakis et al., 2010).

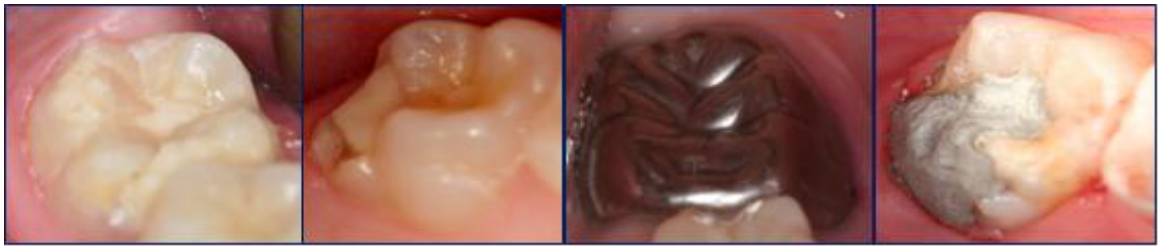


Fig. 18: First permanent molar (46) with demarcated opacities and atypical GIC restoration

Fig. 19: First permanent molar (16) with demarcated opacities, composite filling and enamel breakdown

Fig. 20: Stainless steel crown in a hypomineralised first permanent molar (36)

Fig. 21: Amalgam filling and demarcated opacities in a hypomineralised first permanent molar (26)

1.8 Aim of the study

The aim of this cross sectional study was to determine the prevalence of MIH in Germany among 7- 10 school children in four different areas of the country (East: Greifswald, North: Hamburg, South: Heidelberg, West: Düsseldorf) and to compare this with other local and international studies.

In addition, this study aims to analyse in each study area the gender-specific MIH distribution, as well as the possible association between the presence of

hypomineralisation in second primary molars and MIH. A possible relationship of hypomineralisation and caries experience (DMFT/dmft value) will be also investigated.

2. Materials and Methods

2.1 Ethical committee approval

The study was approved by the ethical committee of the Ernst-Moritz-Arndt University of Greifswald/Germany (Reg.-Nr.: BB 48/10) and took place from February 2011 to March 2012 (chapter 10).

2.2. Sample of the Study

All children who took part on the compulsory dental school examination in the four study sites (n= 2395) were examined for the presence of MIH according to the criteria of EAPD (Weerheijm et al., 2003; Lygidakis et al., 2010). The children attended the second to fourth grade of primary school, aged 7- 10 years (mean 8.1 ±0.8), Examinations were performed in 20 primary schools in four study sites in Germany (East: Greifswald, North: Hamburg, South: Heidelberg, West: Düsseldorf). The schools were selected randomly by the city's community medicine office (Gesundheitsamt, Jugendzahnärztlicher Dienst).

In Greifswald, 440 children were examined in 3 out of 6 primary schools, in Hamburg/Bezirk Eimsbüttel 279 children corresponding to 3 out of 32 primary schools, in Heidelberg 713 children corresponding to 6 out of 136 primary schools and in Düsseldorf 963 children corresponding to 8 out of 86 primary schools. In Heidelberg, four schools belonged to the surrounding county (Rhein-Neckar-Kreis) which belongs to the same community medicine office.

Children who were not present during the examinations as well as those not having at least one eruptive first permanent molar were excluded from the study. The schools were previously informed and all necessary procedures were arranged before children examination. 2396 children proceeded with the dental examination but one felt sick during examination (Heidelberg) and was excluded from the study sample. Figure 22 illustrates the selection of the sample.

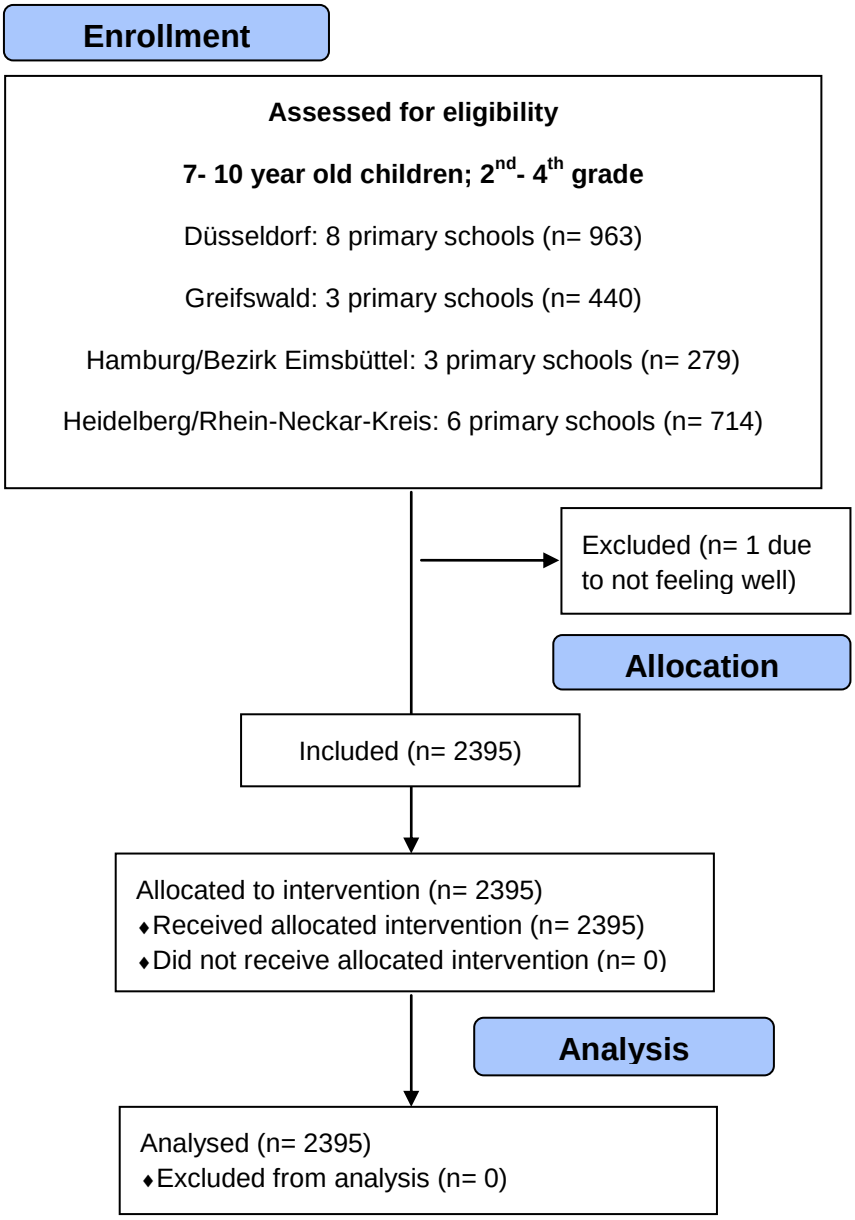


Fig. 22: CONSORT 2010 flow diagram for recruitment of study sample

The fluoride levels in drinking water in Germany are controlled and only low levels of fluoride are present in the drinking water as compare with national standards (Momeni et al., 2007). According to the Federal Institute for Risk Assessment (Bundesinstitut für Risikobewertung) the fluoride content in drinking water in Germany in 90 % of the country correspond to less than 0.3 mg/L.

2.3 Clinical examination

Dental school examinations in Germany are compulsory to all children and follow standard procedures (Pieper, 2010). Socio-demographic data (gender, age and city), caries experience (DMFT/dmft values) according to WHO (1997) and orthodontic disorders of the children are documented. Within this examination, the first permanent molars and permanent incisors were examined according to the MIH EAPD criteria (Tab. 1; Weerheijm et al., 2003; Lygidakis et al., 2010) for presence of:

- demarcated opacities
- post-eruptive enamel breakdown
- atypical restorations
- possible failure of eruption or extractions due to MIH.

Children were considered as having MIH if at least one permanent molar had one of the above clinical appearances. Defects less than 1mm or contrast opacities occurring in incisors but not in at least one first molar were not recorded.

The affected index-teeth as well as the affected surfaces of each tooth analog to their clinical view and in case of atypical restorations the material used were recorded in printed forms for each child separately (chapter 10). Possible failure of eruption or extractions due to MIH was recorded as “missing tooth” because no access to the dental files of the children was allowed. Teeth with atypical restorations and without another MIH sign were not classified as having MIH.

In case of co-existence of more than one clinical figure of MIH in one tooth, the tooth was categorized according to its severest form following the order: demarcated opacity, post-eruptive enamel breakdown, atypical restoration. The combinations of MIH figures in one tooth as well as co-existence of caries were also noted.

The diagnosis of MIH was made by five calibrated examiners (Kappa> 0.9) on clean teeth after supervised tooth brushing, normally without drying the teeth. The examiners used a head light, a portable light, mirrors and dental explorers, which were used without force to assess the roughness of the defects. When necessary, cotton rolls were used to control extensive salivation.

In order to investigate a possible association between hypomineralisation of second primary molars and the presence of MIH in the permanent dentition, all second primary molars of children diagnosed with MIH were examined with the same criteria and procedures.

The hypersensitivity of the teeth was documented according to the discomfort of the children while brushing their teeth or during their daily activities. The following standardized questions were asked to all children with MIH in order to determine lack or presence of discomfort. The questions were formulated originally in German and, therefore, the original text in German is presented next to the English translation:

- Does it hurt when you brush your teeth? Does it hurt when you brush your back teeth? (German: „Zieht es ein bisschen an deinen Zähne, wenn du sie putzt? Tut es weh, wenn du die Backenzähne putzt?“)

- Does it hurt when you drink a hot tea or cacao? Do you enjoy having ice-creams in summer or does the cold make your teeth hurt? (German: „Wenn du einen heißen Tee/Kakao trinkst, tun dann deine Zähne weh? Isst du im Sommer gern Eis, oder ist dies zu kalt für deine Zähne?“)

The degree of severity was recorded according to the findings as mild or severe (Tab. 4; Lygidakis et al., 2010).

Electronic tables or designed printed tables with the same labels (chapter 10) were used for documentation of sample characteristics. In Greifswald, the examiner used a Microsoft Excel table, in Düsseldorf the documentation was entered in the electronic program of the community dentistry, in Hamburg

preformed tables of the community service were used and in Heidelberg an already designed table was introduced for the study.

The names of the schools and children were coded and the charts were anonymously sent to the Ernst-Moritz-Arndt University of Greifswald/Germany to the department of Preventive and Paediatric dentistry for the analysis. The data from Düsseldorf and Heidelberg were sent as printed version of the tables and incorporated into to final data basis in Greifswald. The data from Hamburg were entered in the study site, using an Excel Microsoft table and sent electronically to Greifswald. Finally, the data from all participating sites were anonymously merged into Microsoft Excel and transferred to SPSS 18 for the subsequent data analysis.

Apart from the examination date and the coded school name, the following characteristics were recorded for each child:

- birthday and age
- caries experience in both dentitions
- gender
- presence of MIH
- presence of hypomineralised second primary molars in MIH cases

The caries experience at tooth level was assessed according to WHO (1997) recommendations. For each examined child decayed (D/d), missing (M/m) and filled (F/f) teeth (T/t) due to caries were scored and documented for both dentitions (DMFT: permanent dentition; dmft: primary dentition). Caries scores at surface level were not possible in all examination sites and, therefore, this information was excluded from the present study.

2.4. Calibration

The examinations were performed by one examiner in each of the participating cities, except for Düsseldorf, where two examiners were responsible for conducting the examination in different schools.

2.4.1 Calibration for DMFT/dmft values

Over the last 15 years, all examiners who took part in the standardized German dental school examinations (Deutsche Arbeitsgemeinschaft für Jugendzahnpflege/DAJ examinations) received standardized caries calibrations trainings, and they were trained to the same "gold standard". This calibration had a robust Kappa value of 0.85 (Pieper, 2010). Therefore, the study examiners were experienced dentists in the public health services and re-calibrated for the last German dental survey (Pieper, 2010).

2.4.2 Calibration for MIH examinations

Prior to the school examination, the examiners were trained to identify MIH defects using international literature referring to differential diagnosis of MIH (Chawla et al., 2008a; Lygidakis et al., 2010). Furthermore, several clinical pictures of MIH and other enamel defects were used for better understanding of the clinical features, especially for demarcated defects/opacities in MIH, as well as reference for differential diagnosis.

The calibration of the dentists was performed by a calibrated examiner (MP; intra and inter-examiner Kappa scores> 0.9), who was considered as "the gold standard" for this study. A series of 20 pictures of MIH affected teeth presenting with defects of variable severity were used. The training was conducted in one session and the examiners reached Kappa values higher than 0.9.

Moreover, the "gold standard" (MP) was always present during the first examinations in all study sites to co-examine the children and to ensure that procedures were performed according to the optimum standards.

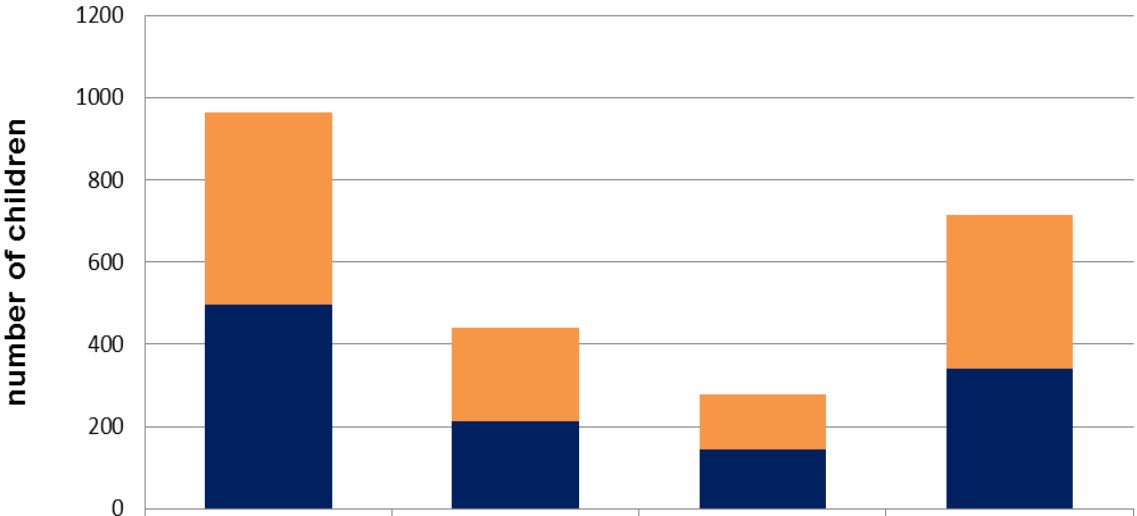
2.5 Statistical analysis

Statistical analysis of the data was performed using the Statistical Package for Social Science (SPSS for Windows, version 18.0, SPSS Inc., Chicago, IL, USA). The mean values for DMFT, dmft and age, as well as the distribution of gender and the prevalence of MIH, its characteristic's distribution and degrees were performed with descriptive statistics. The differences and the probable associations of the children's age, gender, region, caries experience, presence of hypomineralised second primary molars and presence of MIH, as well as the severity of MIH cases and number/surfaces of affected teeth were statistically analyzed using t-test, χ^2-test and Spearman's correlation. The level of statistical significance was p= 0.05.

3. Results

Study group

A total of 2395 children (age: 8.1 ±0.8) were examined for MIH. From the total sample, 963 children participated in Düsseldorf, 440 in Greifswald, 713 in Heidelberg and 279 in Hamburg. The number of males (n= 1195) and females (n= 1200) was evenly distributed in this study (Fig. 23).



	Düsseldorf	Greifswald	Hamburg	Heidelberg
females	465	228	135	372
males	498	212	144	341

Fig. 23: Distribution of children according their gender and the city of examination

Prevalence of MIH

The total prevalence of MIH was found to be 10.1 % (n= 242) and the prevalence of each city were as follows: 14.6 % in Düsseldorf (n= 141), 4.3 % in Greifswald (n= 19), 14.0 % in Hamburg (n= 39) and 6.0 % in Heidelberg (n= 43). The difference in MIH prevalence between the study sites was statistically significant (χ^{2}-test: $p < 0.01$).

As far as the participants' gender was concerned (males: 10.7 %; females: 9.5 %; Tab. 5), no statistically significant difference was found (χ^{2}-test: $p = 0.57$).

Table 5: Distribution of MIH (n; %) between genders and study sample

Diagnosis	Study sample					
	males (n= 1195)		females (n= 1200)		total (n= 2395)	
	n	%	n	%	n	%
MIH	128	**10.7**	114	**9.5**	242	**10.1**
no MIH	1067	89.3	1086	90.5	2153	89.9

When the different age groups (Tab. 6) were compared, once again no statistically significant difference was found (χ^2-test: p= 0.4).

Table 6: Distribution of MIH (n, %) among children in different age groups (in years)

Diagnosis	Age groups						Total sample	
	7 – 7.99 yrs (n= 647)		8 – 8.99 yrs (n= 835)		9 +yrs (n= 913)		(n= 2395)	
	n	%	n	%	n	%	n	%
MIH	66	**10.2**	77	**9.2**	99	**10.8**	242	**10.1**
no MIH	581	89.8	758	90.8	814	89.2	2153	89.9

Hypomineralised second primary molars among children with MIH

In all of 242 children, having MIH 12.0 % (n= 29) had hypomineralisation defects in at least one second primary molar. This figure corresponds to 11.3 % in

Düsseldorf, 36.8 % in Greifswald, 12.8 % in Hamburg and 2.3 % in Heidelberg. The existence of hypomineralisation defects in second primary molars is significant positive correlated to the presence of MIH (Spearman‘s correlation: r= 0.330, p< 0.001).

MIH characteristics

Distribution of hypomineralised index teeth among children with MIH

The overall number of affected permanent index teeth found in children diagnosed with MIH was 686 (molars: n= 490; incisors: n= 196). The overall mean of affected teeth in children with MIH was 2.8 ±1.7 teeth (Fig. 24) and 3.0 ±2.0 if primary teeth (n= 54) were included. The mean value of affected primary teeth was 0.2 ±0.6 per child.

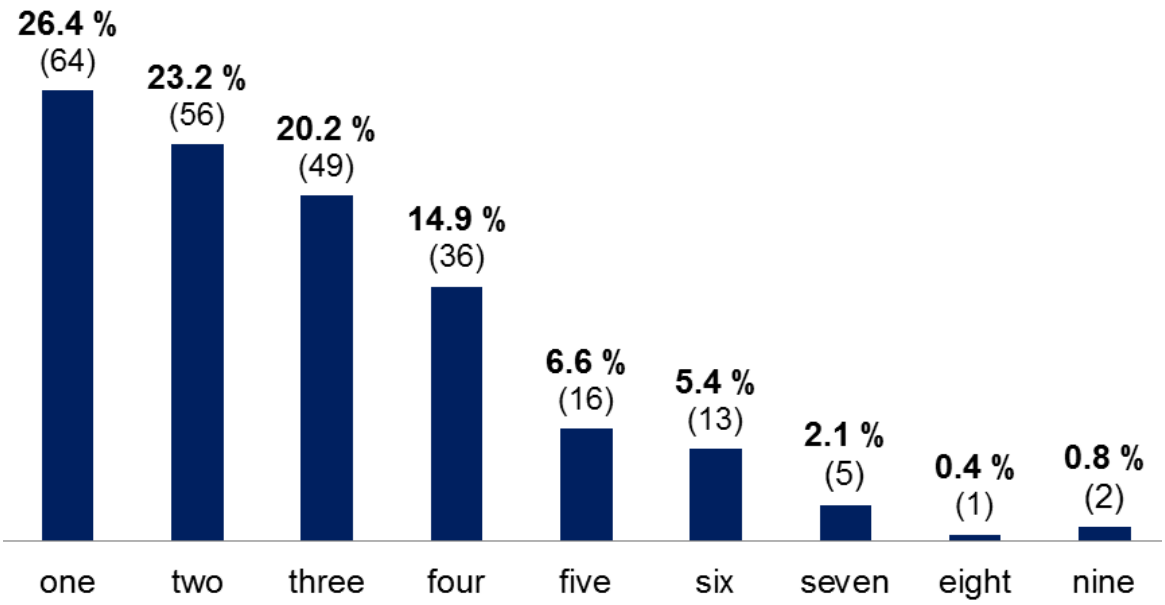


Fig. 24: Prevalence (%) and number (n) of children diagnosed with MIH according the number of their hypomineralised permanent teeth (first permanent molars and incisors)

The mean number of affected permanent molars was 2.0 ±1.1. 57.8 % of the MIH cases (n= 140) presented hypomineralised first permanent molars without presence of affected incisors (MH) and the majority of the children (60.8 %; n= 147) had more than one affected first permanent molar (Fig. 25).

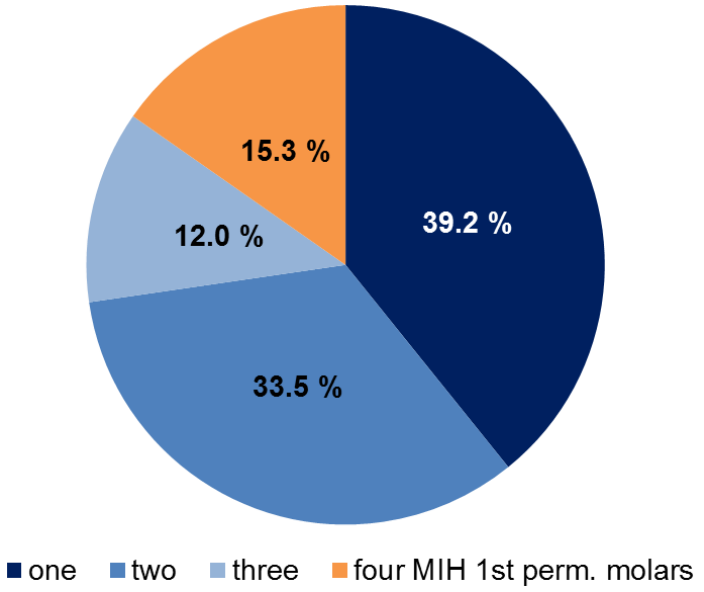


Fig. 25: Distribution (%) of MIH first permanent molars (n= 490) in child level

The prevalence of MIH in different teeth is presented in Figure 26. There was no difference between the mandibular and maxillary molars. On the other hand, the central maxillary incisors are the most MIH affected incisors.

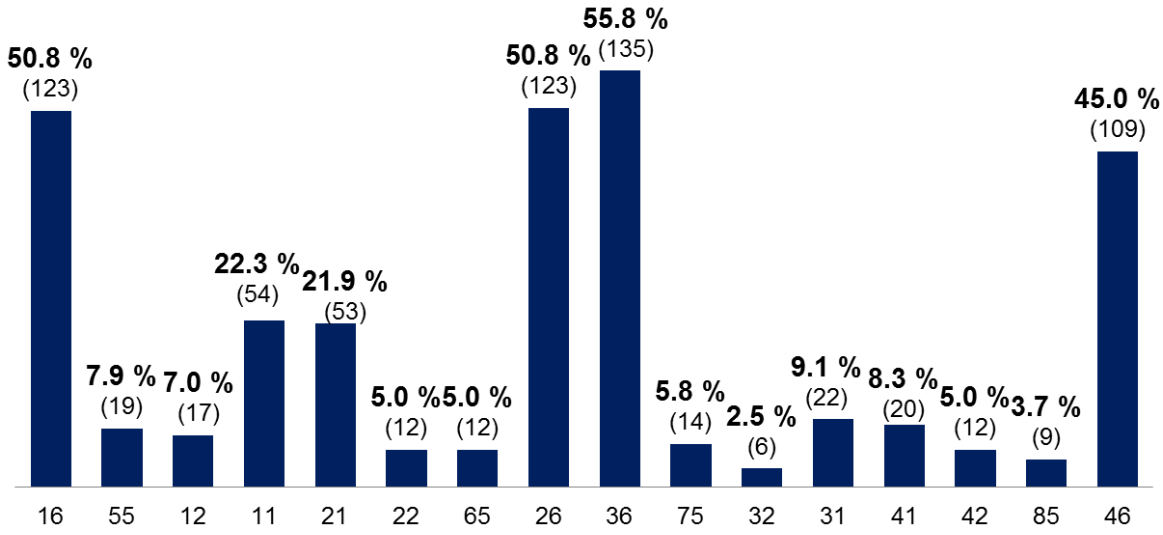


Fig. 26: Prevalence of MIH in children, according to the affected tooth (%; n)

Distribution of MIH criteria in tooth level

The demarcated opacities were the most common form of MIH, whereas post-eruptive breakdown and atypical restorations were observed less often (Fig. 27-

28). The presence of breakdown was almost exclusively restricted to molars and no atypical restoration was observed in incisors teeth. In one nine-year-old child (dmft= 6), who was diagnosed with MIH, a first permanent molar was missing, but the reason could not be determined.

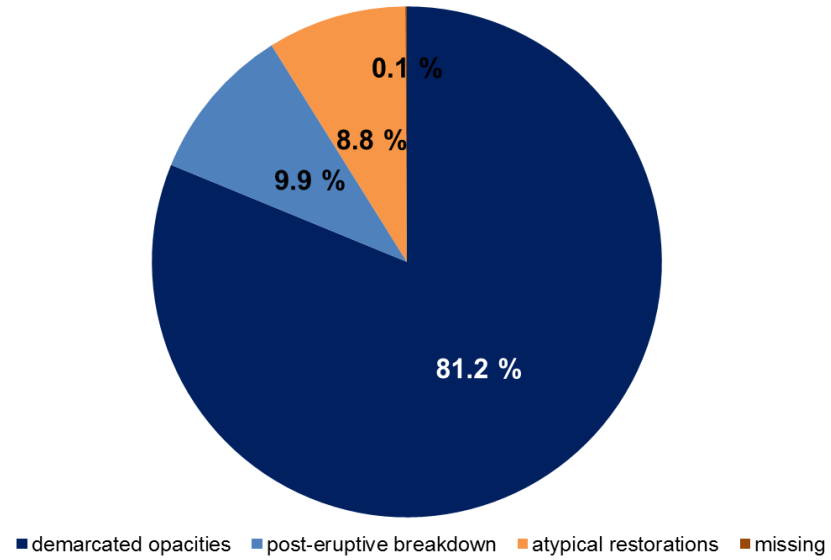


Fig. 27: Distribution of MIH criteria among hypomineralised teeth (n= 740)

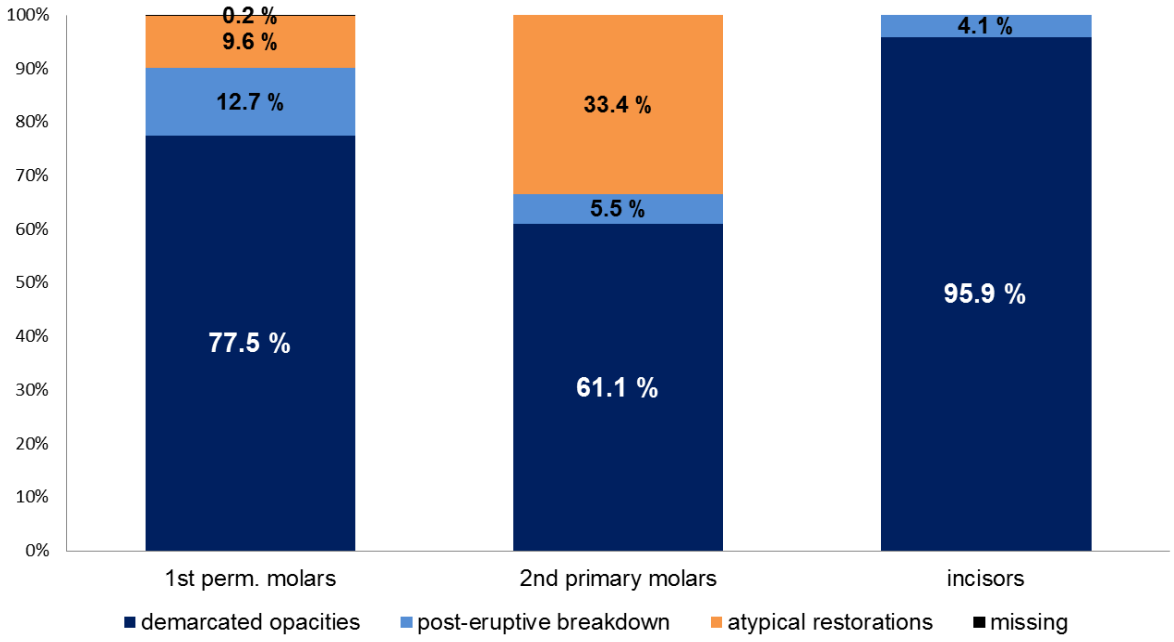


Fig. 28: Distribution of MIH criteria for each group of teeth (first permanent molars: 490; second primary molars: 54; incisors: 196)

Three teeth with clinical evidence of post-eruptive breakdown were also diagnosed with caries and 14.9 % (n= 110) of the affected teeth (n= 740) presented with different clinical pictures of hypomineralisation among their surfaces. The most common combination for the first permanent molars was the post-eruptive enamel breakdown and atypical restorations, whereas incisors combined demarcated opacities and post-eruptive breakdown. The combination of demarcated opacities among the different surfaces and atypical restorations was found mainly in second primary molars. In details the combinations of the distribution of MIH criteria are described in the following table (Tab. 7).

Table 7: Combinations of MIH criteria at tooth level (n; %)

Combinations of MIH	**Tooth category**					
	first permanent molars (92; 18.8 %)		**permanent incisors (3; 1.5 %)**		**second primary molars (15; 7.6 %)**	
	n	%	n	%	n	%
demarcated opacity and post-eruptive breakdown	51	55.4	3	100	2	13.3
demarcated opacity and atypical restoration	13	14.2	0	0	12	80.0
demarcated opacity, post-eruptive breakdown and atypical restoration	8	8.7	0	0	1	6.7
post-eruptive breakdown and atypical restoration	20	21.7	0	0	0	0

The most common material of atypical restorations was composite (74.0 %; 48) followed by glass ionomer cement (GIC, 16) and amalgam (2) (Fig. 29).

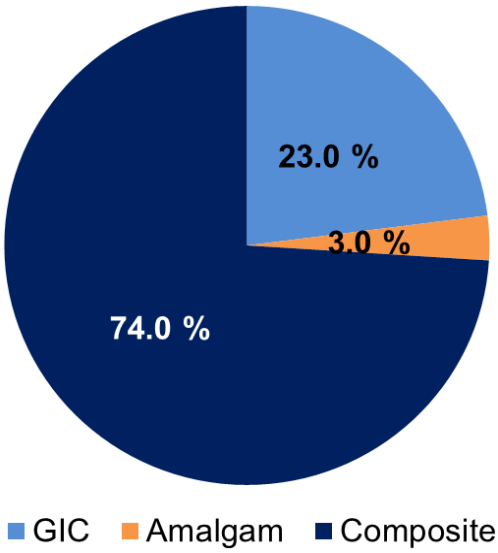


Fig. 29: Distribution of materials used in atypical restorations of affected teeth

Experience of pain and severity of MIH in child level

30.6 % (n= 74) of the children with MIH reported that they had experienced pain either during tooth brushing and/or they have had difficulties to consume hot or cold beverages (Fig. 30). According the EAPD-guidelines (Lygidakis et al., 2010) 52.1 % (n= 126) of the MIH children exhibit a severe form of MIH at least one of their affected teeth (Fig. 31).

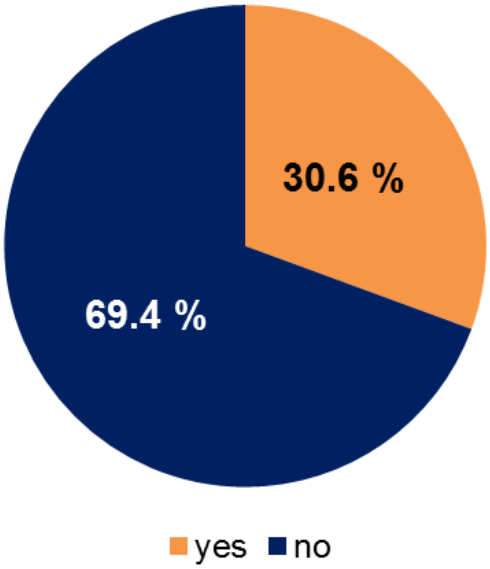


Fig. 30: Distribution of hypersensitivity's presence (yes) at child level (n= 242)

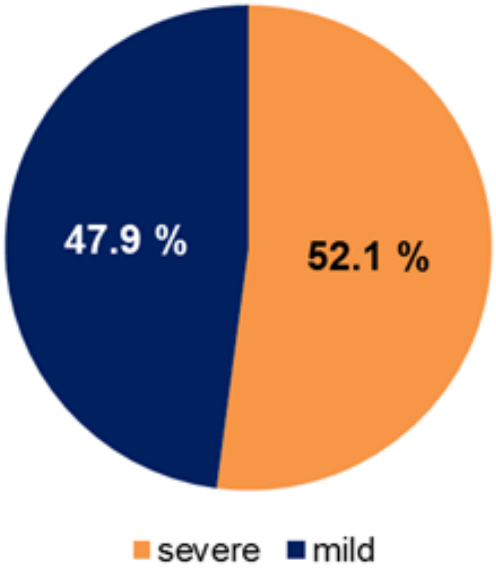


Fig. 31: Distribution of the severity grad of MIH in child level (n= 242)

The severity of MIH was significantly associated with the number of affected permanent teeth per child (Spearman's correlation: r= 0.147; p= 0.022; Fig. 32). The correlation was higher when primary teeth were included (Spearman's correlation: r= 0.148; p= 0.022).

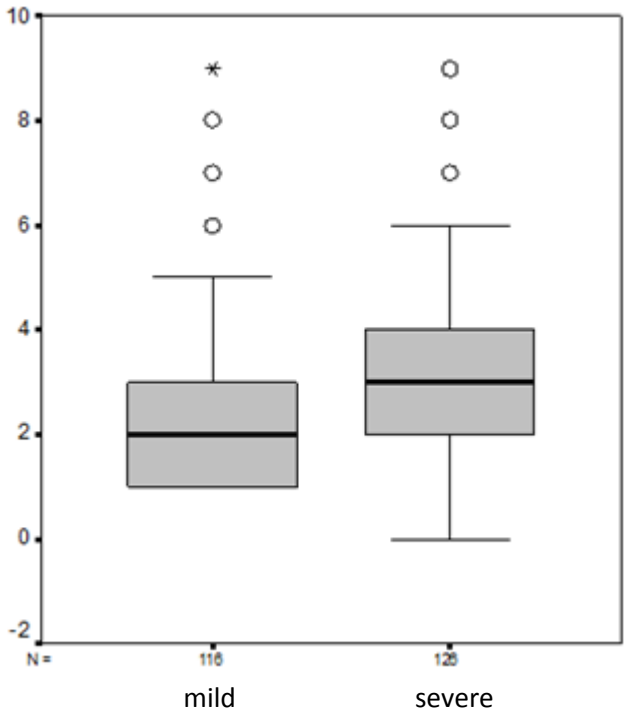


Fig. 32: Distribution of number of affected permanent teeth and severity of the MIH defects (Spearman's correlation: r= 0.147; p= 0.022)

Distribution of MIH characteristics at tooth surface level

Among children with MIH, the mean number of affected surfaces in permanent dentition was 4.5 ±3.8, the mean number of surfaces of affected molars was 3.9 ±3.4 (Fig. 33) and the mean number of affected surfaces of index teeth (first permanent molars, incisors and second primary molars) was 5.1 ±4.2. There was a significant correlation between the number of affected molars surfaces and the presence of more severe forms of MIH (Spearman's correlation: r= 0.366; p< 0.001) as well as number of affected surfaces and severity (permanent index teeth: Spearman's correlation, r= 0.321, p< 0.001; all index teeth: Spearman's correlation, r= 0.300, p< 0.001).

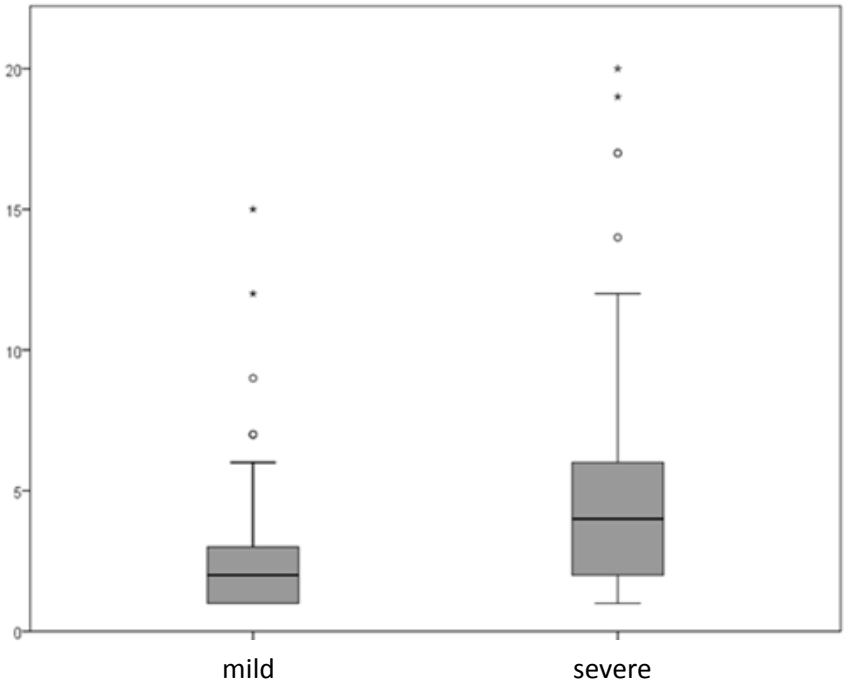
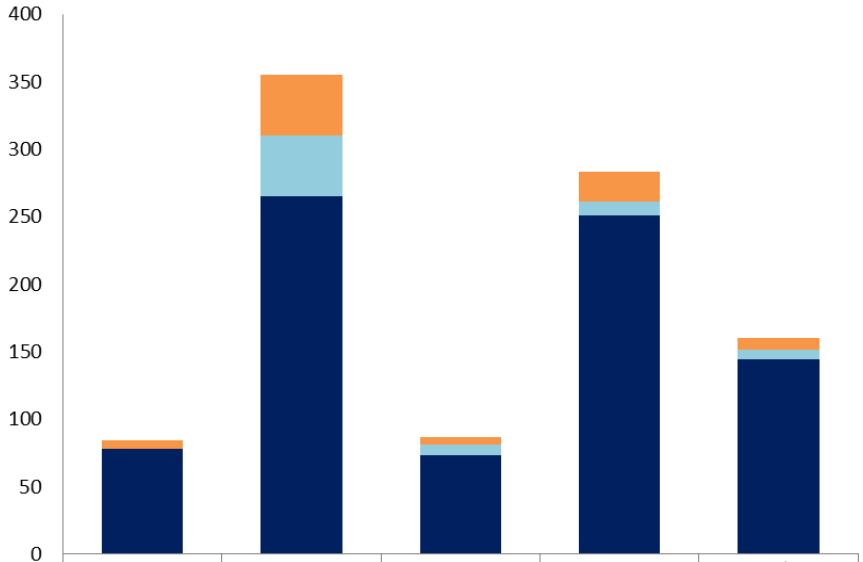


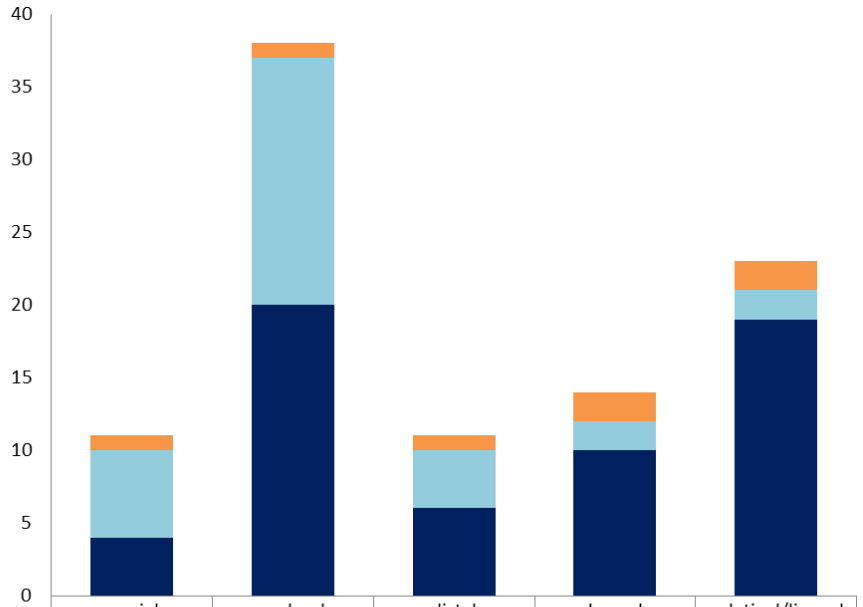
Fig. 33: Distribution of number of affected surfaces of MIH molars and severity of MIH (Spearman's correlation: r= 0.366, p< 0.001)

The occlusal surface was the most common affected surface in permanent and primary molars (36.6 % and 39.2 %, respectively), whereas the most common affected surface in incisors was the buccal (68.2%; Fig. 34- 36).



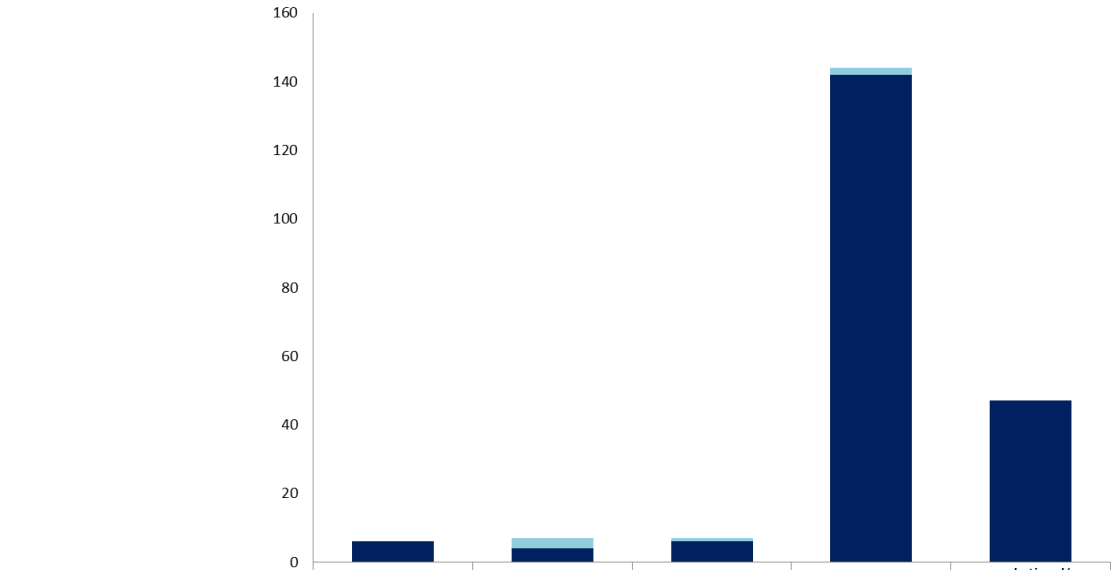
	mesial	occlusal	distal	buccal	paltinal/lingual
atypical restoration	6	45	6	22	9
post-eruptive enamel breakdown	0	45	8	10	7
demarcate opacity	78	265	73	251	144

Fig. 34: Number of hypomineralised surfaces of MIH first permanent molars



	mesial	occlusal	distal	buccal	palatinal/lingual
atypical restoration	1	1	1	2	2
post-eruptive enamel breakdown	6	17	4	2	2
demarcate opacity	4	20	6	10	19

Fig. 35: Number of hypomineralised surfaces of hypomineralised second primary molars



	mesial	incisal	distal	buccal	palatinal/ lingual
post-eruptive enamel breakdown	0	3	1	2	0
demarcate opacity	6	4	6	142	47

Fig. 36: Number of hypomineralised surfaces of hypomineralised permanent incisors

Caries experience of the sample

The sample had mean caries experience of 0.1 DMFT ±0.5 and 1.5 dmft ±2.2 with some regional variation (Tab. 8).

Table 8: Caries experience in permanent (mean DMFT ±SD) and primary (mean dmft ±SD) dentition of the study sample in each study area

Caries experience	City of examination				
	Düsseldorf	**Greifswald**	**Hamburg**	**Heidelberg**	**total**
DMFT ±SD	0.1 ±0.5	0.1 ±0.4	0.3 ±0.7	0.1 ±0.3	0.1 ±0.5
dmft ±SD	1.7 ±2.4	0.9 ±1.7	2.3 ±2.8	1.3 ±2.1	1.5 ±2.2

The majority of the children (92.1 %; 2205) had a DMFT of 0 (Tab. 9) and 88.2 % of the children presented with dmft≤ 2 (Tab. 10).The MIH group presented statistically significantly higher caries values (DMFT 0.2 ±0.6; dmft 2.0 ±2.5; t-test:

p< 0.001 and 0.001) compared to the children without MIH (DMFT 0.1 ±0.5; dmft 1.5 ±2.2).

Table 9: Distribution of the caries experience in permanent dentition (DMFT) in children with and without MIH

Number of children	DMFT value									
	0		1		2		3		4	
	n	%	n	%	n	%	n	%	n	%
with MIH (n= 242)	200	8.3	30	1.3	7	0.3	4	0.2	1	0.1
without MIH (n= 2153)	2005	83.7	93	3.8	35	1.5	10	0.4	10	0.4
total (n= 2395)	2205	92.0	123	5.1	42	1.8	14	0.6	11	0.5

Table 10: Distribution of caries experience in primary dentition (dmft value) of children with and without MIH

Number of children	dmft value									
	0		0<dmft≤2		2<dmft≤4		4<dmft≤7		dmft>7	
	n	%	n	%	n	%	n	%	n	%
with MIH	111	4.6	56	2.3	30	1.2	37	1.5	8	0.3
without MIH	1208	50.4	443	18.5	265	11.1	169	7.1	68	2.8
total	1319	55.0	499	20.8	295	23.3	206	8.6	76	3.1

Conclusively, the first permanent molars dominate the clinical picture of MIH. Meanwhile more than half of the children show a severe form of MIH with tooth breakdowns and hypersensitivity.

4. Discussion

The present study is the first German MIH study carried out in more than one regions of the country. The materials and methods of the study were identical for all the participating areas as well as in accordance with the latest European guidelines (Weerheijm et al., 2003; Lygidakis et al., 2010). The results of the study bring forward important information regarding the MIH phenomenon, thereby stressing the need for further research on this conflicting subject.

4.1 Discussion of methods

Selection of the sample

The sample was collected during regular compulsory dental examinations conducted in German schools ensuring a representative sampling. Limiting studies to those children attending the university dental clinics carries a high risk of a selection bias, as university clinics serve as reference centers for children who seek dental treatment because of unusual defects (e.g. MIH) or health problems (Jälevik, 2010). The schools participating in the study were randomly selected by the health centers of the regions minimizing a possible selection bias and increasing the internal validity of the study.

Calibration

A calibrated examiner (MP) with prior high Kappa scores acted as “gold standard” and she conducted calibration at the different sites ensuring a high inter-examiner reliability. A training session took place with 20 photographs representing different MIH grades and other enamel defects. The validity of this method has been proved as a reliable method for MIH identification and calibration in other studies (Elfrink et al., 2009; Wong et al., 2005). Although in this study only 20 photos have been used, in each photo a variety of defects of different severity was presented, thereby helping in diagnosing defects at surface level.

Due to time restrains, it was not possible to perform an intra-examiner calibration. To compensate this drawback, the main examiner (MP) was present during the first examinations (70- 100 children at each site) co-examining the children, so that any initial difficulties would be overcome in an appropriate and time-efficient manner.

Data collection forms

The MIH data sheet was the same for all the children with MIH according to the EAPD criteria (Weerheijm et al., 2003; Lygidakis et al., 2010). In addition information on demographic parameters (age, gender, etc.) was obtained and DMFT/dmft values were documented, because according to Weerheijm (2003; 2004), MIH defects are often associated with co-existing carious lesions. As the tooth most affected by caries in the early permanent dentition is the first permanent molar (Raadal et al., 2001; Runnel et al., 2012) the detailed recording of all defects on these teeth is also of pathognomonic value for the MIH phenomenon.

MIH criteria

The characteristics of MIH were recorded according to the EAPD criteria (Weerheijm et al., 2003). These criteria were established with the aim to solve the problem of differentially diagnosing MIH from other enamel defects, as various studies conducted in the past using pre-2003 criteria may not report its actual prevalence (Lygidakis et al., 2008a). A variety of indices had been developed (Tab. 4). The mDDE (modified Developmental Defects of Enamel) index for example, used by Dietrich et al. (2003), failed to differentiate post-eruptive breakdown (which constitutes a characteristic manifestation of MIH) from enamel hypoplasia (Jälevik, 2010). Nevertheless, a recent study by Balmer et al. (2012), with the aim of identifying the prevalence of MIH in 12-year-olds and being partly conducted in a highly fluoridated area, made use of the same index (mDDE), as it enabled them to distinguish between fluorotic and MIH defects. Furthermore, the Koch index, which was developed in 1987 in order to determine the prevalence of idiopathic enamel hypomineralisation in permanent teeth (Koch et al., 1987), was

implemented in the study of Preusser et al. (2007). However, according to Willmott et al. (2008) by using this index only an approximate MIH prevalence could be extracted. In the present study, as performed also by Leppäniemi et al. (2001) and Ghanim et al. (2012), the most severe form of MIH was registered for each tooth (demarcated opacity, post-eruptive breakdown, atypical restoration). "Atypical restoration" was categorized as the most severe form of MIH due to its invasiveness, in spite of the uncertainty of the previous status of the restored MIH teeth (Wogelius et al., 2008). To achieve a more representative analysis of the clinical variations of MIH, the surface-specific documentation of the different defects allows a more detailed analysis.

As the examinations were performed in classrooms and not in dental chairs the means of hypersensitivity measurements were limited. Therefore the examiners concentrated on questions regarding the children's experienced discomfort during daily activities. According to the EAPD guidelines (Lygidakis et al., 2010) experience of pain during brushing MIH teeth reveals a severe form of defect. Furthermore enamel defects in relation with eating could affect the quality of life (Castro et al., 2010). The hypersensitivity was recorded at child level and therefore a severity categorization at tooth level was not possible

Thus, the EAPD criteria (Weerheijm et al., 2003; Lygidakis et al., 2010) used in the present study are the best compromise for the assessment of MIH and allow a good comparison with other studies.

Differential diagnosis

The caries prevalence in Germany has been reduced over the last decades (Pieper, 2010). In accordance to this fact, the DMFT and dmft values of the children examined (DMFT= 0.1 ±0.5; dmft= 1.5 ±2.2) were low in all regions (DAJ, 2000; Kühnisch et al., 2010), so that a masking of the MIH defects was hardly possible (Willmott et al., 2008) and atypical restorations were easy to recognize. Additionally, the fluorosis prevalence has been very low in Germany (4.9 %-11.3 %) and its severity has generally been recorded as mild (Pieper et al., 2008; Momeni et al., 2007). This almost excludes fluorosis as a differential diagnosis of MIH. The frequent combination of MIH defects found in different dental surfaces

of the same teeth also confirms the validity of the diagnosis, particularly in cases of atypical restorations or demarcated opacities.

MIH examinations procedure

The examinations were performed on wet teeth according to the EAPD criteria (Weerheijm et al., 2003), even though a number of previous studies suggested that a higher prevalence of enamel defects can be reported when the teeth are dried first (Jälevik, 2010; Balmer et al., 2012). The same concern for underestimation of the prevalence of enamel defects was expressed by Balmer et al. (2012) regarding the limitations of the defects size. On the other hand, using no size limit carries the risk of misdiagnosis (Jälevik, 2010).

According to the definition of MIH, only if at least one first permanent molar was presented with MIH, the case was diagnosed as MIH. Children with enamel defects only in incisors or other non-index teeth were not included in the MIH group which could lead to an underestimation of MIH. On the other hand, defects in permanent incisors could be the result of a traumatic injury (Chawla et al., 2008a) in the primary dentition and, therefore, could prove misleading, resulting to an overestimation of the MIH prevalence. Still, authors such as Balmer et al. (2012) included MIH incisors even if molars with MIH were not present.

The age range of this study's with 7- 10-years of age is ideal, as the first permanent molars and incisors have just erupted. Later, caries and extractions of severely affected molars mask the detection of MIH (Balmer et al., 2012).

MIH in primary molars

In the present study the hypomineralisation of second primary molars in cases of MIH was recorded as an additional characteristic in MIH cases. Recent studies (Elfrink et al., 2012; Ghahim et al., 2012) record a relationship between hypomineralisation of the two dentitions. Elfrink et al. (2012) suggest that hypomineralisation of second primary molars could share the same cause and could be a predictor of MIH. Indeed there is a small overlap in the mineralization period of these teeth (32^{nd} week in utero- first year of life; Schroeder, 1987;

Weerheijm, 2003). Clinicians and investigators of MIH should consider these findings. It may be important in further epidemiological studies of MIH that the second primary teeth are co-examined among all the children of the sample.

4.2 Discussion of results

Prevalence of MIH

The majority of the MIH studies are carried out only in one city or region of a country. Due to the statistically significant variations (p= 0.001) of the prevalence of MIH (4- 14 %) between the four sites of Germany, it has become clear that a sample gathered from one region only cannot be representative for the whole land. Among the studies with samples from different regions or cities in a country (Höllta et al., 2001; Kusku et al., 2009; Mahoney et al., 2011; Muratbegovic et al., 2007; Jasulaityte et al., 2008; Weerheijm et al., 2001b; Wogelius et al., 2008; Zawaideh et al., 2011), only Kusku et al. (2009), Mahoney et al. (2011) and Weerheijm et al. (2001) reported no differences in occurrence of MIH among the different country sites, whereas Höltta et al. (2001) found a high difference between two cities in Finland along the same river contaminated with dioxins and furans (Kotka: 14.2%, Anjalankosk: 5.6 %). Similarly, Kosma et al. (2012) assessed the prevalence of MIH in 8 and 14 year old children in two cities in Greece, reporting significant differences between two cities (Ioannina: 22.5 %, Ptolemaida: 15.4 %). Furthermore, Souza et al. (2012) in their resent research in children from urban and rural areas concluded that environment has an important role in the analysis of the possible MIH aetiological factors.

Taking into account the different study criteria of previous studies, the overall prevalence of 10.1 % for the whole sample as well as the prevalence in each study area (Greifswald: 4.3 %, Heidelberg: 6.4 %, Hamburg: 14.0 %, Düsseldorf: 14.6 %) is comparable to the previous German (Dietrich et al., 2003; Heitmüller et al., 2012; Preusser et al., 2007) and other international studies (Jälevik, 2010).

The prevalence in Düsseldorf with 14.6 % and in Hamburg with 14.0% proved to be significantly higher than in the other two sites (p= 0.001). Considering the prior calibration (Kappa> 0.9) and the presence of the “gold standard” investigator during all first examinations of each participating city, this difference could not be caused by an examiner bias.

Since the aetiology of MIH is not yet clear (Alaluusua, 2010; Chawla et al., 2008a; Chawla et al., 2008b; Lygidakis et al., 2008b; Willmott et al., 2008) such variation in prevalence could be caused because of particular differences in the four regions taking part in the study. According to health insurances’ data, the prescription of antibiotics for children up to six years old in Germany, often considered as a cause of MIH (Alaluusua, 2010; Chawla et al., 2008a-b; Lygidakis et al., 2008b; Lygidakis et al., 2010), is the highest in Greifswald with the lowest MIH rate, while Düsseldorf with the highest prevalence of MIH showed a clearly lower antibiotics consumption. (BARMER GEK, 2010; de With et al., 2004). This does not support the hypothesis of antibiotics, but the data were not analysed on a child level.

The differences in the numbers of Caesarian sections performed in each region are also unable to justify the differences amongst MIH prevalences. According to national data (Statistisches Bundesamt, 2009), the percentage of Caesarian sections in Nordrhein-Westfalen (region of Düsseldorf) and in Baden-Württemberg (region of Heidelberg) is almost at the same level (32.5 % and 32.6 %, respectively) as in Mecklenburg-Vorpommern (region of Greifswald) and Hamburg (27.9 % and 28.0 %) whereas the MIH prevalences vary greatly.

The majority of aetiological studies were conducted on an individual basis. Information about possible aetiological parameters was extracted with questionnaires (Lygidakis et al., 2008b). The air pollution and the toxins alone (Kusku et al., 2009) or in combination with breast feeding (Alaluusua et al., 1996a; 1996b) were also investigated. The conclusions of these studies seem to differ as Alaluusua et al. (1996a-b) found a possible connection of MIH and toxins in breast milk, whereas Kusku et al. (2009) found no differences in MIH prevalence between a polluted and a non-polluted area.

The obvious variation among the different regions of a country opens a new dimension of research. As Souza et al. (2012) suggested, there seems to be a "link between MIH and environmental factors". In the present study, there was a clear increase in MIH from the almost rural and touristic town of Greifswald to Heidelberg and its surrounding countryside and finally to the cities Hamburg and Düsseldorf. This result contrasts with the study by Souza et al. (2012), who found that children from the rural areas of a Brazilian town (Bothelos) had a significantly higher prevalence of MIH than those coming from the urban areas (24.9% and 17.8%, respectively).

An investigation of all related aetiological factors and their regulating parameters on a local as well as regional and/or national basis may lead to a further step of understanding the nature of MIH.

MIH in primary molars

Weerheijm et al. (2003) and Lygidakis et al. (2010) already stated that the existence of MIH defects is also possible in the second primary molars. MIH defects were also documented in primary molars (4.9 %) according to EAPD criteria in the study of Elfrink et al. (2008). Casanova-Rasado et al. (2011) found a connection between the dental opacities and hypoplasia of both dentitions. Thus, the relationship between MIH in both dentitions found by Elfrink et al. (2012) and Ghanim et al. (2012) was confirmed by the present study and primary second molar hypomineralisation could be used as a predictor for MIH.

Distribution of MIH

The results of this study are in agreement with the findings of other German and international studies:

- no gender-specific difference in the distribution of MIH prevalence (Calderara et al., 2005; Chawla et al., 2008a; Fteita et al., 2006; Jälevik et al., 2001; Jasulaityte et al., 2008; Martinez Gomez et al., 2012; Muratbegovic et al., 2007; Leppäniemi et al., 2001),

- a similar distribution of defects in the upper and lower jaw (Chawla et al., 2008a; Cho et al., 2008; Ghanim et al., 2011; Weerheijm et al., 2001b),
- the mean value of about 2.8 ±1.7 affected teeth per affected child is consistent with other reports (Calderara et al., 2005; Cho et al., 2008; Jälevik et al., 2001),
- the frequency of affected incisors (40%, n= 196 in 490 cases with affected molars; Jasulaityte et al., 2008; Lygidakis et al., 2008),
- the mean value of about 2.0 ±1.1 MIH molars per affected child (Dietrich et al., 2003; Jälevik et al., 2001),
- the upper central incisors (right: 22.3 %, left: 21.9 %) are the most frequent affected incisors (Lygidakis et al., 2008; Zawaideh et al., 2011; Jasulaityte et al., 2008),
- demarcated opacities (81.2 %) are the most frequent form of MIH (Jasulaityte et al., 2007; Muratbegovic et al., 2008; Ghanim et al., 2011; Heimüller et al., 2012; Soviero et al., 2009),
- the positive correlation between number of affected teeth and the severity (hypersensitivity, structural loss) of MIH (Chawla et al., 2008a-b; Ghanim et al., 2011; Jälevik et al., 2001; Jasulaityte et al., 2007; Leppäniemi et al., 2001)
- as well as the most commonly affected surface of molars (occlusal) and incisors (buccal) (da Costa-Silva et al., 2011; Lygidakis et al. 2008a; Muratbegovic et al., 2007; Preusser et al., 2007).

Even though older children tend to show severer lesions than younger ones (Leppäniemi et al., 2001; Lygidakis et al., 2008a; Jasulaityte et al., 2008), this difference was not statistical proved in the present study (p= 0.4). A probable reason for this finding could be the small variation in the age groups (7- 10 years) of the study sample.

The treatment costs and the fear of experiencing pain are relevant parameters for children with MIH (Jasulaityte et al., 2008). According to Jälevik and Klingberg (2002), nine-year-old children with MIH were treated 10 times more often than children without MIH. This corresponds to the results of the present study, because almost half of the cases had a severe form of MIH (52.1 %) and 18.8 % of the hypomineralised first permanent molars showed a combination of MIH defects.

In Germany, health insurances cover most of the costs for dental treatment. Unfortunately, composite fillings and stainless steel crowns in permanent teeth, which are often needed to ensure the optimum restoration of MIH molars, are not included. An adaptation of these rules for MIH patients would be helpful.

Although a detailed knowledge of the intra-oral distribution of MIH at surface level would be beneficial to assess the treatment need, it is rarely examined. A study on the distribution of “post-eruptive breakdown” among molars surfaces is in agreement with the present study (Ghanim et al., 2011). The thesis of Mach (2009) also clearly revealed a mean of more than one affected surfaces per tooth (755 surfaces in 601 teeth).

Caries experience and MIH

In spite of the low caries prevalence (0.1 ±0.5 DMFT), the caries experience in the permanent dentition for children with MIH was statistically significantly elevated, which is not in agreement with the recent study of Heitmüller et al. (2012).

In the primary dentition, the difference was even more pronounced (2.0 ±2.5 vs. 1.5 ±2.2) which may indicate a masking of possible hypomineralisation of second primary molars.

In accordance with the higher caries prevalence for children with MIH in other studies (Leppäniemi et al., 2001; Weerheijm, 2003), the presence of MIH defects as a risk factor for caries development may also be due to pain or discomfort

during tooth brushing (Lygidakis et al., 2010). This would call for early capping of hypersensitive teeth which affects almost half of the children.

The hypomineralisation defects in the second primary molars may be related to the reported high caries prevalence in the same teeth (Elfrink et al., 2006). Whether the fact that caries incidence in first primary molars is lower compared to the second ones (Gizani et al., 1999) can be explained by the higher occurrence of hypomineralisation in the latter is still speculative.

5. Conclusions and clinical considerations

In spite of the regional variation for MIH from 4.3 to 14.6 %, the estimated mean prevalence of about 10 % for Germany is comparable to other international studies and poses an epidemiologically relevant problem. It corresponds with the necessity of an early diagnosis, intensified caries-preventive measures and an adequate treatment of the affected teeth soon after eruption. This is of special interest as more than half of the children showed a severe form of MIH with tooth breakdowns or hypersensitivity. The positive relationship between caries experience and the presence of MIH found in the permanent as well the primary dentition stresses the importance of additional caries prevention in order to prevent a further reduction in oral health. Furthermore, the presence of MIH in the second primary molars could be of predictive value for the presence of MIH in permanent dentition. As other studies point out, MIH might not be a problem strictly limited to first permanent molars or incisors (Elfrink et al., 2012; Ghanim et al., 2012; Heitmüller et al., 2012).

Therefore, diagnosing and treating MIH should be part of the basic undergraduate education in German universities. As the interest in MIH is very recent, continuing education should also address this topic to bring it to the attention of all dental practitioners. The general practitioner should be able to recognise MIH defects in order to perform an adequate treatment or to refer complicated cases for specialized treatment. The necessity of these measures becomes clearer when the prevalence of MIH is compared with the prevalence of other challenging conditions, such as early childhood caries (13.6 %; Robke and Buitkamp, 2002) or dental trauma (12.7 %; Martins et al., 2012).

Specialists should be trained to treat complex MIH cases routinely. The training should optimally include stainless steel crowns for intermediate coverage of severely affected first permanent molars, a mixed dentition analysis and the decision making between extracting or preserving these teeth right before the eruption of the second permanent molars.

The reason there is a need for adequate awareness of the dental service for MIH cases is the socio-psychological stress (Lygidakis et al., 2010) that these children undergo. Restrictions during tooth brushing or eating, mentioned in 30.6 % of the MIH cases, are often associated with a reduction in the quality of life (Castro et al. 2011, Vargas-Ferreira et al., 2011). The involvement of discolorations in incisors of about 40% can also be of esthetical concern.

Another clinical problem is the conditioning for dental pain which can reinforce dental fear, anxiety and management problems commonly found in children with MIH (Jälevik and Klingberg, 2002). A follow-up study (Jälevik and Klingberg, 2012) revealed that 18-year-old adults with severe MIH defects continued having the same oral and anxiety problems as in their youth.

Generally, representative samples are necessary for MIH studies in order to estimate the countries' prevalences. As long as aetiology of MIH remains unclear, preventive approaches are not possible. On the contrary, the prevention of further destruction of MIH defects, using appropriate restorative techniques, as well as reducing the caries activity with an intensive preventive program during the early eruption stage, is ideal for the prognosis of MIH teeth (Lygidakis et al., 2010). In spite of a variety of potential causes of MIH, the biological pathways for presence and severity which differ even within the same dentition, are not clear (Chawla et al., 2008a-b; Lygidakis et al., 2010). Further clinical and, especially, epidemiological research could be helpful to identify potential aetiological factors due to their regional variation. Moreover, the distribution of defects among surfaces of affected teeth gives a full clinical view of MIH and, therefore, it is recommended that at least a part of the future epidemiological studies should include the tooth and surface level.

Since MIH is not a classical disease, parents may not pay attention to the discolorations or even the enamel breakdown of their children's teeth before the child itself starts to complain of pain or discomfort during daily activities (e.g. eating). This could lead to the deterioration of the prognosis of the affected tooth since sensitivity and the avoidance of brushing the affected area favor rapid caries development (Leppäniemi et al., 2001; Weerheijm, 2003; Weerheijm,

2004). Hence information regarding MIH should be made available to the public and parents in particular should be made aware of the features of MIH, the high necessity of tooth brushing and of regular visits at the dental practice for early preventive and therapeutic steps.

6. Abstract

Due to the wide range of reported prevalence of Molar-Incisor-Hypomineralisation (MIH) found in regional studies, the aim of this study was to determine the prevalence of MIH in school children at different areas in Germany and to compare the findings to other studies.

In the compulsory dental school examination, the first permanent molars, permanent incisors and second primary molars were examined for the presence of MIH according to EAPD criteria (Lygidakis et al., 2010; Weerheijm et al., 2003) in 2395 children attending 2^{nd} to 4^{th} grade (mean age 8.1 ±0.8 years, range 7- 10 years) in four regions in Germany. Examinations were performed by five calibrated examiners (Kappa> 0.9) on clean teeth after brushing.

The MIH prevalence at the four regions differed considerably (Düsseldorf 14.6 %, Hamburg 14.0 %, Heidelberg 6.0 %, Greifswald 4.3%) with a mean prevalence of 10.1 % (10.7 % boys, 9.5 % girls, χ^2-test: p= 0.57). The caries prevalence was low in general, but children with MIH exhibited statistically significantly higher caries experience in the primary and permanent dentition (MIH group: dmft 2.0 ±2.5; DMFT 0.2 ±0.6; other children: dmft 1.5 ±2.2; DMFT 0.1 ±0.5; t-test: p= 0.001 and p< 0.001, respectively). The mean number of permanent teeth affected by MIH was 2.8 (±1.7). 12.0 % of the children with MIH also had at least one affected primary molar which resulted in a statistically significant correlation for MIH in primary and permanent teeth (p< 0.01, Spearman`s correlation). Most of the affected teeth had demarcated opacities (81.2 %), but more than half of the affected children showed at least one tooth with a severe form of MIH characterized by breakdown of the tooth, atypical restorations or pain during brushing or eating.

In conclusion, MIH is a clinically and epidemiologically relevant problem in German school children. The prevalence which is highly varying in different regions requires more research on the aetiology of MIH. The high rate of severe forms is of clinical concern. The findings of the present study stress the need for

educating present and future dentists and pediatric specialists in MIH, as well as for developing public health policies for the prevention and adequate treatment of MIH.

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8. Data collection forms

8.1 Data collection form used for each MIH case (German version)

Schule: **Prävalenz von MIH in 2.-4. Klasse** __/__/201_

Klasse: ____Geschlecht: m w Alter: ____Geb.Dat.:__/__/XX N. im Befundbogen: ____

Wenn es MIH gibt:

	1.Farbe Veränderung					Substanzen Verlust					Zerstörte / fehlende Zähne	Sensibilität (beim Putzen oder fragen ob Zähne empf. sind)	Atypische Restorationen (Füllungsmaterial; VS auch vermerken)					
	m	o	d	b	p/l	m	o	d	B	p/l			m	o	d	b	p/l	Welche:
16																		
55																		
12																		
11																		
21																		
22																		
65																		
26																		
36																		
75																		
32																		
31																		
41																		
42																		
85																		
46																		

Index von EAPD 2003:

1. Farbe	Demarcated opacities
2. Schmelzsubstanzverlust	Post-eruptive enamel breakdown
3. Nicht durchgebrochene Zähne oder extarierte Zähne wegen MIH	Failure of eruption or extraction due to MIH
4. Atypische Restorations	Atypical restorations

8.2 Data collection form for demographic data and caries experience (German version)

MIH Studie

Datum:
Schule:
Klasse:

	Geb. Datum (--/--/XX)	Geschlecht (m/w)	Alter	dmft	DMFT	MIH nur perm.	MIH in Milchmolaren (nur wenn MIH perm.)
1							
2							
3							
4							
5							
6							
7							
8							
9							
10							
11							
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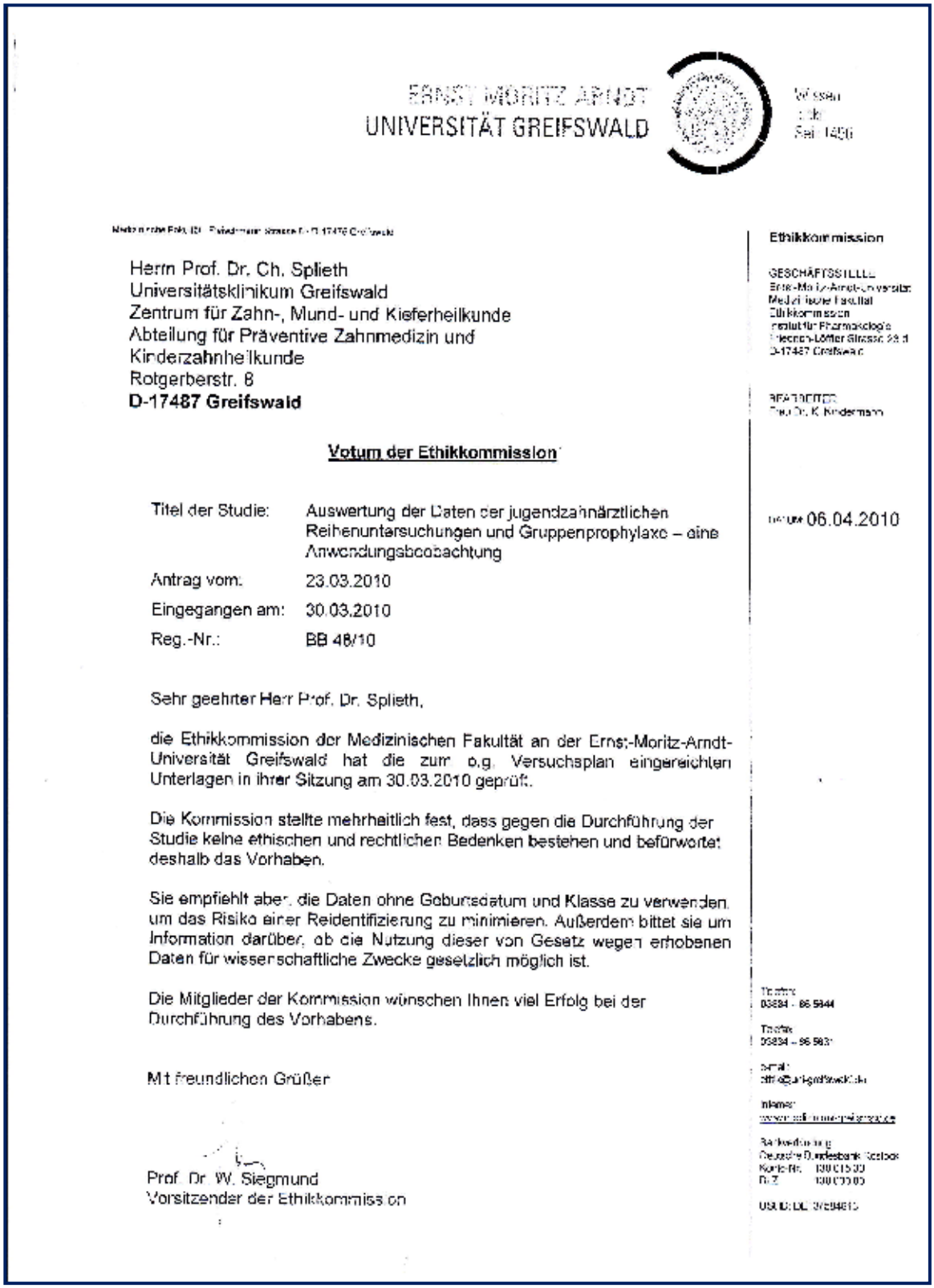
28							

9. Approval of ethical committee



ERNST MORITZ ARNDT
UNIVERSITÄT GREIFSWALD

Wissen
Seit 1456

Ethikkommission

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Ethikkommission
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Rotgerberstr. 8
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Votum der Ethikkommission

datum 06.04.2010

Titel der Studie:	Auswertung der Daten der jugendzahnärztlichen Reihenuntersuchungen und Gruppenprophylaxe – eine Anwendungsbeobachtung
Antrag vom:	23.03.2010
Eingegangen am:	30.03.2010
Reg.-Nr.:	BB 48/10

Sehr geehrter Herr Prof. Dr. Splieth,

die Ethikkommission der Medizinischen Fakultät an der Ernst-Moritz-Arndt-Universität Greifswald hat die zum o.g. Versuchsplan eingereichten Unterlagen in ihrer Sitzung am 30.03.2010 geprüft.

Die Kommission stellte mehrheitlich fest, dass gegen die Durchführung der Studie keine ethischen und rechtlichen Bedenken bestehen und befürwortet deshalb das Vorhaben.

Sie empfiehlt aber, die Daten ohne Geburtsdatum und Klasse zu verwenden, um das Risiko einer Reidentifizierung zu minimieren. Außerdem bittet sie um Information darüber, ob die Nutzung dieser von Gesetz wegen erhobenen Daten für wissenschaftliche Zwecke gesetzlich möglich ist.

Die Mitglieder der Kommission wünschen Ihnen viel Erfolg bei der Durchführung des Vorhabens.

Mit freundlichen Grüßen

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Vorsitzender der Ethikkommission

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Zur Begutachtung haben der Kommission vorgelegen:

- Antrag an die Ethikkommission mit Beschreibung des Vorhabens vom 23.03.2010

Der Ethikkommission gehören an:

reguläre Mitglieder	ständige Stellvertreter
Prof. Dr. M. Lerch Klinik für Innere Medizin A	*Prof. Dr. J. Mayerle ** *Klinik für Innere Medizin A*
Prof. Dr. R. Biffar Zentrum für Zahn-, Mund- und Kieferheilkunde	*Dr. I. Polzer ** *Zentrum für Zahn-, Mund- und Kieferheilkunde*
Prof. Dr. U. Runge Klinik und Poliklinik für Neurologie	*Prof. Dr. A. Hamm* *Institut für Psychologie*
OA Dr. M. Gründling Klinik für Anästhesiologie und Intensivmedizin	*OÄ Dr. S. Friesecke* *Klinik für Innere Medizin B*
Prof. Dr. W. Siegmund * Institut für Pharmakologie	*Dr. Dr. G. Engel* *universitätsapotheke*
Prof. Dr. Th. Kohlmann * Institut für Community Medicine	*Prof. Dr. W. Hoffmann* *Institut für Community Medicine*
PD Dr. B. Bockholdt Institut für Rechtsmedizin	*Prof. Dr. W. Jocks ** *Fakultät für Rechts- und Staatswissenschaft*
Prof. Dr. H.-W. Eckert Fakultät für Rechts- und Staatswissenschaft	*Prof. Dr. J. Lege * und Prof. Dr. C. D. Classen* *Fakultät für Rechts- und Staatswissenschaft*
Prof. Dr. H. Asse Theologische Fakultät	*Prof. Dr. K. Ott* *HB Biologie*
Prof. Dr. H. Laufer Klinik und Poliklinik für Kindermedizin	*PD Dr. R. Brums* *Klinik und Poliklinik für Kindermedizin*
Prof. Dr. R. Sudick * Klinik und Poliklinik für Frauenheilkunde Klinikum Neubrandenburg	*Prof. Dr. M. Zygmunt* *Klinik und Poliklinik für Frauenheilkunde und Geburtshilfe*
PD Dr. H.-C. Schober * Klinik für Innere Medizin Klinikum Südstadt Rostock	*PD Dr. R. Möllmann* *niedergelassener Internist, Greifswald*
Katharina Schade, Medizinstudentin *	*Rahel Österreicher-Cuiz, Medizinstudentin*

* bei der Sitzung am 30.03.2010 anwesend

10. Eidesstattliche Erklärung

Hiermit erkläre ich, dass ich die vorliegende Dissertation selbstständig verfasst und keine anderen als die angegebenen Hilfsmittel benutzt habe.
Die Dissertation ist bisher keiner anderen Fakultät und keiner anderen wissenschaftlichen Einrichtung vorgelegt worden.
Ich erkläre, dass ich bisher kein Promotionsverfahren erfolglos beendet habe und dass eine Aberkennung eines bereits erworbenen Doktorgrades nicht vorliegt.

Marina Agathi Petrou

Greifswald, 22/11/2012

(Affirmation

I hereby declare that I have written this thesis independently and have used no other than the means and sources mentioned. The thesis has so far not been submitted to any other faculty. I declare that I have not completed any doctoral process unsuccessfully and no withdrawal exists of an already acquired doctoral degree.

Greifswald, 22/11/2012 *Marina Agathi Petrou*

Place, date *Signature)*

11. Dedication

This work is dedicated to my husband Nikolaos P. Parthymos for his entire and incessant support. Without it, the fulfillment of this study would not be possible.

12. Acknowledgements

This multi-center study was conducted by the public health centers and universities of Düsseldorf, Greifswald, Hamburg and Heidelberg. I would like to express my gratitude for their contribution and great hospitality to all the examiners, co-workers and heads of the departments.

Using a chronological order of participation in the study, I would like to thank the scientists who contributed to it: My sincere thanks to Dr. Basner[1] and Prof. Dr. Splieth[1] in Greifswald, Dr. Bissar[2, 3] and Prof. Dr. Schulter[2] in Heidelberg, Dr. Giraki[4], Dr. Schaeffer[5], Dr. Schraven[5], Ms Brenneis[5] and Prof. Dr. Beilke[4] in Düsseldorf and last but not least Dr. Wempe[6] and Prof. Dr. Schiffner[7] in Hamburg ([1]Dept. of Preventive and Pediatric Dentistry, University of Greifswald; [2]Dept. of Conservative Dentistry, University of Heidelberg; [3]Gesundheitsamt Rhein-Neckar- Kreis, Heidelberg; [4]Dept. of Operative Dentistry, Periodontics, and Endodontics, University of Düsseldorf; [5]Gesundheitsamt, Düsseldorf; [6]Gesundheitsamt, Eimsbüttel; [7]Dept of Restorative and Preventive Dentistry, University of Hamburg).

I would like to express my immense gratitude to my supervisor, Prof. Dr. Splieth, Head of the Department of Preventive and Pediatric Dentistry of Greifswald University, for his constant support and direction, as well as for his invaluable contribution to the statistical analysis of the data.

A great acknowledgment and my deepest appreciation go to all my teachers for their guidance and support to my constant effort of self- improvement as a person and a scientist.

I would also like to thank my parents, Andreas Petrou and Eleni Arvaniti, as well as my sisters, Vasiliki, Maria and Foteini, for the support they provided me through my entire life.

As for my friends and colleagues, Ms Ruth Santamaria and Ms Aikaterini Tachou, I own them a big thank not only for their psychological support but also for their tips and tricks that made my work easier.

Όρκος του Ιπποκράτη

Ὄμνυμι Ἀπόλλωνα ἰητρὸν, καὶ Ἀσκληπιὸν, καὶ Ὑγείαν, καὶ Πανάκειαν, καὶ θεοὺς πάντας τε καὶ πάσας, ἵστορας ποιεύμενος, ἐπιτελέα ποιήσειν κατὰ δύναμιν καὶ κρίσιν ἐμὴν ὅρκον τόνδε καὶ ξυγγραφὴν τήνδε.

Ἡγήσασθαι μὲν τὸν διδάξαντά με τὴν τέχνην ταύτην ἴσα γενέτῃσιν ἐμοῖσι, καὶ βίου κοινώσασθαι, καὶ χρεῶν χρηίζοντι μετάδοσιν ποιήσασθαι, καὶ γένος τὸ ἐξ ωὐτέου ἀδελφοῖς ἴσον ἐπικρινέειν ἄῤῥεσι, καὶ διδάξειν τὴν τέχνην ταύτην, ἢν χρηίζωσι μανθάνειν, ἄνευ μισθοῦ καὶ ξυγγραφῆς, παραγγελίης τε καὶ ἀκροήσιος καὶ τῆς λοιπῆς ἁπάσης μαθήσιος μετάδοσιν ποιήσασθαι υἱοῖσί τε ἐμοῖσι, καὶ τοῖσι τοῦ ἐμὲ διδάξαντος, καὶ μαθηταῖσι συγγεγραμμένοισί τε καὶ ὡρκισμένοις νόμῳ ἰητρικῷ, ἄλλῳ δὲ οὐδενί.

Διαιτήμασί τε χρήσομαι ἐπ' ὠφελείῃ καμνόντων κατὰ δύναμιν καὶ κρίσιν ἐμὴν, ἐπὶ δηλήσει δὲ καὶ ἀδικίῃ εἴρξειν.

Οὐ δώσω δὲ οὐδὲ φάρμακον οὐδενὶ αἰτηθεὶς θανάσιμον, οὐδὲ ὑφηγήσομαι ξυμβουλίην τοιήνδε. Ὁμοίως δὲ οὐδὲ γυναικὶ πεσσὸν φθόριον δώσω. Ἁγνῶς δὲ καὶ ὁσίως διατηρήσω βίον τὸν ἐμὸν καὶ τέχνην τὴν ἐμήν.

Οὐ τεμέω δὲ οὐδὲ μὴν λιθιῶντας, ἐκχωρήσω δὲ ἐργάτῃσιν ἀνδράσι πρήξιος τῆσδε.

Ἐς οἰκίας δὲ ὁκόσας ἂν ἐσίω, ἐσελεύσομαι ἐπ' ὠφελείῃ καμνόντων, ἐκτὸς ἐὼν πάσης ἀδικίης ἑκουσίης καὶ φθορίης, τῆς τε ἄλλης καὶ ἀφροδισίων ἔργων ἐπί τε γυναικείων σωμάτων καὶ ἀνδρῴων, ἐλευθέρων τε καὶ δούλων.

Ἃ δ' ἂν ἐν θεραπείῃ ἢ ἴδω, ἢ ἀκούσω, ἢ καὶ ἄνευ θεραπηίης κατὰ βίον ἀνθρώπων, ἃ μὴ χρή ποτε ἐκλαλέεσθαι ἔξω, σιγήσομαι, ἄῤῥητα ἡγεύμενος εἶναι τὰ τοιαῦτα.

Ὅρκον μὲν οὖν μοι τόνδε ἐπιτελέα ποιέοντι, καὶ μὴ ξυγχέοντι, εἴη ἐπαύρασθαι καὶ βίου καὶ τέχνης δοξαζομένῳ παρὰ πᾶσιν ἀνθρώποις ἐς τὸν αἰεὶ χρόνον. Παραβαίνοντι δὲ καὶ ἐπιορκοῦντι, τἀναντία τουτέων. *(Ιπποκράτης 460-370 π. Χ.)*

Hippocratic Oath (Original, translated into English)

"I swear by Apollo, the healer, Asclepius, Hygieia, and Panacea, and I take to witness all the gods, all the goddesses, to keep according to my ability and my judgment, the following Oath and agreement:

To consider dear to me, as my parents, him who taught me this art; to live in common with him and, if necessary, to share my goods with him; To look upon his children as my own brothers, to teach them this art; and that by my teaching, I will impart a knowledge of this art to my own sons, and to my teacher's sons, and to disciples bound by an indenture and oath according to the medical laws, and no others.

I will prescribe regimens for the good of my patients according to my ability and my judgment and never do harm to anyone.

I will give no deadly medicine to any one if asked, nor suggest any such counsel; and similarly I will not give a woman a pessary to cause an abortion.

But I will preserve the purity of my life and my arts.

I will not cut for stone, even for patients in whom the disease is manifest; I will leave this operation to be performed by practitioners, specialists in this art.

In every house where I come I will enter only for the good of my patients, keeping myself far from all intentional ill-doing and all seduction and especially from the pleasures of love with women or with men, be they free or slaves.

All that may come to my knowledge in the exercise of my profession or in daily commerce with men, which ought not to be spread abroad, I will keep secret and will never reveal.

If I keep this oath faithfully, may I enjoy my life and practice my art, respected by all humanity and in all times; but if I swerve from it or violate it, may the reverse be my life." (Hippocrates 460- 370 BC; *http://en.wikipedia.org/wiki/Hippocratic_Oath)*