Hypomineralised Second Primary Molars: Prevalence, characteristics and perception of management by Irish dentists

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Summary

This thesis comprises three different studies with a shared focus on Hypomineralised Second Primary Molars (HSPM). HSPM is defined as idiopathic hypomineralisation affecting between one and four second primary molars (SPMs). The first part (Study 1) of the thesis aimed to investigate the global prevalence of HSPM by conducting a systematic review and meta-analysis. The prevalence of HSPM was 6.8% (95%CI 4.98 to 8.86%) on a child level and 4.08% on a tooth level (95%CI=2.80 to 5.59%). Part two (Study 2) of the thesis presents preliminary data from a cross-sectional study that aimed to investigate the prevalence of HSPM in Dublin 4–6-year-old children. Due to Covid 19 restrictions in 2020 data collection from other Dublin schools was not possible. The prevalence of HSPM was 38.3%.The mean number of affected teeth per child was 2.16±1.13. The most common defects were creamy-white demarcated opacities (81.8%). No association was found between caries experience and HSPM prevalence (p=.25). The final part of the thesis (Study 3) aimed to explore how general dentists in the Republic of Ireland perceive and manage HSPM. A validated structured questionnaire was developed and was sent to Irish dentists using Survey Monkey. A total of 279 general dentists responded to the questionnaire and were grouped according to age, years of practice and workplace. The majority of dentists (75%) were aware of HSPM and were confident in its diagnosis (71%). Only 58% of respondents were aware of the predictive nature of HSPM for Molar Incisor Hypomineralisation (MIH) development highlighting a potential gap in knowledge. MIH has been defined as hypomineralisation of systemic origin involving one to four first permanent molars (FPMs) with frequently affected incisors. Dentists who had

practiced for ≥ 15 years were significantly more likely to document HSPM frequently compared to those with less experience. Conservative and biological based treatment approaches were the most popular choices in the clinical scenarios.

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Glossary of terms

ABBREVIATION	DESCRIPTION
HSPM(s)	Hypomineralised Second Primary Molar(s)
SPM(s)	Second Primary Molar(s)
FPM(s)	First Permanent Molar(s)
MIH	Molar Incisor Hypomineralisation
DMH	Deciduous Molar Hypomineralisation
PEB	Post Eruptive Breakdown
DDE	Developmental Defects of Enamel
mDDE index	Modified Developmental Defects of Enamel
EAPD	European Academy of Paediatric Dentistry
OHRQoL	Oral Health Related Quality of Life
d_{v3}mf	Decayed to the level of visual dentine cavitation, missing, filled
GIC	Glass Ionomer Cement
RMGIC	Resin Modified Glass Ionomer Cement
ART	Atraumatic Restorative Treatment
SSC(s)	Stainless Steel Crown(s)

1 Literature Review

1.1 Background

Dental caries and developmental defects of enamel (DDE) are common oral health conditions affecting children worldwide. (Tinanoff and Reisine, 2009, AAPD, 2014). There is increasing interest as to whether these two conditions are associated. DDE can occur in the primary and permanent dentition and can be classified under two main categories including hypoplasia and hypomineralisation. Enamel hypoplasia is a quantitative defect of enamel caused by a disturbance to the ameloblasts during matrix formation (Jalevik and Noren, 2000, Weerheijm, 2003). Enamel hypomineralisation is a qualitative defect of the enamel resulting from a disturbance during initial calcification and/or maturation (Jalevik and Noren, 2000, Weerheijm, 2003). In the permanent dentition, hypomineralised FPMs are often associated with affected incisors with the term MIH being used (Weerheijm, 2003). In the primary dentition, hypomineralisation of the SPM has been observed (Weerheijm, 2003, Elfrink et al., 2008, Elfrink et al., 2012). The term HSPM has been accepted and is defined as idiopathic hypomineralisation of one to four SPMs (Elfrink et al., 2008, Ghanim et al., 2013). MIH studies have formed the basis for our understanding of HSPM and have informed areas of research such as potential aetiological factors and management.

Research conducted by Koch et al. in the 1980s reported an increasing number of children with both extensive and severe FPM enamel hypomineralisation of idiopathic origin (Koch et al., 1987). Defect characteristics included that of a demarcated opacity frequently associated with breakdown of the enamel

especially at the occlusal surfaces and cusps (Koch et al., 1987). The marginal areas of breakdown were rough and irregular differentiating them from hypoplastic defects (FDI Commission on Oral Health Research and Epidemiology, 1982). Historically, many terms have been used to describe MIH including cheese molars and idiopathic enamel hypomineralisation (Weerheijm, 2003). In 2001, the term MIH was coined defined as hypomineralisation of systemic origin involving one to four FPMs with frequently affected incisors (Weerheijm et al., 2001). Reference to MIH-like defects affecting the SPMs was reported soon after this (Weerheijm et al., 2003). The global term of Deciduous Molar Hypomineralisation (DMH) was proposed by Elfrink in 2009 reflecting the lack of detailed studies on the issue (Elfrink et al., 2009, Elfrink et al., 2010). This was later revised to the now accepted term HSPM, highlighting the localisation of the defect to the SPM (Ghanim et al., 2013).

1.2 Aetiology

Tooth development while genetically controlled is sensitive to environmental disturbances (Alaluusua, 2010). Enamel formation occurs slowly and insults that occur during this process leave a permanent record in the tooth (Fearne et al., 1994). Enamel as a hard tissue has been described as a kymograph, facilitating the dating of events with relatively good accuracy (Sarnat and Schour, 1942). This function is necessary when trying to relate developmental disturbances to possible aetiological factors.

Teeth affected by demarcated hypomineralisation defects are believed to have a multifactorial aetiology with disturbances occurring during the prenatal, perinatal or postnatal periods hypothesised (Ghanim et al., 2012). SPM crown

calcification commences around the 18th gestational week and is complete by the end of the first year of childhood (McDonald and Avery, 2004). Mineralisation of the SPM overlaps with that of the permanent incisors and FPMs with these teeth beginning calcification later, during the third gestational trimester and finishing by the end of the third year of childhood. The causes of both HSPM and MIH are anticipated to be the same however with an earlier timed disturbance for HSPM (Weerheijm et al., 2003). Potential HSPM aetiological factors have been divided into three chronological phases: prenatal (0-36/38 weeks), perinatal (birth to 28 days) and postnatal periods (29 days+). It has been hypothesised that prenatal or perinatal insults occurring concomitant with crown calcification are more likely to cause a HSPM defect (Ghanim et al., 2012). Table 1.1 summarises studies investigating HSPM determinants.

1.2.1 *Genetics and ethnicity*

The genetic contribution to HSPM development remains inconclusive. Studies on MIH suggest a shared input of both environmental exposures and genetic/epigenetic factors (Vieira and Kup, 2016, Teixeira et al., 2018). Several MIH associative genes (ENAM, AMBN, *TUFT1* and *TFIP11*) have been identified with no association found between AMELX (a gene involved in amelogenesis imperfecta) (AI) with a primary function of amelogenin deposition and MIH (Jeremias et al., 2013). The strongest evidence supporting the genetic contribution to MIH has been obtained from analysing its distribution in twins. It has been shown that not only are twins at greater risk of MIH than the normal population, but monozygotic twins are twice more likely to have this condition than dizygotic twins (Teixera et al, 2018). Silva et al. (2019) used a longitudinal

twin cohort study to prospectively assess the contribution of genes to HSPM aetiology (Silva et al., 2019). Little evidence for genetic influence was found even after adjustment for known risk factors suggesting the role of other shared environmental factors in HSPM causation. Past research suggests a commonality in the genetic aetiology of various dental anomalies with one observational study displaying strong reciprocal relationships between missing second premolars, hypoplasia and other anomalies such as infraocclusion and diminutive maxillary lateral incisors (Baccetti, 1998). Walshaw et al. (2020) investigated the relationship between MIH and other dental anomalies by examining the radiographs (orthopantograms) of 101 children affected by the condition in their convenience based sample (Walshaw et al., 2020). Coexisting hypodontia was found in 12% with other anomalies such as concurrent ectopic eruption of FPMs (8%), infraocclusion of primary molars (9%) and abnormal morphology (9%) also identified. The authors advised the need for further epidemiological studies to corroborate the association of MIH and dental anomalies in a general population as their findings were limited to a referred sample. The prevalence and variety of dental anomalies in children with HSPM requires further exploration.

The role of social and demographic factors in HSPM aetiology remains unclear. A lower threshold for HSPM and MIH in Caucasian populations has been suggested however is not confirmed (Elfrink et al., 2014). In 2014, Elfrink et al. (2014) conducted a large prospective multi-ethnic cohort study and Dutch ethnicity was identified as a HSPM determinant (Elfrink et al., 2014). However, the proportion of mothers with non-Dutch ethnicity was lower than anticipated from the population data influencing the generalisability of this result (Jaddoe et al., 2010). Silva et al. (2019) showed increased socio-demographic status was

associated with HSPM using an index of Relative Socio-economic Disadvantage based on area post code (Silva et al., 2019). This measure of SES may not accurately reflect individual status. Similarly, Goyal et al. (2019) found a higher prevalence of HSPM amongst private school participants compared to those attending a public school (Goyal et al., 2019). Alternatively in Nigeria, a non-significant association between HSPM prevalence and socioeconomic background was found (Oyedele et al., 2016a, Temilola et al., 2015b). Table 1.2 summarises the role of social, ethnic and educational factors in HSPM development.

1.2.2 *Prenatal factors*

There is inconclusive evidence on the relationship between HSPM and In Vitro Fertilisation (IVF) (Silva et al., 2019, Kar et al., 2014). Higher rates of perinatal adverse outcomes and congenital abnormalities from pregnancies conceived via IVF have been reported (Pinborg et al., 2013). HSPM demonstrated a moderate to strong association with IVF in a prospective twin study (Silva et al., 2019). Conflictingly Kar et al. (2014) revealed no association between IVF and DDE in the primary dentition (Kar et al., 2014).

Maternal alcohol consumption during pregnancy was found to be associated with HSPM development (Elfrink et al., 2014). In animal research, ethanol can cause changes in cellular differentiation and enamel mineralisation (Jimenez-Farfan et al., 2005). Further research is required to explore other issues including dose related effects of alcohol as there were only small numbers of the high exposure category in this study (Jaddoe et al., 2007, Elfrink et al., 2014).

The use of tobacco during pregnancy has been found to be associated with HSPM (Lopes-Fatturi et al., 2019). In addition, Silva et al. (2019) identified maternal smoking beyond the first trimester of pregnancy as a risk factor (Silva et al., 2019). Animal studies have demonstrated smoke exposure in utero as an influential factor in ameloblast function (Dong et al., 2011). Animals exposed to nicotine presented with an alteration in dental morphology hypothesising that nicotine could affect dental development (Chowdhury and Bromage, 2000).

The effects of maternal medication during pregnancy have also been studied with no significant association reported. Elfrink et al. (2013) found no associations between anti-bacterial agents and medicines used in asthma and allergy and HSPM. The authors stated that the influence of dosage, mode of intake and extent of use requires further investigation. (Elfrink et al., 2013). A systematic review by Serna Munoz et al. (2020) concluded that there was no clear evidence of an association between HSPM and maternal medication use, and further well designed prospective cohort studies were needed. The limitations of this study included multiple diagnostic criteria between the studies and inclusion of non HSPM defects including hypoplasia and diffuse opacities. (Serna Munoz et al., 2020). The use of folic acid during pregnancy was also studied in a prospective cohort study (Elfrink et al., 2014). While univariate analysis showed that maternal folic acid supplementation resulted in a significantly higher prevalence of HSPM compared to the control group, significance was lost upon accounting for confounding factors.

Recent results from a double-blind clinical trial suggest a protective role of vitamin D supplementation during pregnancy against enamel defects (Nørrisgaard et al., 2019). Six year follow up results found that high-dose

vitamin D supplementation during pregnancy was associated with a reduced risk of primary teeth enamel defects in the offspring. The authors recommended prenatal vitamin D supplementation should be considered as a preventive intervention for enamel defects in pregnant woman.

Gestational illness has been identified as a significant risk factor for HSPM with an emphasis on timing of the illness (Ghanim et al., 2012, Lopes-Fatturi et al., 2019). Ghanim et al. (2012) used a previously validated questionnaire to explore the role of maternal health (gestational diabetes, rhesus disease, hypertension and pre-eclampsia) during pregnancy and HSPM (Ghanim et al., 2012). Significantly more children were affected by the defect if their mothers had experienced illness during the second/third trimester compared with the first trimester. Similarly, findings of a recent systematic review found a positive association between HSPM and presence of hypertension during pregnancy (Lopes-Fatturi et al., 2019).

1.2.3 *Perinatal factors*

Perinatal factors have been examined including low birth weight, prematurity and preterm delivery. The relationship between DDE and low birth weight has been established (Seow et al., 1984, Fearne et al., 1990, Ferrini et al., 2008, Jacobsen et al., 2014). A recent systematic review by Wu et al. (2018) found that low birth weight (< 2500g) neonates were approximately three times more likely to have MIH (Wu et al., 2018). Both Ghanim et al. (2012) and Elfrink et al. (2014) identified low birth weight as a significant risk factor for HSPM (Ghanim et al., 2012, Elfrink et al., 2014). Elfrink et al. (2014) stated that low birth weight can be associated with HSPM but is likely to be biased with other potential interacting factors. Prematurity and low birth weight are often associated

(Nelson et al., 2010). A preterm infant is defined as is any infant born before 37 weeks gestation (Beck et al., 2010). A recent cross sectional study found that those born preterm had a higher prevalence of HSPM (Lima et al., 2019). This finding is supported by an earlier meta-analysis on MIH aetiology concluding pre-term individuals were 1.57 times more likely to develop MIH enamel defects in permanent teeth (Wu et al., 2018).

In the field of MIH, Kuhnisch et al. (2015) showed a protective effect of vitamin D with higher serum concentrations associated with less MIH and dental caries in 1048 German children at age 10 (Kühnisch et al., 2015). There appears to be conflicting evidence regarding the role of vitamin D at birth and HSPM. Silva et al. (2019) found an unexpected association between HSPM and increased levels of vitamin D however following further analysis this association was likely to reflect confounding data (Silva et al., 2019). In contrast, Van der Tas et al. (2018) found no evidence for an association between vitamin D status and presence of HSPM (van der Tas et al., 2018). Interestingly, there was a tendency towards a lower likelihood of developing HSPM in those with lower vitamin D concentrations, however associations were not sustained after adjusting for confounding factors.

Ghanim et al (2012) identified delivery complications as a potential perinatal risk factor for HSPM with complications including prolonged labour, retained placenta, bleeding and maternal hypoxia (Ghanim et al., 2012). Lopes-Fatturi et al. (2019) used a cross sectional study design to explore delivery complications. The initial significant association was lost following adjustment by prenatal exposures (Lopes-Fatturi et al., 2019).

Neonatal complications including jaundice, neonatal hypoxia, incubation, respiratory distress and hypocalcaemia have demonstrated inconsistent associations with HSPM. Ghanim et al. (2012) identified neonatal illness as a potential HSPM risk factor (Ghanim et al., 2012). Elfrink and colleagues (2014) studied neonatal morbidities using Apgar scores and hospitalisation in first week of life as parameters (Elfrink et al., 2014). Apgar scoring refers to a method of assessment of the physical health of a new born infant assessing functions such as respiration, pulse and reflexes (American Academy of Pediatrics and Gynecologists, 2015). These factors were not found to be of significance following statistical analysis.

1.2.4 *Postnatal factors*

Febrile illness has often been mentioned in MIH research as a possible determinant (Alaluusua, 2010, Silva et al., 2016b, Fatturi et al., 2019). Animal based studies have found that enamel hypomineralisation of incisors can be induced by fever in rats (Tung et al., 2006). Fever episodes in the first year of life was reported as a significant risk factor for HSPM by Elfrink et al. in 2014 (Elfrink et al., 2014). This finding was supported by Ghanim et al. (2012) who assessed acute illness (ear infection, tonsillitis, pneumonia, fever) and found that children with unexplained high fever presented with a higher prevalence of HSPM defects (Ghanim et al., 2012). As a risk factor, the presence of otitis media in the first year of life has been identified with affected children presenting with 68% more prevalence of HSPM (Lopes-Fatturi et al., 2019). The authors have advised that this finding be carefully interpreted as otitis media is an infectious condition that could co-exist with fever and use of

medications. This association with otitis media has been supported in MIH research (Allazzam et al., 2014, Hernandez et al., 2018)

Silva et al. (2019) identified infantile eczema as a risk factor for HSPM (Silva et al., 2019). The authors stated that this association was more likely to reflect common developmental pathways occurring prenatally as infantile eczema occurs after the period when SPMs would be considered to be susceptible to HSPM (Silva et al., 2019). HSPM's connection with infantile eczema may have a cause similar to allergy and atopy, instigated through microbiome and immunity however this requires future study (Lewis and Britton, 1998).

Preterm birth in conjunction with asthma reported in the first year of life was found to be associated with HSPM (Lima et al., 2019). Children born preterm may have an increased susceptibility to respiratory symptoms including asthma (Medsker et al., 2015). Lima's study has been the first to identify asthma as a HSPM risk factor and is supported by earlier MIH research showing MIH to be linked to respiratory conditions in general including asthma (Hernandez et al., 2018). Oxygen deprivation which is inherent to asthma can play an inhibitory role in enzymatic action during the maturation stage of amelogenesis potentially interrupting the mineralisation process (Hernandez et al., 2018).

No significant associations were found between HSPM and chronic illness of childhood (Ghanim et al., 2012). This highlights the importance of event timing in HSPM aetiology with earlier occurring insults prenatally and perinatally potentially playing a more significant role.

Ghanim et al. (2012) found duration of breastfeeding to be influential with children who breastfed for less than six months after birth over three times

more likely to have HSPM than those who breastfed for the first year of childhood (Ghanim et al., 2012). Ghanim et al. (2012) suggested early weaning (i.e. breastfeeding up to 6 months) could be a HSPM risk factor by exacerbating the child's nutritional deficiencies. Both Elfrink et al. (2014) and Lopes Fatturi et al. (2019) studied breastfeeding and duration as a postnatal risk factor for HSPM development. In Elfrink's study breastfeeding at 6 months was of significance in univariate analysis but did not enter the final risk factor model (Elfrink et al., 2014). Lopes- Fatturi et al. (2019) found breastfeeding activity and duration not to be of significance in their cross sectional study (Lopes-Fatturi et al., 2019).

The relationship between antibacterial use and MIH, especially for the commonly prescribed antibacterial amoxicillin has been demonstrated in animal experimental research (Laisi et al., 2009). In human studies, evidence has been contradictory regarding the role of antibiotics in early childhood and MIH development. However, confounding factors cannot be excluded as it is still unclear as to whether it is the disease or the medications used to treat the disease that cause the hypomineralisation (Elfrink et al., 2013). In a systematic review by Serna Munoz et al. (2020), no clear evidence was found for medications taken in the first year of life and HSPM (Serna Munoz et al., 2020). Of the studies included, only one used a diagnostic criteria suitable for HSPM diagnosis (Elfrink et al., 2014). Antibiotic use in the first year of life was assessed by Elfrink et al. in 2014 with no significant association found (Elfrink et al., 2014).

Table 1. 1: Studies exploring prenatal, perinatal and postnatal determinants of HSPM

Reference	**Prenatal factors**					
	IVF	**Maternal medication**	**Maternal illness**	**Maternal smoking**	**Maternal alcohol consumption**	**Maternal vitamin D**
Elfrink et al. 2013		-				
Elfrink et al. 2014			-	-	+	
Ghanim et al. 2012			+			
Lopes-Fatturi et al. 2019			+	+		
Silva et al. 2019	+		-	+	-	
Serna Munoz et al. 2019		-				
van der Tas et al. 2018						-
	Perinatal factors					
Reference	**Delivery complications**	**Low birth weight**	**Preterm birth**	**Neo natal illness**	**Vitamin D levels neonate at birth**	
Elfrink et al. 2014		+		-		
Silva et al. 2019		-	-	-	+	
Lima et al. 2019			+			
Ghanim et al. 2012	+	+		+		
van der Tas et al. 2018					-	
Lopes-Fatturi et al. 2019	-					
	Post-natal factors					
Reference	**Fever in 1st year of life**	**Illnesses**	**Medications in early childhood**	**Breastfeeding duration**	**Vitamin D**	
Elfrink et al. 2014	+		-	-		
Ghanim et al..2012	+	+		+		
Lima et al. 2019		+ (Asthma, 1st year)				
Silva et al. 2019		+ (Infantile eczema 1st 18 mths)				
van der Tas et al. 2018					-	
Lopes-Fatturi et al. 2019		+ (Otitis media 1st year)		-		
Serna Munoz et al. 2019			-			

+ Positive influence; - No influence; Empty cells=not reported/investigated by the study

Table 1. 2: Studies exploring social, ethnic and educational factors in HSPM aetiology

Reference	Ethnic/Lifestyle/Social factors				
	Ethnicity	**Socio economic status (SES)**	**Education level Mother**	**Maternal occupation**	**Child Education**
Elfrink et al. 2014	+		-		
Ghanim et al. 2012				-	
Silva et al. 2019		+ (increased SES)			
Goyal et al. 2019					+ (Private school education)

+ Positive influence; - No influence; Empty cells=not reported/investigated by the study

1.2.5 *Exposure timing and confounding factors*

Previous research on MIH aetiology has described the importance of a combined effect of several factors (Alaluusua, 2010). Beentjes et al. (2002) postulated that MIH is caused by a combination of factors and that these factors need to reach a certain threshold level before enamel hypomineralisation is caused (Beentjes et al., 2002). The importance of this has been reinforced in HSPM aetiological studies. Lopes-Fatturi et al. (2019) hypothesised a combined effect in HSPM which occurs according to a chronological period of amelogenesis by increment (Lopes-Fatturi et al., 2019). Their study employed a unique multiple model approach which was hierarchical to evaluate potential exposures. Exposures were divided according to their timing with previous chronological events considered in the assessment of later exposures. This analysis was based on the concept that a prenatal exposure could potentially determine perinatal events as well as postnatal comorbidities (Victora et al., 1997). The authors concluded that this incremental process might be an explanation for why demarcated opacities occur in different areas of a crown (Lopes-Fatturi et al., 2019). Ghanim et al. (2012) was unable to identify one

single factor predisposing to HSPM but rather several factors of systemic nature (Ghanim et al., 2012). Furthermore, Silva et al. (2019) referred to shared environmental factors as instrumental in HSPM aetiology (Silva et al., 2019). Several studies have supported the importance of exposure timing in HSPM development. Ghanim et al. (2012) reported that perinatal health events such as neonatal illness of the child was the most frequently reported associated factor with prenatal conditions second in importance (Ghanim et al., 2012). Elfrink et al. (2014) referred to the role of 'general perinatal morbidity' in HSPM aetiology (Elfrink et al., 2014).

The association between potential aetiological factors and HSPM can only be assessed through studies of an observational nature. The absence of randomisation means that a real relationship may be masked or exaggerated/ diminished by confounding factors (Silva et al., 2016b). The majority of HSPM aetiological studies have accounted for confounding factors and provided information on how adjustment was performed (Ghanim et al., 2012, Elfrink et al., 2014, Elfrink et al., 2013, Silva et al., 2019, Lopes-Fatturi et al., 2019). Some studies have attempted to collect data prospectively (Elfrink et al., 2013, Elfrink et al., 2014, Silva et al., 2019) however the majority of the evidence comes from cross sectional studies which inherently have recall and memory biases as a limitation. These biases can occur because parents often wish to give answers they believe to be 'the best' or they may overlook some incidentally happening events such as fever (Ghanim et al., 2012, Elfrink et al., 2014, Lima et al., 2019). Evidence suggests certain perinatal factors such as gestational age, birthweight and mode of delivery are more accurately remembered even years after the event (Rice et al., 2007). Alternatively, some aspects of maternal health during illness, child illness and medication use were

less likely to be recalled correctly (Liu et al., 2013). Conflicting results from studies regarding recall of breast feeding duration have been obtained also (Natland et al., 2012, Tienboon et al., 1994).

1.3 HSPM diagnostic criteria

Correct scoring of DDE requires a reproducible and valid index (Elfrink, 2012). Regardless of the index used, teeth should be examined clean and wet with an artificial light source (Ghanim et al., 2015). Indices used for scoring MIH/HSPM defects have included the modified index of DDE (mDDE) and the European Academy of Paediatric Dentistry (EAPD) judgement criteria (Clarkson and O'Mullane, 1989, Weerheijm et al., 2003). Self-devised criteria have also been used. Despite widespread use of the EAPD diagnostic criteria, MIH and HSPM prevalence rates have varied greatly (Elfrink et al., 2015). This vast disparity has been attributed to a lack of a standardised, internationally utilised and reliable criteria for diagnosis (Elfrink et al., 2015, Ghanim et al., 2019). In 2015, the MIH/HSPM index was developed to address this drawback, combining elements of both the EAPD and mDDE criteria (Ghanim et al., 2015).

Historically, enamel defect indices based on clinical appearance have been proposed by several investigators (Young, 1973, Murray and Shaw, 1979). These indices have been criticised as they have not covered the full range of defects with no effort made in differentiating between the configuration and demarcation of opacities (Clarkson, 1989). In 1982, the DDE index was created by the Federation Dentaire International (FDI) and was based on descriptive criteria which possessed flexibility for recording enamel defects on a surface, tooth and individual level (FDI, 1982). This index was further modified to become the mDDE in 1989 (Clarkson & O’ Mullane, 1989).

1.3.1 *DDE Index (DDE)*

The type, number and demarcation of defects affecting enamel on the buccal/ lingual surfaces of all teeth are described. Information on the location, treatment needs, dental and medical history, and the aetiology of defects are also included. While the creation of this index was a step towards a more standardised measurement of developmental enamel defects, several drawbacks of the DDE system have been cited. Firstly, due to the multiple codes and requirement to assess each tooth surface, the DDE Index is time-consuming and complicated to use and analyse. This complexity may hamper one's ability to understand and therefore reproduce data using the index (Clarkson, 1989). Secondly, the section which describes defect type primarily refers to white and yellow opacities and hypoplasia. Studies conducted close to the time of DDE development highlighted the fact that colour was less important than the need to differentiate between diffuse and demarcated opacities (Suckling and Pearce, 1984, Clarkson and O'Mullane, 1989). Thirdly, severity of defects cannot be recorded with no differentiation between mild and severe defects (Clarkson, 1989).

1.3.2 *Modified DDE Index (mDDE)*

To overcome the shortcomings of the DDE index, several modifications were made to the existing index (Table 1.3). The modified DDE Index (mDDE) was developed by Clarkson and O'Mullane in 1989 (Clarkson and O'Mullane, 1989). The main changes related to defect coding and weighting of certain factors. To simplify the index, a single scoring system was suggested comprising three broad categories of defects- demarcated opacities, diffuse opacities and hypoplasia- with provision for recording other defects also. The demarcation of

an opacity (demarcated or diffuse) instead of its colour became the main factor recorded. Surface extent was also included to reflect defect severity by visually condensing all areas affected by the defect and then relating the total area affected to that of the total visible tooth surface area. For MIH/HSPM diagnosis, this index has major limitations. Post eruptive breakdown (PEB) cannot be scored or may be described as hypoplasia. Furthermore, atypical caries, atypical restorations and atypical extractions cannot be recorded (Elfrink et al., 2015, Weerheijm et al., 2003).

Table 1.3: Description of mDDE index (Clarkson & O'Mullane, 1989)

Diagnostic criteria	**Description**
Modified index of DDE (mDDE)	***Categories*** *Normal* *Demarcated opacity* *White/cream* *Yellow/brown* *Diffuse opacity* *Lines* *Patchy* *Confluent* *Confluent/patchy + staining + loss of enamel* *Hypoplasia* *Pits* *Missing enamel* *Any other defects* *Extent of Defect* *Normal* *<1/3* *At least 1/3 < 2/3* *At least 2/3*

1.3.3 *EAPD judgement criteria*

In response to a lack of a standardised MIH diagnostic criteria, the EAPD judgement criteria was developed in 2003 in Athens (Weerheijm et al., 2003). The criteria consists of five main definitions including demaracted opacities, PEB, atypical restorations, extracted molar due to MIH and failure of eruption of a molar or incisor (Table 1.4). It has been used commonly as a measure of

HSPM due to the similar defect characteristics. While the EAPD criteria is purpose fit for MIH/HSPM diagnosis, it lacks clarification as regards data collection. Descriptions of the various types of defects are provided but there is an absence of practical direction for researchers in terms of coding and recording the extent of the defect.

A best clinical practice guideline on MIH was developed in 2010 following an EAPD interim Seminar and Workshop in Helsinki in May 2009 (Lygidakis et al., 2010). This guideline recommended continued use of the EAPD criteria for MIH diagnosis with reference to SPMs. Additional criteria were also added including enamel disintegration, tooth sensitivity and recording of defect severity (Table 1.5).

Table 1.4: Description of EAPD diagnostic criteria (Weerheijm et al, 2003)

EAPD Criteria Clinical characteristic	Description
Demarcated opacities	'A demaracted defect involving an alteration in the translucency of the enamel which is variable in degree. The enamel affected has a smooth surface and is of a normal thickness with a well defined boundary. These opacities can be white, yellow or brown in colour'.
PEB	'A defect that indicates loss of initially formed surface enamel after tooth eruption. Enamel loss is often associated with a pre-existing demarcated opacity'
Atypical restorations	'Restorations vary in terms of their size and shape that do not conform to the temporary caries picture. Restorations can extend to the buccal or palatal smooth surface with demaracted opacities often present at the restorations border. In incisors a buccal restoration can be present that is not trauma related'.
Extracted molar due to MIH	'Absence of a FPM should be viewed in the context of the whole dentition. An MIH diagnosis should be suspected where a FPM is missing in conjunction with visible opacities/atypical restorations in remaining FPMs. In addition, absence of FPMs in an intact dentition in combination with demarcated opacities on the incisors is suspicious for MIH diagnosis'
Atypical caries	Reference is also made to 'FPMs affected by large carious lesions in association with demarcated opacities' and how this occurrence should be described as MIH.

Table 1.5: Additions to EAPD diagnostic criteria (Lygidakis et al, 2010)

EAPD criteria	Description
Enamel disintegration	'The level of porosity varies in affected areas. Severely hypomineralised enamel, which is subjected to occlusal loading soon breaks down, exposing dentine and causes rapid caries development'
Tooth sensitivity	'Sensitivity of affected teeth may be reported. Variation in severity ranges from a mild response to external stimuli to spontaneous hypersensitivity. Affected teeth may be challenging to anaesthetise'.
Recording of defect severity	• 'Mild defects involve demarcated opacities only without breakdown of enamel, occasional sensitivity to external stimuli e.g., air/water but not brushing'. • 'Severe defects refer to teeth affected by demarcated opacities with enamel breakdown, caries ongoing/spontaneous hypersensitivity affecting function'.

1.3.4 *MIH/HSPM index*

The MIH/HSPM index was developed in 2015 integrating elements of the EAPD and mDDE and is currently used in data collection for HSPM (Ghanim et al., 2015). The scoring sheets classify MIH/HSPM defects based on their visual appearance with consideration for defect extent. Each index tooth is scored based on its eruption status, clinical status and the extent of the lesion (Table 1.6). Studies will present with differing needs and objectives and therefore a short and long scoring form are provided. The short form is suitable for simple screening surveys while the long form is more detailed and may be used for community based studies. The detailed nature of the index also may highlight defect patterns among different populations. The reproducibility and validity of the MIH/HSPM index was recently assessed (Ghanim et al., 2019). The index codes and their descriptions showed face, content, and construct validities with

a high agreement level. Substantial to almost perfect scores were obtained for MIH/HSPM inter and intra observer reliability. These findings support this index as a valid and reliable MIH/HSPM assessment tool in both clinical practice and larger field studies.

Several indices have been devised for MIH/HSPM diagnosis. These indices have evolved over time with progress achieved in terms of their suitability for diagnosing MIH/HSPM. The 2003 EAPD judgement criteria was a product of this progress and added much needed methodological rigour to MIH/HSPM prevalence and aetiological studies (Weerheijm et al., 2003, Elfrink et al., 2015). More recently, the MIH index was devised facilitating the total spectra of MIH/HSPM to be determined (Ghanim et al., 2015). It is hoped that this charting system will enable the accrual of improved quality information leading to better decision making on MIH/HSPM diagnosis at both an individual and population level.

Table 1.6: Description of MIH/HSPM index (Ghanim et al, 2015)

MIH/HSPM criteria: Clinical feature	**Description**
Eruption status criteria	• A tooth that is unerupted or partially erupted does not receive a score • Partially erupted refers to a tooth that is not visible or less than 1/3 of the occlusal table is visible
Clinical status criteria	• Includes demarcated opacities, PEB, atypical restorations, atypical caries and extracted molar due to MIH/HSPM • Demarcated opacities are differentiated according to colour (white or creamy versus yellow or brown) • A 'cannot be scored' code also exists which relates to an index tooth with extensive coronal breakdown where the potential cause is impossible to ascertain • A score is allocated for non MIH/HSPM defects including diffuse opacities, hypoplasia, amelogenesis imperfecta and hypomineralisation defects (not MIH/HSPM)
Lesion Extension criteria	• Defects which are greater than 1 mm in diameter are recommended to be reported (Lygidakis et al., 2010, Ghanim et al., 2015). • The amount affected should be related to the total visible surface area and where more than one type of MIH/HSPM defect exists per tooth, all areas affected should be visually combined. • **Code I**: Less than a 1/3 of the tooth surface is affected • **Code II**: More than a 1/3 but less than 2/3s of tooth surface affected • **Code III**: At least 2/3 of the tooth surface involved
Severity Evaluation	• MIH/HSPM severity are deduced from the clinical status criteria and the defect extent

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1.3.5 *Training and calibration*

Training in the diagnostic criteria must be performed prior to data collection. A common training method includes the use of reference photos covering the full range of HSPM diagnosis and non HSPM/MIH enamel defects to ensure examiners are familiar with the differential diagnosis. Following satisfactory training, calibration is required to determine inter and intra examiner reliability by calculating a Kappa score. Values of Kappa from 0.41 to 0.60 are considered moderate, 0.61–0.80 substantial, and 0.81 onwards are considered outstanding (Landis and Koch, 1977). It is recommended to repeat the same scoring process more than once with at least a one week interval between each scoring session (Ghanim et al., 2017). The same scoring conditions should be maintained throughout the sessions e.g. room lighting and score timing per image (Ghanim et al., 2017).

1.3.6 *Differential diagnosis*

Differential diagnosis of demarcated hypomineralisation lesions from other enamel defects is integral to avoiding misdiagnosis and ensuring best management of individuals with HSPM/MIH (Table 1.7).

Table 1.7: Differential diagnoses for HSPM/MIH (Ghanim et al, 2015; Ghanim et al, 2017)

Differential diagnosis	Description
Diffuse opacities	Diffuse opacities involve a defect in the translucency of the enamel which can be variable in degree. The enamel is of a normal thickness and has a relatively smooth surface (FDI., 1992). Unlike HSPM, it can have a linear, patchy or confluent distribution with no clear boundary with adjacent normal enamel (Rozier, 1994). The lack of opacity demarcation is a significant factor differentiating diffuse opacities from HSPM. In addition, the distribution of diffuse opacities tends to be symmetrical and bilateral which differs from HSPM where specific teeth are involved (Weerheijm et al., 2004). These opacities are induced by excess fluoride ingestion at time of enamel development and a positive history of excess fluoride intake at time of affected teeth formation may be recalled aiding diagnosis (Rozier, 1994).
Hypoplasia	Hypoplasia refers to a quantitative defect, characterised by reduced enamel thickness (FDI., 1992). Three main clinical presentations (FDI., 1992): **Pits** Minute areas of enamel loss, which could be single, multiple, shallow or deep, scattered or in rows. **Grooves/linear** Grooves of enamel loss that could be single or multiple, narrow or wide (maximum 2 mm). **Area** Partial or complete absence of enamel over a considerable area of a tooth crown. Compared to HSPM, great variation exists in its distribution in terms of number of teeth affected and affected areas are rarely of a regular shape (Elcock et al., 2006). Challenges exist in differentiating between hypoplasia and PEB (Ghanim et al., 2015). An important differentiating factor relates to the defect border. With hypoplasia, the borders are mostly smooth and regular reflecting a developmental, pre-eruptive lack of enamel matrix formation. Contrastingly, MIH/HSPM borders tend to be sharp and irregular due to the post eruptive shearing or weakened enamel (Ghanim et al., 2015).
Amelogenesis Imperfecta (AI)	Refers to a range of genetic developmental enamel defects Enamel can be classified as hypoplastic, hypo-mature, hypomineralised or a

	combination of these (Crawford et al., 2007) Unlike MIH/HSPM, the distribution of AI tends to be generalised affecting both primary and permanent dentitions In addition, there are specific characteristics relating to AI including anterior open bite and taurodontic molars which can aid in the diagnosis. Family history/history of systemic disorders/illnesses provide valuable clues to diagnosis (Weerheijm, 2004, Crawford et al., 2007).
White Spot Lesions	Lesions are characterised by being chalky/white in colour. Surface characteristics may be smooth or irregular depending on lesion activity (Ghanim et al. 2017). White spot lesions can be distinguished from MIH/HSPM lesions based on their location. These lesions tend to occur in areas of plaque stagnation such as contact areas adjacent to the cervical margins of the tooth or at the gingival margin, areas where enamel hypo mineralisation rarely occurs (Seow, 1997a).
Hypo mineralisation defect (non MIH/HSPM)	This refers to MIH/HSPM-like demarcated defects diagnosed in primary/permanent teeth other than MIH/HSPM index teeth. Distinguishing factors include both the timing of coronal mineralisation and source of defect aetiology (Ghanim et al, 2015). For non MIH/HSPM defects, timing of crown mineralisation is not simultaneous with that of FPMs and SPMs. Additionally, the cause of the defect could be due to a local disturbance rather than an aetiological factor of systemic origin e.g. trauma/infection of primary predecessors (Lo et al., 2003, Broadbent et al., 2005).

1.4 Patterns in HSPM presentation and defect characteristics

Several studies have found no significant difference in HSPM prevalence between males and females (Elfrink et al., 2008, Ghanim et al., 2013, Mittal and Sharma, 2015b, Oyedele et al., 2016a, da Silva Figueiredo Se et al., 2017, Halal and Raslan, 2020). There has been conflicting evidence regarding the most common location of HSPM defects. Several studies investigating HSPM prevalence have found no difference in HSPM levels according to arch location e.g., maxillary versus mandibular arches (Elfrink et al., 2008, Elfrink et al., 2012, Temilola et al., 2015a, Owen et al., 2018, Lima et al., 2019). A number of

studies found the maxillary molars to be most commonly affected by HSPM (Ghanim et al., 2013, Oyedele et al., 2016a, Goyal et al., 2019). Alternatively, other studies have reported the mandibular molars to be most often affected by the defect (Mittal and Sharma, 2015b, Halal and Raslan, 2020).

Studies have reported no significant difference in HSPM prevalence or lesion characteristics according to arch side (right or left) (Elfrink et al., 2008, Elfrink et al., 2012, Temilola et al., 2015b, Zakirulla et al., 2018, Goyal et al., 2019, Ghanim et al., 2013, Owen et al., 2018, Zakirulla et al., 2020).

Several studies have found demarcated opacities to be the most prevalent form of HSPM (Elfrink et al., 2008, Ghanim et al., 2013, Elfrink et al., 2012, Owen et al., 2018, Zakirulla et al., 2018, Goyal et al., 2019, Halal and Raslan, 2020). This finding is supported by earlier literature where all primary teeth were scored and SPMs were mostly affected by demarcated opacities (Seow, 1997b, Slayton et al., 2001, Lunardelli and Peres, 2005). Creamy white opacities have been found to be the most common colour of HSPM opacities (Ghanim et al., 2013, Mittal and Sharma, 2015b, Owen et al., 2018).

Several studies have reported PEB as the second most common form of the defect (Elfrink et al., 2008, Elfrink et al., 2012, Ghanim et al., 2013, Owen et al., 2018). The latter two studies found a higher prevalence of PEB associated with yellow-brown demarcated opacities compared to PEB with creamy-white opacities.

Atypical caries, atypical restorations and extractions due to HSPM have accounted for lower prevalence levels in several studies (Elfrink et al., 2008, Elfrink et al., 2012). EAPD judgement criteria which has been used in most studies for HSPM diagnosis does not include atypical caries and therefore

several studies do not have data on this HSPM defect (Elfrink et al., 2008, Ghanim et al., 2013, Ng et al., 2014). The lower prevalence has often been attributed to diagnostic challenges where lesions with extensive caries cannot be scored. The MIH/HSPM index developed by Ghanim et al. (2015) which includes atypical caries in its criteria has been used in more recent HSPM prevalence studies (Ghanim et al., 2015). Using this index, Gambetta-Tessini et al. (2018) reported atypical carious lesions to be the most common defect with 24.6% of affected teeth having this defect. This was closely followed by demarcated opacities which represented 21.5% of defects (Gambetta-Tessini et al., 2018).

Atypical restorations in HSPM are infrequently reported. This finding may be related to the young age of the children at time of examination. Cooperation challenges and access to care in young children may also be contributory factors. The generally low level of atypical caries and restorations may also be related to the fact that the most common presentation of HSPM are demarcated opacities. (Elfrink et al., 2008, Elfrink et al., 2012, Ghanim et al., 2013, Owen et al., 2018, Halal and Raslan, 2020).

Extractions due to HSPM represent the most severe manifestation of the defect and accounts for the lowest prevalence level. Several studies have found no form of this defect in their sample (Mittal and Sharma, 2015b, Ng et al., 2014, Owen et al., 2018, Halal and Raslan, 2020). Other studies have reported low prevalence levels (6.9%-11.2%). (Elfrink et al., 2012, Ghanim et al., 2013, Goyal et al., 2019).

The relationship between the type of HSPM defect and tooth surface have been explored in many studies. Most studies agree that the buccal and occlusal

surfaces are the most frequently affected (Ghanim et al., 2013, Mittal and Sharma, 2015b, Goyal et al., 2019). Sidhu et al. (2019) reported single surface lesions to be most common in teeth affected by HSPM (Sidhu et al., 2019). Alternatively, Mittal et al. (2015) reported the majority of subjects had ≤2 surfaces affected (Mittal and Sharma, 2015b).

Severity of HSPM can be related to clinical criteria or defect extent. A positive relationship between defect extent and clinical severity has been reported (Owen et al., 2018). There is conflicting evidence as to whether mild, moderate or severe presentations of HSPM are most common. Elfrink et al. (2012) reported that most children diagnosed with HSPM were severely affected (demarcated opacities in combination with PEB (Elfrink et al., 2012). Alternatively, Mittal et al. (2015) reported moderately extensive defects as most prevalent i.e. >1/3 but <2/3 surface involvement (Mittal and Sharma, 2015b). In contrast, some studies have reported the majority of HSPM lesions to be of mild severity (Lima et al., 2019, Sidhu et al., 2019).

HSPM can affect between one and four SPMs. Most studies have reported an average of 1-2 affected teeth (Elfrink et al., 2008, Elfrink et al., 2012, Ghanim et al., 2013, Mittal and Sharma, 2015b, Owen et al., 2018, Sidhu et al., 2019, Goyal et al., 2019, Zakirulla et al., 2020). In contrast, Halal and Raslan (2020) found that nearly 50% of their sample had four SPMs affected (Halal and Raslan, 2020).

A relationship between the number of HSPM teeth and defect severity has been observed in some studies (Owen et al., 2018). In one study, children with one to two affected SPMs were more likely to have mild lesions without PEB, whilst

participants with three/four affected teeth were more likely to be affected by PEB and atypical restorations (Owen et al., 2018).

1.5 HSPM and Caries

Normal enamel displays a well-organised and distinctive prism and crystal structure. Hypomineralised enamel contains a higher protein content, less distinct prism edges and crystals with a more marked interprismatic space (Farah et al., 2010, Fagrell et al., 2010). Consequently, hypomineralised enamel is more porous resulting in reduced strength and increased likelihood of PEB (Fagrell et al., 2010). This breakdown may occur soon after tooth eruption or at a later stage following occlusal loading (Weerheijm et al., 2001, Lygidakis et al., 2010). A microCT analysis of teeth affected by HSPM showed reduced mineral density (Elfrink et al., 2016). Defective molars with yellow opacities had a 30% lower mineral density compared to unaffected molars. The authors concluded that the total reduction in enamel mineral content in HSPM teeth was similar to white spot lesions highlighting the increased susceptibility of defective SPMs to caries. Furthermore, surfaces affected by breakdown favour plaque accumulation and subsequent caries development (Weerheijm et al., 2001, Lygidakis et al., 2010, Weerheijm, 2003).

The SPM erupts 10-12 months after the first primary molar at the age of 24-30 months (Elfrink et al., 2010). This eruption timing difference often leads to the assumption that the first primary molar has a greater caries prevalence due to a longer duration in the mouth (Elfrink et al., 2010). Although in the typical pattern of early childhood caries, the teeth are affected by caries in sequence of eruption (Veerkamp and Weerheijm, 1995), overall the SPM has found to be more commonly affected by caries especially the occlusal surface (Holland and

Crowley, 1982, Li et al., 1993, Holt, 1995, Gizani et al., 1999, Elfrink et al., 2006, Halal and Raslan, 2020). DDE may be a significant explanation for the differences in caries prevalence's between the first and SPM.

The likelihood of caries developing in a tooth affected by HSPM appears to be influenced by overall caries risk and severity of the defect, although this relationship remains weakly understood (Elfrink et al., 2012, Ghanim et al., 2013). Historically, there has remained a lack of consensus regarding the relationship between DDE and caries in the primary dentition (Costa et al., 2017). Recent studies including a systematic review and meta-analysis have confirmed an association between these two entities (Massignan et al., 2016, Costa et al., 2017). These studies broadly considered all DDE and did not use criteria suitable for HSPM diagnosis. In 2010, Elfrink and colleagues (2010) explored factors increasing the caries risk of SPMs in five year old Dutch children (Elfrink et al., 2010). HSPM had a significant effect on caries prevalence with children affected by HSPM 3.2 times more likely to have caries (Elfrink et al., 2010). Similarly in Syria, Halal and Raslan (2020) reported that the risk of caries for children with HSPM was about seven times more likely when compared to those unaffected (Halal and Raslan, 2020). The higher caries risk of the latter study may be related to the overall increased caries risk on a population level.

The relationship between HSPM and defect severity has also been investigated with some studies finding a positive association between HSPM and increasing caries severity (Ghanim et al., 2013, Oyedele et al., 2016b, Gambetta-Tessini et al., 2019). Ghanim et al. (2013) found that the chance of having more severe caries (ICDAS codes 4-6) were three times higher in

HSPMs than in defect free molars. They also found that PEB was twelve times more likely in teeth with more advanced caries compared to milder lesions (Ghanim et al., 2013). In Chile, Gambetta-Tessini et al. (2018) found a positive relationship between the presence of HSPM/MIH and pulpal involvement using the PUFA index (Pulp/ulceration/fistula/abscess) as an outcome of caries (Gambetta-Tessini et al., 2018). A cross sectional study from Melbourne Australia in children aged 6-12 years where the reported caries prevalence is low found that demarcated lesions had a great effect on caries severity as those affected had an increased likelihood of presenting untreated severe atypical carious lesions (Gambetta-Tessini et al., 2018). Interestingly, another cross sectional study from Melbourne Australia found the differences between caries risk according to defect severity not to be significant. (Owen et al., 2018). They concluded that in a low caries prevalence population, the presence of demarcated hypomineralised enamel lesions cannot be viewed as an important risk factor. Of interest, the defect extent rather than the defect severity was more crucial in terms of developing caries.

The pathogenesis of these lesions over time and how this may modify caries risk in different populations remains unclear. Further study of these lesions in populations with differing caries experiences may give a more nuanced appreciation of HSPM activity. Table 1.8 summarises findings from studies which have investigated the relationship between HSPM and caries.

Table 1.8: Studies investigating relationship between HSPM and caries

Article and study type	Year	Country	Age range	Reported caries risk of population	Diagnostic criteria	Findings
Elfrink et al. Cross sectional	2010	Netherlands	5	Low	EAPD dmfs	HSPM positively associated with caries prevalence in Dutch 5 year olds.
Ghanim et al. Cross sectional	2013	Iraq	7-9	High	EAPD ICDAS II	Increased likelihood of having more severe caries in HSPM teeth compared to defect free molars.
Oyedele et al. Cross sectional	2016	Nigeria	8-10	Not described	EAPD dmft	Positive correlation between caries and increasing severity of the HSPM defect
Owen et al. Cross sectional	2018	Australia	3-5	Low	Modified EAPD ICDAS II	Defect extent rather than severity more crucial in caries development
Gambetta-Tessini et al. Cross sectional	2018	Australia	6-12	Low	MIH/HSPM index ICDAS II PUFA	Increased likelihood of presenting untreated severe carious lesions compared with defect free children
Gambetta-Tessini et al. Cross Sectional	2018	Chile	6-12	High	MIH/HSPM index ICDAS II PUFA	HSPM lesions were associated with carious lesion occurrence and increased disease severity
Mittal et al. Cross sectional	2016	India	3-5 6-12	Not described	EAPD ICDAS II	Increased likelihood caries and positive relationship between increased caries and defect severity in hypomineralised molars
Halal & Raslan Cross sectional	2020	Syria	4-5	Not described	MIH/HSPM index dmft	Children with HSPM had a higher prevalence of caries (OR 6.69) when compared with children without HSPM. In each quadrant, SPM significantly more affected by caries when compared to first primary molars

OR=Odds Ratio; dmft= decayed, missing, filled teeth; PUFA= pain, ulcer, fistulae and abscess; ICDAS= International Caries Detection and Assessment System.

1.6 HSPM and MIH

Periods of mineralisation of the FPM and SPM overlap with a significantly longer maturation phase for the FPM (Butler, 1967). If a risk factor were to occur during this overlapping period, hypomineralisation might occur in the primary as well as the permanent dentition (Aine et al., 2000, Elfrink et al., 2012). This parallel mineralisation period both developmentally and with respect to their location in the jaw strengthens the argument for a shared cause (Elfrink et al., 2012).

Table 1.9 summarises the studies which have investigated the predictive nature of HSPM for MIH. Several studies have found the presence of HSPM to be significantly predictive for MIH (Elfrink et al., 2012, Mittal and Sharma, 2015b, Mittal et al., 2016, Negre-Barber et al., 2016, da Silva Figueiredo Se et al., 2017, Gambetta-Tessini et al., 2018, Gambetta-Tessini et al., 2019). Alternatively, some studies have not supported an association between the two entities (Ghanim et al., 2013, Costa-Silva et al., 2013, Sidhu et al., 2019) A systematic review which included five studies with meta-analysis demonstrated that children affected by HSPM were approximately five times more likely to develop MIH (Garot et al., 2018, Elfrink et al., 2012, Ghanim et al., 2013, Costa-Silva et al., 2013, Mittal and Sharma, 2015b, Negre-Barber et al., 2016). The fact that few studies were suitable for analysis should be considered and therefore the authors advised careful interpretation of results. Reference to variation in sample size, calibration protocols and examination conditions was also discussed and attributed to the observed heterogeneity between the studies.

In those children affected by HSPM, factors such as number of teeth affected and defect severity have been assessed as to how this may affect predictability for MIH. A number of studies have found that the likelihood of developing MIH is related to the number of SPM affected by HSPM, in particular when more than two SPMs are involved (Elfrink et al., 2012, Ghanim et al., 2013, Mittal and Sharma, 2015a).

It has been reported that those with milder HSPM defects (without PEB) have a higher odds ratio for developing MIH compared to those with severe HSPM defects (Elfrink et al., 2012, Mittal and Sharma, 2015a, Garot et al., 2018). It may be that the aetiological disturbance resulting in milder HSPM defects occurs during later stages of mineralisation/maturation and overlaps with earlier, more active phases of ameloblast activity of the FPM (Mittal and Sharma, 2015a).

As HSPM/MIH aetiology continues to remain unclear the predictive nature of HSPM for MIH is an additional diagnostic tool for clinicians and may be the only available dental risk indicator in predicting MIH (Leith, 2019). From a clinical perspective, children with HSPM, even mild presentations, should be closely reviewed during eruption of FPMs to facilitate early diagnosis of MIH (Mittal et al., 2016). The significance of anticipating an MIH diagnosis relates to the role of early education and prevention in that parents can be informed and provided with the necessary information on sequelae and home oral care (Lygidakis et al., 2010).

Table 1.9: Studies investigating the predictive nature of HSPM for MIH

Study	Country	Design	No.	Age (Years)	Diagnostic criteria	Setting	Exam conditions	Outcome(s)
Elfrink et al. 2012	Netherlands	Cohort	2327	5-6	EAPD	Medical centre	Photos	Children with HSPM were 4.4 times more likely to develop MIH compared to those unaffected (OR) Children with mild HSPM had higher OR for developing MIH OR increased with increasing number of HSPM affected molars
Ghanim et al. 2013	Iraq	Cross sectional	809	7-9	EAPD	Public school	Artificial light	No significant relationship between HSPM and MIH
Costa-Silva et al. 2013	Brazil	Cohort	134	3-6	EAPD	Public School	Natural light	No significant relationship between HSPM and MIH
Mittal et al. 2015	India	Cross sectional	978	6-8	EAPD	School	Artificial light	Children with HSPM were 7.8 times more likely to develop MIH compared to those unaffected (OR) Slightly higher OR for mild HSPM defects (8.9) compared to severe. Subjects with ≥2 HSPM had significantly higher OR for MIH
Temilola et al. 2015	Nigeria	Cross sectional	563	Group 1: 3-5 Group 2: 8-10	Self-devised	School	Natural light	34.8 % of the children with MIH had MIH/DMH co-morbidity

Negre-barber et al. 2016	Spain	Cross sectional	414	8-9	EAPD	Medical centre	Artificial light	HSPM high predictive power for MIH (Likelihood ratio of 10.3) Children with HSPM 18.2 times more likely to develop MIH compared to those unaffected (OR)
Mittal et al. 2016	India	Cross sectional	1109	Group 1: 3-5 Group 2: 6-12	EAPD	Public School	Natural light	48% of children with MIH had at least one HSPM
da Silva Figueiredo et al. 2017	Brazil	Cross sectional	1963	6-11	EAPD	School	Artificial light	Children with HSPM were 6.3 times more likely to develop MIH compared to those unaffected (OR)
Gambetta-Tessini et al. 2018	Australia	Cross Sectional	327	6-12	EAPD	School	Artificial light	Children with HSPM were 2.9 times more likely to develop MIH compared to those unaffected (OR)
Sidhu et al. 2019	Canada	Cross sectional	429	Not specified	MIH/HSPM index	Hospital	Artificial light	No significant relationship between MIH and HSPM
Gambetta-Tessini et al. 2019	Chile	Cross sectional	527	6-12	MIH/HSPM index	School	Artificial light	Children with HSPM were 3.7 times more likely to develop MIH (OR)

OR=Odds ratio

1.7 HSPM Management

The evidence base for HSPM management is limited. Currently, there are no clinical guidelines for management of HSPM with treatment options following similar recommendations established for MIH. An extensive range of treatments exist for those affected by HSPM from preventive care to restoration and extraction (Lygidakis et al., 2010). Like MIH, several factors must be considered when deciding a suitable treatment plan for HSPM with particular reference to defect severity and behaviour management (Lygidakis et al., 2010). Children with HSPM may present with an extensive treatment need at a very young age and treatment delivery may not be possible under local anaesthesia. The clinician must holistically consider all available options bearing in mind the individual condition of each patient and of each tooth, as well as parental input (Quintero et al., 2019). Table 1.10 describes the management options available for HSPM.

The relationship between HSPM and impact of dental interventions is poorly understood. One recent study explored the impact of HSPM on oral health related quality of life (OHRQoL) in pre-school children (Cerqueira Silva et al., 2021). While the presence of severe HSPM resulted in a negative impact on the OHRQoL of pre-schoolers and their families, the presence of dental caries neutralised this impact. While difficulties in achieving adequate local anaesthesia have been reported for MIH teeth, this challenge has not been explored in children with HSPM (Fagrell et al., 2008, Jalevik and Klingberg, 2002). Furthermore, unlike MIH, there is no evidence suggesting that these teeth are hypersensitive.

Children with HSPM should be viewed as high caries risk and managed as per high caries risk guidelines (Gambetta-Tessini et al., 2019). As for MIH, intense prevention for HSPM teeth should commence as soon as they erupt due to their increased susceptibility to breakdown and caries (Elfrink et al., 2010, Ghanim et al., 2017). Measures should incorporate oral hygiene, dietary counselling and correct use of fluorides (Leith, 2019, Health Service Executive et al., 2009). Studies have found that like demineralisation lesions caused by caries, hypomineralised enamel defects have been shown to form a thin but well mineralised surface layer preventing further mineral loss following fluoride use (Crombie et al., 2013).

Casein Phosphopepetide-Amorphus Calcium Phosphate (CPP-ACP) has been effectively used to manage sensitivity and remineralise MIH molars, however there is no evidence for its use in HSPM (Lygidakis et al., 2010, Restrepo et al., 2016, Özgül et al., 2013).

The caries preventive benefit of fissure sealing sound, non-hypomineralised primary molars has been reported (Beauchamp et al., 2008, Joshi et al., 2019, Hong et al., 2019). Challenges have been reported in the use of resin sealants for MIH molars due to bonding difficulties (Kotsanos et al., 2005, Lygidakis et al., 2010). There is contradictory results regarding the use of sodium hypochlorite to remove the protein layer prior to sealant placement (Sönmez and Saat, 2017, Gandhi et al., 2012). These studies have focused on permanent molars only. Emerging evidence supports the caries preventive effect of high viscosity glass ionomer cement (GIC) in primary molars with favourable retention rates reported (de Amorim et al., 2012, Holmgren et al., 2013). GIC is advantageous in terms of its ease of application with good patient

acceptability reported (Holmgren et al., 2000). Fissure sealant application for defective SPMs requires further investigation in terms of clinical outcomes.

While Atraumatic Restorative Treatment (ART) has been shown to be effective in the management of single surface carious primary molars, there is no specific evidence to support its use in HSPM molars (de Amorim et al., 2018, Tedesco et al., 2017). In early post-eruptive stages of MIH molars, temporisation with GIC may be advantageous as an intermediate treatment where moisture control is not achievable (Lygidakis et al., 2010). Anecdotally, this stabilisation technique can be applied to HSPMs.

While composite has shown relatively favourable outcomes for MIH molars, caution should be exercised in extrapolating to the primary dentition. While strong evidence exists for the success of class 1 composite restorations in primary molars, an overall less predictable clinical behaviour has been observed in primary teeth (Soncini et al., 2007, Chisini et al., 2018). A recent systematic review reported the annual failure rate of composites in primary teeth to be between 1.7 to 12.9% (Chisini et al., 2018). This finding compares poorly to annual failure rates reported in permanent teeth of between 1 and 3% (Demarco et al., 2012, Opdam et al., 2014, Manhart et al., 2004). Patient related factors such as age and behaviour management must be considered when viewing these results. Composite placement is highly technique sensitive and will be jeopardised if optimal conditions are not achieved. The use of rubber dam has been shown to increase the longevity of composite restorations and possibly decrease restoration failure in relation to cotton rolls (Heintze and Rousson, 2012, Wang et al., 2016). Given the limitations of multi-surface composites in primary molars, best practice guidelines have supported the use

of stainless steel crowns (SSCs) for teeth with enamel developmental defects (Kindelan et al., 2008). Furthermore, a recent Cochrane review reported that the use of full coverage restorations outperform conventional fillings for carious primary molars (Innes et al., 2015). While there is limited research comparing SSC to intracoronal restorations for HSPM, case reports have described its suitability (Quintero et al., 2019). Placement of SSCs conventionally using local anaesthesia may not be possible in the younger child due to limited cooperation. The Hall technique provides a useful alternative and its success has been established (Innes et al., 2011). SCCs are placed without any tooth reduction or need for local anaesthesia leading to improved patient acceptability compared to conventional restorative approaches (Santamaria et al., 2015). Unlike other interventions, the use of the Hall technique in HSPM has an evidence base (albeit limited as the study in question involved a small sample size with only a 12 month follow up) (Declerck and Mampay, 2021). This prospective cohort study demonstrated favourable clinical and radiographic results when the Hall technique was used to restore HSPM affected teeth. Clinical outcomes were fully successful in 64.1% and radiographically successful in 93.3%. The main reason for not being viewed as fully successful was deterioration of the gingival condition. Overall, the treatment was well tolerated and accepted by the patients. It is worth mentioning that the criteria used in this study was stricter when compared to past studies where the criteria for success has been limited to no clinical signs/symptoms of pulpal pathology, no intervention required and no pathology radiographically present (Innes et al., 2007). If this criteria was applied, crowns rated as ‘acceptable’ would also be incorporated, leading to a 100% success rate.

Extraction of a defective SPM may be necessary in cases of severely affected or symptomatic molars (Leith, 2019). In paediatric patients, maintenance of the SPM is important as it contributes towards bone development, function and occlusion (Quintero et al., 2019). Premature loss of a SPM may result in space loss and negative sequelae such as dental arch crowding, ectopic eruption/impaction of the permanent tooth and tipping of the FPM (Richardson, 1965, Clinch and Healy, 1960). The negative psychological impact of dental extractions early in childhood has been reported (Karjalainen et al., 2003, Milsom et al., 2003). Further research is needed exploring the impact of early SPM loss in HSPM affected children both clinically and psychologically.

Table 1.10: Management options for HSPM (William et al., 2006, Leith, 2019)

Management option	**Description**
Risk identification	Review of prenatal, perinatal and postnatal periods
Early diagnosis	Teeth should be examined as soon as they erupt
Remineralisation	Dietary advice; assisted brushing with fluoride toothpaste (1000-1450ppm) Professionally applied fluoride varnish (22,600ppm F)
Fissure sealants	Use of GIC, RMGIC or resin
Restorative or extractions	RMGIC; composite resin Hall technique; conventional SSC; extraction
Maintenance	Frequent review and careful monitoring during eruption of FPMs

1.8 Dentists' perception and clinical management of HSPM

There is limited research around dentists' perceptions and clinical management of HSPM. One recent questionnaire study conducted in Saudi Arabia explored this area providing a much needed insight into how dental professionals perceive and clinically manage this condition (Meer et al., 2020). The study

used a cross sectional design involving 206 dentists with a young age profile (53% of participants <30 years of age with 48% of participants having < 5 years of dental experience). Most participants were general dentists (84%) with 16% of the sample having completed masters training. 60% of respondents were aware of HSPM with 48% citing white demarcated opacities as the most common presentation. 51% reported being confident in diagnosis with a higher percentage (70%) being confident in management. GIC represented the most popular choice for restoring these teeth (46%).

One area which has been explored relates to the perceived frequency of observing HSPM. Most studies have used the same form of questioning and have used the FPM as a reference i.e. do participants feel HSPM is more or less frequent when compared to MIH in the FPMs**.** Most studies have been in agreement that HSPM features less commonly when compared to MIH (Ghanim et al., 2011, Silva et al., 2016a, Kumar and Dhillon, 2020, Serna-Muñoz et al., 2020, Meer et al., 2020). HSPM is a relatively new condition and general dentists may not be as familiar with or as vigilant in diagnosing compared to the more widely recognised MIH. This theory was supported by Humphries et al. (2021) in their vignette survey where they found that correct diagnosis of HSPM was much lower than for MIH amongst general dentists (Humphreys et al., 2021). They cited a lack of awareness of HSPM terminology as a potential influencing factor.

1.9 Concluding remarks

The aetiology of HSPM remains unclear however this is not surprising considering the likely multifactorial aetiology and complex interplay of factors at a surface, tooth, child and family level. While much of the research has focused

on systemic disturbances to the ameloblast there is a lack of evidence relating to the role of genetics in HSPM development. The relationship between HSPM and other dental anomalies requires further exploration and would be of value as it has potential implications for assessment and treatment planning. The role of social factors such as socio-economic and demographic factors remains poorly understood and requires further investigation. The diagnosis and clinical presentation of HSPM has been well explored in the literature adding a methodological robustness to prevalence and aetiological studies. Despite widespread use of standardised criteria, a broad variation in reported prevalence levels exists. The likely impact of the diagnostic criteria on HSPM prevalence has been discussed in the literature but has yet to be confirmed as to whether it significantly affects prevalence. The relationship between HSPM and caries remains poorly understood although evidence to date highlights the importance of overall caries experience of the populations being studied and the underlying severity of the condition when interpreting this relationship. The predictive nature of HSPM for MIH has been demonstrated however this finding should be interpreted with caution as the evidence is limited with high variability between the studies involved. There is a scarcity of evidence relating to management of HSPM with a need for HSPM specific treatment guidelines. In addition, our understanding of how clinicians perceive and clinically manage this condition is very limited and requires further investigation.

1.10 Introduction to current research study

The overall aim of this thesis was to provide more insight into HSPM including both its prevalence worldwide and its prevalence in the Irish population. The influence of the diagnostic criteria on global HSPM prevalence was also of

interest. The current understanding around HSPM awareness and clinical management is very limited. This study sought to investigate perception and management of HSPM by Irish dentists.

1.10.1 *Research questions*

Study 1

What is the pooled prevalence of HSPM worldwide and what effect does diagnostic criteria have on HSPM prevalence levels?

Study 2

What is the prevalence of HSPM in an Irish population?

Study 3

How do Irish dentists perceive and manage HSPM?

Study 1:

Prevalence of Hypomineralised Second Primary Molars:

a systematic review and meta-analysis

2. Study 1 - Prevalence of Hypomineralised Second Primary Molars: a systematic review and meta-analysis

2.1 Abstract

Background*:** Several prevalence studies on HSPM have now been published with a wide variation in defect prevalence reported. Despite the development of the 2003 EAPD criteria, comparability between studies remains challenging because of the use of different diagnostic criteria, examination variability and different age groups. To date, no systematic review on HSPM prevalence has been conducted. ***Aim: To evaluate the prevalence of HSPM worldwide on a child and tooth level and investigate the influence of diagnostic criteria on the prevalence of HSPM. ***Methods:*** A comprehensive literature search was performed through MEDLINE/PubMed, Scopus and Web of Science databases. An adaptation of the Newcastle-Ottawa Scale was used to evaluate the quality of the studies. A meta-analysis was performed to determine the pooled prevalence of HSPM. ***Results:*** The search strategy identified 1,987 articles, 486 were retrieved for full text evaluation and 37 studies were included in the meta-analysis (32 for child and 23 for tooth level prevalence), providing data from 26,805 individuals and 81,107 molars. The prevalence of HSPM was 6.8% (95%CI 4.98 to 8.86%) on a child level and 4.08% on a tooth level (95%CI 2.80 to 5.59%). The diagnostic criteria used did not seem to influence the prevalence results (p≥.05). The majority of the papers (75%) showed low to moderate risk of bias. ***Conclusion:*** There was a broad variation in the prevalence reported that may be attributed to differences in the study population. The present meta-analysis showed a HSPM prevalence worldwide of 6.8% on a child level and 4.08% on a tooth level.

2.2 Study aims and objectives

2.2.1 Aims

- To determine the child and tooth level prevalence of HSPM worldwide
- To investigate the influence of the diagnostic criteria employed on the prevalence of HSPM

2.2.2 Objectives

- To systematically review the literature so that all relevant articles were included on HSPM prevalence
- To perform a meta-analysis to determine the pooled prevalence of HSPM
- To perform a sub-group meta-analysis to determine the effect of diagnostic criteria on HSPM prevalence

2.3 Methods

This systematic review and meta-analysis was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA Statement) checklist recommendations and was registered on PROSPERO (International prospective register of systematic reviews) (protocol number CRD42020220498).

2.3.1 Search strategy

A comprehensive literature search was performed through MEDLINE/PubMed, Scopus and Web of Science databases to identify relevant papers published up to March 2021. The reference lists of the included studies were manually searched to retrieve all eligible papers that could not have been identified during the main search. A language restriction existed with only English publications included.

MEDLINE/PubMed search strategy:

("primary tooth" OR "primary teeth" OR "deciduous tooth" OR "deciduous teeth" OR "primary molar*" OR "deciduous molar*" OR child* OR pre-schooler*) AND ("hypomineralized SPM*" OR "hypomineralised SPM*" OR HSPM OR "deciduous molar hypomineralization" OR "deciduous molar hypomineralisation" OR hypomineralisation OR hypomineralization OR "demarcated opacities" OR opacity OR "deciduous molar hypoplasia" OR "hypoplastic primary teeth" OR "hypoplastic primary tooth" OR "primary molar hypoplasia" OR "hypoplasia of primary molars") AND (Prevalence (MeSH) OR prevalence (all) OR incidence OR epidemiolog*)

Scopus search strategy:

TITLE-ABS-KEY (prevalence OR incidence OR epidemiolog*) AND ("primary tooth" OR "primary teeth" OR "deciduous tooth" OR "deciduous teeth" OR "primary molar*" OR "deciduous molar*" OR child* OR pre-schooler*) AND ("hypomineralized SPM* " OR "hypomineralised SPM*" OR "HSPM" OR "deciduous molar hypomineralization" OR "deciduous molar hypomineralisation" OR "hypomineralisation" OR "hypomineralization" OR "demarcated opacities" OR "deciduous molar hypoplasia" OR "hypoplastic primary teeth" OR "hypoplastic primary tooth" OR "primary molar hypoplasia" OR "hypoplasia of primary molars")

Web of Science search strategy (combined searches):

TS = ("primary tooth" OR "primary teeth" OR "deciduous tooth" OR "deciduous teeth" OR "primary molar*" OR "deciduous molar*" OR child* OR pre-schooler*)

TS=("hypomineralized SPM*" OR "hypomineralised SPM*" OR "HSPM" OR "deciduous molar hypomineralization" OR "deciduous molar hypomineralisation" OR "hypomineralisation" OR "hypomineralization" OR "demarcated opacities" OR "deciduous molar hypoplasia" OR "hypoplastic primary teeth" OR "hypoplastic primary tooth" OR “primary molar hypoplasia” OR “hypoplasia of primary molars”)

TS=(prevalence OR incidence OR epidemiolog*)

2.3.2 Selection Criteria

Inclusion criteria

Potentially eligible references were imported into an Excel file. Databases were merged into one spreadsheet file and organised in an alphabetical order with duplicates removed manually. Two independent reviewers (CMC and IOC) were involved in the screening of articles by title and abstract according to pre-determined inclusion criteria. In the case of disagreement regarding inclusion, a third reviewer (RL) was involved in reaching consensus. If there was a lack of clarity in any of the criteria evaluated, the study was included for full text evaluation. The inclusion criteria incorporated four of the following categories and is summarised in Table 2.1.

Criteria 1- DDE/enamel defect description

This related to the presence of any DDE including both quantitative and qualitative enamel defects such as enamel hypoplasia, enamel hypomineralisation, diffuse opacities (fluorosis) and Amelogenesis Imperfecta (AI).

Criteria 2- Child population

It was required that the study population included children. Studies involving adult participants (defined as an individual aged 18 years and over) were not included.

Criteria 3- Epidemiological study design

Epidemiological study design was a requirement for inclusion which included cohort, case control and cross-sectional studies. Systematic reviews, literature reviews, case reports and case-series were not included.

Criteria 4- English language

Only articles published in the English language were accepted.

Table 2.1: Inclusion criteria used in screening of article title/abstract

Inclusion category	Question
1. Developmental defect of enamel (DDE)	Was a DDE/enamel defect described?
2. Child/paediatric population	Did the study involve a child population?
3. Epidemiological	Was it an epidemiological study?
4. Language	Was the abstract in English?

Exclusion criteria

Table 2.2 summaries the exclusion criteria. The full texts of articles were read by the same two examiners involved in the inclusion process (CMC & IOC) and excluded based on pre-determined criteria. When a disagreement arose, a third examiner (RL) was involved in reaching consensus. Articles were excluded when any one of five exclusion criteria described below were not met.

Criteria 1- Was the defect described HSPM?

HSPM was defined as enamel hypomineralisation affecting one to four SPMs characterised by demarcated opacities, PEB, atypical caries, atypical restorations and extractions due to HSPM. Criteria which have been designed specifically for HSPM diagnosis include the EAPD judgement criteria and MIH/HSPM diagnostic criteria and articles using these criteria were retained (Weerheijm et al., 2003, Ghanim et al., 2015). Description of demarcated opacity was required to be classified as a HSPM diagnosis. Therefore, other diagnostic criteria, such as mDDE and other self-devised indices were included as long a clear description of the above was provided.

Criteria 2- Prevalence data

The authors needed to provide sufficient data in order to calculate the prevalence of HSPM. It was a requirement of the meta-analysis to include child and tooth level prevalence, and therefore, the total sample size (children/SPM) and the total number (children/SPM) affected by HSPM needed to be available for calculation.

Criteria 3- Full text

Unavailability of the full text resulted in the article being excluded. Full texts were requested by the library team and a period of 6 weeks was given to source after which articles were excluded.

Criteria 4- Missing data

Incomplete data included missing the total sample size or missing the total number of participants affected by HSPM. In the case of missing data, authors were emailed and given a period of 6 weeks to provide required information after which articles were excluded if not provided.

Category 5- No repeated data

When more than one study was conducted using the same sample, only the original or the most complete article was included.

Table 2.2: Summary of exclusion criteria used in reading of full-text articles

Exclusion category	**Question**
1. HSPM	Is the DDE described HSPM?
2. Prevalence	Is HSPM prevalence data provided?
3. Full text	Is the full text available?
4. No missing data	Is data complete?
5. No repeated data	Refers to when more than one study was conducted using the same sample

2.3.3 Training and calibration

Reviewers (CMC & IOC) were trained and calibrated in paper selection. The calibration exercise involved a randomised selection of papers (10% of included articles; n=147) which were screened for eligibility. Kappa analysis was carried out to determine inter-examiner reliability for inclusion of selected papers (yes/no) (K=0.954). Kappa analysis was also performed for reason (1-4 according to Table 1) for 'not including' (K=0.899).

2.3.4 Data extraction

Information on the included studies was collected by two teams of reviewers CMC & RL; IOC & AOC). Should disagreement exist consensus was reached by all authors. A data collection proforma was developed (Appendix 1). The following data were systematically collected from each included study: publication details (authors, country, year and study type), population details (location, population type -general or specific, age range, gender), evaluation (examination conditions), diagnostic criteria (standardised and self-devised

options given), outcomes (child and tooth level prevalence) and extra information (defect characteristics).

2.3.5 Risk of bias of included studies

Following data extraction, the same two reviewer teams independently assessed possible risk of bias amongst eligible studies using a bias assessment tool (Modified Newcastle Ottawa Quality Assessment Scale-adapted for cross sectional studies) (Herzog et al., 2013, Tibúrcio-Machado et al., 2021). This tool was adapted further with minor modifications made to the starring system (Appendix 2). Reviewers scored the articles that sufficiently fulfilled each methodological criterion and provided a score with a maximum of 13 stars. The tool consisted of three sections which included selection, comparability and outcome. Section 1 (selection criteria) included sample representativeness, sample size and non-respondents (maximum of 6 stars). Section 2 described comparability referring only to studies which included different groups (maximum of 2 stars). The final section described outcome criteria including diagnostic criteria, training and calibration (maximum of 5 stars). Studies which received ≥ 9 stars were considered to be high quality or to have low risk of bias. Those with 7-8 stars were of medium quality or moderate risk of bias. Those with ≤ 6 stars had low methodological quality or high risk of bias. In the case that a certain area was not described in the study a ‘not reported’ or ‘NR’ was entered.

2.3.6 Data analysis

MedCalc 20 (MedCalc Software Ltd.) statistical software was used to determine inter-examiner reliability for inclusion of selected articles using Kappa calculation.

All searches' results were exported and managed in an Excel file (Microsoft Inc., USA). Data collection for the meta-analysis included the number of children evaluated in the study and respective number of children with HSPM. In relation to tooth prevalence, the total number of SPMs evaluated and how many presented HSPM were calculated.

A forest plot was generated using Stata 17.0 statistical (StataCorp LLC, Texas, USA) using a random-effects model including the subgroup prevalence data and the overall pooled effects. Jamovi software (The Jamovi Project 2021; version 1.6) was used for meta-regression analysis using criteria as a moderator. Paul-Mandel mixed-effects model was used for estimating overall pooled prevalence and between-study variability in the meta-regression.

2.4 Results

2.4.1 Study selection

One thousand, nine hundred and eighty seven (1987) potentially relevant articles were identified in the systematic literature search; 519 were considered duplicated and were therefore removed. After screening of titles and abstracts, 983 were considered as non-eligible. The principal reason for non-inclusion was that studies did not describe a DDE (n=756), followed by non-clinical studies (n=123), studies not involving children (n=68) and non-English studies (n=36). A total of 485 studies were retrieved for full-text evaluation with an additional one article sourced manually, from which 449 articles were excluded. The main reason for exclusion was that the article did not describe HSPM (n=373). Other reasons included no prevalence data (n=44), missing data (n=17), duplicated data (n=11) and no full text (n=4). Finally, 37 papers were included in the systematic review (32 papers showed appropriate data for child prevalence and 23 papers for tooth prevalence meta-analysis). Figure 2.1 displays the study selection process.

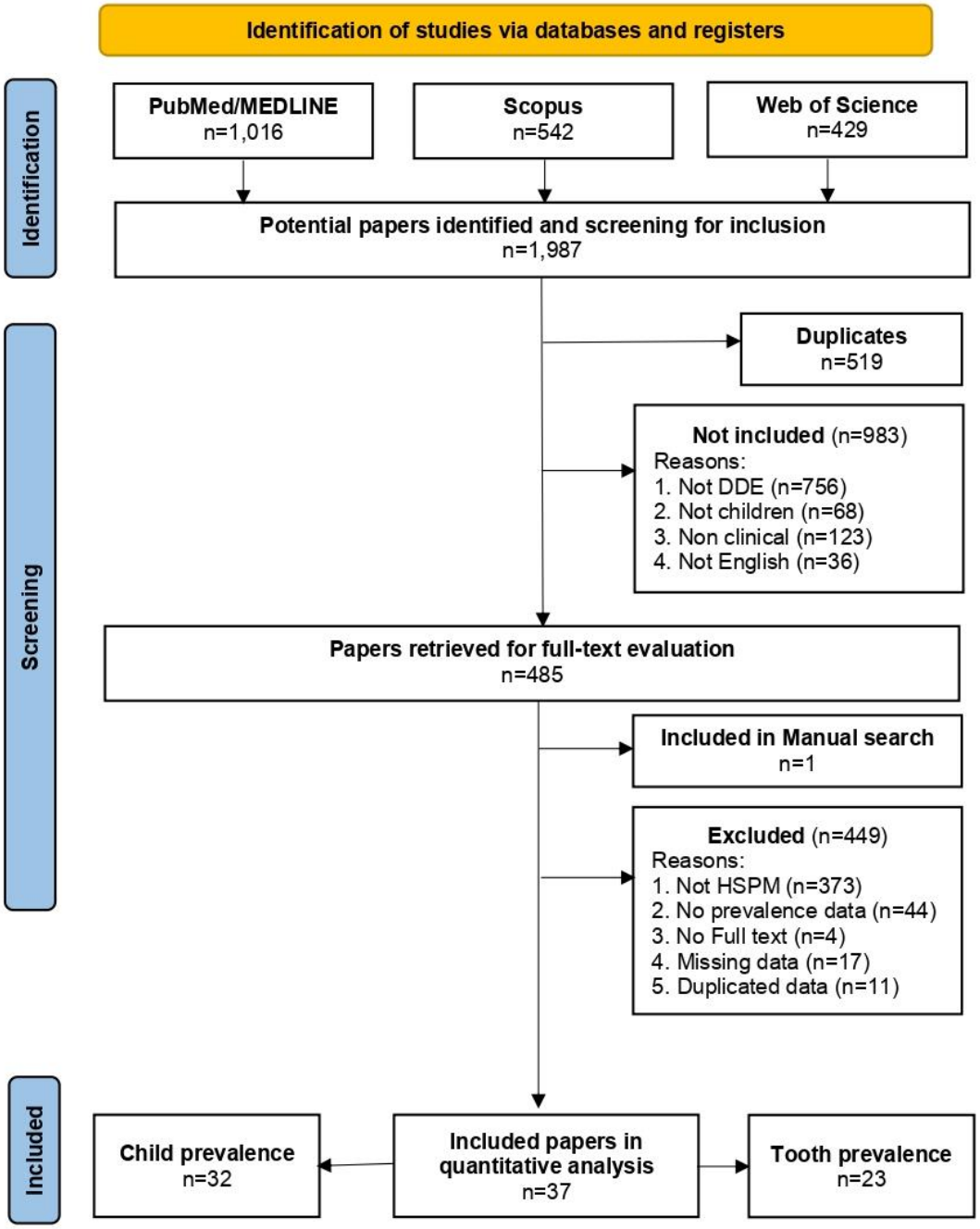


Figure 2.1: Flow chart of study selection process

2.4.2 *Study characteristics*

Table 2.3 presents the main characteristics of the included studies. The included studies provided data from 26,805 individuals (ranging from 31 to 5561 children) and 81,107 primary second molars (ranging from 124 to 23,722 teeth). Articles were published between 1979 and 2020 and included countries in Europe, Australia, Asia, Africa, South America, USA and Canada (Figure 2.2). Twenty-nine of the studies were cross sectional in nature, followed by seven cohort studies and one randomised control trial. Thirty-four studies involved general populations and three studies involved select groups. 16 studies were carried out in schools/early childhood centres, five in dental clinics, four with portable dental chairs, five in medical centres/hospitals, three in research facilities, two in households, one in the field and one in a sub-urban area.

Nineteen of the studies used the EAPD criteria for diagnosis and six used the Ghanim et al. criteria (2015). An equal number of studies (4 each) used the mDDE or DDE indices. Two studies used a combination of the above criteria with two using self-devised criteria.

Twenty-two studies described the light source as being artificial, nine used natural light, two used photographs and four did not record the lighting conditions. Seventeen studies described teeth as wet, ten were described as dried with cotton rolls/gauze, two studies described the teeth as air dried and eight studies did not record this area.

As regards cleaning of the teeth, fifteen used toothbrushes, ten used gauze/cotton rolls, two used prophylaxis, two described the teeth as clean but did not specify how so, seven did not record if the teeth were cleaned and one study stated that the teeth were not cleaned.

2.4.3 Prevalence of HSPM worldwide

Europe

Eight of the included studies from Europe provided data on child prevalence with an overall range of 0% and 14.5% reported. In the Netherlands, a range of 4.9 to 9% was reported (Elfrink et al., 2008, Elfrink et al., 2012). These studies applied the EAPD diagnostic criteria with an age range of 5-to-6 years. Research populations for these studies mainly included a specific group of children including groups from referred populations and were all based in urban locations. Photos were used in one of the studies to score HSPM with good to excellent inter- and intra- observer reliability reported (Elfrink et al., 2012). Studies in Germany have been conducted also. Both Kuhnisch et al. (2014) and Elgar et al. (2020) reported a similar HSPM prevalence of 4% (Kuhnisch et al., 2014, Elger et al., 2020). Both studies employed the same diagnostic criteria with similar sample sizes however a difference existed in the age range with Kuhnisch et al. (2014) employing an older age group. Schuttfort et al. (2020) and Wagner et al. (2017) reported similar prevalence levels (Schüttfort et al., 2020, Wagner, 2017). Schuttfort et al. (2020) reported a prevalence of 0% (Schüttfort et al., 2020). This study involved a select group (HIV exposed children) and involved an age group of 2 years (potentially prior to age SPMs erupt). The sample size was small (31 participants) which may have resulted in an under reporting of defect prevalence. Wagner et al. (2017) reported a prevalence of 1.6% in their sample and involved a similar age group of 3 years (Wagner, 2017). In Spain, Negre-Barber et al. (2016) reported a higher prevalence of 14.5% with an age range of 8-9 years (Negre-Barber et al., 2016). In Denmark, Nørrisgaard et al. (2019) reported a similarly high

prevalence of 12.3% (Nørrisgaard et al., 2019). Both studies were performed in dental clinics with comparable diagnostic criteria. A slightly older age group was used in Negre-Barber's study (8-9 years) compared to the 6 year old sample employed in the Danish study.

One study from England was included which reported a tooth prevalence of 5.1%. This study employed an index developed by Young (1973) & Al-Alousi (1977). The criteria included white and coloured opaque spots well demarcated from the surrounding area. The full spectrum of HSPM including PEB, atypical caries, restorations or extractions due to HSPM were not included which likely resulted in an under reporting. However, considering this article was published in 1979, prior to the recognition of MIH/HSPM this is not a surprising finding. In the Netherlands, studies have reported similar tooth prevalence levels - 4% and 3.7% respectively (Elfrink et al., 2012, Elfrink et al., 2008). In Germany, Schuttfort et al. (2020) reported a 0% tooth prevalence in their select group of 2 year old children (Schüttfort et al., 2020). Kuhnisch et al. (2014) reported a slightly higher tooth prevalence of 1.8% in their German study (Kuhnisch et al., 2014). Representation from several European countries has been absent including but not limited to France, Italy and Ireland.

Asia

Nine studies were conducted in Asia. Ghanim et al. (2013) conducted a cross sectional study involving 809 Iraqi children aged 7-to 9 years (Ghanim et al., 2013). EAPD diagnostic criteria were applied with favourable conditions for diagnosis. A HSPM prevalence of 6.6% was reported. Four studies from India have been published showing a prevalence range of 0 to 7.9% (Kar et al., 2014, Mittal and Sharma, 2015b, Mittal et al., 2016, Goyal et al., 2019). The study by

Kar et al. in 2014 reported a 0% HSPM prevalence with the sample including 306 3-to-5-year-olds. Study limitations included use of the mDDE diagnostic criteria and examinations conducted under natural light. The studies conducted by Mittal et al. in 2015 and 2016 produced similar prevalence rates of 4.5% and 5.6% however comparison is challenged by different sample sizes, age groups and examination conditions (Mittal and Sharma, 2015b, Mittal et al., 2016). Goyal et al. (2019) reported a prevalence of 7.9% in their cross sectional study of 3013 3-6 year old school children (Goyal et al., 2019). This is higher than previous published prevalence studies in India. Singapore's first prevalence study was conducted in 2014 with a low prevalence of 2.9% reported (Ng et al., 2014). This study consisted of a convenience sample of 1083 children with an average age of 7 years. Atypical caries was not included in the judgement criteria and therefore prevalence may have been under reported. As the sample was convenient in nature, true representation of the population may not have been achieved. In 2020, a cross sectional study consisting of 600 4-5 year old Syrian preschool children was carried out with a HSPM prevalence of 41% calculated (Halal and Raslan, 2020). Teeth were examined clean and wet according to the diagnostic criteria developed by Ghanim et al. in 2015. The examination was performed in the children's kindergarten. This is the highest reported HSPM prevalence level worldwide. The authors postulated that the increased prevalence may have been related to the use of a purpose fit diagnostic criteria and also a suitable age group of children as other studies have not always employed appropriate diagnostic measures and used older age cohorts which can result in an under reporting of HSPM prevalence. However, several studies have used suitable diagnostic criteria, examination conditions and appropriate age groups and have not demonstrated such a high

rate of prevalence (Goyal et al., 2019, Lima et al., 2020). The authors also reflected on the impact the war in Syria may have had on the higher prevalence rate considering the likely increase in adverse environmental conditions (Halal and Raslan, 2020). Saudia Arabia's first prevalence study was conducted in 2020 (Zakirulla et al., 2020). This cross sectional study comprised 596 children (80% male participants) with an age range of 7-10 years. The EAPD diagnostic criteria was applied with clean, wet, teeth examined in a dental setting using an artificial light source. A HSPM prevalence of 5.4% was reported amongst the sample which is comparable to the findings reported in India and also some parts of Europe.

In India similar tooth prevalence levels have been reported. Mittal & Sharma reported a level of 3.5% and Goyal et al. reported a level of 4% (Mittal and Sharma, 2015b, Goyal et al., 2019). Comparability has also been seen in Saudi Arabia where a tooth prevalence of 3.1% and 4.8% have been demonstrated (Farsi, 2010, Zakirulla et al., 2020). In Singapore, one study has been published with a tooth prevalence of 1.2% reported. A high tooth prevalence of 29.8% has been reported in Syria (Halal and Raslan, 2020)

Africa

Representation from Africa is emerging with four studies from Nigeria included in the systematic review. Temilola and Folayan (2015) reported a prevalence of 1.3% in their cross sectional survey of 1-19 year olds (Temilola and Folayan, 2015). Foyalan et al. (2020) reported a similar prevalence of 2.1% in their sample of 3-5 years (Folayan et al., 2020). Both studies employed the same diagnostic criteria. Oyedele et al. (2016) reported a higher prevalence of 5.8% which involved a school environment and 8-10 year old children (Oyedele et al.,

2016b). Another study conducted by Temilola et al. (2015) used an alternative diagnostic criterion and reported a prevalence of 4.6% (Temilola et al., 2015b, Kemoli, 2008). The criteria by Kemoli et al. (2008) was similar to EAPD including demarcated opacities, atypical restorations and PEB. Both studies were carried out using natural light which may have hampered diagnosis.

One African study has published data on HSPM tooth prevalence with a level of 4% reported (Oyedele et al., 2016b).

Australia

In Australia, three studies have been conducted investigating HSPM prevalence (Owen et al., 2018, Gambetta-Tessini et al., 2018, Silva et al., 2019). Owen et al. (2018) conducted the first Australian HSPM prevalence study in 2018 with a reported child prevalence of 14.1% and tooth prevalence of 5.80% (Owen et al., 2018). A slightly lower child prevalence of 8% was found by Gambetta-Tessini and colleagues (2018) however defect prevalence may have been under reported due to the older age group being examined (Gambetta-Tessini et al., 2018). Alternatively, Silva et al. (2019) conducted a prospective, twin study involving 172 twin pairs and found an increased child and tooth prevalence of 20% and 10.20% respectively (Silva et al., 2019). Given the increased likelihood of prenatal and perinatal complications in twin cohorts this is not surprising (Taji et al., 2011).

South America

In recent years, an increasing body of literature has emerged from South America on HSPM prevalence with four studies included in this review on child prevalence. Brazilian studies have reported a prevalence range of between

1.2% and 20.2% (Costa-Silva et al., 2013, Lima et al., 2019, Reyes et al., 2019, Fernandes et al., 2020). The study by Costa-Silva (2013) was an outlier with a reported prevalence of 20.2% (Costa-Silva et al., 2013). Compared to the two other Brazilian studies, the sample size was small with only 134 participants leading to a likely over estimation of defect prevalence. In Chile, Gambetta-Tessini (2019) reported a HSPM prevalence of 5% in their cross sectional study of 577 children (Gambetta-Tessini et al., 2019). This result is comparable to findings in Brazil and also internationally where similar prevalence levels have been reported (Ghanim et al., 2013, Sidhu et al., 2019, da Silva Figueiredo Se et al., 2017). Six Brazilian studies have reported on HSPM tooth prevalence with a range of between 0.55% to 3.8% reported (Chaves et al., 2007, Corrêa-Faria et al., 2013, de Lima Mde et al., 2015, da Silva Figueiredo Se et al., 2017, Fernandes et al., 2020).

North America and Canada

There is a dearth of literature from North America on HSPM and MIH prevalence with two studies included in this review. Slayton et al. (2001) reported a child prevalence of 14.3% and a tooth prevalence of 5.7% in their cross sectional study using the DDE index (Slayton et al., 2001). Contrastingly, Ahmed et al. (2020) reported a lower child prevalence of 2.4% (Tagelsir Ahmed et al., 2020). This study employed the more recently developed index by Ghanim et al. (2015) with an age range of 8-10 years. One study from Canada has provided some insight into the countries prevalence with a reported child level of 5.2% reported (Sidhu et al., 2019). This cross sectional study was hospital based and included a mixture of healthy and medically compromised participants. While an adequate sample size was used with appropriate

diagnostic criteria/ calibration, the robustness of the study was compromised by not describing the age group of participants or providing calibration kappa scores.

Distribution of included studies

Europe, Australia, Asia, Africa, North America and South America were represented in the included studies. Disparity existed in the number of studies across continents. Europe, South America and Asia were well represented. Contrastingly, there were fewer studies from Africa, North America and Australia. Figure 2.2 illustrates the geographical distribution of HSPM worldwide.

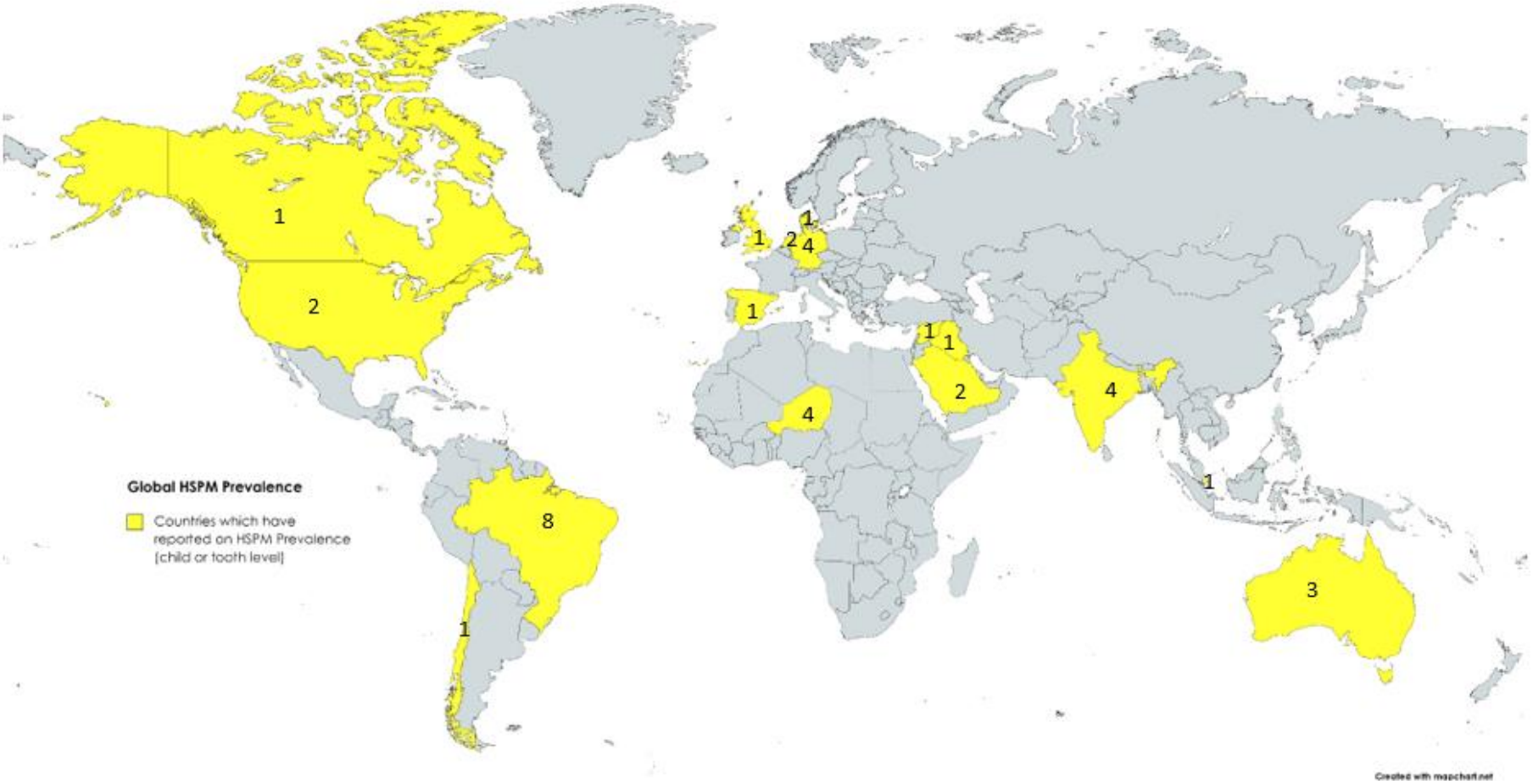


Figure 2.2: Geographical distribution of HSPM worldwide – yellow zones reflect number of studies in each country which have reported on HSPM prevalence (child or tooth level).

2.4.4 Risk of bias assessment

Risk of bias within studies is shown for each article in Table 2.4.

Selection criteria

Representativeness (Maximum 3 stars)

Sixteen of the studies were truly representative of the average in the target population (all subjects or random sampling). Seventeen studies were somewhat representative, and three studies involved a selected group of users. One study provided no description of the sampling strategy.

Sample Size (Maximum 1 star)

Eighteen of the studies provided a justified and satisfactory sample size with the sample size calculation reported. Nineteen of the studies did not report on sample size.

Non respondents (Maximum 2 stars)

Comparability between respondents and non-respondents' with a satisfactory response rate (>80%) was provided by thirteen of the studies. Eight of the studies had an unsatisfactory response rate (<80%), or the comparability between respondents and non-respondents was unsatisfactory. Sixteen of the studies provided no description of the response rate or the characteristics of the responders and the non-responders.

Comparability (Maximum of 2 stars)

For thirty-four of the studies this area was not applicable. Two of the studies controlled for the most important factor (location of recruitment). One study controlled for any additional factor (age).

Outcome

Criteria (Maximum of 1 star)

Twenty-eight of the studies used the EAPD or Ghanim et al. (2015) criteria. Nine studies used an alternative diagnostic criterion such as the mDDE/DDE or self-devised.

Training (Maximum 1 star)

Twenty-five of the studies described the training of the examiners. The remaining twelve studies did not provide a description of the training performed**.**

Calibration (Maximum 3 stars)

Twenty-eight of the studies described the calibration for the methodology of HSPM, with inter- and intra-agreement values provided greater than 0.70. Two studies described the calibration with inter- and intra-agreement values provided lower than 0.70. Four studies described the calibration but provided no agreement values. Three studies did not mention calibration.

Overall bias of studies

Bias scores ranged from 3 to 11 stars, and the majority of the papers showed a low to moderate risk of bias with only nine studies displaying a high risk of bias (≤6 stars). An equal number of studies (14 each) presented with a low (≥9 stars) and moderate (7-8 stars) risk of bias.

Table 2.3: Characteristics of the selected studies

Study	Country	Study Design	Examination Details					Sample			Age (years)
			Setting	Criteria	Wet/Dry	Light	Clean	Child (Total/HSPM)	Teeth (Total/HSPM)	HSPM defect characteristics	
(da Silva Figueiredo Se et al., 2017)	Brazil	Cross-sectional	School	EAPD	Wet	Artificial	Toothbrush	1590/103	6360/139	By tooth Demarcated opacities n=80 (57.6%) PEB enamel only n=17 (12.2%) PEB dentine/ atypical restoration/extraction n=42 (30.2%)	6-11
(Mittal et al., 2016)	India	Cross-sectional	School	EAPD	NR	Natural	NR	223/10	-	By child Demarcated opacities = 8 (80%) PEB = 2 (20%)	3-5
(Nørrisgaard et al., 2019)	Denmark	RCT	Dental clinic	EAPD	NR	Artificial	No	496/61	-	NR	6
(Gambetta-Tessini et al., 2018)	Australia	Cross-sectional	School	Ghanim et al. 2015	Dry (Cotton rolls/ gauze)	Artificial	Toothbrush	327/26	-	NR	6-12
(Murray and Shaw, 1979)	England	Cross-sectional	Portable chair	Young 1973 Al-Alousi 1977	Dry (air)	Artificial	NR	-	1140/58	NR	6
(Elfrink et al., 2012)	Netherlands	Cohort	Medical Centre	EAPD	Wet	Photos	Toothbrush	5561/499	23722/955	By child Demarcated opacities n=382 (76.6%) PEB n=159 (31.9%) Atypical restoration n=97 (19.4%) Atypical caries n=73 (14.6%) Atypical extraction n=56 (11.2%)	5-6
(Reyes et al., 2019)	Brazil	Cross-sectional	School	mDDE	Wet	Artificial	Gauze	731/69	-	NR	8
(Wagner,	Germany	Cohort	Dental	mDDE	Dry (Cotton	Artificial	Gauze	377/6	-	NR	3

2017)			clinic		rolls/ gauze)						
(Corrêa-Faria et al., 2013)	Brazil	Cross-sectional	Health care unit	DDE	NR	Natural	Gauze	-	1509/16	NR	3-5
(Farsi, 2010)	Saudi Arabia	Cross-sectional	School	mDDE	Wet	Artificial	Clean (not specified)	-	2003/62	NR	4-5
(Temilola and Folayan, 2015)	Nigeria	Cross-sectional	House	EAPD	Wet	Natural	Gauze	1169/15	-	NR	1-19
(Chaves et al., 2007)	Brazil	Cohort	House	DDE	Dry (Cotton rolls/ gauze)	Natural	Gauze	-	816/31	NR	1-3
(de Lima Mde et al., 2015)	Brazil	Cross-sectional	School	EAPD	NR	Artificial	Toothbrush	-	583/7	NR	11-14
(Silva et al., 2019)	Australia	Cohort	Research facility/ House	Ghanim et al. 2015/ DDE	Wet	Artificial	Cotton rolls	344/68	1382/141	By child Demarcated opacities n=36 (52.9%) PEB/atypical caries/restorations/extractions n=32 (47.1%)	6
(Mittal and Sharma, 2015b)	India	Cross-sectional	School	EAPD	Wet	Artificial	Clean (not specified)	978/55	3912/136	By surface Demarcated opacities n=177 (69.4%) PEB = 77 (30.2%)	6-8
(Oyedele et al., 2016b)	Nigeria	Cross-sectional	School	EAPD	Wet	Natural	Gauze	469/27	1876/73	By child Demarcated opacities n=13 (48.14%) PEB/atypical caries/restorations/extractions n=14 (51.8%)	8-10
(Negre-Barber et al., 2016)	Spain	Cross-sectional	Dental Clinic	Ghanim et al. 2015	Wet	Artificial	Gauze	414/60	-	By child Demarcated opacities n=55 (91.7%) PEB/atypical	8-9

									caries/restorations/extractions n=5 (8.3%)	
(Elfrink et al., 2008)	Netherlands	Cross-sectional	Portable chair	EAPD	NR	NR	NR	386/19	1517/55	By tooth Demarcated opacities n=48 (87%) PEB = 22 (40%) Atypical restorations n=8 (15%)	5
(Costa-Silva et al., 2013)	Brazil	Cohort	School	EAPD	Wet	Natural	Toothbrush	134/27	864/64	Demarcated opacities n=134 (100%)	4-6
(Schüttfort et al., 2020)	Germany	Cross-sectional	Hospital	DDE	Dry (Gauze)	Artificial	Gauze	31/0	124/0	NR	2
(Folayan et al., 2020)	Nigeria	Cross-sectional	Sub-urban area	EAPD	NR	NR	NR	1173/25	-	NR	3-5
(Fernandes et al., 2020)	Brazil	Cross-sectional	School	EAPD	Dry (air)	Natural	Toothbrush	610/7	1804/10	By tooth Demarcated opacities n=9 (90%) PEB = 1 (10%)	6-12
(Lima et al., 2020)	Brazil	Cross-sectional	School	EAPD	Dry (Gauze)	Artificial	Toothbrush	811/121	3244/238	By tooth White/cream Demarcated opacities n=170 (71.4%) Yellow/brown Demarcated opacities n=68 (28.6%) PEB n=27 (11.34%) Atypical restorations n=4 (1.7%) Atypical caries n=27 (11.34%)	5
(Sidhu et al., 2019)	Canada	Cross-sectional	Hospital	Ghanim et al. 2015	Wet	Artificial	Prophylaxis	365/19	-	By tooth White/cream Demarcated opacities n=170 (71.4%) Yellow/brown Demarcated opacities n=68 (28.6%); PEB n=27 (11.34%) Atypical restorations n=4 (1.7%) Atypical caries n=27 (11.34%)	
(Slayton et al., 2001)	U.S.A.	Cross-sectional	Portable chair	DDE (Clarkso-n 1992)	Wet	Artificial	NR	694/99	2743/155	By surface White Demarcated opacities 67% Brown Demarcated opacities 9% PEB 24%	4-5

(Halal and Raslan, 2020)	Syria	Cross-sectional	School	Ghanim et al. 2015	Wet	Photos	Toothbrush	600/246	2400/715	NR	4-5
(Zakirulla et al., 2020)	Saudi Arabia	Cross-sectional	Dental chair	EAPD	Wet	Artificial	Toothbrush	596/32	2292/110	NR	7-10
(Ng et al., 2015)	Singapore	Cross-sectional	School on-site dental clinic	EAPD	NR	NR	NR	1083/31	4277/52	By tooth White/cream Demarcated opacities n=15 (28.8%) Yellow/brown demarcated opacities n =37 (71.2%)	7-8
(Tagelsir Ahmed et al., 2020)	U.S.A.	Cross-sectional	School on portable unit	Ghanim et al. 2015	Wet	Artificial	Toothbrush	337/8	-	NR	8-10
(Goyal et al., 2019)	India	Cross-sectional	School	EAPD	Dry (Cotton rolls)	Artificial	Toothbrush	3013/249	12029/479	By tooth Cream demarcated opacities n=176 (36.7%) Yellow demarcated opacities n =138 (28.8%) Brown demarcated opacities n=165 (34.4%) PEB n=101 (21.1%) Atypical restoration n=20 (4.1%) Atypical extraction n=33 (6.9%)	3-6
(Kuhnisch et al., 2014)	Germany	Cohort	Hospital	EAPD	Wet	Artificial	Toothbrush	693/28	2722/49	NR	10
(Elger et al., 2020)	Germany	Cohort	Research centre	EAPD	NR	NR	NR	958/38	-	NR	1-6
(Gambetta-Tessini et al., 2019)	Chile	Cross-sectional	School	Ghanim et al. 2015	Dry (Cotton roll)	Artificial	Toothbrush	577/29	-	NR	6-12
(Temilola et al.,	Nigeria	Cross-sectional	Field (chair)	Kemoli et al.	Wet	Natural	Gauze	327/15	1305/45	NR	3-5

2015b)				2008							
(Owen et al., 2018)	Australia	Cross-sectional	Early childhood centre	EAPD/ M-DDE	Dry (Cotton roll)	Artificial	Toothbrush	623/88	2483/144	NR	3-5
(Ghanim et al., 2013)	Iraq	Cross-sectional	School	EAPD	Dry (Cotton roll)	Artificial	Toothbrush	809/53	-	NR	7-9
(Kar et al., 2014)	India	Cross-sectional	Dental Science and Research Institute	mDDE	Dry (Gauze)	Natural	Prophylaxis	306/0	-	NR	3-5

NR= Not Reported

Table 2.4: Quality assessment of the primary studies

Study	Country	1. Selection			2. Comparability	3. Outcome				BIAS
		Representativeness Max 3*	Sample Size Max 1 *	Non respondents Max 2*	Specific groups Max 2*	Criteria Max 1*	Training Max 1*	Calibration Max 3*	Stars	Risk ≤6 = high 7-8 = moderate ≥9 = low
da Silva et al. 2017	Brazil	**	NR	**	NA	*	*	*	7	Moderate
Mittal et al. 2016	India	**	NR	NR	NA	*	*	***	7	Moderate
Norrisgaard et al., 2019	Denmark	*	*	**	*	*	*	***	10	Low
Gambetta-Tessini et al. 2018	Australia	***	*	*	NA	*	*	***	10	Low
Murray & Shaw 1979	England	**	NR	NR	NA	No	NR	***	5	High
Elfrink et al. 2012	Netherlands	**	NR	**	NA	*	NR	**	7	Moderate
Reyes et al.2019	Brazil	***	*	**	NA	No	*	***	10	Low
Wagner 2017	Germany	**	NR	*	NA	No	*	***	7	Moderate
Corrêa-Faria et al. 2013	Brazil	**	*	**	NA	No	*	***	9	Low
Farsi 2010	Saudi Arabia	***	*	NR	NA	No	*	***	8	Moderate
Temilola et al. 2015	Nigeria	**	*	NR	NA	*	NR	***	7	Moderate
Chaves et al. 2007	Brazil	**	*	**	NA	*	NR	***	9	Low
de Lima et al. 2015	Brazil	***	*	**	NA	*	NR	***	10	Low
Silva et al. 2019	Australia	*	NR	*	**	*	NR	*	6	High
Mittal & Sharma 2015	India	***	NR	**	NA	*	*	***	10	Low
Oyedele et al. 2016	Nigeria	***	*	NR	NA	*	NR	***	8	Moderate

Negre-Barber et al. 2016	Spain	**	*	NR	NA	*	*	***	8	Moderate
Elfrink et al. 2008	Netherlands	**	NR	*	NA	*	*	***	8	Moderate
Costa-Silva et al. 2013	Brazil	**	NR	NR	NA	*	NR	*	4	High
Schüttfort et al. 2020	Germany	*	NR	NR	NA	No	*	*	3	High
Folayan et al. 2020	Nigeria	***	*	NR	NA	*	NR	NR	5	High
Fernandes et al. 2020	Brazil	***	NA	**	NA	*	*	***	10	Low
Lima et al. 2020	Brazil	***	*	**	NA	*	*	***	11	Low
Sidhu et al. 2019	Canada	**	*	**	NA	*	*	***	10	Low
Slayton et al. 2001	U.S.A.	**	NR	NR	NA	No	*	**	5	High
Halal & Raslan 2020	Syria	***	*	NR	NA	*	NR	***	8	Moderate
Zakirulla et al. 2020	Saudi Arabia	***	NR	NR	NA	*	NR	***	7	Moderate
Ng et al. 2015	Singapore	***	NR	NR	NA	*	NR	NR	4	High
Ahmed et al. 2020	U.S.A.	**	NR	*	NA	*	*	***	8	Moderate
Goyal et al. 2019	India	***	*	**	NA	*	*	***	11	Low
Kühnisch et al. 2014	Germany	**	NR	*	NA	*	*	***	8	Moderate
Elger et al. 2020	Germany	NR	NR	NR	NA	*	*	***	5	High
Gambetta-Tessini et al. 2019	Chile	***	*	*	NA	*	*	***	10	Low
Temilola et al. 2015	Nigeria	**	*	NR	NA	No	*	***	7	Moderate
Owen et al. 2018	Australia	***	*	*	NA	*	*	***	10	Low
Ghanin et al. 2013	Iraq	***	NR	**	NA	*	*	***	10	Low
Kar et al. 2014	India	**	NR	NR	**	No	*	NR	5	High

NR= Not Reported; NA=Not Applicable

2.4.5 Data synthesis

A forest plot depicting child prevalence is shown in Figure 2.3. A total of 32 studies were included in the meta-analysis. Great variation existed between studies with a range of between 0 and 41% prevalence reported. The overall pooled child prevalence of HSPM was 6.80% (95% CI 4.98-8.86%; I2 = 97.35%).

For tooth prevalence, a total of 23 studies were included in the meta-analysis. A broad variation existed between studies with a reported prevalence ranging from 0 and 29.79%. The overall pooled prevalence of HSPM was 4.08% (95% CI 2.80-5.59%; I2 = 98.92%) (Figure 2.4).

The studies in which the EAPD or MIH/HSPM index was used (Figure 2.3), we observed a child level pooled prevalence of 7.54% (95% CI 5.48%-9.89%), while those who used other indices the pooled prevalence was 3.65% (95% CI 0.43% to 9.33%). Figure 2.4 depicts the pooled prevalence at tooth level as 4.65% (95% CI 2.96% to 6.70%; weight = 70.34%) for studies that used EAPD or MIH/HSPM index, which represented the majority of the studies included in the meta-analysis. When other indices were used, the prevalence was 2.98% (95% CI 1.73% to 4.55%; weight = 29.66%). However, the diagnostic criteria did not influence the pooled prevalence on a child level (estimate -0.034; CI -0.104 to 0.037; p=0.347) or tooth level (estimate -0.024; CI -0.077 to 0.028; p=0.359).

Fifteen studies provided information on HSPM defect characteristics. Demarcated opacities represented the most common HSPM presentation on both a child and tooth level in the majority of studies. PEB, atypical

caries/restorations/extractions were less commonly reported, and data was often incomplete.

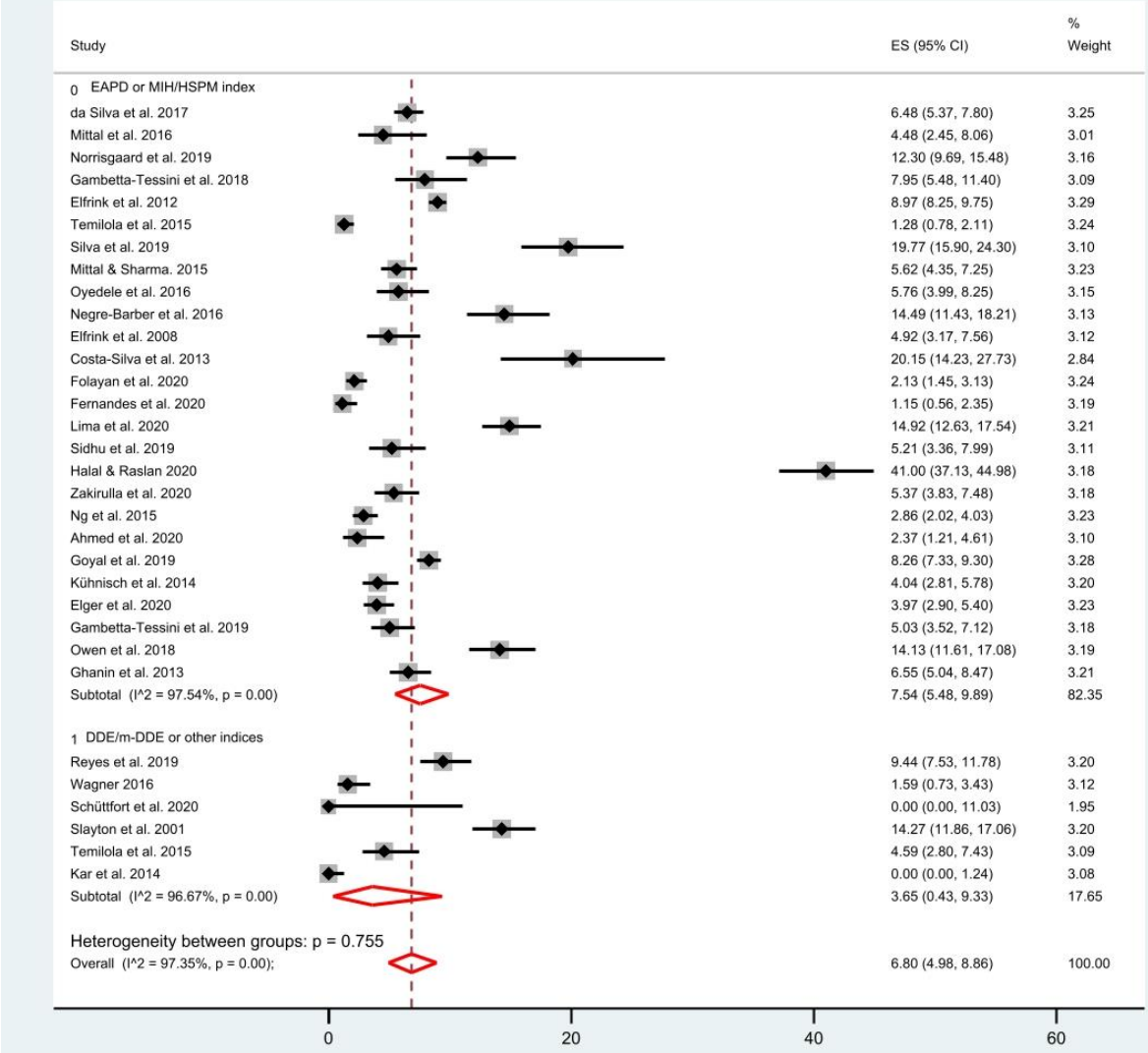


Figure 2.3: Forest-plot of Sub-group analysis using mixed-effects models for determining child prevalence according to the diagnostic criteria used

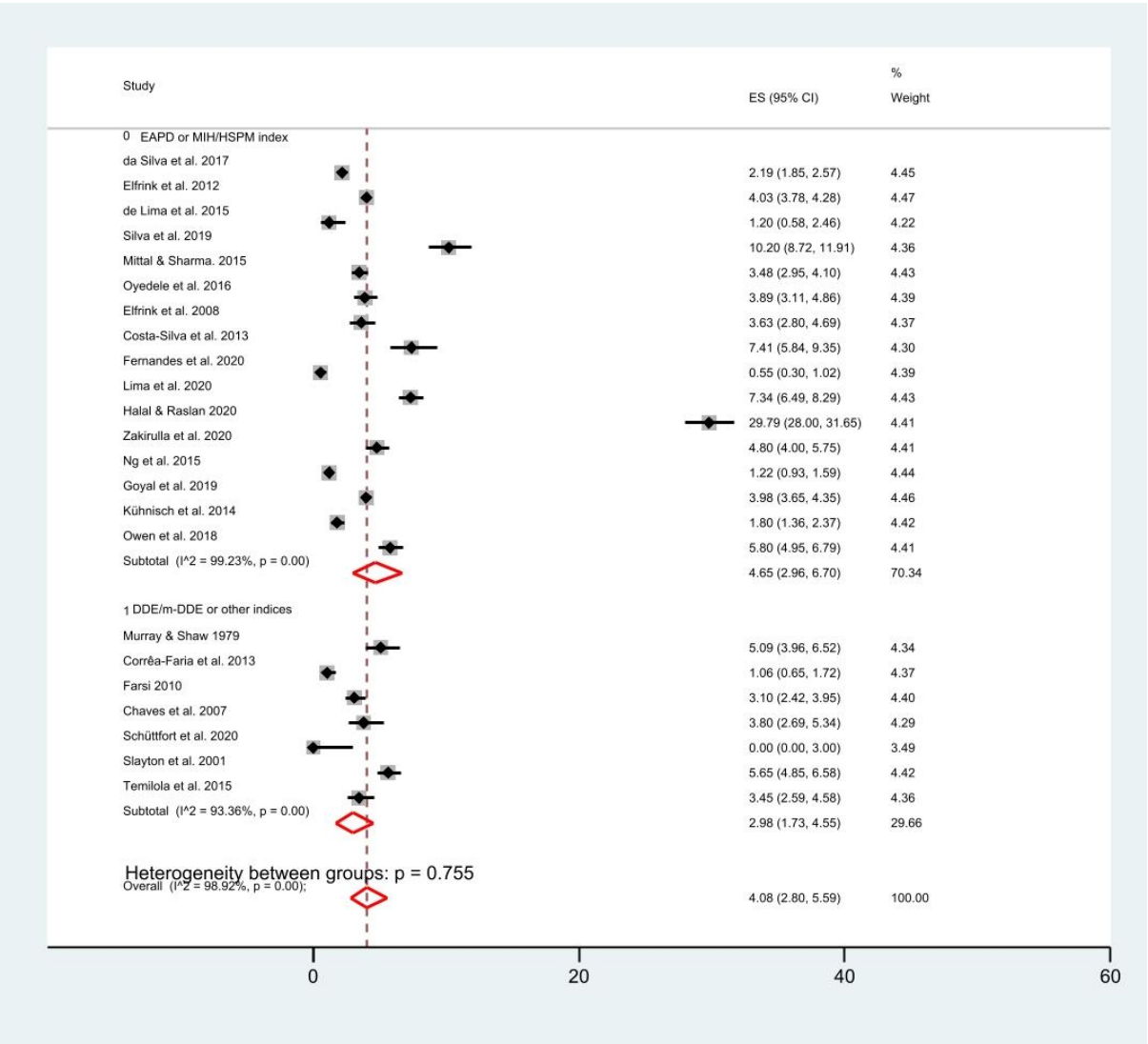


Figure 2.4: Forest-plot of Sub-group analysis using mixed-effects models for determining tooth prevalence according to the diagnostic criteria used

2.5 Discussion

The present systematic review is the first to explore HSPM prevalence on a global level. Great variation existed between studies with a range in child prevalence of between 0 and 41% reported. The overall pooled prevalence of HSPM was 6.80% (95% CI 4.98 to 8.86%).

In the sub-group analysis, we observed a pooled prevalence of 7.54% (95% CI 5.48%-9.89%) in the studies in which the EAPD or MIH/HSPM index was used (n=26). Alternatively, a lower pooled prevalence of 3.65% (95% CI 0.43% to 9.33%) was found in those studies which used other indices (n=6). While we initially hypothesised that the diagnostic criteria may influence the prevalence results, following meta-regression we found no differences in the prevalence regardless of the criteria used. This can be explained by the fact that demarcated opacities were the most common presentation reported, which is captured by all indices as reported in Table 2.3. Although 26 studies used the EAPD/MIH/HSPM criteria, only 14 studies used the index in its entirety (including PEB, atypical caries/restorations and extractions related to HSPM).

I^2 statistics identifies what proportion of the observed variance reflects differences in the true effect sizes rather than sampling error (proportion of observed dispersion that is real, rather than spurious). The I^2 statistic revealed that 99.75% of the observed variance reflected differences in true effect sizes rather than sampling error. This variance could be explained by the characteristics of the population (age group, environmental factors, socio-economic characteristics, etc.) and study methodology (training/calibration of the examiners, examination conditions).

A tooth prevalence range of 0% and 29.8% was reported, with a pooled HSPM tooth prevalence of 4.08% (95%CI 2.80 to 5.59%). As expected, the tooth prevalence was lower than the child prevalence, since not every SPM is affected by HSPM. This result is comparable to MIH prevalence studies where not all FPMs are involved (Beentjes et al., 2002, William et al., 2006).

Although the age at examination varied among the studies, the optimal age for HSPM diagnosis has been suggested as 5 years (Elfrink et al., 2015). Examining this age group is advantageous as gross destruction masking the original defect is less likely to occur in earlier years (Elfrink et al., 2015). Several studies have used older age groups which could influence the reporting of true defect prevalence (Ghanim et al., 2013, Kuhnisch et al., 2014, de Lima Mde et al., 2015, Oyedele et al., 2016b, Negre-Barber et al., 2016, Reyes et al., 2019, Tagelsir Ahmed et al., 2020). As age increases, so too does potential for PEB, atypical caries lesions and restorations which can mask any underlying hypomineralisation defect (Ghanim et al., 2013, Oyedele et al., 2016b).

The majority of the studies were cross sectional in nature. Examining a sample at one point in time has proven to be an effective method of assessing defect prevalence (Elfrink et al., 2015). Examination setting and conditions of assessment varied between studies. Several studies were carried out in the school environment. Recommended conditions for HSPM diagnosis include a dental chair and several studies involved a portable dental chair or dental clinic for the examination. The location is not as significant as the examination conditions in terms of adequate artificial lighting and examination of clean, wet teeth. Ghanim et al. (2017) advised a transillumination/fibre-optic light source with a disposable non magnifying, front surface mirror (Ghanim et al., 2017).

Several studies have been carried out using natural light to examine which is not favourable due to changes in light during the day depending on weather conditions (Elfrink et al., 2015, Ghanim et al., 2017). Two studies used photographs for HSPM scoring (Elfrink et al., 2008, Halal and Raslan, 2020) which has demonstrated a high sensitivity and specificity (Elfrink et al., 2009). Teeth should be examined wet with no air drying applied to surfaces before examination (Ghanim et al., 2017). The majority of studies recorded that the teeth were wet or that they were dried with guaze/cotton rolls so still moist prior to examination. Furthermore, teeth should be clean prior to assessment with several of the included studies accounting for this requirement with teeth brushed prior to exam or use of cotton wool/gauze to remove surface debris

The EAPD judgement criteria was used by 19 of the included studies. The criteria was established in 2003 and was specifically designed for MIH diagnosis (Weerheijm et al., 2003). The criteria is based on the clinical presentation of MIH which includes demarcated opacities, PEB, atypical restoration, and extraction due to MIH/HSPM. More recently, a new diagnostic criterion, the MIH/HSPM index has been developed combining elements of EAPD and mDDE indices (Ghanim et al., 2015). This index was used in six of the included studies and represents the full spectrum of HSPM/MIH diagnosis. The criteria has been validated and offers a standardised approach to researchers in their data collection (Ghanim et al., 2019). As the MIH/HSPM index was developed based on the EAPD criteria (sharing similar diagnostic features), a decision was made to merge those indices for the meta-analysis. In contrast, the use of DDE/mDDE that only considered the presence of demarcated opacities was grouped into a different diagnostic category.

Eight of the studies used the DDE or mDDE criteria which presents major drawbacks. This index does not allow for scoring of PEB or is mistakenly classified as hypoplasia. Furthermore, caries, restorations and extractions that are atypical in nature are not accounted for (Elfrink et al., 2015). Demarcated opacities were often the only aspect of HSPM which was scored in included studies resulting in a limited picture of HSPM prevalence. Adherence to a standardised specific HSPM diagnostic criterion is recommended to decrease the variation between studies. Criteria that include all aspects of HSPM presentation may be helpful in determining the true spectrum of HSPM defects. Moreover, this may also improve the quality of studies recording defect progression over time.

Although the majority of the papers (75%) showed low to moderate risk of bias, flaws were identified in the methodology of included studies. Few studies followed the STROBE guidelines for reporting observational data. Regarding sampling procedure, 19 of the studies did not report on sample size, lowering the study quality. Prevalence studies require a minimum number of randomly selected children. Sample sizes ranged from a minimum of 31 to a maximum of 5561 children. Naing et al. (2006) developed a formula to calculate sample sizes based on estimated prevalence levels (Naing et al., 2006). For an estimated prevalence of 5%, a recommended minimum of 300 children are needed to conduct a valid prevalence study.

A total of 13 studies did not describe the training provided for their examiners in applying the diagnostic criteria. A Kappa statistic is required for both inter and intra observer reliability and should be provided in the study's methodology. Although data quality depends critically on the examiners ability to apply the

diagnostic criteria consistently over time, not all studies described the calibration procedure.

Demarcated opacities represented the most common clinical presentation of HSPM which is favourable considering that this is the mildest form of the detect that usually requires preventive care alone and monitoring. However, those affected by PEB and atypical caries may present with an increased treatment burden including restorative care (atypical restorations) and loss of the SPM affected by HSPM. The clinical significance of a child presenting with demarcated opacities also relates to the predictive nature of HSPM for MIH development (Garot et al., 2018). This awareness may aid dentists in increasing surveillance of erupting FPMs and enabling an earlier MIH diagnosis.

As a limitation of the present study, we have only included articles published in English indexed on MEDLINE/PubMed, Scopus and Web of Science databases. Moreover, although an attempt was made to cross check all references in the included studies, the authors did not include a grey literature source for the present systematic review. This may have resulted in relevant articles being excluded and therefore, increase the likelihood of selection bias. Finally, the high heterogeneity observed between the studies may have resulted in bias and influenced the estimated pooled prevalence reported.

2.6 Conclusions

The present systematic review is the first to explore HSPM prevalence on a global level. Great variation existed between studies with a range in child prevalence of between 0 and 41% reported. The overall pooled prevalence of HSPM was 6.80% (95%CI 4.98 to 8.86%). The diagnostic criteria was not as strong an influence as previously hypothesised, and the role of other factors must be considered when attempting to understand this variation.

There is a need for more standardised information to be provided on the type of HSPM defect, presence of sensitivity and respective treatment needs. Further research is also required in certain countries where no prevalence data exists. Determining the prevalence of HSPM will inform early detection and management strategies according to the defect severity.

Study 2:

Prevalence of Hypomineralised Second Primary Molars in one Dublin school — preliminary findings of a cross-sectional study

3. Study 2 - Prevalence of Hypomineralised Second Primary Molars in one Dublin school — preliminary findings of a cross-sectional study

3.1 Abstract

Background: Prevalence of HSPM is unreported in the Irish population. This study provides preliminary data on HSPM prevalence in one Dublin primary school. Defect characteristics of HSPM were recorded including commonly seen clinical presentations. In addition to determining HSPM prevalence, the relationship between HSPM and caries experience was also explored. ***Aims:*** The study sought to determine the prevalence of HSPM in 4-to-6-year-old children attending a Dublin primary school. ***Methods:*** A cross sectional study was carried out using a sample of 4-6 year old boys from one Dublin primary school. Due to Covid 19 restrictions in 2020 data collection from other Dublin schools was not possible. Ethical approval and parental/guardian consent were obtained, and 81 boys were examined in the school environment. HSPM were recorded using the MIH/HSPM index developed by Ghanim et al. (2015). Five examiners were calibrated in the diagnosis of enamel defects and dental caries. Inter-examiner and intra-examiner agreement had a kappa score of ≥0.70 for both HSPM and caries. Caries was recorded using the modified WHO caries index to the level of visual caries into dentine (dv_3mft). The association between dental caries prevalence and HSPM was tested using Chi square ($\alpha = 5\%$).

Results: A total of 81 children were examined and 31 had HSPM defects (38.27% prevalence). The mean number of affected teeth per child was 2.16±1.13. The most common defects were creamy-white demarcated opacities (81.8% of affected teeth). This was significantly greater than the prevalence of

yellow-brown demarcated opacities (7.6%), HSPM associated missing SPMs (6.1%), atypical caries (3.0%) and PEB (1.5%). The most common form of extension reported was extension of less than one third of tooth surface affected. 18 out of the 81 participants had dental caries (22.22%). No association was found between caries experience and HSPM prevalence (p= .25). ***Conclusions:*** The prevalence of HSPM in this sample was 38.2% which is higher than existing studies in Europe. Demarcated opacities were the most common form of the defect. The caries rate was high (22%) but there was no association with HSPM in this sample. Continued investigation of HSPM prevalence is justified in a broader selection of children to determine true HSPM prevalence in the population**.**

3.2 Aim and Objectives:

3.2.1 Aim

- To determine the prevalence of HSPM in 4-to-6-year-old children attending one Dublin school.

3.2.2 Objectives

- To examine the dentitions of a sample of 4-to-6-year-old primary school children attending one Dublin school.

3.3 Materials and Methods

3.3.1 Ethical Approval

The Faculty of Health Sciences Research Ethics Committee in Trinity College Dublin granted ethical approval for this study in May 2019 (Appendix 2.1).

3.3.2 Study design, age profile and sample size calculation

This was a cross-sectional pilot study involving 4-to 6-year-old primary school children in Dublin, Ireland. For an estimated prevalence of 5% a sample minimum of nearly 300 children was calculated based on a validated formula by Naing et al. (Naing et al., 2006; Elfrink et al., 2015). The formula proposed: (n) = [Z2 x P(1-P)]/d2 where Z is the statistical level of confidence [95% confidence interval (CI>Z=1.96], P is the expected prevalence and d is the precision.

3.3.3 Inclusion and exclusion criteria

Table 3.1: Inclusion and exclusion criteria

Inclusion criteria	**Exclusion criteria**
• Age 4 to 6 • Parental/guardian consent for participation • Present on day of assessment	• Outside required age range • Not consented for participation • Absent on day of assessment

3.3.4 Recruitment

In August 2019, several primary schools in the Dublin city and suburban areas were invited to participate in the study. The Department of Education website was used to access information on primary school demographics. In Irish schools a system of DEIS (Delivering Equality of Opportunity in Schools) exists which aims to support children who are at greatest risk of educational disadvantage.

An equal number of DEIS and non DEIS schools were invited to participate and an information pack including a letter of invitation, participant information leaflet, consent form and proforma (should child have dental needs) were delivered to selected schools. (Appendices 2.2-2.5). Schools were invited to contact the Dublin Dental University Hospital (DDUH) division 1 administrative staff should they be interested in participating.

Class teachers acted as gate keepers distributing the forms to each pupil to return home to their parent/guardian. A period of two weeks was given for parents/guardians to read the information leaflet and provide consent should they wish for their child to participate. Teachers from each class collected the signed consent forms which were stored securely prior to collection.

3.3.5 Confidentiality

Each subject (parent/child pair) had a unique numerical code assigned to them. This code was used for all data relating to the subject e.g. data collection sheet. All hard copy records were stored in a secure locker in the DDUH. All electronic data was password protected on a DDUH desktop.

3.3.6 HSPM diagnostic criteria

The MIH/HSPM index developed by Ghanim et al. in 2015 was used for HSPM diagnosis with one modification (Ghanim et al., 2015). This modification included the addition of a code (7b) to the clinical criteria which described a SPM with a SSC in an otherwise caries free dentition with clinical signs of HSPM affecting one or more remaining SPMs. Each index tooth i.e. FPM (if present) and SPMs were scored based on their clinical status and extent of the lesion.

Clinical status criteria

A predetermined numerical score was assigned to each HSPM clinical diagnosis (Table 3.2). Where uncertainty existed regarding the rating of the defect the less severe score was assigned. In cases where two defects existed in a tooth e.g. demarcated opacities and PEB, the more severe form of the defect was given i.e. PEB.

Table 3.2: HSPM clinical status criteria (Ghanim et al., 2015)

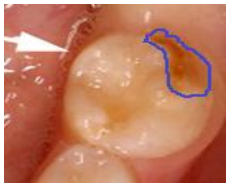
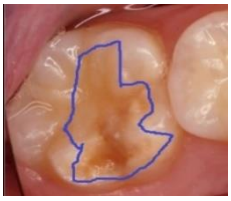
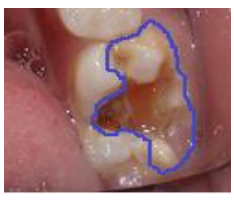
Code	Description	
0	**No visible enamel defect**	'Tooth is free of enamel defects including diffuse opacities, hypoplasia, demarcated hypomineralisation lesions and AI'
1	**Enamel defect, not MIH/HSPM**	'These defects include diffuse opacities, hypoplasia, AI and hypomineralisation defects (non MIH/HSPM)'
2a **Demarcated opacities- white or creamy** **2b** **Demarcated opacities- yellow or brown**		'Alteration in the translucency of the enamel with a clear distinct border with adjacent enamel. Opacities are variable in degree and can be white, yellow or brown in colour . The defective enamel is of a normal thickness with a smooth surface'
3	**PEB**	'Loss of initially formed surface enamel after eruption. Commonly associated with a pre-existing demarcated opacity and found on surfaces that are traditionally low caries risk such as cuspal ridges/smooth surfaces. Areas affected are characteristically rough with uneven margins'
4	**Atypical restoration**	'Atypical restorations do not conform to the traditional picture of caries in terms of their size and shape and commonly involve buccal and palatal/lingual surfaces. Pre-existing demarcated opacities may be present at the restoration border'
5	**Atypical caries**	'Caries onset can be atypical involving surfaces that are not usually prone such as the buccal and palatal/lingual surfaces. Pre-existing demarcated opacities may be present. These lesions are typically seen in an otherwise caries-free mouth'
6	**Missing due to MIH/HSPM**	'Absence of a SPM in an otherwise healthy

		dentition and associated with opacities, PEB, atypical restorations or caries in at least one SPM'
7a	**Cannot be scored**	'A tooth with extensive coronal breakdown where potential cause is impossible to determine'
7b	**Stainless Steel Crown (due to HSPM)**	A SPM with a stainless steel crown in an otherwise caries free dentition with clinical signs of HSPM affecting one or more remaining SPMs
X	**Unerupted/partially erupted**	'Partially erupted refers to a tooth that is not visible or less than 1/3 of the occlusal table is visible'

Lesion Extension criteria

Defects which were greater than 1 mm in diameter were recorded (Ghanim et al., 2015). Three codes were allocated for lesion extension and referred to the total amount of enamel affected by the defect (Table 3.3).

Table 3.3: HSPM lesion extension criteria

Code	Description	Example
I	Less than 1/3 affected	
II	At least 1/3 but less than 2/3 affected	
III	At least 2/3 of tooth surface	

3.3.7 HSPM calibration

Before clinical examination, five paediatric dentists (CMC, EC, ES, RL, AOC) were calibrated in detection and diagnosis of enamel defects in the DDUH. In November 2019, a 2 hour training session involving an introductory PowerPoint presentation on the HSPM diagnostic criteria and non-HSPM enamel defects was carried out. The presentation involved an interactive discussion with photographic examples of the criteria and differential diagnosis. Two calibration exercises were subsequently performed one week apart. The calibration involved a series of 40 photographs with each photo requiring a HSPM numerical score and extent score (Figure 3.1). Photographs included teeth with enamel defects other than MIH or HSPM to reduce risk of overestimation of HSPM prevalence (Figure 3.2). Prior to calibration a 'gold standard score' was allocated for each photograph based on reference photos with pre-determined scores (Ghanim et al., 2017). Additional images from consented DDUH patients were also used. Examiner's scores were compared to this 'gold standard' and used to calculate Kohen's Kappa score for inter and intra examiner reliability.

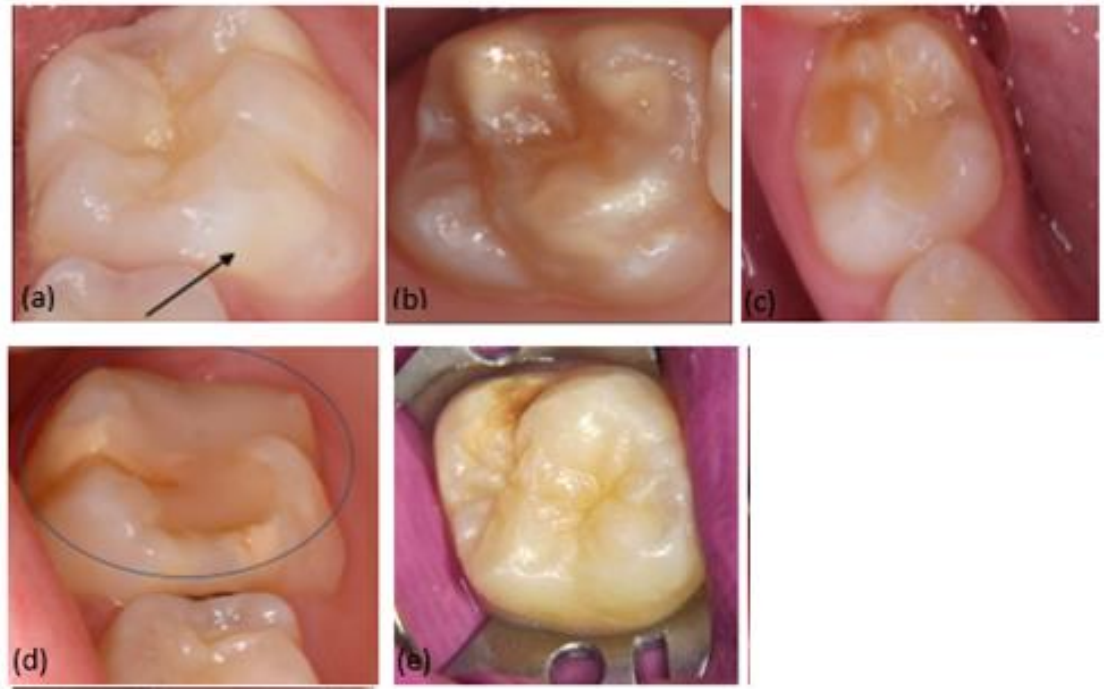


Figure 3.1: Examples of MIH/HSPM clinical diagnostic criteria used in calibration exercise. (a) Hypomineralised molar (HM) with white demarcated opacities (b) HM with yellow-brown demarcated opacities (c) HM with PEB and associated demarcated opacities (d) HM with atypical restoration (e) HM with atypical caries

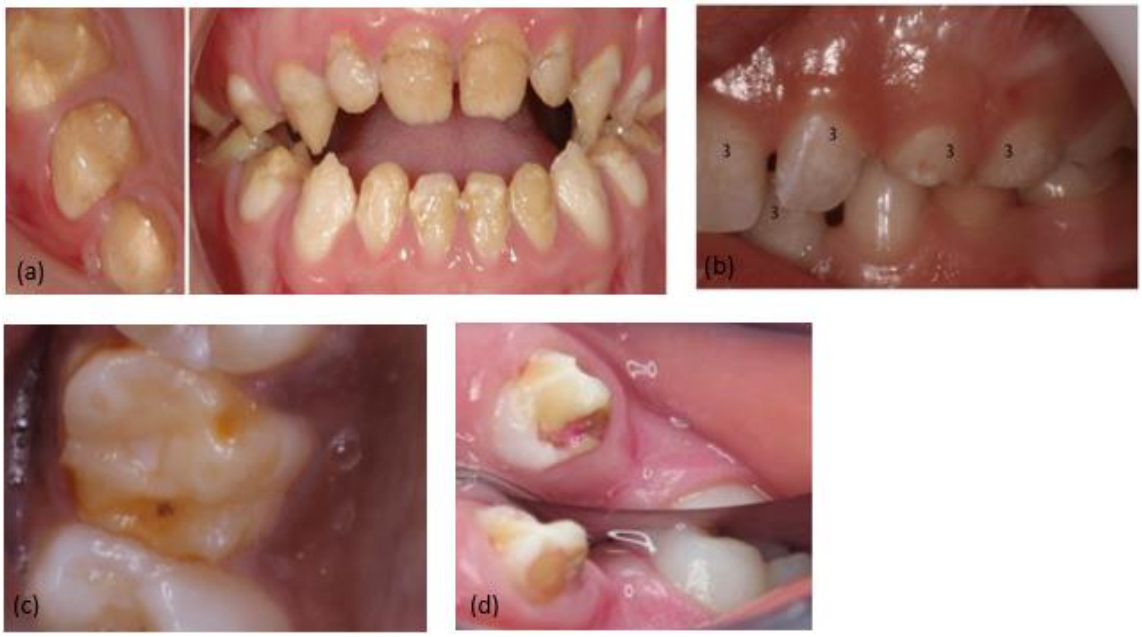


Figure 3.2: Examples of enamel defects other than MIH/HSPM used in calibration exercise (a) Dentition affected by Amelogenesis Imperfecta (b) Dentition affected by fluorosis (diffuse opacities) (c) SPM affected by hypoplasia (d) Hypomineralised mandibular premolar (turner tooth)

3.3.8 Caries diagnostic criteria

Caries status in primary molars was assessed using the modified WHO decayed missing filled index to the level of visual caries into dentine (dv_3mft) (World Health Organization, 1997). The caries experience for a child was expressed as the number of first and SPMs that were decayed with dentine involvement (dv_3), missing (m), or filled (f) (Table 3.4). A tooth that was caries free was described as having no visible caries into dentine and was denoted a horizontal line (---) in the data collection sheet.

Table 3.4: Description of dv_3mft caries index (WHO, 1997)

Code	**Description**
Decayed (dv_3)	'Any tooth whose crown has an unmistakable cavitation on the pits and fissures, or on a tooth surface or a filled crown with decay, when it has one or more restorations with decay'
Filled (f)	Filled crown with no decay, when it has one or more permanent restorations, and there is no caries anywhere on the crown
Missing (m)	Missing tooth due to caries, when a tooth has been extracted due to caries

3.3.9 Caries calibration

Training on caries diagnosis involved a one hour introductory PowerPoint presentation on the caries diagnostic criteria, which was carried out in the DDUH in November 2019 (following the HSPM diagnostic criteria presentation). The same five examiners (CMC, EC, ES, RL, AOC) were involved in the calibration exercises. The presentation included a series of photographs reflecting dv_3mft components which were discussed (Figure 3.3). As for HSPM calibration, two calibration exercises one week apart were conducted. The same 40 photographs involved in HSPM calibration were used with an

additional score required for caries. Cohen's Kappa score was calculated for inter and intra examiner reliability.

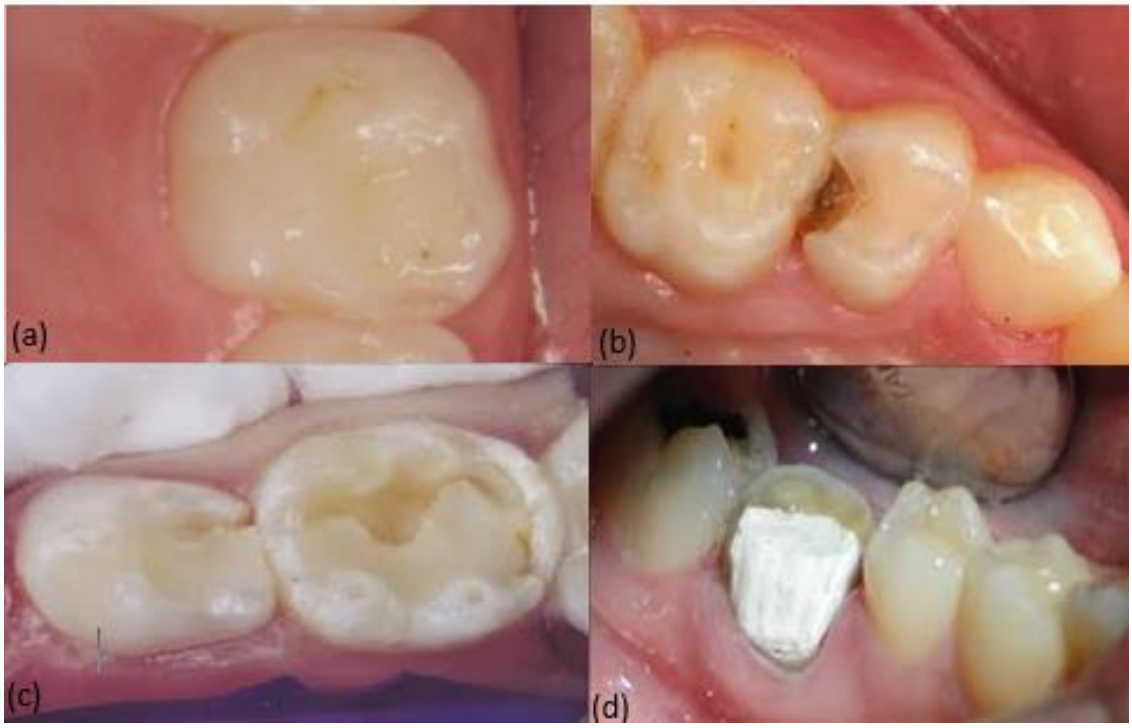


Figure 3.3: Examples of photos used in caries calibration. (a) Caries free SPM. (b) Cavitated caries in first primary molar. (c) Glass ionomer restorations in first and SPMs. (d) Example of tooth restored with temporary restoration

3.3.10 Examination

The assessment of participants included a dental screening of approximately two minutes in duration which was carried out over two days. The exam was carried out in an available classroom in the presence of the class teachers (Figure 3.4). Four teams, each consisting of a calibrated examiner and trained nurse assistant were present. The examiner conducted the dental screening while the nurse assistant was responsible for data recording and assisting in cross infection measures. Each team was assigned to a different colour zone (yellow, green, blue and orange) to facilitate ease of participant allocation. Upon

presenting for exam, participant information was confirmed by the assistant and recorded.

Figure 3.4: (a) Classroom where screening was conducted. (b) Example of zone where screening was conducted

Children were examined sitting upright in the school chair, using an illuminated mirror system (Denlite®) with extra illumination provided by a LED head lamp. Teeth were examined wet for HSPM however gauze was available to remove any surface debris/plaque (Figure 3.5). For assessment of caries, air drying was not feasible. Gauze was used to remove plaque and excess saliva from tooth surfaces.

Figure 3.5: Materials required for each screening. (a) Sterile gauze, Denlite® mirror, surgical mask, gloves. (b) Denlite® illuminated mirror system with single use mirror head (c) Head light for additional light

3.3.11 Data collection

A data collection sheet was developed based on the short form by Ghanim et al. (2015) with some modifications in the format for ease of use (Ghanim et al., 2015) (Appendix 2.7). A reference coding table was present on the datasheet to familiarise examiners with the scoring system. Teeth assessed as part of the HSPM screening included index teeth only i.e. FPMs/SPMs and first and SPMs in the case of caries. Sequence of scoring involved first entering the HSPM numerical score followed by the HSPM extent score and finally the caries score into the data sheet. Teeth were assessed systematically according to the data collection tool. Examiners and assistants were familiarised with the collection sheet and instructed on its use prior to the screening days. Table 3.5 summaries the data collection workflow on the screening day.

3.3.12 Cross infection protocol

A cross infection protocol was in place for the dental screening with appropriate disinfection between each participant. To ensure universal precautions were complied with, personal protective equipment was utilised by all examiners. Disposable nitrile gloves (Transform® 100 Nitrile Powder Free Gloves) were brought to the school and used for each subject. Each Denlite® mirror consisted of a disposable mirror head (single use) that was replaced for each participant. A disposable sleeve was used to cover the non-removable component which was replaced for each participant and disinfected with Clinell Universal Wipes after each use (Universal Sanitising Wipes, Clinell®, GAMA Healthcare Ltd., Hertfordshire, UK). Clean and contaminated zones were kept separate and were identifiable. Clinical waste was collected after each screening and disposed of through the clinical waste disposal process at the DDUH. Alcohol hand gel (PURELL® Advanced Hygienic Hand Rub, GOJO Industries, Frankfurt, Germany) was used to disinfect examiners hands between each participant, before/after each participant and before/after cross infection control measures.

Table 3.5: Description of data collection workflow and management

One month prior to data collection	
Consent forms collected from class teachers. Data organized and numerical code assigned to each consented participant Participants categorized according to class and assigned to examining teams in advance of screening	
At the time of data collection	
Preparation	Four examining zones (orange, green, blue and yellow) were set up in classroom Teams consisted of an 'examiner' who conducted the dental screening and carried out cross infection and an 'assistant' who ensured participant information was correct and recorded screening data
Arrival of participants	Participants arrived in groups accompanied by class teacher Children were pre-assigned to zones and given a matching colour card upon arrival
Screening	**Examination sequence:** Child sat in chair and name/consent status confirmed Data collection sheet checked to ensure correct numerical code match Index teeth examined and results recorded by dental assistant on data sheet Should any dental disease be detected, a proforma sheet was given to the child for attention of parents indicating need to see dentist Cross infection measures employed prior to next examination
After completion of screening	Cross infection control verified Data collection sheets collected, stored in sealed envelope and returned to lead researcher
After data collection	
Data input	Data from examination sheets was entered into google forms manually and then exported to excel spreadsheet

3.3.13 Data analysis

Clinical and calibration data was tabulated in an Excel spreadsheet (Microsoft Inc., USA). HSPM and caries prevalence on a child and tooth level were analysed with the total number and percentages calculated. For quantitative data, mean and standard deviation values were calculated.

SPSS software was used to determine if any association existed between dental caries prevalence and HSPM using Chi square analysis (α = 5%). Further statistical analysis was not possible due to the small sample size.

3.4 Results

3.4.1 Calibration

A Kappa score of ≥0.70 was achieved for both intra and inter examiner reliability for all examiners in HSPM diagnosis. Regarding caries diagnosis, an inter examiner reliability of ≥ 0.80 and intra examiner reliability of ≥ 0.70 was achieved for all examiners.

3.4.2 Participant characteristics

One non DEIS school from Dublin North (Dublin 7 area) expressed interest in participating and was recruited in October 2019 (Appendix 2.6). All pupils in junior and senior infants' classes (118 pupils) were invited to participate. A total of 91 parents/guardians consented to participate: 45 from junior infants and 46 from senior infants' classes respectively (response rate of 77%). On the day of screenings, 87 children presented for examination. Two children were not cooperative for examination and five children were absent on the scheduled screening days. Following screening, four children were excluded as they did not meet the inclusion criteria for age reasons leading to a final sample of 81 participants for analysis.

The age range of the participants was 4 to 6 years old. 17 of the participants were 4 years of age with an equal number (32) aged 5 and 6 years (Figure 3.6). Two further schools from Dublin South and Southwest were recruited in January and February 2020. Scheduled screening days for these schools in March and April 2020 were deferred due to the COVID 19 pandemic and subsequent school closures. Irish primary schools reopened in September 2020

however restrictions remained in place with no access permitted.

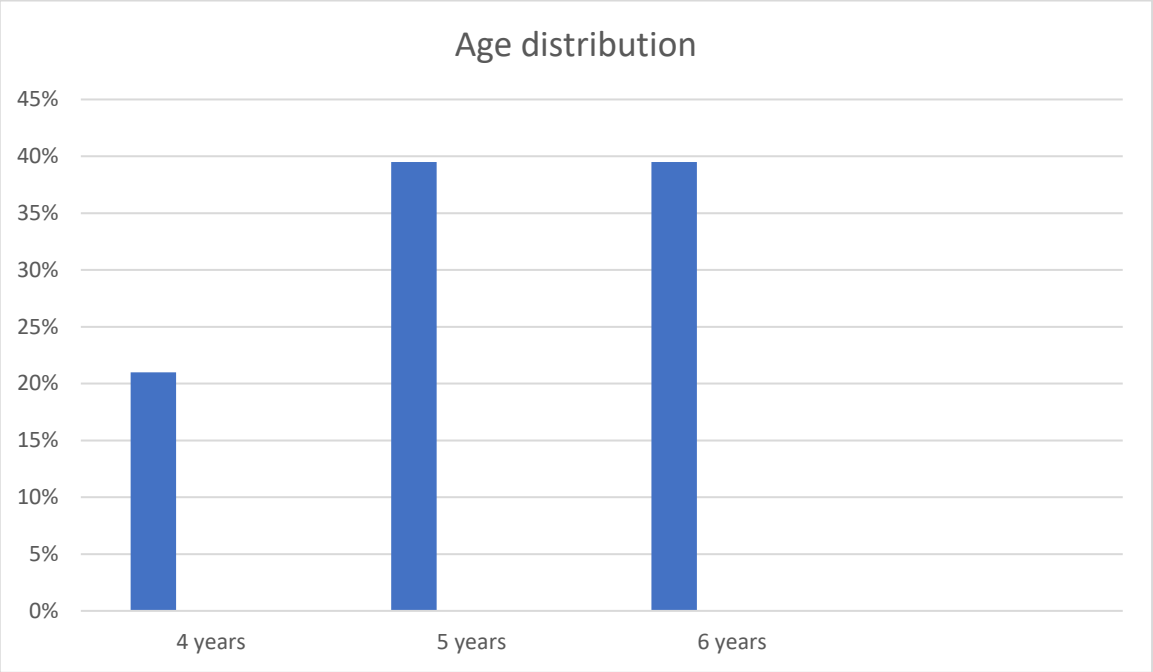


Figure 3.6: Age distribution of participants

3.4.3 HSPM prevalence

A total of 81 children were examined and 31 had HSPM defects (38.27%). Twenty-three children (74.19%) had white or creamy demarcated opacities. Two children had yellow or brown demarcated opacities (6.45%). 2 children had a combination of both opacity colours (6.45%). Two children had atypical caries (6.45%). One child had PEB (3.22%). One child was missing all SPMs due to HSPM (3.22%). The majority of children had either one (35.48%) or two (32.26%) SPMs affected. 12.90% of children had three SPMs affected followed by 19.35% with four HSPM. The mean number of affected teeth per child was 2.16±1.13.

A total of 324 SPMs were examined and 66 were affected by HSPM; tooth prevalence of 20.37% (Table 3.6). Creamy-white demarcated opacities were

the most common defect accounting for 81.82% of affected SPMs. In order of frequency this was followed by yellow or brown opacities (7.58%), missing due to HSPM (6.06%), atypical caries (3.03%) and PEB (1.51%).

Table 3.6: Distribution according to lesion type by teeth affected by HSPM

Lesion Type	**Tooth number**				
	55 n (%)	**65 n (%)**	**75 n (%)**	**85 n (%)**	**Total n (%)**
Demarcated creamy-white opacity	16 (29.63)	13(24.07)	11 (20.37)	14(25.93)	54
Demarcated yellow-brown opacity	2 (40)	0 (0)	1 (20)	2 (40)	5
Demarcated opacity with PEB	0(0)	0 (0)	1 (100)	0 (0)	1
Atypical caries	1 (50)	0 (0)	1 (50)	0 (0)	2
Missing due to HSPM	1 (25)	1 (25)	1 (25)	1 (25)	4
Total	20 (30.30)	14 (21.21)	15 (22.73)	17 (25.76)	66

3.4.4 HSPM lesion extension

A lesion extension of <1/3 of tooth surface affected (code I) was the most common form of extension reported (Table 3.7). According to lesion type, 88.88% of affected SPMs with creamy-white opacities presented with this degree of extension. An extension of >1/3 but less than 2/3s (II) was seen for demarcated creamy-white opacities (11.12%); PEB (100%) and atypical caries (50%). No SPM had an extension of >2/3s of surface area (III) affected.

Table 3.7: Lesion extension of affected SPMs according to lesion type

Lesion Type	**Extension**			
	I n(%)	**II n(%)**	**III n(%)**	**Total n(%)**
Demarcated creamy-white opacity	48 (88.88)	6 (11.12)	0 (0)	54
Demarcated yellow-brown opacity	5 (100)	0 (0)	0 (0)	5
Demarcated opacity with PEB	0 (0)	1 (100)	0 (0)	1
Atypical caries	1 (50)	1 (50)	0 (0)	2
Total	54 (87.09)	8 (12.91)	0 (0)	62

3.4.5 Caries prevalence

18 out of the 81 participants had dental caries (22.22%; dmft ≥1). Of those affected, 16 (19.75%) children were diagnosed as having cavitated caries into dentine. Two children were missing first or SPMs due to caries (2.47%). No children had restored or filled primary molars. 36 out of the 721 primary molars were affected by dental caries; a tooth prevalence of 4.99%.

3.4.6 Relationship between dental caries and HSPM

No significant association was found between dental caries and HSPM (p= .246) (Table 3.8).

Table 3.8: Relationship between dental caries and HSPM

	HSPM		**Total** X^2**=1.347** ***p*=0.246**
Caries	No n (%)	Yes n (%)	
No	41 (65.08)	22 (34.92)	63 (77.78)
Yes	9 (50)	9 (50)	18 (22.22)
Total	50 (61.73)	31 (38.27)	81

3.5 Discussion

The present study presents data on HSPM prevalence in Ireland. While a representative, adequately powered sample was not fully achieved, this study does provide preliminary data and an insight into levels of HSPM and caries prevalence in one part of Dublin. The HSPM diagnostic criteria was validated and represented the full range of HSPM presentations. Examiners were calibrated using standardised photographs and substantial Kappa scores were achieved for all team members. The screenings were conducted in the school environment however the examination conditions were standardised.

The sample size calculation required a minimum of 300 participants, however due to Covid-19 restrictions in 2020, data collection in several primary schools was deferred. A total of 81 children from one Dublin school were included in the final analysis.

Child ages ranged from 4-6 years old. The data was relatively evenly distributed with an equal number aged between 5 and 6 years with a smaller number aged 4 years. This age range was chosen as the SPM would be present for examination and co-operation achievable (Elfrink et al., 2015). The age profile of participants is also important in HSPM diagnosis as there is a potential for under reporting of enamel hypomineralisations in older age groups (Ghanim et al., 2013). With increasing age, gross destruction of severely hypomineralised primary molars may have already occurred masking the original defect and resulting in an under reporting of HSPM. (Elfrink et al., 2010). An older sample may have greater levels of PEB present due to prolonged periods of function. In addition, other factors such as caries, tooth wear and restorations may be more commonly seen in older cohorts and may

complicate a HSPM diagnosis. Furthermore, in an older age group the SPM may have been lost for several reasons including natural exfoliation or extraction. Several studies using older age profiles have reported this as a limitation to their results (Ghanim et al., 2013, Negre-Barber et al., 2016, Oyedele et al., 2016b). In our study sample, all participants were male. Several studies have demonstrated no differences between HSPM prevalence and gender however a gender balanced sample would have been preferrable (Elfrink et al., 2008, Ghanim et al., 2013, da Silva Figueiredo Se et al., 2017).

Of the 81 children examined, 31 had HSPM defects, a child prevalence of 38.27%. This prevalence falls within the higher range compared to other studies looking at HSPM prevalence. However, this data is preliminary in nature and representative of only one area of Dublin. Further data collection in a broader section of children is required before conclusions can be drawn.

A broad variation in HSPM prevalence has been reported in the literature with a range of between 0 and 41% reported (Elfrink et al., 2015, Halal and Raslan, 2020). This variation may be related to inherent differences in the populations being studied including genetic predisposition, environment, socio-behavioural factors or indeed a combination of the above (Elfrink et al., 2015). The methodology employed in a study in terms of its diagnostic criteria, calibration and examination conditions must also be considered when analysing this disparity. Some studies have used the mDDE index which is unsuitable to fully capture the spectrum of HSPM defects, while others have developed their own criteria which hampers comparison (Kar et al., 2014, Temilola et al., 2015b). Furthermore, examination conditions have often not been ideal in some studies with some examinations occurring in natural light and others failing to adequately describe such conditions (Costa-Silva et al., 2013, Kar et al., 2014,

Mittal et al., 2016, Halal and Raslan, 2020).

Over time, efforts have been made to standardise HSPM prevalence studies with improved reporting of the study methods and use of more suitable diagnostic criteria. In spite of this, variation has persisted in reported prevalence levels. When compared to this research, other European studies have reported lower prevalence levels with the Netherlands and Germany reporting a range of between 4 and 9% (Elfrink et al., 2008, Elfrink et al., 2012, Kühnisch et al., 2015). A slightly higher prevalence has been reported in Spain with 14.5% affected by the defect (Negre-Barber et al., 2016). Australia and South America have displayed similar ranges to Europe (8-14% in Australia and 5-14.9% in South America). In Asia, studies have predominantly taken place in India with a range of 0-7.9% reported (Kar et al., 2014, Mittal and Sharma, 2015b, Mittal et al., 2016, Goyal et al., 2019). Interestingly, one recent cross sectional survey conducted in Syria demonstrated comparable results to this study. This cross sectional survey involved a similar age group (4-5 years) and the same diagnostic criteria (MIH/HSPM index) with a prevalence of 41% reported (Halal and Raslan, 2020). The authors postulated this increased prevalence may have been related to the war in Sryia which resulted in higher levels of pollution, malnutrition, stress and poor quality food for large portions of the population. However, this relationship requires further exploration as the present study did not examine socioeconomic backgrounds of the participant's families.

The mean number of affected teeth per child was 2.16±1.13. This finding is comparable to other HSPM studies. Elfrink et al. (2008) reported a mean number of 2.5 HSPMs per child in their Dutch study (Elfrink et al., 2008). Outside of Europe similar findings have been observed. Ghanim et al. (2013) reported that 58.5% of Iraqi children only had one tooth affected followed by

30.2 % with two teeth affected (Ghanim et al., 2013). In India, Mittal & Sharma (2015) reported an average of two HSPMs per child (Mittal and Sharma, 2015b). MIH prevalence studies have reported a similar trend where not all molars are affected by the defect (Beentjes et al., 2002, William et al., 2006). The relationship between number of HSPMs and defect severity has been explored with interesting results. Owen et al. (2018) reported that those affected by one to two SPMs were more likely to have milder defects (Owen et al., 2018). Contrastingly, those affected by severe defects were more likely to have between three and four primary molars affected. In this study, most children were affected by demarcated opacities and had an average of two SPMs affected.

Out of a total of 324 SPMs, 66 were affected by HSPM; giving a tooth prevalence of 20.37%. Demarcated opacities (creamy-white) were the most common form of the defect accounting for 81.82% of affected SPMs. This finding is comparable to several HSPM studies where lighter demarcated opacities have been the most common type of defect (Ghanim et al., 2013, Mittal and Sharma, 2015b, Owen et al., 2018, Halal and Raslan, 2020, Vlachou et al., 2020). Creamy-white demarcated opacities represent the mildest form of the defect and are considered less severely affected than a tooth with PEB, atypical restoration, or atypical caries. Yellow-brown demarcated opacities were the second most common HSPM presentation with 7.58% of SPMs affected. Darker opacities represent a more severe form of hypomineralisation and are more commonly associated with PEB (Ghanim et al., 2013, Owen et al., 2018). Several studies have found PEB to be the most common form of HSPM after demarcated opacities (Ghanim et al., 2013, Elfrink et al., 2012, Vlachou et al., 2020). In this study, missing due to HSPM and atypical caries were more

common than PEB, however the numbers were low in these categories and therefore any meaningful interpretation was not possible.

HSPM severity was also assessed according to lesion extension. The component of lesion extension is a relatively new concept in HSPM diagnosis and therefore fewer studies are available to analyse. In this study, the majority of affected SPMs had a lesion extension of <1/3 of tooth surface affected. A similar finding has been reported in other HSPM prevalence studies where the same index has been used (Owen et al., 2018, Vlachou et al., 2020, Sidhu et al., 2019) Furthermore, 88.88% of affected SPMs with creamy-white opacities presented with this degree of extension suggesting the relationship between milder HSPM severity and a smaller defect surface area, a finding which has been supported in other studies (Owen et al., 2018). In this study, as defect severity increased so too did lesion extent with those teeth affected by PEB and atypical caries affected by a moderate extension (> 1/3 less than 2/3s). No SPMs were affected by a severe extension (<2/3s) in this study.

No significant relationship was found between HSPM and dental caries in this study (p=.246). However, this is not surprising considering the very low numbers (only two children with HSPM had atypical caries). Therefore, this result should be interpreted with caution until a larger sample of children have been examined.

Out of the 81 participants, 18 had dental caries (22.22%). This level is comparable to recent data published on caries prevalence in Dublin with 24% of five-year-olds in fluoridated areas affected by the disease (Oral Health Services Research Centre, 2018). The latter study examined caries in primary molars and canines using a similar index to the one used in our study with the addition of visible non-cavitated dentinal caries. In 2017, among children with full water

fluoridation in Dublin, caries prevalence was high with 55% of 8 year olds affected (James et al., 2020). It was also reported that the first opportunity for these children to avail of free routine dental care was at age 7 to 9 years. In our study, of those children affected by caries, most were affected by cavitated caries into dentine (19.75%). Furthermore, no children had restored or filled primary molars supporting the theory that this may have been their first dental assessment as there were no signs of dental intervention. Two children were missing first or SPMs due to caries (2.47%).

In our study, 36 out of 721 primary molars were affected by dental caries: giving a tooth prevalence of 4.99%. The drawback of the dv_3mft index to the level of visual caries into dentine is that this may have resulted in an under estimation of caries prevalence as only cavitated caries into dentine was reported. In this study, only the primary molars were examined for caries, so data collected was not reflective of full mouth caries prevalence.

The sample size in this study was small and representative of only one Dublin area. Caries has been shown to vary in both prevalence and severity according to geographical area, level of deprivation and ethnic group (Public Health England, 2019). In an Irish national survey conducted in 2002, results supported the link between oral health and level of disadvantage with caries experience higher in disadvantaged groups and most pronounced among 5 and 8 year old groups (Whelton et al., 2006). Due to deferred data collection, we were unable to explore how caries prevalence in Irish children interacts with regionality and social factors. This would be of value in future research as at present there is limited data in Ireland exploring this relationship.

Several countries have investigated HSPM prevalence with varying levels reported (Elfrink et al., 2015). Determining HSPM prevalence in Irish children is

of value as it reflects the potential burden of this condition and has implications for a child's oral health and treatment need. Furthermore, hypomineralisation defects can be a significant explanation for the difference in caries prevalence between first and SPMs and may be a contributing factor to caries prevalence in the Irish population (Elfrink et al., 2010).

The school in our study was non DEIS however included catchment areas of varying social advantage. MIH aetiological studies have demonstrated a relationship between increased socioeconomic status and MIH development (Balmer et al., 2012). HSPM prevalence may also be influenced by social factors such as socio-demographics/socio-economics however the evidence remains inconclusive with conflicting results reported (Silva et al., 2019, Oyedele et al., 2016b)

The drawback of this study relates to the representativeness of the sample as opposed to the sample size as only a narrow section of the population were screened. The study involved only one school limited to a relatively small geographic location. Other counties in Ireland should also be involved. Our sample was not gender balanced as only boys were examined. An even distribution of boys and girls would have been favourable.

3.6 Conclusions

HSPM prevalence was high in this study with 38.27% of children affected by the condition. This was higher than anticipated and when compared to other HSPM prevalence studies in Europe. Demarcated creamy-white opacities of mild extension were the more prevalent lesion type accounting for 81.82% of affected SPMs. 22.22% of children had caries affecting their primary molars with 19.75% presenting with cavitated caries. No children had restored primary molars perhaps reflecting the low uptake of dental interventions in this cohort of children.

Study 3:

A questionnaire study of Irish dentists' perceptions and clinical management of Hypomineralised Second Primary Molars

4. Study 3- A questionnaire study of Irish dentists' perceptions and clinical management of Hypomineralised Second Primary Molars

4.1 Abstract

Background: The perception and clinical management of HSPM amongst Irish dentists has not been explored. ***Aims:*** This questionnaire aimed to explore how general dentists in the Republic of Ireland perceive and manage HSPM. ***Methods:*** Following ethical approval, a validated structured questionnaire containing 19 questions on awareness, experience and clinical management of HSPM was sent to Irish dentists using Survey Monkey. Binary outcomes and independent variables were compared using logistic regression analysis (α = 5%). ***Results:*** The total number of respondents was 356; of which 279 were general dentists , 66 were specialists from different disciplines and 11 represented incomplete returned surveys. The main analysis represented general dentists only and were grouped according to age, years of practice and workplace. 72.40% of dentists reported awareness of HSPM with most observing the condition monthly (28.22%) or yearly (36.63%). Most dentists felt confident in diagnosing HSPM (70.79%) with demarcated yellow-brown opacities representing the most reported presentation. A similar number of participants believed the prevalence of HSPM to be between 5-10% (36.14%) and <5% (32.67%). 58% of respondents were aware of the predictive nature of HSPM for MIH development and awareness was highest in private practice (OR 0.44 p=.006) and lowest in those who practiced < 5 years (OR 0.21; p= .030). Dentists who had practiced for ≥ 15 years were significantly more likely to document HSPM frequently compared to those with less experience (OR 0.29;

p=.012) . No significant association was found between age group, years of practice and workplace and confidence in HSPM diagnosis. Dentists working outside of private practice reported to be less comfortable in management (OR 0.49; p=.030). The most cited barrier to care was child's behaviour. A broad variation was observed in the clinical scenarios with preventive treatments and biological approaches commonly selected options. Paediatric dentists were significantly more confident in HSPM diagnosis when compared to general dentists (OR 6.53; p=<.001). ***Conclusions:*** In general, Irish dentists are aware of HSPM and are confident in diagnosis and management. Variation existed in treatment options reflecting the disparity that exists in clinical management. Specialisation favourably influenced diagnostic confidence and comfort in management

4.2 Aims and Objectives

4.2.1 Aims

- To determine awareness of HSPM amongst Irish general dentists
- To gain an improved understanding of how Irish dentists perceive HSPM
- To determine how HSPM is clinically managed

4.2.2 Objective

- To survey Irish general dentists using an online questionnaire to establish their awareness, knowledge, and clinical management of HSPM

4.3 Materials and Methods:

4.3.1 Ethical approval

Ethical approval was granted by the DDUH Research Ethics Committee in June 2020 (Appendix 3.1)

4.3.2 Questionnaire development

This questionnaire was formulated based on a questionnaire published by a previous Irish Study investigating the perception and management of MIH by Irish dentists (Wall and Leith, 2020). The questionnaire developed by Wall and Leith was based on previously validated questionnaires with minor modifications made (Gambetta-Tessini et al., 2016, Kopperud et al., 2016, Alanzi et al., 2018).

This questionnaire was modified to determine HSPM awareness and clinical management with the term ‘MIH’ substituted for HSPM in seven of the questions. The questionnaire was also modified to include additional questions in relation to a dentist’s experience of HSPM and the relationship between HSPM presence and MIH development. Clinical scenario questions were changed to include photographic examples of HSPM affected teeth. Written consent was obtained for use of photographs by parents/guardians prior to questionnaire dissemination.

In total, there were 19 questions with a combination of yes/no, multiple choice and ‘select all that apply’ styled questions (Appendix 3.2). Several questions had the option of adding the participants own answer should the options available not match their own choice. The first four questions focused on

participant characteristics including participants age, duration of practicing dentistry, place of work and area of practice.

The second section addressed the areas of HSPM awareness (Figure 4.1), perceived prevalence and frequency of noticing the defect. Questions also assessed participants confidence in diagnosing the condition and preferred restorative material choices for these teeth. Regarding defect severity, participants were asked what type of defect they most commonly see with options including demarcated opacities or PEB.

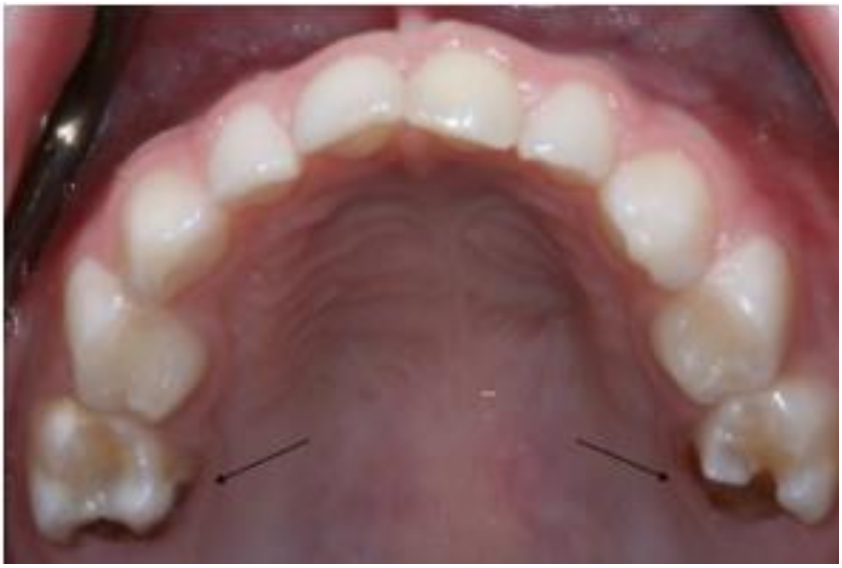


Figure 4.1: Are you aware of a condition known as Hypomineralised Second Primary Molars (HSPM) or hypomineralised Es?

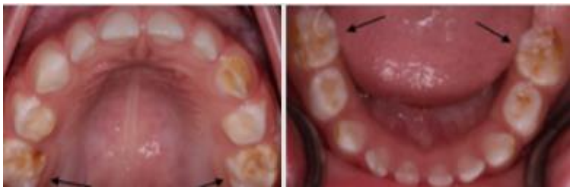
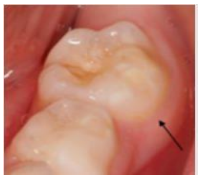
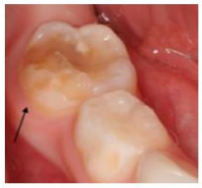
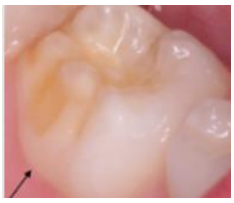
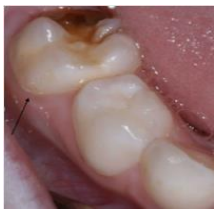
The third section (comprising of 8 questions) focused on the clinical management of teeth affected by HSPM and also participants awareness of HSPM as a predictor of MIH. Clinical photographs of HSPM affected teeth were provided with a short description including information on the child's age, behaviour, clinical and radiographic details. The participants were asked what treatment they would provide with a list of options available (Table 4.1).

Participants were able to choose a combination of options should they wish. The scenarios involved varying degrees of defect severity so as to ensure the full spectrum of HSPM was represented (Table 4.2).

Table 4.1: Treatment options provided in clinical scenario questions

Treatment options available for clinical scenario questions (15-18)
1. No treatment with preventive advice
2. Fluoride varnish
3. Fissure sealant (glass ionomer)
4. Fissure sealant (resin)
5. Glass ionomer restoration
6. Composite restoration
7. Stainless steel crown with Hall technique (no LA/no tooth preparation)
8. Conventional stainless steel crown (with LA and tooth preparation)
9. Extraction

Table 4.2: Clinical scenario questions

Question	Description	Photo
Questions 12-14 Case A	Below photos represent a five year old child with hypomineralisation and PEB of all SPMs (Es). All Es are asymptomatic, radiographic findings are normal and the child is very cooperative	
Question 15 Case B	Which treatment would you provide for this hypomineralised, caries free SPM (E) with demarcated opacities? The patient is 5 years old, has good oral hygiene and is very cooperative.	
Question 16 Case C	Which treatment would you provide for this hypomineralised, asymptomatic SPM (E) with PEB and atypical caries? The patient is five years old, has good oral hygiene and is very cooperative.	
Question 17 Case D	Which treatment would you provide for this caries free, hypomineralised SPM (E) with PEB? The patient is 8 years old, has good oral hygiene and is cooperative	
Question 18 Case E	Which treatment would you provide for this hypomineralised SPM (E) with PEB and atypical caries? The tooth is asymptomatic and there are no signs of clinical or radiographic infection. The patient is 8 years old, has good oral hygiene and is very cooperative.	

To ensure questionnaire validity and reliability, piloting was conducted prior to its distribution (Appendix 3.3). Five general dentists with backgrounds in private dental practice and community dentistry were invited to participate in the piloting phase. Questions were categorised according to six key areas: readability, clarity, layout, sequence, relevance / representativeness and

appropriateness. Questions were dichotomous in nature (yes or no) with a comment section available should feedback wish to be given. The final question was open ended and asked if there were any areas the participants believed to be important to the study that were not already included.

4.3.3 Distribution

The survey was distributed online using Survey monkey® as the host and remained open for four weeks. Dentists were invited to participate via two principal avenues. A link to the questionnaire was emailed to members of the Irish Dental Association following a paediatric dentistry online webinar. Principal dental surgeons in the public dental service (Health Service Executive) were also contacted with the survey disseminated to its dentists.

4.3.4 Confidentiality

Participant information was anonymous. On survey monkey, settings were selected which ensured respondent's email/IP address was not visible upon completing the questionnaire.

4.3.5 Data collection

Survey monkey software was used to automatically collate survey responses.

4.3.6 Data analysis

Data was exported from survey monkey to an excel spreadsheet and re-organised before exporting to SPSS for statistical analysis. Missing data (where participants did not provide an answer) were accounted for on SPSS in the missing values section of the variable data view.

Variables relating to participants were analysed. The total number and percentages were calculated for each categorical variable. Following this, certain dependant variables (confidence, perceived frequency) and independent variables (age, years of practice and place of work) were collapsed into smaller categories to facilitate logistic regression analysis.

4.3.7 Statistical analysis

In the sample comprising general dentists only, binary logistic regression models including univariate and adjusted analysis were performed to determine if any association existed between the dependant variables (HSPM awareness, confidence in diagnosis, competency/comfort in management, perceived frequency and awareness of HSPM as predictor for MIH) and the independent variables (age, years of practice and place of work) ($\alpha = 5\%$).

In the broader sample including specialist groups, ordinal logistic regression was performed to determine if a difference existed between general dentists and specialty groups in relation to confidence in diagnosis. Fisher's exact test was performed to determine if any difference existed between general dentists and specialists in the areas of HSPM awareness, comfort in management and awareness of the predictive nature of HSPM for MIH analysis ($\alpha = 5\%$).

4.4 Results

4.4.1 Sample size

The total number of respondents was 356; of which 66 were specialists from different disciplines (including 17 paediatric dental specialists). These 66 specialists were excluded from the main analysis and eleven of the returned surveys were incomplete, leaving a final figure of 279 for analysis. This sample represented general dental practitioners.

In 8 of the questions (12-19) there were missed answers. While survey settings were set so that all questions required an answer, in some instances, participants exited the questionnaire prematurely resulting in a partially completed survey being submitted. These submissions remained included and missing values were accounted for in the statistical analysis.

4.4.2 Response rate

According to the dental council of Ireland, there are an estimated 2100 dentists practicing in the Republic of Ireland. Using this as a total figure, the response rate was estimated as 16.95% (356 dentists out of an estimated total of 2100 email recipients).

4.4.3 Participant Characteristics

Regarding age, the majority of the sample were aged between 36-45 years (26.16%) and between 46-55 years (25.81%). The third largest group were aged between 26-35 years (24.01%). 16.13% of the sample were aged over 55 and 7.89% were less than 25 years (Figure 4.2).

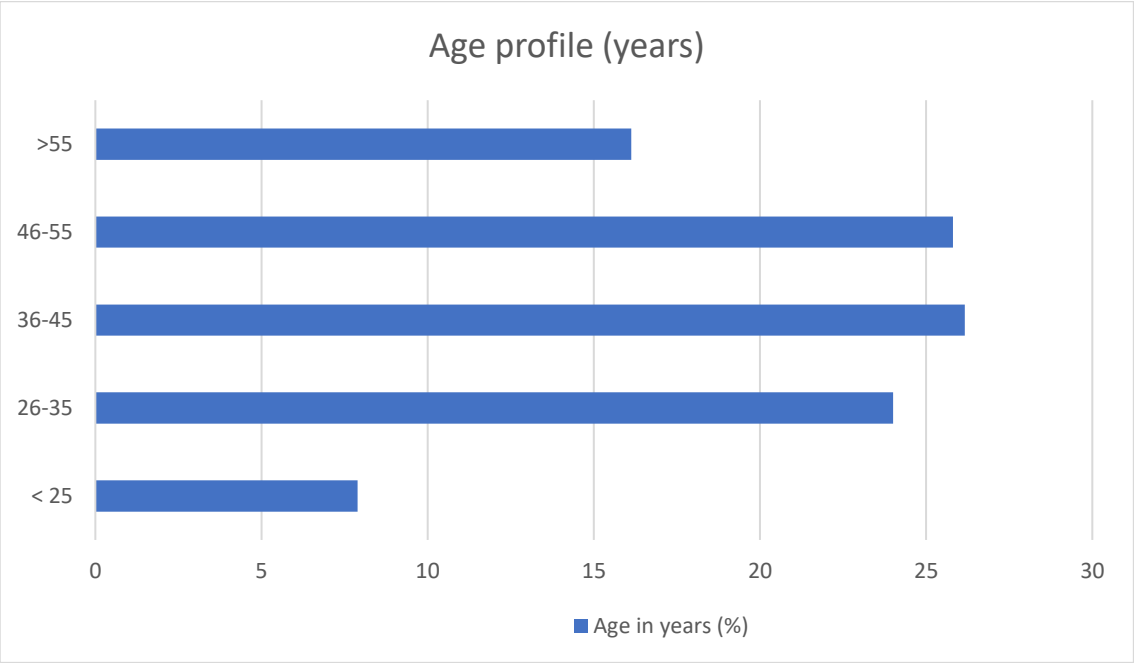


Figure 4.2: Age profile of general dentist respondents

Regarding years of work, most respondents (42.66%) had more than 20 years' experience; this was followed by 16.13% who had between five to ten years' experience. The remaining categories (<5 years,10-15 years, 15-20 years) were evenly dispersed; 13.98%, 13.98% and 13.25% respectively (Figure 4.3).

Figure 4.3: Participants' years of practicing dentistry

Of the 279 general dentists that completed the survey, 188 worked in private practice exclusively (67.38%). The remaining 91 respondents represented those working in the public sector, university, and a combination of private practice/public sector/university (Figure 4.4). Table 4.3 summarises participant characteristics with counts and percentages provided.

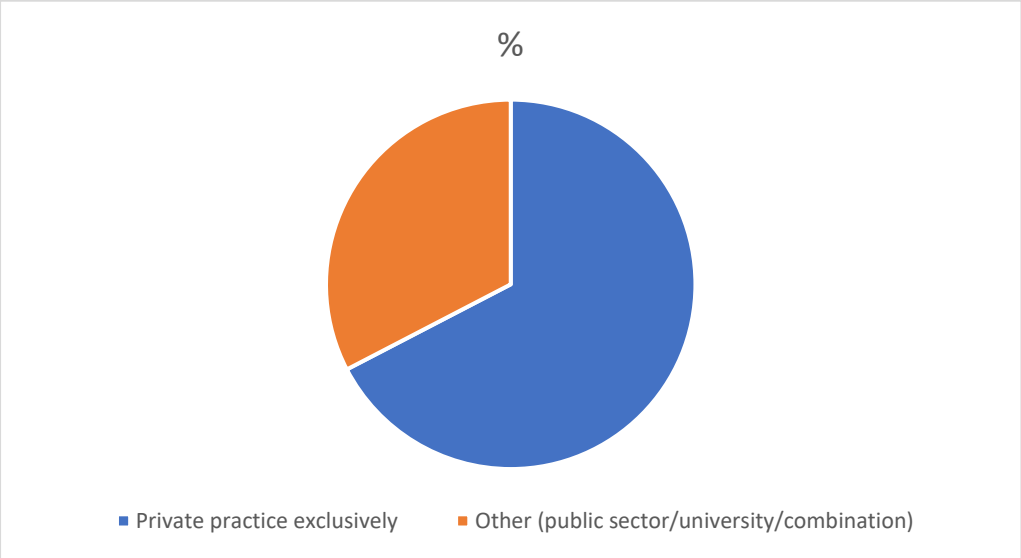


Figure 4.4: Pie chart demonstrating participants workplace (general dentists)

Table 4.3: General dentist's participant characteristics (age, years of practice and place of work)

Variable	Count (/279)	Valid Percent (%)
Q1 Age		
<25 years	22	7.89
26-35 years	67	24.01
36-45 years	73	26.16
46-55 years	72	25.81
>55 years	45	16.13
Q2 Years practicing		
<5 years	39	13.98
5-10 years	45	16.13
10-15 years	39	13.98
15-20 years	37	13.25
>20 years	119	42.66
Q3 Place of work		
Private Practice exclusively	188	67.38
Other (Public sector/university/ combination)	91	32.62
Total	**279**	**100**

4.4.4 Awareness, perceived frequency and prevalence

When asked about their awareness of HSPM as a condition, most dentists (72.40%) reported that they were aware of the condition.

Regarding the frequency of noticing the condition, 36.63% of participants reported that they observed HSPM on a yearly basis, while 28.22% observed it monthly and 9.90% weekly. 2.87% reported never seeing the condition.15.41% of the sample were not sure regards its frequency (Figure 4.5).

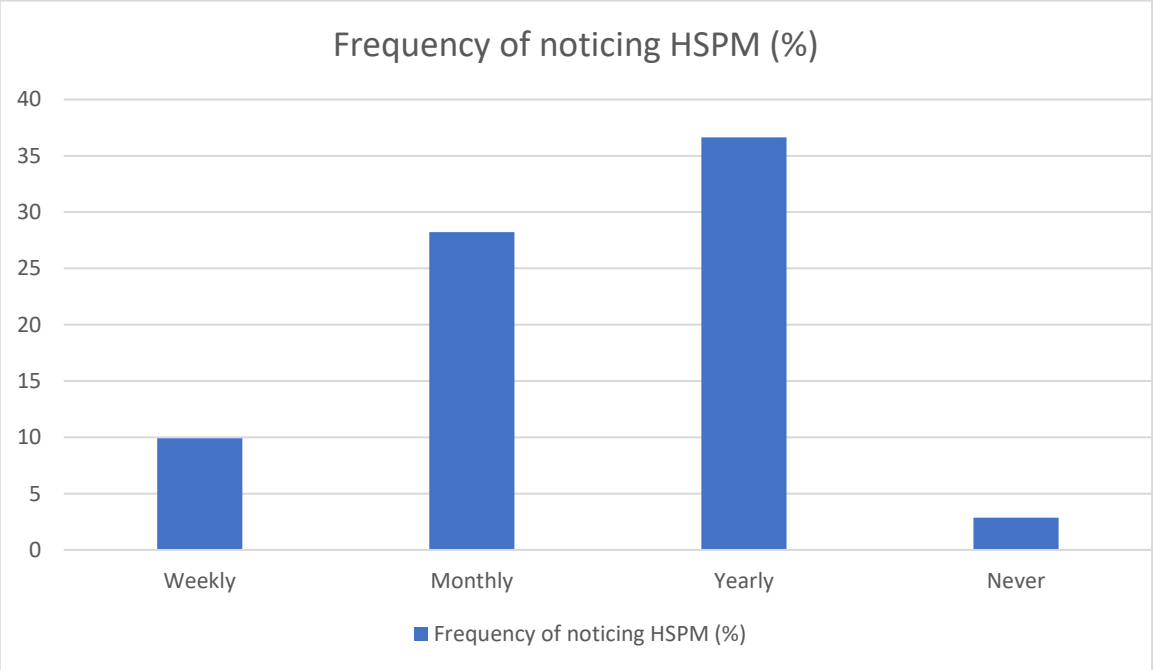


Figure 4.5: Frequency of noticing HSPM amongst Irish general dentists

A similar number of participants believed the prevalence of HSPM to be between 5-10% (36.14%) and <5% (32.67%). 16.83% of the sample perceived the prevalence to be higher; between 10 and 20%. A small percentage (3.47%)

believed the prevalence to be greater than 20%. 10.89% of participants were unsure regarding HSPM prevalence in their community (Figure 4.6).

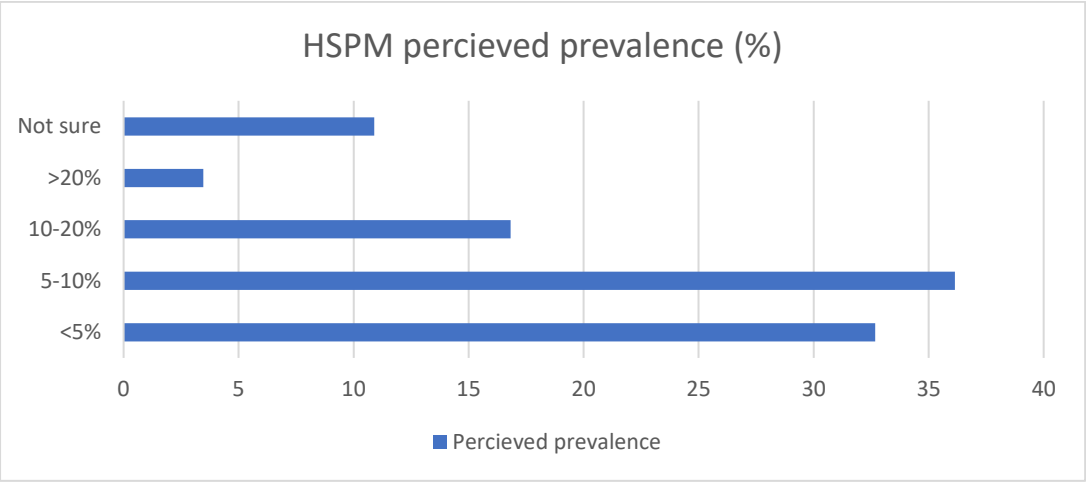


Figure 4.6: Perceived prevalence of HSPM amongst Irish general dentists

4.4.5 Defect severity, confidence in diagnosis and caries pattern

Regarding the severity of the defect, 52.97% of participants reported seeing yellow/brown demarcated opacities most frequently. This was followed by PEB with associated demarcated opacities (24.25%) and white demarcated opacities (22.77%) (Figure 4.7).

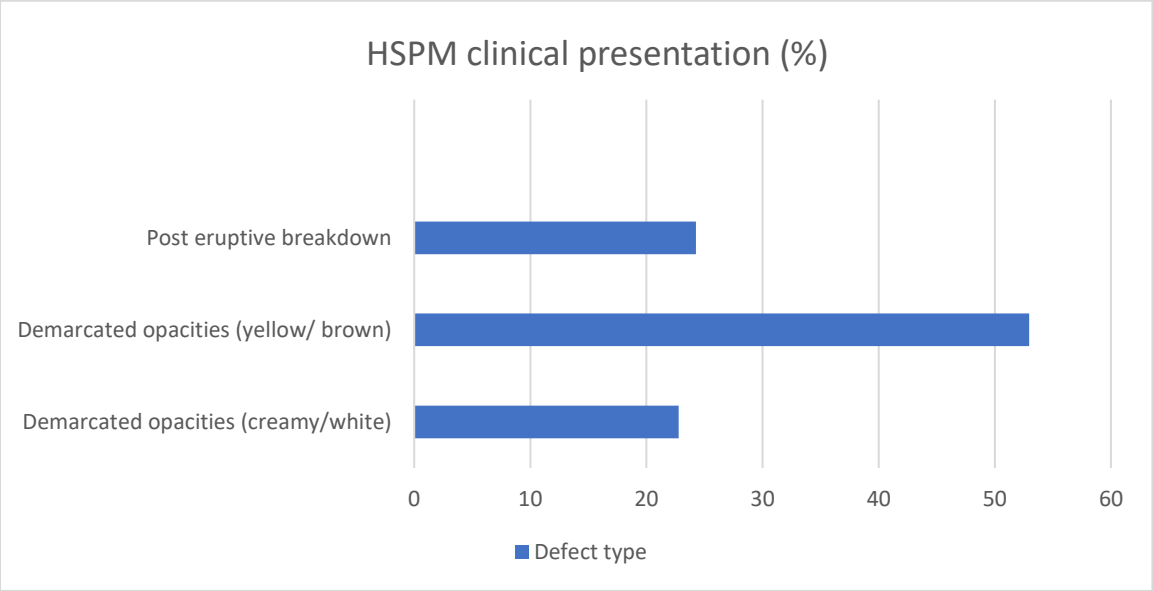


Figure 4.7: Perceived clinical presentations of HSPM seen by Irish general dentists

Regarding confidence in diagnosing HSPM, 70.79% of dentists either felt extremely or very confident in diagnosis. 27.72% felt unconfident in diagnosis with 1.49% very unconfident. Most of the participants (95.54%) recognised the difference between atypical caries associated with HSPM and the classical caries pattern.

4.4.6 Material selection for HSPM

When asked about commonly used materials in the treatment of HSPM affected teeth (multiple responses allowed), the most common response was conventional GI (54.95%) followed closely by resin modified glass ionomer (RMGI) (40.59%). Composite resin (29.21) and preformed crowns (29.70) represented the next most frequent material choices. Compomer and 'other' were less commonly selected options (Figure 4.8). Table 4.4 provides the counts and percentages for questions 5-10.

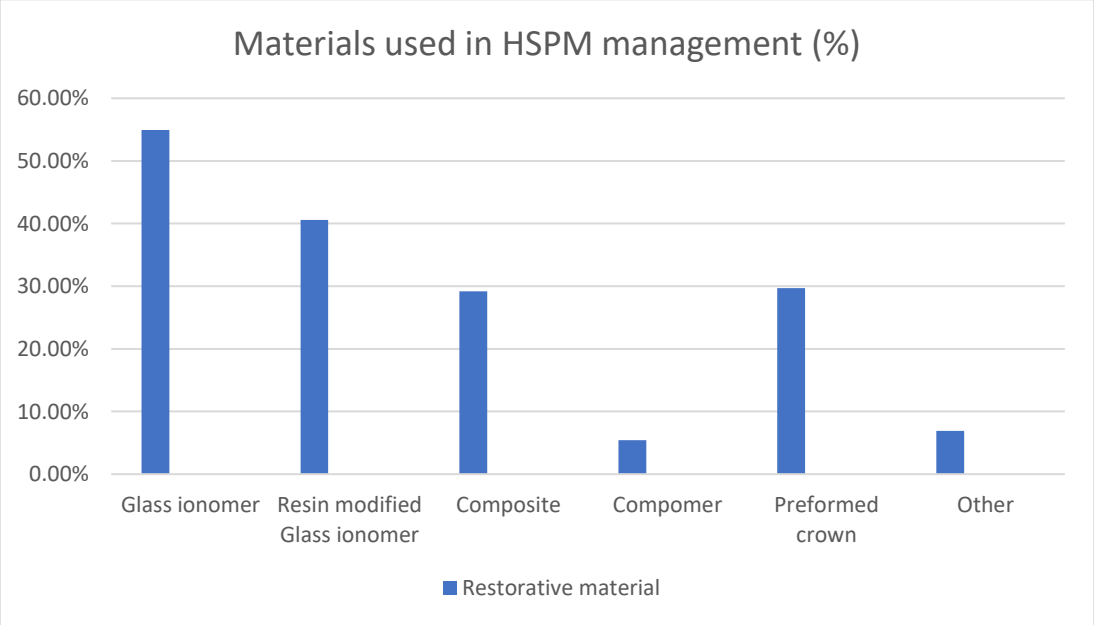


Figure 4.8: Materials commonly used in the management of HSPM

Table 4.4: Questions 5-10 with counts and valid percentages

Variable	Count (/279)	Valid Percent (%)
Q5 Are you aware of HSPM?		
Yes	202	72.40
No	77	27.60
Total	**279**	**100**
Q6 How often do you notice this condition? (If answered yes to Q5 (n = number of yes participants /202)		
Weekly basis	20	9.90
Monthly basis	57	28.22
Yearly basis	74	36.63
Not sure/never	51	25.25
Q7 How prevalent do you think hypomineralised Es might be in your community?		
<5%	66	32.67
5-10%	73	36.14
10-20%	34	16.83
>20%	7	3.47
Not sure	22	10.89
8. Regarding the severity of the defect; which of the following do you most frequently notice in your practice?		
White demarcated opacities	46	22.77
Yellow/brown demarcated opacities	107	52.97
PEB (PEB)	20	9.90
Demarcated opacities and PEB	29	14.36
Q9. How confident do you feel in diagnosing teeth affected by this condition?		
Extremely confident	28	13.86
Very confident	115	56.93
Unconfident	56	27.72
Very unconfident	3	1.49
10. Do you think the pattern (shape, size, location) of caries due to HSPM (hypomineralised Es) is different from the classical caries pattern?		
Yes	193	95.54
No	9	4.46
11. What type of material do you often use in treating these teeth? (Select all that apply)		
Glass ionomer	111	54.95
Resin modified Glass Ionomer	82	40.59
Composite	59	29.21
Compomer	11	5.45
Preformed crowns (SSC)	60	29.70
Other	14	6.93

4.4.7 Case scenarios

Respondents assessed five case scenarios with associated questions on clinical management. Multiple options were available for selection in each scenario. Table 4.6 describes treatment options selected for each case scenario.

Case scenario A (Questions 12-14) described a five year child with hypomineralisation and PEB of all SPMs. Participants were asked would they be comfortable providing care for this case with the majority responding yes (75.45%). For those who responded as not being comfortable, 91.66% said they would refer to a paediatric specialist. When asked regarding barriers to care (where multiple answers were allowed), the majority (83.67%) indicated the child's behaviour as a barrier. This was followed by young age (41.03%). Less commonly reported reasons included repeated failure of restorations (33.47%), dental treatment that needs a long time to be accomplished (20.32%), insufficient training to treat children with this condition (23.90%) and difficulty deciding how to restore teeth/what materials to use (15.14%). A number of respondents (7.97%) indicated 'other' barriers to treating HSPM teeth including financial barriers and constraints of their working environment (Table 4.5).

Table 4.5: Cited barriers to care

Q14. Would any of the following be a barrier to you for managing this child. n=251;28 not answered. Multiple options can be selected.		
Young age	103	41.03
Child's behavior	210	83.67
Dental treatment that needs long time to be accomplished	51	20.32
Difficulty deciding how to restore teeth and what materials to use	38	15.14
Repeated failure of restorations	84	33.47
Insufficient training to treat children with this condition	60	23.90
Other	20	7.97

Case scenario B asked participants what treatment they would provide for a hypomineralised, caries free SPM with demarcated opacities This case involved a five year old child with good oral hygiene and cooperation. The most popular choices were non-operative approaches including fluoride varnish application (55.78%) and glass ionomer fissure sealant (40.24%). 25.10% of respondents said they would provide no treatment but would offer preventive advice followed by resin fissure sealant which was selected by 20.32%. Least popular choices included hall crown technique (7.17%), composite resin (2.79%) and conventional SSC (1.20%) (Figure 3.9).

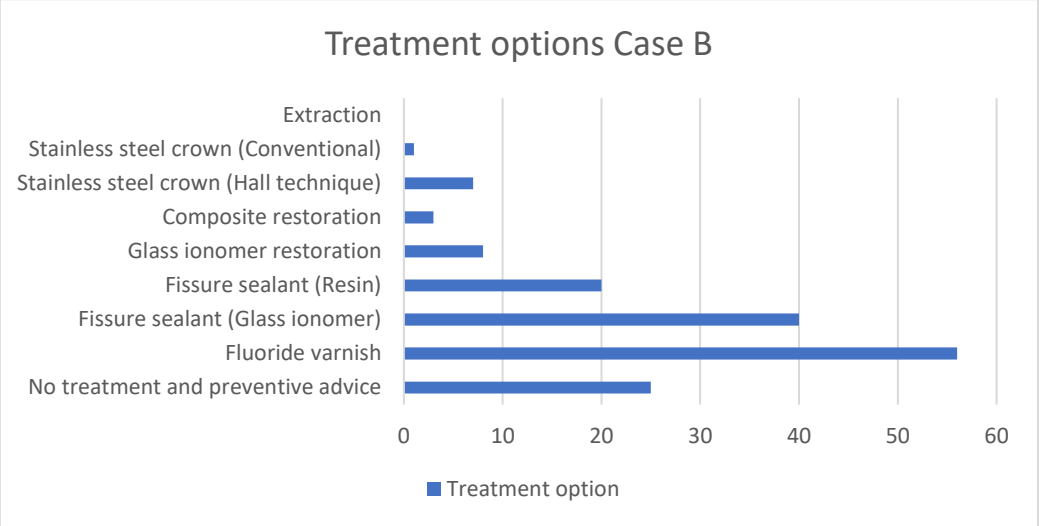


Figure 4.9: Treatment options selected for case B

Case scenario C asked participants what treatment they would provide for a hypomineralised, asymptomatic SPM with PEB and atypical caries. The child was five years old with good cooperation and hygiene. The most popular choices included placement of a SSC using the hall technique (45.02%) and restoring with GI (38.24%). Non-operative, preventive measures were also selected such as fluoride varnish application (19.52%). Restoration with composite resin was chosen by 14.34% of participants. A minority of respondents chose GI sealant (6.37%), resin sealant (1.99%), conventional SSC (3.59%) and extraction (0.40%) (Figure 4.10).

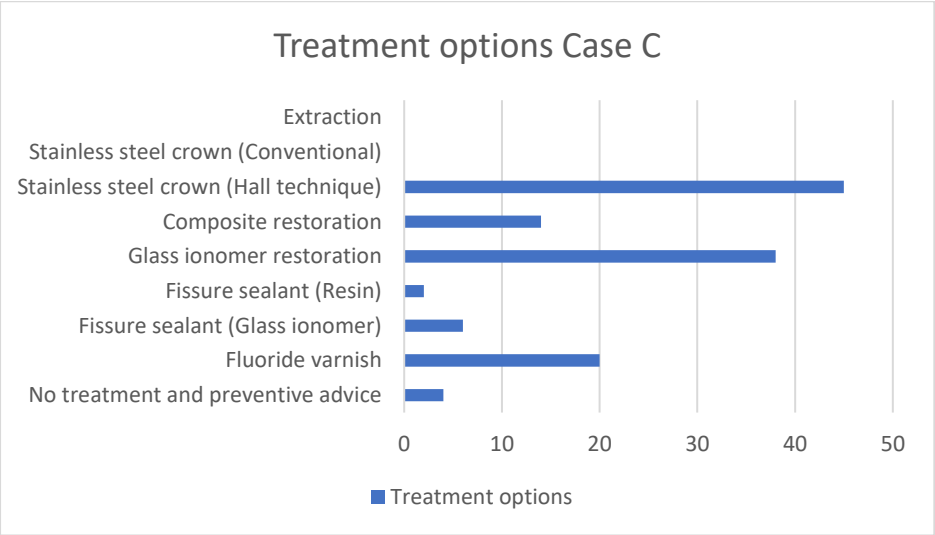


Figure 4.10: Treatment options selected for case C

Case scenario D (question 17) asked participants what treatment they would provide for a caries free, hypomineralised SPM with PEB. The child was 8 years old with good oral hygiene and cooperation. The most popular treatments were fluoride varnish (55.39%) and no treatment with preventive advice (27.89%). A smaller percentage of respondents chose GI fissure sealant (15.94%), composite resin restoration (11.16%), resin fissure sealant (9.56%) and SSC placed with the hall technique (7.97%). Two participants (0.80%) chose conventional SSC with none choosing the extraction option (Figure 4.11).

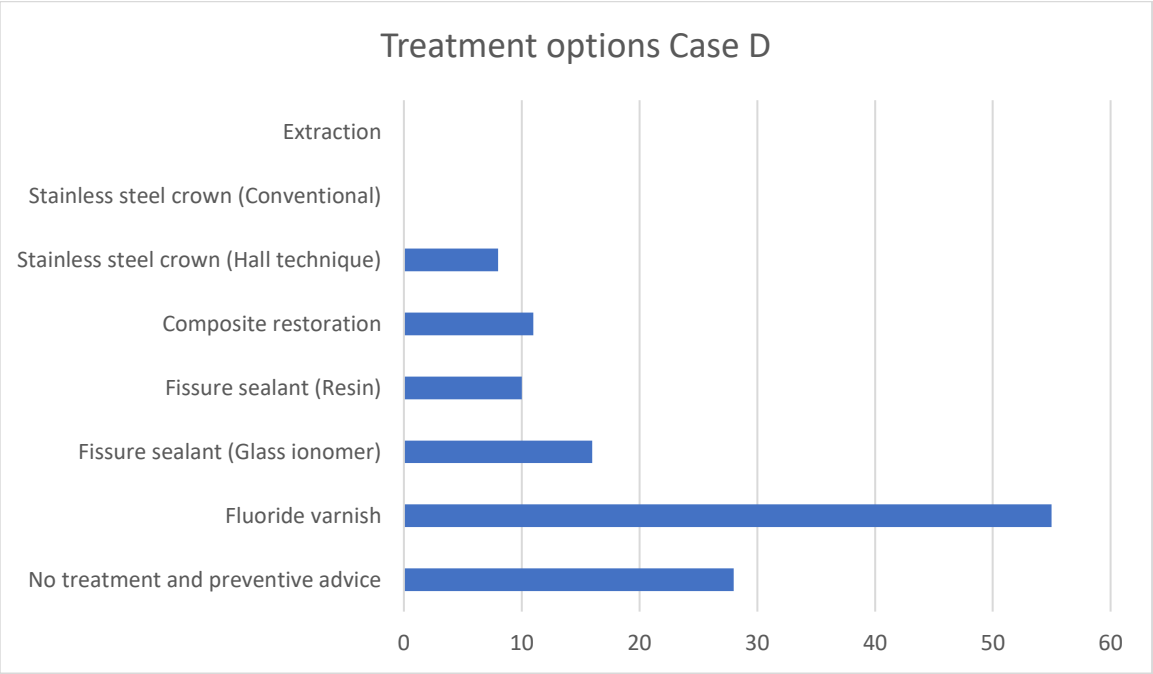


Figure 4.11: Treatment options selected for case D

Case Scenario E (question 18) asked participants what treatment they would provide for a hypomineralised SPM with PEB and atypical caries. The tooth was described as asymptomatic with no signs of clinical/radiographic infection. In terms of restorative treatment, 41.43% of participants selected the hall technique as a suitable treatment option which was followed by GI restoration (26.29%), composite restoration (12.35%) and conventional SSC (10.76%). Non-operative approaches were also selected including fluoride varnish (13.94%), no treatment and preventive advice (5.98%) and fissure sealant (5.57%). 10 participants (3.98%) selected extraction (Figure 4.12).

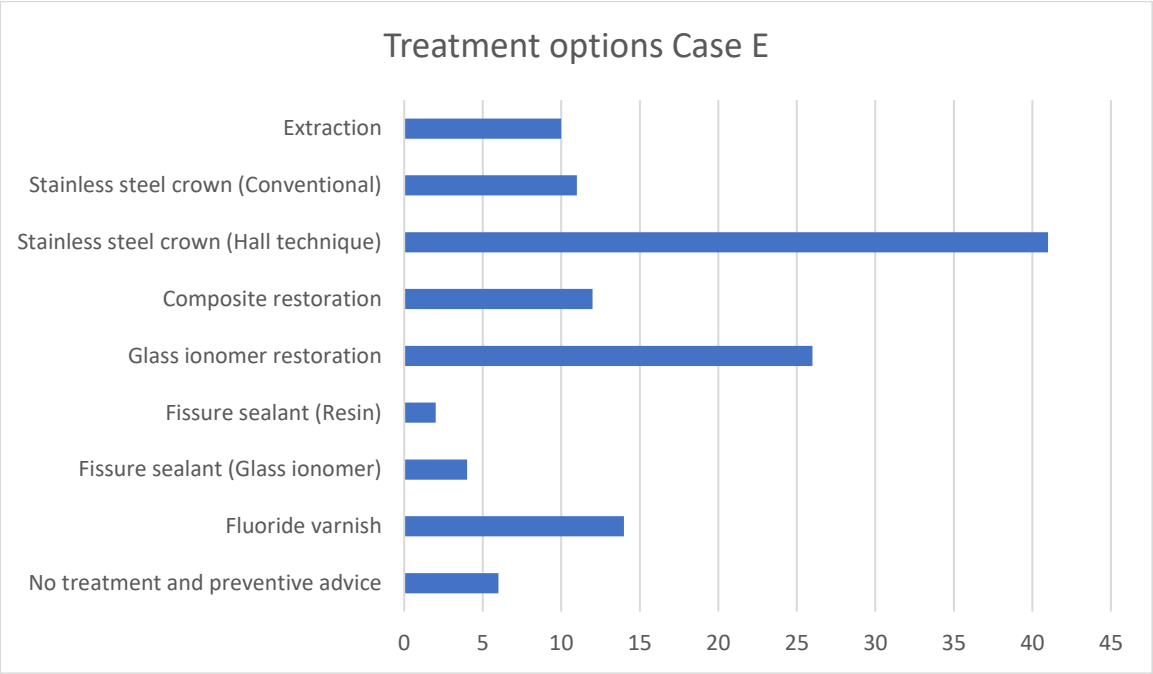


Figure 4.12: Treatment options selected for case E

Only 58% of respondents were aware of the predictive value of HSPM for MIH development. Table 4.6 describes the treatment options selected for the clinical scenarios.

Table 4.6: Treatment options selected for clinical scenarios (questions 12-18)

Q12. (Case A) Would you be comfortable providing restorative care for this child (n= 277; 2 not answered)		
	Count	Valid Percent (%)
Yes	209	75.45
No	68	24.55
Total	**277**	**100.00**
Q13. If answered No to Question 12 (n=60) (10 not answered)		
Another general dentist	1	1.67
Paediatric Specialist (private)	55	91.66
Hospital setting	1	1.67
Community HSE clinic	0	0.00
Other	3	5.00
Total	**60**	**100.00**
Q15. (Case B) Which treatment would you provide for this hypomineralised, caries free SPM (E) with demarcated opacities? The patient is 5 years old, has good oral hygiene and is very cooperative. (n=251; 28 not answered). Multiple options can be selected.		
No treatment and preventive advice	63	25.10
Fluoride varnish	140	55.78
Fissure sealant (Glass ionomer)	101	40.24
Fissure sealant (Resin)	51	20.32

Glass ionomer restoration	19	7.57
Composite restoration	7	2.79
Stainless steel crown (Hall technique)	18	7.17
Stainless steel crown (Conventional)	3	1.20
Extraction	0	0.00

Q16. (Case C) Which treatment would you provide for this hypomineralised, asymptomatic SPM (E) with PEB and atypical caries. The patient is five years old, has good oral hygiene and is very cooperative. (n=251;28 not answered). Multiple options can be selected.

No treatment and preventive advice	8	3.19
Fluoride varnish	49	19.52
Fissure sealant (Glass ionomer)	16	6.37
Fissure sealant (Resin)	5	1.99
Glass ionomer restoration	96	38.24
Composite restoration	36	14.34
Stainless steel crown (Hall technique)	113	45.02
Stainless steel crown (Conventional)	9	3.59
Extraction	1	0.40

Q17. (Case D) Which treatment would you provide for this caries free, hypomineralised SPM (E) with PEB? The patient is 8 years old, has good oral hygiene and is cooperative. (n=251;28 not answered). Multiple options can be selected.

No treatment and preventive advice	70	27.89
Fluoride varnish	139	55.39
Fissure sealant (Glass ionomer)	40	15.94
Fissure sealant (Resin)	24	9.56
Glass ionomer restoration	39	15.54
Composite restoration	28	11.16
Stainless steel crown (Hall technique)	20	7.97
Stainless steel crown (Conventional)	2	0.80
Extraction	0	0.00

Q18. (Case E) Which treatment would you provide for this hypomineralised SPM (E) with PEB and atypical caries? The tooth is asymptomatic and there are no signs of clinical or radiographic infection. The patient is 8 years old, has good oral hygiene and is very cooperative. (n=251;28 not answered). Multiple options can be selected.

No treatment and preventive advice	15	5.98
Fluoride varnish	35	13.94
Fissure sealant (Glass ionomer)	10	3.98
Fissure sealant (Resin)	4	1.59
Glass ionomer restoration	66	26.29
Composite restoration	31	12.35
Stainless steel crown (Hall technique)	104	41.43
Stainless steel crown (Conventional)	27	10.76
Extraction	10	3.98

Q19. Are you aware that hypomineralised SPMs (Es) may be predictive of Molar Incisor Hypomineralisation in the FPM teeth (MIH)? (n=250; 29 not answered)

Yes	145	58.00
No	105	42.00
Total:	**250**	**100.00**

4.4.8 Relationship between dependant (awareness, perceived frequency, confidence in diagnosis, comfort in management) and independent variables

Binary logistic regression was performed to investigate the relationship between a number of variables. No statistically significant relationship was found between awareness of HSPM and participants age, years of practice or place work (Table 4.7).

Table 4.7: Binary logistic regression of participants awareness of HSPM and independent variables

Variable	**Awareness**		**Univariate**		**Adjusted**	
	No n (%)	Yes n (%)	OR (95% CI)	p-value	OR (95% CI)	p-value
Q1 Age						
≥36 years (ref)	55 (28.95)	135 (71.05)				
<36 years	22 (24.72)	67 (75.28)	1.24 (0.69-2.20)	0.462	1.27 (0.52-3.13	0.602
Q2 Years in practice						
≥15 years (ref)	42 (26.92)	114 73.08)				
< 5 years	5 (12.82)	34 (87.18)	2.50 (0.92-6.83)	0.073	1.93 (0.51-7.34)	0.335
5-15 years	30 (35.71)	54(64.29)	0.66 (0.38-1.17)	0.157	0.56 (0.26-1.23)	0.148
Q3 Place of work						
Private Practice (ref)	56 (29.79)	132 (70.21)				
Other	21 (23.08)	70 (76.92)	1.41 (0.79-2.52)	0.241	1.42 (0.79-2.57)	0.240

Binary logistic regression was performed to determine if any association existed between participant's confidence in HSPM diagnosis and independent variables. Confidence outcomes were collapsed down into two categories: very and extremely confident (reference group) and unconfident/very unconfident. Following univariate and adjusted analysis no significant association was found to exist (Table 4.8).

Table 4.8: Binary logistic regression of participant's confidence in HSPM diagnosis and independent variables

Variable	Confidence		Univariate		Adjusted	
	Very unconfident/ unconfident (%)	Very and extremely confident (%)	OR (95% CI)	p-value	OR (95% CI)	p-value
Q1 Age						
≥36 years (ref)	40 (29.63)	95 (70.37)				
< 36 years	19 (28.36)	48 (71.64)	0.94 (0.49-1.80)	0.852	1.23 (0.33-4.66)	0.760
Q2 Years in practice						
≥15 years (ref)	36 (31.58)	78 (68.42)				
< 5 years	12 (35.29)	22 (64.71)	1.18 (0.53-2.65)	0.685	0.92(0.20-4.25)	0.918
5-15 years	11 (20.37)	43 (79.63)	0.55 (0.26-1.20)	0.134	0.47(0.15-1.52)	0.205
Q3 Place of work						
Private Practice (ref)	34 (25.76)	98 (74.24)				
Other	25 (35.71)	45 (64.29)	1.60 (0.86-2.99)	0.140	1.63(0.87-3.08)	0.129

A statistically significant relationship was found to exist between years of practice and perceived frequency. Those practicing for between 5-15 years were less likely to note frequent HSPM compared to those practicing for greater than 15 years (p=.012). No significant association was found to exist in the areas of age and place of work. (Table 4.9).

Table 4.9: Binary logistic regression of participant's perceived frequency of noting HSPM and independent variables

Variable	Frequency of noticing HSPM		Univariate		Adjusted	
	Frequently	Infrequently	OR (95% CI)	p-value	OR (95% CI)	p-value
Q1 Age (years)						
≥36 (ref)	50 (37.04)	85 (62.96)	-		-	-
< 36	27 (40.30)	40 (59.70)	0.87 (0.48-1.59)	0.653	1.62 (0.55-4.84)	0.384
Q2 Years in practice						
≥15 (ref)	37 (32.46)	77 (67.54)	-	-	-	-
< 5	10 (29.41)	24 (70.59)	1.15 (0.50-2.66)	0.738	0.76 (1.98-2.93)	0.690
5-15	30 (55.56)	24 (44.44)	0.38 (0.20-0.75)	0.005*	0.29 (0.11-0.76)	0.012*
Q3 Place of work						
Private (ref)	45 (34.09)	87 (65.91)				
Other	32 (45.71)	38 (54.29)	0.61 (0.34-1.11)	0.107	0.61 (0.33-1.12)	0.113

The relationship between competency in HSPM management and independent variables was also explored. A statistically significant relationship was found to exist between place of work and competency with those not exclusively working in private practice less comfortable in managing HSPM compared to those working in private practice exclusively (p= .030) (Table 4.10).

Table 4.10: Binary logistic regression for participant's comfort in managing Case A in Question 12 and independent variables

Variable	Comfort in HSPM management (Q12)		Univariate		Adjusted	
	Yes	No	OR (95% CI)	p-value	OR (95% CI)	p-value
Q1 Age (years)						
≥36 (ref)	142 (75.13)	47 (24.87)				
<36	67 (76.14)	21 (23.86)	0.95 (0.53-1.71)	0.857	0.85 (0.32-2.31)	0.754
Q2 Years in practice						
≥15 (ref)	117 (75.48)	38 (24.52)				
< 5	29 (76.32)	9 (23.68)	0.96 (0.42-2.20)	0.915	1.19 (0.33-4.32)	0.790
5-15	63 (75.00)	21 (25.00)	1.03 (0.56-1.90)	0.934	1.18 (0.50-2.77)	0.711
Q3 Place of work						
Private (ref)	133 (71.51)	53 (28.49)				
Other	76 (83.52)	15 (16.48)	0.50 (0.26-0.94)	0.031*	0.49 (0.26-0.94)	0.030*

The relationship between independent variables and awareness of HSPM as a predictor of MIH was assessed (Table 4.11). In the univariate analysis, a statistically significant relationship was found to exist between all independent variables (age, years in practice and place of work). However, after bringing forward these variables for adjusted analysis, years of practice and place of work only remained significant. Those working for < 5 years were less likely to have awareness on the predictive nature of HSPM for MIH (p= .030) compared to those working for ≥ 15 years . Furthermore, those whose workplace was not exclusive to private practice were less likely to have awareness compared to those who worked exclusively in private practice (p=.006).

Table 4.11: Binary logistic regression for participants awareness of HSPM as a predictor of MIH and independent variables.

Variable	Awareness of HSPM as a predictor MIH		Univariate		Adjusted	
	Yes	No	OR (95% CI)	p-value	OR (95% CI)	p-value
Q1 Age (years)						
≥36 (ref)	85 (50.90)	82 (49.10)				
<36	60 (72.29)	23 (27.71)	0.40 (0.23-0.70)	0.001*	0.63(0.25-1.60)	0.331
Q2 Years in practice						
≥15 (ref)	69 (50.74)	67 (49.26)				
< 5	32 (88.89)	4 (11.11)	0.13(0.04-0.38)	0.000*	0.21(0.05-0.86)	0.030*
5-15	44 (56.41)	34 (43.59)	0.80 (0.46-1.39)	0.424	1.08(0.48-2.42)	0.849
Q3 Place of work						
Private (ref)	88 (51.76)	82(48.24)				
Other	57 (71.25)	23 (28.75)	0.43(0.25-0.77)	0.004*	0.44(0.24-0.79)	0.006*

4.4.9 Comparison between general dentists and specialists in diagnostic confidence, awareness and comfort in HSPM management

In order to compare confidence in HSPM diagnosis amongst the different subgroups, ordinal logistic regression analysis was carried out (ranging from very unconfident to extremely confident) (Table 4.12). When comparing paediatric dentists and other specialties to general dentists, paediatric specialists displayed a higher confidence level and were 6.5 times more likely to feel confident in diagnosis when compared to general dentists (p <.001).

Table 4.12: Ordinal logistic regression for participants confidence (varying from very unconfident to extremely confident) and area of practice

Variable	**Univariate analysis (participants confidence in diagnosis)**	
Q4 Area of practice	**OR (95% CI)**	**P value**
General dentist (ref)		
Specialist - Paediatric	6.53 (2.47-17.22)	<0.001*
Specialist - Other	0.48 (0.23-1.0)	0.051

Fishers exact test was performed with a significant difference being found between paediatric dentists and the other groups for awareness, comfort in management and predictive nature of HSPM for MIH. 100% of paediatric dentists were aware of the condition HSPM and there was a significant difference found between the groups (p=.006). Regarding comfort in management, paediatric dentists were significantly more comfortable in HSPM management when compared to other groups (p=.002). The awareness of the predictive nature of HSPM for MIH was lower amongst general dentists and other specialty groups when compared to paediatric dentists (p=.011).

Table 4.13: Analysis investigating relationship between area of practice and dependant variables (HSPM awareness/Comfort in HSPM management/Awareness of predictive nature of HSPM for MIH)

	HSPM Awareness		
	No n (%)	**Yes n (%)**	**Fisher exact test p value**
Area of practice			
Specialist – Paediatric (ref)	0 (0.00)	17 (100.00)	
General dentist	77(27.60)	202(72.40)	0.006*
Specialist - Other	18(36.73)	31(63.27)	
Total	95(27.54)	250(72.46)	
Comfort in HSPM management (Case A)			
	No n (%)	**Yes n (%)**	
Specialist – Paediatric (ref)	1 (5.88)	16 (94.12)	
General dentist	68 (24.55)	209 (75.45)	0.002*
Specialist - Other	22 (44.90)	27 (55.10)	
Total	91 (26.53)	252 (73.47)	
Awareness that HSPM is predictive of MIH			
	No n (%)	**Yes n (%)**	
Specialist – Paediatric (ref)	0(00.00)	10 (100.00)	
General dentist	105(42.00)	145(58.00)	0.011*
Specialist - Other	22(47.83)	24(52.17)	
Total	127 (41.50)	179(58.50)	

4.5 Discussion

Several surveys have been published regarding dentists' perception and clinical management of MIH (Ghanim et al., 2011, Alanzi et al., 2018, Wall and Leith, 2020). In contrast, there is a lack of information pertaining to dentist's knowledge and perception of HSPM. This is not surprising considering MIH as a clinical entity has been recognised for longer and therefore has established itself in the scientific literature. The majority of HSPM studies have addressed the areas of prevalence and aetiology with little emphasis on how clinicians perceive and manage the condition. This is disappointing since the detection and awareness of HSPM is related to its recognition by dental practitioners. It is difficult to determine at present how Irish dentists perceive HSPM and whether any concern exists in terms of its management. The viewpoints of Irish general dentists may be of benefit in identifying any gaps in knowledge and in understanding what clinical challenges exist for this group.

In this study, the total number of respondents were 356, sampled from across the Republic of Ireland. All specialist dental practitioners were excluded from the main analysis (66 respondents). The inclusion of 17 paediatric dentists may have introduced bias as patients with HSPM are often referred to specialist practice and may present with a more severe form of the defect (Crombie et al., 2008). In addition, we wished to gain an understanding of the viewpoint of general dental practitioners whose treatment approach may differ when compared to paediatric specialists and other specialties. A separate subgroup analysis including the full sample was conducted to determine if any significant difference existed between general dentists and specialists and dependent variables.

The response rate was low (16.95%). However, it cannot be determined if all dentists received an email and therefore this figure may not be fully accurate. A recently conducted Irish MIH perception study reported a similarly low response rate of 11%. (Wall and Leith, 2020). Furthermore, the number of respondents in this study is comparable when one looks at both MIH and HSPM perception studies outside of Ireland (Ghanim et al., 2011, Alanzi et al., 2018, Meer et al., 2020).

The questionnaire was distributed online using Survey monkey as the host. Due to the COVID 19 pandemic and restrictions in conference attendance, online distribution was anticipated to be the most suitable circulation method.

The age ranges of 26-35, 36-45 and 46-55 years were evenly distributed. Those aged < 25 and > 55 represented a smaller proportion of participants. Regarding years of practice, most of the sample had > 20 years of experience. This response profile differed to the study by Meer et al. (2020) where most respondents had < 10 years of experience (Meer et al., 2020). Direct comparability of results may be hampered by such inherent differences in the profile of dentists surveyed. In Ireland, dentistry is mostly private, which was reflected by the responders (67.38% worked exclusively in private practice). A similar number worked in public sector/private practice and public sector exclusively.

Most general dentists (72.40%) were aware of the condition HSPM. This was comparable to the findings by Meer et al. (2020) where 60% of participants reported encountering HSPM defects (Meer et al., 2020). Independent variables such as age, years of practice and place of work did not influence HSPM awareness ($p = \geq .05$). HSPM is a relatively new condition, and it could be

hypothesised that years of practice may have been important with those more recently qualified potentially having more awareness. This association was not shown in our study and therefore one must consider other factors. A participant's continued professional development and further education may be more important in determining HSPM awareness compared to more general factors such as age and years of practice. On analysis of the entire sample including paediatric dentists and other specialties, unsurprisingly all paediatric dentists had awareness of HSPM and there was a significant difference between the groups (p=.006).

Most respondents either noticed the condition monthly or yearly. These findings differ from a Saudi Arabian study where the majority of respondents noticed HSPM on a weekly basis (Meer et al., 2020). Several MIH perception studies have asked its participants how frequently they notice HSPM defects in relation to MIH. Consensus has been reached by most studies in that participants feel HSPM is less commonly observed when compared to MIH (Ghanim et al., 2011, Alanzi et al., 2018, Serna-Muñoz et al., 2020). No statistically significant association was found to exist between frequency of noticing HSPM and participants age or place of work. However, those with ≥15 years of experience were significantly more likely to report frequent HSPM compared to those with between 5-15 years of experience (p=.012). Those with a greater number of years of experience may be more familiar with the clinical presentation of HSPM and therefore may be more competent in diagnosing this condition.

Most respondents perceived the prevalence of HSPM to be between 5-10% (36.14%) or < 5% (32.67%). It is important to note that this finding represents the perceptions of dentists rather than the actual prevalence. In Europe, the

reported prevalence of HSPM varies with a range of between 0-14.5% which is line with the perceived prevalence reported in this study (Elfrink et al., 2008, Negre-Barber et al., 2016, Elfrink et al., 2012).

52.97% reported seeing yellow/brown demarcated opacities. This is similar to the findings by Wall and Leith (2020) where Irish dentists were questioned regarding the severity of MIH defects and 57% encountered yellow-brown demarcated opacites most frequently (Wall and Leith, 2020). This finding provides some insight into what may represent the most common clinical presentation of HSPM in Ireland. However, caution should be taken in interpreting this result as it reflects only perceived observation. Contrastingly, this finding differs from the study by Meer et al. (2020) where white demarcated opacities were the most commonly observed form of the defect accounting for 48% of the respondents (Meer et al., 2020).

70.79% of respondents reported being either very or extremely confident in diagnosing HSPM. The confidence level in this study was lower when compared to the confidence reported by Irish dentists in MIH diagnosis. In Wall and Leith's study, 91% of respondents felt confident in diagnosing MIH (Wall and Leith, 2020). MIH is a well-established condition when compared to HSPM and therefore practitioners may feel more comfortable in its diagnosis. Other studies have demonstrated lower confidence levels in HSPM diagnosis (Meer et al., 2020, Humphreys et al., 2021). Meer et al. (2020) reported that only 51% of their respondents felt confident in diagnosis. The majority of this sample had under 5 years of experience which may have influenced this result. Humphreys et al. (2021) reported that general dentists were more likely to misdiagnose HSPM in comparison to MIH (Humphreys et al., 2021).

No significant association was found to exist between age, years of practice or place of work and confidence in HSPM diagnosis. This result was surprising as one may have believed years of practice to have some effect on confidence level. In the full sample including general dentists and specialists, a statistically significant relationship was found with paediatric specialists being 6.5 times more confident in HSPM diagnosis when compared to general dentists (p=<.0001; OR= 6.53). This finding is unsurprising considering children affected by DDE including HSPM are commonly referred to paediatric specialists. Studies investigating perceived confidence in MIH diagnosis have reported similar findings with improved confidence in specialty groups (Ghanim et al., 2011, Kalkani et al., 2016)

The vast majority of dentists (95.54%) agreed that the caries pattern caused by HSPM is different to the classical caries pattern. This is in agreement with another Irish study where 98% of respondents acknowledged the difference between MIH breakdown resulting in atypical caries and conventional caries (Wall and Leith, 2020).

Material choices for HSPM affected teeth varied amongst respondents with the most popular materials being conventional GI (54.95%) and RMGI (40.59%) (where multiple options were available). Meer et al. (2020) reported a similar finding in their study where GI cement was the most popular choice for treatment of HSPM affected teeth (46%) (Meer et al., 2020). GI placement is less technique sensitive and displays forgiving properties in the presence of moisture and can prevent caries lesion progression but not PEB in MIH molars (Schraverus et al., 2021). GIC offers an interim solution to protect affected SPMs however due its poorer mechanical properties in load bearing areas it is

not a long term option. Poor survival rates of GIC have been demonstrated for MIH affected molars with a recent systematic review reporting an annual failure rate of 12% (Elhennawy and Schwendicke, 2016).

A smaller number of respondents reported use of composite resin (29.21%). In MIH, composite resin has been advocated as a favourable choice due to its high success rates (Lygidakis et al., 2003, Mejare et al., 2005, Elhennawy and Schwendicke, 2016). However, successful outcomes are heavily determined by conditions of placement which are sometimes not ideal in the younger child. While not directly related to HSPM, single surface composite restorations have demonstrated favourable outcomes in the management of non hypomineralised carious primary molars (Ribeiro et al., 2018, Alves dos Santos et al., 2010, Guelmann et al., 2005). In MIH, the use of composite has been supported in the restoration of milder defects with one to two surface involvement (Lygidakis et al., 2010).

29.70% of respondents selected SSCs as a commonly used material. In the study by Meer et al. (2020), the use of SSCs for HSPM management was lower (11% of respondents selected this material) (Meer et al., 2020). In MIH, full coverage preformed crowns have been recommended for FPMs affected by moderate to severe PEB (Fayle, 2003). In HSPM, a similar treatment approach has been adopted and preformed crowns have been advocated in teeth with DDE where insufficient tooth structure remains for placement of an intra-coronal restoration (Kindelan et al., 2008). In the younger child, placement of a preformed crown conventionally with the use of local anaesthesia and tooth preparation may not be feasible. The Hall technique has demonstrated favourable clinical and radiographic outcomes for HSPM affected teeth

(Declerck and Mampay, 2021). Eight respondents listed ‘other materials’ in their restorative material selection. Popular other choices included the use of topical fluorides including fluoride varnish and silver diamine fluoride (SDF). Three respondents included amalgam as a restorative choice. The use of amalgam has been heavily restricted (Minamata Convention 2018) and advised against in the treatment of primary teeth, except when deemed strictly necessary by the dentist based on the specific dental needs of the patient (Irish Dental Association., 2017). Amalgam has shown high failure rates in atypically shaped MIH cavity preparations and therefore cannot be recommended as a favourable restorative material (IAPD., 2020, Elhennawy and Schwendicke, 2016).

In question 12, 75.45% of respondents reported they would be comfortable providing restorative care. The case involved a five year old child with all four SPMs affected by moderate HSPM with PEB. This finding is comparable to the study by Meer et al. (2020) where 70% of participants reported feeling confident in HSPM management (Meer et al., 2020). A statistically significant association was found between participant’s place of work and comfort in management with those working exclusively in private practice more comfortable in HSPM management when compared to the other subgroup (p=.030). This was an interesting result as one may have perceived those working in the other groups which included public sector to be more comfortable as they tend to see mainly children. The result from this study highlights the competency private practitioners possess in treating HSPM. In Ireland, the principal route of accessing paediatric dental care is private. Private practitioners are not limited in terms of treatment provision and may be more equipped in dealing with restorative management as they are more likely to see and actively treat these primary molar defects compared to those in the public sector.

For those who were not comfortable in managing HSPM, 91.66% would refer to a paediatric specialist. In Ireland, paediatric dentists are a commonly chosen referral pathway for those dentists uncomfortable in the management of DDE or in the dental management of young children.

Where multiple answers were available for selection, most cited barriers to care were the child's behaviour and young age. This is not surprising considering the clinical scenario which involved a very young child. Overall, there is limited comparable evidence in the literature regarding HSPM and this area. A recent Irish MIH study demonstrated a similar result to our findings where 81% of respondents cited the child's behaviour as a potential barrier in MIH management (Wall and Leith, 2020). In addition, dental treatment that needed a long time to be accomplished was also reported by several respondents (20.32%) which may also be related to behavioural factors.

A total of 33.47% of respondents cited repeated failure of restorations as a barrier to care. This may be because GI restorative materials were the most popular choice amongst this sample in restoring HSPM. Insufficient training to treat children with this condition was reported by 23.90%. This finding highlights a need for clear management guidelines and continued professional development including hands on, practical training. Difficulty deciding how to restore teeth and what materials to use represented 15.14% of respondents concerns in HSPM management. This challenge may relate to several factors such as the clinical presentation of HSPM (intra-coronal restorations may not be suitable for restoring more extensive defects) and dentist's access to certain restorative materials (practices may not stock restorative materials such as SSCs).

7.97% of respondents reported ‘other reasons’ as barriers to care. Common themes included financial barriers, place of work and parental attitude/ acceptance. From a financial perspective, respondents cited that parents may be unable to afford the cost of treatment, which maybe be related to the fact that the majority of respondents were dentists in private practice where fees are applicable. Other respondents mentioned their place of work as a barrier to care, in particular limited resources available within the community dental service. Other concerns included the aesthetic appearance of SSC and how some parents were unaccepting of this material. On the contrary, several studies have shown a high level of child and parental acceptability for SSC (Bell et al., 2010, Santamaria et al., 2015).

Across the clinical scenarios, there was a disparity in the general management of HSPM. Regarding Case B, non-operative approaches were commonly chosen by respondents such as fluoride varnish and GI fissure sealant. Best practice guidelines for MIH support the use of conservative measures such as prevention and fissure sealant application in the management of milder defects (Lygidakis et al., 2010). In a recently conducted Irish study, similar options were chosen by dentists in the management of a moderately hypomineralised FPM with no breakdown with respondents favouring fissure sealants and fluoride varnish (Wall and Leith, 2020).

In Case C, popular management options included restoring this tooth using the Hall technique (45.02%) and also placement of a GI restoration (38.24). It is an interesting finding as the use of crowns amongst general dentists has not always been the most favoured approach with a preferred tendency towards intracoronal restorations (McKnight-Hanes et al., 1991, Tran and Messer,

2004). On a national level, online webinars and publications discussing the Hall technique have increased recently which may have led to more dentists being aware of this approach. A similar result was found in Case E where 41.3% of respondents selected the Hall technique representing the most popular option. Full coverage restorations have been advocated for severe presentations of MIH and also represent a suitable approach for broken down HSPMs (Lygidakis et al., 2010). Furthermore, the ease of application that this technique may offer is favourable when we consider the potential barriers cited in our study. Difficult behaviour and young age were the most commonly selected barriers to care and therefore the Hall technique may provide a suitable alternative to the more traditional treatments often requiring local anaesthetic and tooth preparation (Nazzal and Duggal, 2018).

Regarding case scenario D, preventive options including fluoride varnish and no treatment with preventive advice were the most commonly chosen options. In this case, the area of PEB was localised to the buccal surface. There is some evidence to suggest that the extension of the defect rather than the defect severity is more significant when it comes to caries risk (Owen et al., 2018). In this case, a severe form of HSPM was present however it was of a mild extension (<1/3 of surface area affected) potentially reducing the likelihood of caries developing. The child's age may also have been considered by participants in their decision making. At age 8, the SPM would have been present in the mouth for several years. It is therefore reasonable to assume that this tooth is relatively stable with the potential for defect progression low.

Only 58% of respondents were aware that HSPM was predictive of MIH highlighting a potential gap in knowledge. Following adjusted analysis, years in

practice and place of work remained significant. Participants who had less than 5 years of experience were less likely to have awareness that HSPM was predictive of MIH when compared to those with ≥ 15 years of experience (p=.030). This finding is surprising as one may have thought that those more recently graduated would be knowledgeable in this emerging area. Those who worked in private practice exclusively were more likely to be aware of this predictive relationship when compared to those working in other groups such as the public sector, university, or a combination (p= .006). Those in private practice may have a better opportunity to follow up their patients and observe this relationship over time.

The results of this study must be viewed in the context of its limitations. The estimated response rate was low (16.95%), although this is characteristic of online surveys. However, the number of respondents in this study was similar, (if not superior in some cases) to several other studies investigating perception and clinical management of MIH. The self-reported nature of the questionnaire may have resulted in a degree of response bias impacting the validity of these results. Respondents may have wished to provide socially desirable answers and therefore may not have answered honestly. For example, in the clinical scenario questions, respondents may have chosen what they perceived to be best practice management instead of what they would choose in everyday circumstances. Furthermore, as with any survey, only the most interested clinicians will complete it also leading to potential response bias. The true results for general dentists across Ireland may be different to the results found in this study.

4.6 Conclusions

HSPM is well-recognised by general dentists in the Republic of Ireland with a high level of confidence in diagnosis reported. Those who worked exclusively in private practice were more comfortable in HSPM management when compared to the other groups. Dentists with more than 15 years of experience and those who worked in private practice were more aware of the predictive nature of HSPM for MIH. Variation existed in the clinical management of HSPM which is unsurprising considering the broad range of clinical HSPM presentations and the individual nature of each patient. Development of evidence based treatment guidelines for HSPM would help dentists in their clinical decision making and provide clarity in what can be a challenging part of everyday practice.

5 Overall conclusions and future directions

The findings of this thesis builds on our existing knowledge of HSPM in several ways.

Firstly, by determining the pooled prevalence of HSPM worldwide (6.8% on a child level and 4.1% on a tooth level) we are given an insight into the burden of this disease worldwide. Prior to conducting this research, data on HSPM prevalence was disconnected with a focus on individual countries and populations. This meta-analysis has facilitated the synthesis of HSPM prevalence data worldwide and allows us to consider both pooled prevalence and regional variation between the included studies. The relationship between the diagnostic criteria and the reported prevalence was also explored with no effect observed. This finding is a reflection of the fact that demarcated opacities represented the most common presentation of HSPM however one must consider that the more severe forms of HSPM were not accounted for in the DDE/mDDE indices and therefore this result has its limitations. The role of other factors such as the characteristics of the population being studied must be considered when attempting to understand the broad variation across the studies.

Secondly, the prevalence of HSPM in one Dublin school was determined with 38.3% of children affected. Creamy-white demarcated opacities of mild extent represented the most common clinical presentation. This study is the first to investigate HSPM prevalence in Irish children and its strength lies in the dissemination of preliminary but new data. While limited by its lack of

representativeness, this data is of value to all stakeholders involved in the allocation and provision of paediatric dental care in Ireland.

Finally, our questionnaire study has contributed to our understanding of how Irish dentists actually perceive and treat this condition. Our results demonstrated an overall high awareness and confidence in diagnosis amongst participants. Those working exclusively in private practice were more comfortable in management when compared to other groups. While great variation existed in the treatment options, respondents mostly favoured conservative, biological based options for the management of HSPM.

Regarding future directions, it is hoped that by conducting this systematic review, future researchers will be guided in terms of appropriate study design and also in the adherence to a standardised diagnostic criterion. Our study highlights the importance of selection and outcome criteria when designing a prevalence study. Future prevalence studies should include all aspects of HSPM presentation including the more severe forms of the defect. Prospective based cohort studies analysing defect progression over time would also be of value as it has implications for treatment planning and clinical management of these teeth.

Regarding Irish HSPM prevalence, further data collection in a wider section of the Irish population is required in order to determine true defect prevalence. Data collection from different parts of Dublin but also from different counties would be of value to provide a broader view of HSPM prevalence and also in showing potential regional variation.

Future questionnaire based studies evaluating participants education and continued professional development would be of value in exploring the influence of these factors on HSPM management.

6 References

AAPD 2014. Policy of Early Childhood Caries (ECC): classification, consequences and preventive strategies. *Pediatr Dent,* 37**,** 50-52.

AINE, L., BACKSTROM, M. C., MAKI, R., KUUSELA, A. L., KOIVISTO, A. M., IKONEN, R. S. & MAKI, M. 2000. Enamel defects in primary and permanent teeth of children born prematurely. *J Oral Pathol Med,* 29**,** 403-9.

ALALUUSUA, S. 2010. Aetiology of Molar-Incisor Hypomineralisation: A systematic review. *Eur Arch Paediatr Dent,* 11**,** 53-8.

ALANZI, A., FARIDOUN, A., KAVVADIA, K. & GHANIM, A. 2018. Dentists' perception, knowledge, and clinical management of molar-incisor-hypomineralisation in Kuwait: A cross-sectional study. *BMC Oral Health,* 18(1):34.

ALLAZZAM, S. M., ALAKI, S. M. & EL MELIGY, O. A. S. 2014. Molar incisor hypomineralization, prevalence, and etiology. *International journal of dentistry,* 2014**,** 234508.

ALVES DOS SANTOS, M. P., LUIZ, R. R. & MAIA, L. C. 2010. Randomised trial of resin-based restorations in Class I and Class II beveled preparations in primary molars: 48-month results. *J Dent,* 38**,** 451-9.

AMERICAN ACADEMY OF PEDIATRICS & GYNECOLOGISTS, A. C. O. O. A. 2015. The Apgar Score. *Pediatrics,* 136**,** 819-22.

BACCETTI, T. 1998. A controlled study of associated dental anomalies. *Angle Orthod,* 68**,** 267-74.

BALMER, R., TOUMBA, J., GODSON, J. & DUGGAL, M. 2012. The prevalence of molar incisor hypomineralisation in Northern England and its relationship to socioeconomic status and water fluoridation. *Int J Paediatr Dent,* 22**,** 250-7.

BEAUCHAMP, J., CAUFIELD, P. W., CRALL, J. J., DONLY, K., FEIGAL, R., GOOCH, B., ISMAIL, A., KOHN, W., SIEGAL, M. & SIMONSEN, R. 2008. Evidence-based clinical recommendations for the use of pit-and-fissure sealants: a report of the American Dental Association Council on Scientific Affairs. *J Am Dent Assoc,* 139**,** 257-68.

BECK, S., WOJDYLA, D., SAY, L., BETRAN, A. P., MERIALDI, M., REQUEJO, J. H., RUBENS, C., MENON, R. & VAN LOOK, P. F. 2010. The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity. *Bull World Health Organ,* 88**,** 31-8.

BEENTJES, V. E., WEERHEIJM, K. L. & GROEN, H. J. 2002. Factors involved in the aetiology of molar-incisor hypomineralisation (MIH). *Eur J Paediatr Dent,* 3**,** 9-13.

BELL, S., MORGAN, A., MARSHMAN, Z. & RODD, H. 2010. Child and parental acceptance of preformed metal crowns. *European archives of paediatric dentistry : official journal of the European Academy of Paediatric Dentistry,* 11**,** 218-24.

BROADBENT, J., THOMSON, W. & WILLIAMS, S. 2005. Does Caries in Primary Teeth Predict Enamel Defects in Permanent Teeth? A Longitudinal Study. *Journal of dental research,* 84**,** 260-4.

BUTLER, P. M. 1967. Comparison of the development of the second deciduous molar and first permanent molar in man. *Arch Oral Biol,* 12**,** 1245-60.

CERQUEIRA SILVA, R. N., LIMA, C. C. B., BENDO, C. B., LIMA, L. R. S., DE MOURA, M. S., MOURA, L. & LIMA, M. D. M. 2021. Impact of hypomineralised second primary molar on preschoolers' oral health-related quality of life-A hierarchical approach. *Int J Paediatr Dent*. doi: 10.1111/ipd.12844. Online ahead of print.

CHAVES, A. M., ROSENBLATT, A. & OLIVEIRA, O. F. 2007. Enamel defects and its relation to life course events in primary dentition of Brazilian children: a longitudinal study. *Community Dent Health,* 24**,** 31-6.

CHISINI, L. A., COLLARES, K., CADEMARTORI, M. G., DE OLIVEIRA, L. J. C., CONDE, M. C. M., DEMARCO, F. F. & CORREA, M. B. 2018. Restorations in primary teeth: a systematic review on survival and reasons for failures. *Int J Paediatr Dent,* 28**,** 123-139.

CHOWDHURY, I. G. & BROMAGE, T. G. 2000. Effects of fetal exposure to nicotine on dental development of the laboratory rat. *Anat Rec,* 258**,** 397-405.

CLARKSON, J. 1989. Review of terminology, classifications, and indices of developmental defects of enamel. *Adv Dent Res,* 3**,** 104-9.

CLARKSON, J. & O'MULLANE, D. 1989. A modified DDE Index for use in epidemiological studies of enamel defects. *J Dent Res,* 68**,** 445-50.

CLINCH, L. & HEALY, M. 1960. A longitudinal study of the results of premature extraction of deciduous teeth between 3-4 and 13-14 years of age. *American Journal of Orthodontics,* 46**,** 862-864.

CORRÊA-FARIA, P., MARTINS-JÚNIOR, P. A., VIEIRA-ANDRADE, R. G., OLIVEIRA-FERREIRA, F., MARQUES, L. S. & RAMOS-JORGE, M. L. 2013. Developmental defects of enamel in primary teeth: Prevalence and associated factors. *International Journal of Paediatric Dentistry,* 23**,** 173-179.

COSTA-SILVA, C. M., PAULA, J. S. D., AMBROSANO, G. M. B. & MIALHE, F. L. 2013. Influence of deciduous molar hypomineralization on the development of molar-incisor hypomineralizarion. *Brazilian Journal of Oral Sciences,* 12**,** 335-338.

COSTA, F. S., SILVEIRA, E. R., PINTO, G. S., NASCIMENTO, G. G., THOMSON, W. M. & DEMARCO, F. F. 2017. Developmental defects of enamel and dental caries in the primary dentition: A systematic review and meta-analysis. *J Dent,* 60**,** 1-7.

CRAWFORD, P. J. M., ALDRED, M. & BLOCH-ZUPAN, A. 2007. Amelogenesis imperfecta. *Orphanet Journal of Rare Diseases,* 2**,** 17.

CROMBIE, F. A., MANTON, D. J., PALAMARA, J. E., ZALIZNIAK, I., COCHRANE, N. J. & REYNOLDS, E. C. 2013. Characterisation of developmentally hypomineralised human enamel. *J Dent,* 41**,** 611-8.

CROMBIE, F. A., MANTON, D. J., WEERHEIJM, K. L. & KILPATRICK, N. M. 2008. Molar incisor hypomineralization: A survey of members of the Australian and New Zealand society of paediatric dentistry. *Australian Dental Journal,* 53**,** 160-166.

DA SILVA FIGUEIREDO SE, M. J., RIBEIRO, A. P. D., DOS SANTOS-PINTO, L. A. M., DE CASSIA LOIOLA CORDEIRO, R., CABRAL, R. N. & LEAL, S. C. 2017. Are Hypomineralized Primary Molars and Canines Associated with Molar-Incisor Hypomineralization? *Pediatr Dent,* 39**,** 445-449.

DE AMORIM, R. G., FRENCKEN, J. E., RAGGIO, D. P., CHEN, X., HU, X. & LEAL, S. C. 2018. Survival percentages of atraumatic restorative treatment (ART) restorations and sealants in posterior teeth: an updated systematic review and meta-analysis. *Clin Oral Investig,* 22**,** 2703-2725.

DE AMORIM, R. G., LEAL, S. C. & FRENCKEN, J. E. 2012. Survival of atraumatic restorative treatment (ART) sealants and restorations: a meta-analysis. *Clinical Oral Investigations,* 16**,** 429-441.

DE LIMA MDE, D., ANDRADE, M. J., DANTAS-NETA, N. B., ANDRADE, N. S., TEIXEIRA, R. J., DE MOURA, M. S. & DE DEUS MOURA LDE, F. 2015. Epidemiologic Study of Molar-incisor Hypomineralization in Schoolchildren in North-eastern Brazil. *Pediatr Dent,* 37**,** 513-9.

DECLERCK, D. & MAMPAY, E. 2021. Non-invasive treatment approach for hypomineralised second primary molars using preformed metal crowns: results after 1-year follow-up. *Eur Arch Paediatr Dent*. 22(3), 479-490.

DEMARCO, F. F., CORREA, M. B., CENCI, M. S., MORAES, R. R. & OPDAM, N. J. 2012. Longevity of posterior composite restorations: not only a matter of materials. *Dent Mater,* 28**,** 87-101.

DONG, Q., WU, H., DONG, G., LOU, B., YANG, L. & ZHANG, L. 2011. The morphology and mineralization of dental hard tissue in the offspring of passive smoking rats. *Arch Oral Biol,* 56**,** 1005-13.

ELCOCK, C., SMITH, R. N., SIMPSON, J., ABDELLATIF, A., BACKMAN, B. & BROOK, A. H. 2006. Comparison of methods for measurement of hypoplastic lesions. *Eur J Oral Sci,* 114 Suppl 1**,** 365-9; discussion 375-6, 382-3.

ELFRINK, M. 2012. Deciduous molar hypomineralisation, its nature and nurture. *Available at: https://www.researchgate.net/publication/254873734_Deciduous_molar_hypomineralisation_its_nature_and_nurture.*

ELFRINK, M., KALIN, K., VAN RUIJVEN, L., TEN CATE, J. & VEERKAMP, J. 2016. MicroCT study on the enamel mineral density of primary molars. *European Journal of Paediatric Dentistry,* 17**,** 60-64.

ELFRINK, M. E., GHANIM, A., MANTON, D. J. & WEERHEIJM, K. L. 2015. Standardised studies on Molar Incisor Hypomineralisation (MIH) and Hypomineralised Second Primary Molars (HSPM): a need. *Eur Arch Paediatr Dent,* 16**,** 247-55.

ELFRINK, M. E., MOLL, H. A., KIEFTE-DE JONG, J. C., EL MARROUN, H., JADDOE, V. W., HOFMAN, A., STRICKER, B. H., TEN CATE, J. M. & VEERKAMP, J. S. 2013. Is maternal use of medicines during pregnancy associated with deciduous molar hypomineralisation in the offspring? A prospective, population-based study. *Drug Saf,* 36**,** 627-33.

ELFRINK, M. E., MOLL, H. A., KIEFTE-DE JONG, J. C., JADDOE, V. W., HOFMAN, A., TEN CATE, J. M. & VEERKAMP, J. S. 2014. Pre- and postnatal determinants of deciduous molar hypomineralisation in 6-year-old children. The generation R study. *PLoS One,* 9**,** e91057.

ELFRINK, M. E., SCHULLER, A. A., VEERKAMP, J. S., POORTERMAN, J. H., MOLL, H. A. & TEN CATE, B. J. 2010. Factors increasing the caries risk of second primary molars in 5-year-old Dutch children. *Int J Paediatr Dent,* 20**,** 151-7.

ELFRINK, M. E., SCHULLER, A. A., WEERHEIJM, K. L. & VEERKAMP, J. S. 2008. Hypomineralized second primary molars: prevalence data in Dutch 5-year-olds. *Caries Res,* 42**,** 282-5.

ELFRINK, M. E., TEN CATE, J. M., JADDOE, V. W., HOFMAN, A., MOLL, H. A. & VEERKAMP, J. S. 2012. Deciduous molar hypomineralization and molar incisor hypomineralization. *J Dent Res,* 91**,** 551-5.

ELFRINK, M. E., VEERKAMP, J. S., AARTMAN, I. H., MOLL, H. A. & TEN CATE, J. M. 2009. Validity of scoring caries and primary molar hypomineralization (DMH) on intraoral photographs. *Eur Arch Paediatr Dent,* 10 Suppl 1**,** 5-10.

ELFRINK, M. E. C., VEERKAMP, J. S. J. & KALSBEEK, H. 2006. Caries pattern in primary molars in Dutch 5-year-old children. *European Archives of Paediatric Dentistry,* 7**,** 236-240.

ELGER, W., ILLGE, C., KIESS, W., KORNER, A., KRATZSCH, J., SCHROCK, A. & HIRSCH, C. 2020. Relationship between deciduous molar hypomineralisation and parameters of bone metabolism in preschool children. *Int Dent J***,** 1-5.

ELHENNAWY, K. & SCHWENDICKE, F. 2016. Managing molar-incisor hypomineralization: A systematic review. *J Dent,* 55**,** 16-24.

FAGRELL, T. G., DIETZ, W., JALEVIK, B. & NOREN, J. G. 2010. Chemical, mechanical and morphological properties of hypomineralized enamel of permanent first molars. *Acta Odontol Scand,* 68**,** 215-22.

FAGRELL, T. G., LINGSTROM, P., OLSSON, S., STEINIGER, F. & NOREN, J. G. 2008. Bacterial invasion of dentinal tubules beneath apparently intact but hypomineralized enamel in molar teeth with molar incisor hypomineralization. *Int J Paediatr Dent,* 18**,** 333-40.

FARAH, R. A., MONK, B. C., SWAIN, M. V. & DRUMMOND, B. K. 2010. Protein content of molar-incisor hypomineralisation enamel. *J Dent,* 38**,** 591-6.

FARSI, N. 2010. Developmental enamel defects and their association with dental caries in preschoolers in Jeddah, Saudi Arabia. *Oral Health and Preventive Dentistry,* 8**,** 85-92.

FATTURI, A. L., WAMBIER, L. M., CHIBINSKI, A. C., ASSUNCAO, L., BRANCHER, J. A., REIS, A. & SOUZA, J. F. 2019. A systematic review and meta-analysis of systemic exposure associated with molar incisor hypomineralization. *Community Dent Oral Epidemiol,* 47**,** 407-415.

FAYLE, S. A. 2003. Molar incisor hypomineralisation: restorative management. *Eur J Paediatr Dent,* 4**,** 121-6.

FDI. 1982. Commission on Oral Health, Research and Epidemiology. An epidemiological index of developmental defects of dental enamel (DDE Index). *Int Dent J,* 32**,** 159-67.

FDI. 1992. Commision on Oral Health, Research and Epidemiology. A review of the developmental defects of enamel index (DDE Index). Report of an FDI Working Group. *Int Dent J,* 42**,** 411-26.

FEARNE, J. M., BRYAN, E. M., ELLIMAN, A. M., BROOK, A. H. & WILLIAMS, D. M. 1990. Enamel defects in the primary dentition of children born weighing less than 2000 g. *Br Dent J,* 168**,** 433-7.

FEARNE, J. M., ELLIOTT, J. C., WONG, F. S., DAVIS, G. R., BOYDE, A. & JONES, S. J. 1994. Deciduous enamel defects in low-birth-weight children: correlated X-ray microtomographic and backscattered electron imaging study of hypoplasia and hypomineralization. *Anat Embryol (Berl),* 189**,** 375-81.

FERNANDES, I. C., FORTE, F. D. S. & SAMPAIO, F. C. 2020. Molar-incisor hypomineralization (MIH), dental fluorosis, and caries in rural areas with different fluoride levels in the drinking water. *International Journal of Paediatric Dentistry*, 31(4), 475-482.

FERRINI, F. R., MARBA, S. T. & GAVIAO, M. B. 2008. Oral conditions in very low and extremely low birth weight children. *J Dent Child (Chic),* 75**,** 235-42.

FOLAYAN, M. O., EL TANTAWI, M., OGINNI, A. B., ALADE, M., ADENIYI, A. & FINLAYSON, T. L. 2020. Malnutrition, enamel defects, and early childhood caries in preschool children in a sub-urban Nigeria population. *PLoS ONE,* 15**,** 1-14.

GAMBETTA-TESSINI, K., MARINO, R., GHANIM, A., CALACHE, H. & MANTON, D. J. 2018. Carious lesion severity and demarcated hypomineralized lesions of tooth enamel in schoolchildren from Melbourne, Australia. *Aust Dent J,* 63**,** 365-373.

GAMBETTA-TESSINI, K., MARINO, R., GHANIM, A., CALACHE, H. & MANTON, D. J. 2019. The impact of MIH/HSPM on the carious lesion severity of schoolchildren from Talca, Chile. *Eur Arch Paediatr Dent,* 20**,** 417-423.

GAMBETTA-TESSINI, K., MARIÑO, R., GHANIM, A., CALACHE, H. & MANTON, D. J. 2016. Knowledge, experience and perceptions regarding Molar-Incisor Hypomineralisation (MIH) amongst Australian and Chilean public oral health care practitioners. *BMC Oral Health,* 16(1), 75.

GANDHI, S., CRAWFORD, P. & SHELLIS, P. 2012. The use of a 'bleach-etch-seal' deproteinization technique on MIH affected enamel. *Int J Paediatr Dent,* 22**,** 427-34.

GAROT, E., DENIS, A., DELBOS, Y., MANTON, D., SILVA, M. & ROUAS, P. 2018. Are hypomineralised lesions on second primary molars (HSPM) a predictive sign of molar incisor hypomineralisation (MIH)? A systematic review and a meta-analysis. *J Dent,* 72**,** 8-13.

GHANIM, A., ELFRINK, M., WEERHEIJM, K., MARIÑO, R. & MANTON, D. 2015. A practical method for use in epidemiological studies on enamel hypomineralisation. *European archives of paediatric dentistry : official journal of the European Academy of Paediatric Dentistry,* 16**,** 235-246.

GHANIM, A., MANTON, D., MARINO, R., MORGAN, M. & BAILEY, D. 2013. Prevalence of demarcated hypomineralisation defects in second primary molars in Iraqi children. *Int J Paediatr Dent,* 23**,** 48-55.

GHANIM, A., MARINO, R. & MANTON, D. J. 2019. Validity and reproducibility testing of the Molar Incisor Hypomineralisation (MIH) Index. *Int J Paediatr Dent,* 29**,** 6-13.

GHANIM, A., MORGAN, M., MARIÑO, R., MANTON, D. & BAILEY, D. 2011. Perception of Molar-Incisor Hypomineralisation (MIH) by Iraqi Dental Academics. *International Journal of Paediatric Dentistry,* 21**,** 261-270.

GHANIM, A., SILVA, M. J., ELFRINK, M. E. C., LYGIDAKIS, N. A., MARINO, R. J., WEERHEIJM, K. L. & MANTON, D. J. 2017. Molar incisor hypomineralisation (MIH) training manual for clinical field surveys and practice. *Eur Arch Paediatr Dent,* 18**,** 225-242.

GHANIM, A. M., MORGAN, M. V., MARINO, R. J., BAILEY, D. L. & MANTON, D. J. 2012. Risk factors of hypomineralised second primary molars in a group of Iraqi schoolchildren. *Eur Arch Paediatr Dent,* 13**,** 111-8.

GIZANI, S., VINCKIER, F. & DECLERCK, D. 1999. Caries pattern and oral health habits in 2- to 6-year-old children exhibiting differing levels of caries. *Clin Oral Investig,* 3**,** 35-40.

GOYAL, A., DHAREULA, A., GAUBA, K. & BHATIA, S. K. 2019. Prevalence, defect characteristics and distribution of other phenotypes in 3- to 6-year-old children affected with Hypomineralised Second Primary Molars. *Eur Arch Paediatr Dent,* 20**,** 585-593.

GUELMANN, M., MCILWAIN, M. F. & PRIMOSCH, R. E. 2005. Radiographic assessment of primary molar pulpotomies restored with resin-based materials. *Pediatr Dent,* 27**,** 24-7.

HALAL, F. & RASLAN, N. 2020. Prevalence of hypomineralised second primary molars (HSPM) in Syrian preschool children. *European Archives of Paediatric Dentistry*, 21(6), 711-717.

HEALTH SERVICE EXECUTIVE, UNIVERSITY COLLEGE CORK & HEALTH RESEARCH BOARD. 2009. Strategies to prevent dental caries in children and adolescents: Evidence-based guidance on identifying high caries risk children and developing preventive strategies for high caries risk children in Ireland. *Available at: https://www.dentalhealth.ie/assets/files/pdf/full_strategies_finaleb.pdf.*

HEINTZE, S. D. & ROUSSON, V. 2012. Clinical effectiveness of direct class II restorations - a meta-analysis. *J Adhes Dent,* 14**,** 407-31.

HERNANDEZ, M., BOJ, J., ESPASA, E., PLANELLS, P. & PERETZ, B. 2018. Molar-Incisor Hypomineralization: Positive Correlation with Atopic Dermatitis and Food Allergies. *J Clin Pediatr Dent,* 42**,** 344-348.

HERZOG, R., ÁLVAREZ-PASQUIN, M. J., DÍAZ, C., DEL BARRIO, J. L., ESTRADA, J. M. & GIL, Á. 2013. Are healthcare workers' intentions to vaccinate related to their knowledge, beliefs and attitudes? a systematic review. *BMC Public Health,* 13**,** 1-17.

HOLLAND, T. J. & CROWLEY, M. J. 1982. Detailed examination of caries progression in 4-year-old children in a non-fluoridated area in Ireland. *Community Dent Oral Epidemiol,* 10**,** 144-7.

HOLMGREN, C. J., LO, E. C. & HU, D. 2013. Glass ionomer ART sealants in Chinese school children-6-year results. *J Dent,* 41**,** 764-70.

HOLMGREN, C. J., LO, E. C., HU, D. & WAN, H. 2000. ART restorations and sealants placed in Chinese school children--results after three years. *Community Dent Oral Epidemiol,* 28**,** 314-20.

HOLT, R. D. 1995. The pattern of caries in a group of 5-year-old children and in the same cohort at 9 years of age. *Community Dent Health,* 12**,** 93-9.

HONG, M., VUONG, C., HERZOG, K., NG, M. W. & SULYANTO, R. 2019. Sealed primary molars are less likely to develop caries. *J Am Dent Assoc,* 150**,** 641-648.

HUMPHREYS, J., JARAD, F. & ALBADRI, S. 2021. Management of molar-incisor hypomineralisation by general dental practitioners - part one: diagnosis. *Br Dent J*. *Available at: https://doi.org/10.1038/s41415-021-2735-3.*

IAPD. 2020. IAPD Foundational Articles and Consensus Recommendations. Management of Molar Incisor Hypomineralization 2020. Available at: https://iapdworld.org/wp-content/uploads/2020/04/07_Management-of-Molar-Incisor-Hypomineralization.pdf.

INNES, N. P., EVANS, D. J. & STIRRUPS, D. R. 2007. The Hall Technique; a randomized controlled clinical trial of a novel method of managing carious primary molars in general dental practice: acceptability of the technique and outcomes at 23 months. *BMC Oral Health,* 7**,** 18.

INNES, N. P., EVANS, D. J. & STIRRUPS, D. R. 2011. Sealing caries in primary molars: randomized control trial, 5-year results. *J Dent Res,* 90**,** 1405-10.

INNES, N. P. T., RICKETTS, D., CHONG, L. Y., KEIGHTLEY, A. J., LAMONT, T. & SANTAMARIA, R. M. 2015. Preformed crowns for decayed primary molar teeth. *Cochrane Database of*

Systematic Reviews, 2015. *Available at: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD005512.pub3/full.*

IRISH DENTAL ASSOCIATION. 2017. The Minamata Convention on Mercury, the EU regulation and dental amalgam and you! Available at: https://www.dentist.ie/_fileupload/members/IDAGuidanceforDentistsMinamataRegulations.pdf.

JACOBSEN, P. E., HAUBEK, D., HENRIKSEN, T. B., OSTERGAARD, J. R. & POULSEN, S. 2014. Developmental enamel defects in children born preterm: a systematic review. *Eur J Oral Sci,* 122**,** 7-14.

JADDOE, V. W., BAKKER, R., HOFMAN, A., MACKENBACH, J. P., MOLL, H. A., STEEGERS, E. A. & WITTEMAN, J. C. 2007. Moderate alcohol consumption during pregnancy and the risk of low birth weight and preterm birth. The generation R study. *Ann Epidemiol,* 17**,** 834-40.

JADDOE, V. W. V., VAN DUIJN, C. M., VAN DER HEIJDEN, A. J., MACKENBACH, J. P., MOLL, H. A., STEEGERS, E. A. P., TIEMEIER, H., UITTERLINDEN, A. G., VERHULST, F. C. & HOFMAN, A. 2010. The Generation R Study: design and cohort update 2010. *European Journal of Epidemiology,* 25**,** 823-841.

JALEVIK, B. & KLINGBERG, G. A. 2002. Dental treatment, dental fear and behaviour management problems in children with severe enamel hypomineralization of their permanent first molars. *Int J Paediatr Dent,* 12**,** 24-32.

JALEVIK, B. & NOREN, J. G. 2000. Enamel hypomineralization of permanent first molars: a morphological study and survey of possible aetiological factors. *Int J Paediatr Dent,* 10**,** 278-89.

JAMES, P., HARDING, M., BEECHER, T., BROWNE, D., CRONIN, M., GUINEY, H., O'MULLANE, D. & WHELTON, H. 2020. Impact of Reducing Water Fluoride on Dental Caries and Fluorosis. *J Dent Res***,** 100(5), 507-514.

JEREMIAS, F., KORUYUCU, M., KÜCHLER, E. C., BAYRAM, M., TUNA, E. B., DEELEY, K., PIERRI, R. A., SOUZA, J. F., FRAGELLI, C. M., PASCHOAL, M. A., GENCAY, K., SEYMEN, F., CAMINAGA, R. M., DOS SANTOS-PINTO, L. & VIEIRA, A. R. 2013. Genes expressed in dental enamel development are associated with molar-incisor hypomineralization. *Arch Oral Biol,* 58**,** 1434-42.

JIMENEZ-FARFAN, D., GUEVARA, J., ZENTENO, E. & HERNANDEZ-GUERRERO, J. C. 2005. Alteration of the sialylation pattern of the murine tooth germ after ethanol exposure. *Birth Defects Res A Clin Mol Teratol,* 73**,** 980-8.

JOSHI, S., SANDHU, M., SOGI, H. P. S., GARG, S. & DHINDSA, A. 2019. Split-mouth Randomised Clinical Trial on the Efficacy of GIC Sealant on Occlusal Surfaces of Primary Second Molar. *Oral Health Prev Dent,* 17**,** 17-24.

KALKANI, M., BALMER, R. C., HOMER, R. M., DAY, P. F. & DUGGAL, M. S. 2016. Molar incisor hypomineralisation: experience and perceived challenges among dentists specialising in paediatric dentistry and a group of general dental practitioners in the UK. *Eur Arch Paediatr Dent,* 17**,** 81-8.

KAR, S., SARKAR, S. & MUKHERJEE, A. 2014. Prevalence and Distribution of Developmental Defects of Enamel in the Primary Dentition of IVF Children of West Bengal. *J Clin Diagn Res,* 8(7)**,** ZC73-6.

KARJALAINEN, S., OLAK, J., SODERLING, E., PIENIHAKKINEN, K. & SIMELL, O. 2003. Frequent exposure to invasive medical care in early childhood and operative dental treatment associated with dental apprehension of children at 9 years of age. *Eur J Paediatr Dent,* 4**,** 186-90.

KEMOLI, A. M. 2008. Prevalence of molar incisor hypomineralisation in six to eight year-olds in two rural divisions in Kenya. *East African Medical Journal,* 85**,** 514-519.

KINDELAN, S. A., DAY, P., NICHOL, R., WILLMOTT, N. & FAYLE, S. A. 2008. UK National Clinical Guidelines in Paediatric Dentistry: stainless steel preformed crowns for primary molars. *Int J Paediatr Dent,* 18 Suppl 1**,** 20-8.

KOCH, G., HALLONSTEN, A. L., LUDVIGSSON, N., HANSSON, B. O., HOLST, A. & ULLBRO, C. 1987. Epidemiologic study of idiopathic enamel hypomineralization in permanent teeth of Swedish children. *Community Dent Oral Epidemiol,* 15**,** 279-85.

KOPPERUD, S. E., PEDERSEN, C. G. & ESPELID, I. 2016. Treatment decisions on Molar-Incisor Hypomineralization (MIH) by Norwegian dentists - a questionnaire study. *BMC Oral Health,* 17(1)**,** 3.

KOTSANOS, N., KAKLAMANOS, E. G. & ARAPOSTATHIS, K. 2005. Treatment management of first permanent molars in children with Molar-Incisor Hypomineralisation. *Eur J Paediatr Dent,* 6**,** 179-84.

KUHNISCH, J., HEITMULLER, D., THIERING, E., BROCKOW, I., HOFFMANN, U., NEUMANN, C., HEINRICH-WELTZIEN, R., BAUER, C. P., VON BERG, A., KOLETZKO, S., GARCIA-GODOY, F., HICKEL, R. & HEINRICH, J. 2014. Proportion and extent of manifestation of molar-incisor-hypomineralizations according to different phenotypes. *J Public Health Dent,* 74**,** 42-9.

KÜHNISCH, J., THIERING, E., KRATZSCH, J., HEINRICH-WELTZIEN, R., HICKEL, R., HEINRICH, J., GROUP, G. I. S. & GROUP, L. I. S. 2015. Elevated serum 25(OH)-vitamin D levels are negatively correlated with molar-incisor hypomineralization. *Journal of dental research,* 94**,** 381-387.

KUMAR, G. & DHILLON, J. 2020. Perception of Indian Dental Surgeons regarding Molar Incisor Hypomineralization. *Int J Clin Pediatr Dent,* 11(2):116-121.

LAISI, S., ESS, A., SAHLBERG, C., ARVIO, P., LUKINMAA, P. L. & ALALUUSUA, S. 2009. Amoxicillin may cause molar incisor hypomineralization. *J Dent Res,* 88**,** 132-6.

LANDIS, J. R. & KOCH, G. G. 1977. The measurement of observer agreement for categorical data. *Biometrics,* 33**,** 159-74.

LEITH, R. 2019. Hypomineralised second primary molars may be indicative of future molar incisor hypomineralisation. *Journal of The Irish Dental Association,* 65 (6)**,** 340-345.

LEWIS, S. A. & BRITTON, J. R. 1998. Consistent effects of high socioeconomic status and low birth order, and the modifying effect of maternal smoking on the risk of allergic disease during childhood. *Respir Med,* 92**,** 1237-44.

LI, S. H., KINGMAN, A., FORTHOFER, R. & SWANGO, P. 1993. Comparison of tooth surface-specific dental caries attack patterns in US schoolchildren from two national surveys. *J Dent Res,* 72**,** 1398-405.

LIMA, L. R. S., PEREIRA, A. S., DE MOURA, M. S., LIMA, C. C. B., PAIVA, S. M., MOURA, L. D. F. A. D. D. & DE DEUS MOURA DE LIMA, M. 2020. Pre-term birth and asthma is associated with hypomineralized second primary molars in pre-schoolers: A population-based study. *International Journal of Paediatric Dentistry,* 30**,** 193-201.

LIU, J., TUVBLAD, C., LI, L., RAINE, A. & BAKER, L. 2013. Medical Record Validation of Maternal Recall of Pregnancy and Birth Events From a Twin Cohort. *Twin research and human genetics : the official journal of the International Society for Twin Studies,* 16**,** 1-16.

LO, E. C., ZHENG, C. G. & KING, N. M. 2003. Relationship between the presence of demarcated opacities and hypoplasia in permanent teeth and caries in their primary predecessors. *Caries Res,* 37**,** 456-61.

LOPES-FATTURI, A., MENEZES, J., FRAIZ, F. C., ASSUNCAO, L. & DE SOUZA, J. F. 2019. Systemic Exposures Associated with Hypomineralized Primary Second Molars. *Pediatr Dent,* 41**,** 364-370.

LUNARDELLI, S. E. & PERES, M. A. 2005. Prevalence and distribution of developmental enamel defects in the primary dentition of pre-school children. *Braz Oral Res,* 19**,** 144-9.

LYGIDAKIS, N. A., CHALIASOU, A. & SIOUNAS, G. 2003. Evaluation of composite restorations in hypomineralised permanent molars: a four year clinical study. *Eur J Paediatr Dent,* 4**,** 143-8.

LYGIDAKIS, N. A., WONG, F., JALEVIK, B., VIERROU, A. M., ALALUUSUA, S. & ESPELID, I. 2010. Best Clinical Practice Guidance for clinicians dealing with children presenting with

Molar-Incisor-Hypomineralisation (MIH): An EAPD Policy Document. *Eur Arch Paediatr Dent,* 11**,** 75-81.
MANHART, J., CHEN, H., HAMM, G. & HICKEL, R. 2004. Buonocore Memorial Lecture. Review of the clinical survival of direct and indirect restorations in posterior teeth of the permanent dentition. *Oper Dent,* 29**,** 481-508.
MASSIGNAN, C., XIMENES, M., DA SILVA PEREIRA, C., DIAS, L., BOLAN, M. & CARDOSO, M. 2016. Prevalence of enamel defects and association with dental caries in preschool children. *Eur Arch Paediatr Dent,* 17**,** 461-466.
MCDONALD, R. E. & AVERY, D. R. 2004. Development and morphology of the primary teeth. *In: McDonald and Avery Dentistry for the child and Adolescent.* 8th ed.: Mosby Co.
MCKNIGHT-HANES, C., MYERS, D. R., DUSHKU, J. C. & BARENIE, J. T. 1991. A comparison of general dentists' and pediatric dentists' treatment recommendations for primary teeth. *Pediatr Dent,* 13**,** 344-8.
MEDSKER, B., FORNO, E., SIMHAN, H. & CELEDÓN, J. C. 2015. Prenatal Stress, Prematurity, and Asthma. *Obstetrical & gynecological survey,* 70**,** 773-779.
MEER, Z., ALMALKI, A., ALSHEHRI, M., ALRASHED, R., HUSSAIN, W., ALWADEI, A., ALHANIF, A., ALHANIF, R., FAGEEH, S., ALI, R., ALSHEHRI, M., ALZAHRANI, F., AL-ALHINYAH, A., MOHAMMED, F. & ALSHAHRANI, F. 2020. Perception of Saudi Dental Surgeons Regarding Hypomineralised Second Primary Molars (HSPM). *Journal of Research in Medical and Dental Science,* 08**,** 71-76.
MEJARE, I., BERGMAN, E. & GRINDEFJORD, M. 2005. Hypomineralized molars and incisors of unknown origin: treatment outcome at age 18 years. *Int J Paediatr Dent,* 15**,** 20-8.
MILSOM, K. M., TICKLE, M., HUMPHRIS, G. M. & BLINKHORN, A. S. 2003. The relationship between anxiety and dental treatment experience in 5-year-old children. *Br Dent J,* 194**,** 503-6; discussion 495.
MITTAL, N. & SHARMA, B. B. 2015a. Hypomineralised second primary molars: prevalence, defect characteristics and possible association with Molar Incisor Hypomineralisation in Indian children. *European Archives of Paediatric Dentistry,* 16**,** 441-447.
MITTAL, R., CHANDAK, S., CHANDWANI, M., SINGH, P. & PIMPALE, J. 2016. Assessment of association between molar incisor hypomineralization and hypomineralized second primary molar. *J Int Soc Prev Community Dent,* 6**,** 34-9.
MURRAY, J. J. & SHAW, L. 1979. Classification and prevalence of enamel opacities in the human deciduous and permanent dentitions. *Arch Oral Biol,* 24**,** 7-13.
NAING, L., WINN, T. & NORDIN, R. 2006. Pratical Issues in Calculating the Sample Size for Prevalence Studies. *Archives of Orofacial Sciences,* 1.
NATLAND, S. T., ANDERSEN, L. F., NILSEN, T. I. L., FORSMO, S. & JACOBSEN, G. W. 2012. Maternal recall of breastfeeding duration twenty years after delivery. *BMC medical research methodology,* 12**,** 179-179.
NAZZAL, H. & DUGGAL, M. 2018. Restorative management of dental enamel defects in the primary dentition. *Clinical Dentistry Reviewed,* 3.
NEGRE-BARBER, A., MONTIEL-COMPANY, J. M., BORONAT-CATALA, M., CATALA-PIZARRO, M. & ALMERICH-SILLA, J. M. 2016. Hypomineralized Second Primary Molars as Predictor of Molar Incisor Hypomineralization. *Sci Rep,* 6**,** 1-6.
NELSON, S., ALBERT, J. M., LOMBARDI, G., WISHNEK, S., ASAAD, G., KIRCHNER, H. L. & SINGER, L. T. 2010. Dental Caries and Enamel Defects in Very Low Birth Weight Adolescents. *Caries Research,* 44**,** 509-518.
NG, J. J., EU, O. C., NAIR, R. & HONG, C. H. 2015. Prevalence of molar incisor hypomineralization (MIH) in Singaporean children. *Int J Paediatr Dent,* 25**,** 73-8.
NØRRISGAARD, P. E., HAUBEK, D., KÜHNISCH, J., CHAWES, B. L., STOKHOLM, J., BØNNELYKKE, K. & BISGAARD, H. 2019. Association of High-Dose Vitamin D Supplementation during Pregnancy with the Risk of Enamel Defects in Offspring: A 6-Year Follow-up of a Randomized Clinical Trial. *JAMA Pediatrics,* 173**,** 924-930.

OPDAM, N. J., VAN DE SANDE, F. H., BRONKHORST, E., CENCI, M. S., BOTTENBERG, P., PALLESEN, U., GAENGLER, P., LINDBERG, A., HUYSMANS, M. C. & VAN DIJKEN, J. W. 2014. Longevity of posterior composite restorations: a systematic review and meta-analysis. *J Dent Res,* 93**,** 943-9.

ORAL HEALTH SERVICES RESEARCH CENTRE 2018. Briefing Document on HRB funded Fluoride and Caring for Children's Teeth study (FACCT). *Available at: https://assets.gov.ie/9587/a7123c5bd5724ca59b3c7e9a64bae54f.pdf.*

OWEN, M. L., GHANIM, A., ELSBY, D. & MANTON, D. J. 2018. Hypomineralized second primary molars: prevalence, defect characteristics and relationship with dental caries in Melbourne preschool children. *Aust Dent J,* 63**,** 72-80.

OYEDELE, T. A., FOLAYAN, M. O. & OZIEGBE, E. O. 2016a. Hypomineralised second primary molars: prevalence, pattern and associated co morbidities in 8- to 10-year-old children in Ile-Ife, Nigeria. *BMC Oral Health,* 16**,** 65.

OYEDELE, T. A., FOLAYAN, M. O. & OZIEGBE, E. O. 2016b. Hypomineralised second primary molars: prevalence, pattern and associated co morbidities in 8-to 10-year-old children in Ile-Ife, Nigeria. *Bmc Oral Health,* 16**,** 1-7.

ÖZGÜL, B. M., SAAT, S., SÖNMEZ, H. & ÖZ, F. T. 2013. Clinical Evaluation of Desensitizing Treatment for Incisor Teeth Affected by Molar-Incisor Hypomineralization. *Journal of Clinical Pediatric Dentistry,* 38**,** 101-105.

PINBORG, A., WENNERHOLM, U. B., ROMUNDSTAD, L. B., LOFT, A., AITTOMAKI, K., SODERSTROM-ANTTILA, V., NYGREN, K. G., HAZEKAMP, J. & BERGH, C. 2013. Why do singletons conceived after assisted reproduction technology have adverse perinatal outcome? Systematic review and meta-analysis. *Hum Reprod Update,* 19**,** 87-104.

PUBLIC HEALTH ENGLAND 2019. Oral health survey of five year olds 2019. A report on the variations in prevalence and severity of dental decay. *Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment data/file/873492/NDEP_for_England_OH_Survey_5yr_2019_v1.0.pdf.*

QUINTERO, Y., RESTREPO, M., SALDARRIAGA, J., SALDARRIAGA, A. & SANTOS-PINTO, L. 2019. Treatment options for deciduous molar hypomineralization: a report of three cases. *Dental Update,* 46**,** 546-553.

RESTREPO, M., JEREMIAS, F., SANTOS-PINTO, L., CORDEIRO, R. C. & ZUANON, A. C. 2016. Effect of Fluoride Varnish on Enamel Remineralization in Anterior Teeth with Molar Incisor Hypomineralization. *J Clin Pediatr Dent,* 40**,** 207-10.

REYES, M. R. T., FATTURI, A. L., MENEZES, J. V. N. B., FRAIZ, F. C., ASSUNCAO, L. R. D. S. & SOUZA, J. F. D. 2019. Demarcated opacity in primary teeth increases the prevalence of molar incisor hypomineralization. *Brazilian oral research,* 33**,** e048.

RIBEIRO, J., FORGERINI, T., PEDROTTI, D., ROCHA, R., ARDENGHI, T., SOARES, F. & LENZI, T. 2018. Performance of resin composite restorations in the primary dentition: A retrospective university-based study. *International Journal of Paediatric Dentistry,* 28. doi: 10.1111/ipd.12404. Epub ahead of print.

RICE, F., LEWIS, A., HAROLD, G., VAN DEN BREE, M., BOIVIN, J., HAY, D., OWEN, M. & THAPAR, A. 2007. Agreement between maternal report and antenatal records for a range of pre and peri-natal factors: The influence of maternal and child characteristics. *Early human development,* 83**,** 497-504.

RICHARDSON, M. E. 1965. The relationship between the relative amount of space present in the deciduous dental arch and the rate and degree of space closure subsequent to the extraction of a deciduous molar. *Dent Pract Dent Rec,* 16**,** 111-8.

ROZIER, R. G. 1994. Epidemiologic indices for measuring the clinical manifestations of dental fluorosis: overview and critique. *Adv Dent Res,* 8**,** 39-55.

SANTAMARIA, R. M., INNES, N. P., MACHIULSKIENE, V., EVANS, D. J., ALKILZY, M. & SPLIETH, C. H. 2015. Acceptability of different caries management methods for primary molars in a RCT. *Int J Paediatr Dent,* 25**,** 9-17.

SARNAT, B. G. & SCHOUR, I. 1942. Enamel Hypoplasia (Chronologic Enamel Aplasia) In Relation to Systemic Disease: A Chronologic, Morphologic and Etiologic Classification. *The Journal of the American Dental Association,* 29**,** 67-75.

SCHRAVERUS, M. S., OLEGÁRIO, I. C., BONIFÁCIO, C. C., GONZÁLEZ, A. P. R., PEDROZA, M. & HESSE, D. 2021. Glass Ionomer Sealants Can Prevent Dental Caries but Cannot Prevent Posteruptive Breakdown on Molars Affected by Molar Incisor Hypomineralization: One-Year Results of a Randomized Clinical Trial. *Caries Res***,** 1-9.

SCHÜTTFORT, G., HÖFLER, S., KANN, G., KÖNIGS, C., DE LEUW, P., HERRMANN, E., STEPHAN, C. & HABERL, A. 2020. Influence of tenofovir exposure in utero on primary dentition. *European Journal of Pediatrics,* 179**,** 1761-1768.

SEOW, W. K. 1997a. Clinical diagnosis of enamel defects: pitfalls and practical guidelines. *Int Dent J,* 47**,** 173-82.

SEOW, W. K. 1997b. Effects of preterm birth on oral growth and development. *Aust Dent J,* 42**,** 85-91.

SEOW, W. K., BROWN, J. P., TUDEHOPE, D. I. & O'CALLAGHAN, M. 1984. Developmental defects in the primary dentition of low birth-weight infants: adverse effects of laryngoscopy and prolonged endotracheal intubation. *Pediatr Dent,* 6**,** 28-31.

SERNA-MUÑOZ, C., MARTÍNEZ-BENEYTO, Y., PÉREZ-SILVA, A., POZA-PASCUAL, A., IBÁÑEZ-LÓPEZ, F. J. & ORTIZ-RUIZ, A. J. 2020. Perception, knowledge, and attitudes towards molar incisor hypomineralization among Spanish dentists: a cross-sectional study. *BMC Oral Health,* 20, 260.

SERNA MUNOZ, C., ORTIZ RUIZ, A. J., PEREZ SILVA, A., BRAVO-GONZALEZ, L. A. & VICENTE, A. 2020. Second primary molar hypomineralisation and drugs used during pregnancy and infancy. A systematic review. *Clin Oral Investig,* 24**,** 1287-1297.

SIDHU, N., WANG, Y., BARRETT, E. & CASAS, M. 2019. Prevalence and presentation patterns of enamel hypomineralisation (MIH and HSPM) among paediatric hospital dental patients in Toronto, Canada: a cross-sectional study. *European Archives of Paediatric Dentistry*, 21(2), 263-270.

SILVA, M. J., ALHOWAISH, L., GHANIM, A. & MANTON, D. J. 2016a. Knowledge and attitudes regarding molar incisor hypomineralisation amongst Saudi Arabian dental practitioners and dental students. *European Archives of Paediatric Dentistry,* 17**,** 215-222.

SILVA, M. J., KILPATRICK, N. M., CRAIG, J. M., MANTON, D. J., LEONG, P., BURGNER, D. & SCURRAH, K. J. 2019. Etiology of Hypomineralized Second Primary Molars: A Prospective Twin Study. *J Dent Res,* 98**,** 77-83.

SILVA, M. J., SCURRAH, K. J., CRAIG, J. M., MANTON, D. J. & KILPATRICK, N. 2016b. Etiology of molar incisor hypomineralization - A systematic review. *Community Dent Oral Epidemiol,* 44**,** 342-53.

SLAYTON, R. L., WARREN, J. J., KANELLIS, M. J., LEVY, S. M. & ISLAM, M. 2001. Prevalence of enamel hypoplasia and isolated opacities in the primary dentition. *Pediatr Dent,* 23**,** 32-6.

SONCINI, J. A., MASEREJIAN, N. N., TRACHTENBERG, F., TAVARES, M. & HAYES, C. 2007. The longevity of amalgam versus compomer/composite restorations in posterior primary and permanent teeth: findings From the New England Children's Amalgam Trial. *J Am Dent Assoc,* 138**,** 763-72.

SÖNMEZ, H. & SAAT, S. 2017. A Clinical Evaluation of Deproteinization and Different Cavity Designs on Resin Restoration Performance in MIH-Affected Molars: Two-Year Results. *Journal of Clinical Pediatric Dentistry,* 41**,** 336-342.

SUCKLING, G. W. & PEARCE, E. I. 1984. Developmental defects of enamel in a group of New Zealand children: their prevalence and some associated etiological factors. *Community Dent Oral Epidemiol,* 12**,** 177-84.

TAGELSIR AHMED, A., SOTO-ROJAS, A. E., DEAN, J. A., ECKERT, G. J. & MARTINEZ-MIER, E. A. 2020. Prevalence of molar-incisor hypomineralization and other enamel defects and associated sociodemographic determinants in Indiana. *J Am Dent Assoc,* 151**,** 491-501.

TAJI, S. S., SEOW, W. K., TOWNSEND, G. C. & HOLCOMBE, T. 2011. Enamel hypoplasia in the primary dentition of monozygotic and dizygotic twins compared with singleton controls. *Int J Paediatr Dent,* 21**,** 175-84.

TEDESCO, T. K., CALVO, A. F., LENZI, T. L., HESSE, D., GUGLIELMI, C. A., CAMARGO, L. B., GIMENEZ, T., BRAGA, M. M. & RAGGIO, D. P. 2017. ART is an alternative for restoring occlusoproximal cavities in primary teeth - evidence from an updated systematic review and meta-analysis. *Int J Paediatr Dent,* 27**,** 201-209.

TEIXEIRA, R., ANDRADE, N. S., QUEIROZ, L. C. C., MENDES, F. M., MOURA, M. S., MOURA, L. & LIMA, M. D. M. 2018. Exploring the association between genetic and environmental factors and molar incisor hypomineralization: evidence from a twin study. *Int J Paediatr Dent,* 28**,** 198-206.

TEMILOLA, O. D. & FOLAYAN, M. O. 2015. Distinguishing predisposing factors for enamel hypoplasia and molar-incisor hypomineralization in children in Ile-Ife, Nigeria. *Brazilian Journal of Oral Sciences,* 14**,** 318-322.

TEMILOLA, O. D., FOLAYAN, M. O. & OYEDELE, T. 2015a. The prevalence and pattern of deciduous molar hypomineralization and molar-incisor hypomineralization in children from a suburban population in Nigeria. *BMC oral health,* 15**,** 73-73.

TIBÚRCIO-MACHADO, C. S., MICHELON, C., ZANATTA, F. B., GOMES, M. S., MARIN, J. A. & BIER, C. A. 2021. The global prevalence of apical periodontitis: a systematic review and meta-analysis. *Int Endod J,* 54**,** 712-735.

TIENBOON, P., RUTISHAUSER, I. H. E. & WAHLQVIST, M. L. 1994. Maternal recall of infant feeding practices after an interval of 14 to 15 years. *Australian journal of nutrition and dietetics.,* 51**,** 25-27.

TINANOFF, N. & REISINE, S. 2009. Update on early childhood caries since the Surgeon General's Report. *Acad Pediatr,* 9**,** 396-403.

TRAN, L. A. & MESSER, L. 2004. Clinicians' choices of restorative materials for children. *Australian dental journal,* 48**,** 221-32.

TUNG, K., FUJITA, H., YAMASHITA, Y. & TAKAGI, Y. 2006. Effect of turpentine-induced fever during the enamel formation of rat incisor. *Arch Oral Biol,* 51**,** 464-70.

VAN DER TAS, J. T., ELFRINK, M. E. C., HEIJBOER, A. C., RIVADENEIRA, F., JADDOE, V. W. V., TIEMEIER, H., SCHOUFOUR, J. D., MOLL, H. A., ONGKOSUWITO, E. M., WOLVIUS, E. B. & VOORTMAN, T. 2018. Foetal, neonatal and child vitamin D status and enamel hypomineralization. *Community Dent Oral Epidemiol,* 46**,** 343-351.

VEERKAMP, J. S. & WEERHEIJM, K. L. 1995. Nursing-bottle caries: the importance of a development perspective. *ASDC J Dent Child,* 62**,** 381-6.

VICTORA, C. G., HUTTLY, S. R., FUCHS, S. C. & OLINTO, M. T. 1997. The role of conceptual frameworks in epidemiological analysis: a hierarchical approach. *Int J Epidemiol,* 26**,** 224-7.

VIEIRA, A. R. & KUP, E. 2016. On the Etiology of Molar-Incisor Hypomineralization. *Caries Res,* 50**,** 166-9.

VLACHOU, C., ARHAKIS, A. & KOTSANOS, N. 2020. Distribution and morphology of enamel hypomineralisation defects in second primary molars. *European Archives of Paediatric Dentistry*, 22(2), 241-246.

WAGNER, Y. 2017. Developmental defects of enamel in primary teeth - findings of a regional German birth cohort study. *BMC Oral Health,* 17**,** 1-8.

WALL, A. & LEITH, R. 2020. A questionnaire study on perception and clinical management of molar incisor hypomineralisation (MIH) by Irish dentists. *European Archives of Paediatric Dentistry,* 21(6), 703-710.

WALSHAW, E. G., NOBLE, F., CONVILLE, R., ANNE LAWSON, J., HASMUN, N. & RODD, H. 2020. Molar incisor hypomineralisation and dental anomalies: A random or real association? *International Journal of Paediatric Dentistry,* 30**,** 342-348.

WANG, Y., LI, C., YUAN, H., WONG, M. C., ZOU, J., SHI, Z. & ZHOU, X. 2016. Rubber dam isolation for restorative treatment in dental patients. *Cochrane Database Syst Rev,* 9**,** Cd009858.

WEERHEIJM, K. L. 2003. Molar incisor hypomineralisation (MIH). *Eur J Paediatr Dent,* 4**,** 114-20.

WEERHEIJM, K. L. 2004. Molar incisor hypomineralization (MIH): clinical presentation, aetiology and management. *Dent Update,* 31**,** 9-12.

WEERHEIJM, K. L., DUGGAL, M., MEJARE, I., PAPAGIANNOULIS, L., KOCH, G., MARTENS, L. C. & HALLONSTEN, A. L. 2003. Judgement criteria for molar incisor hypomineralisation (MIH) in epidemiologic studies: a summary of the European meeting on MIH held in Athens, 2003. *Eur J Paediatr Dent,* 4**,** 110-3.

WEERHEIJM, K. L., JALEVIK, B. & ALALUUSUA, S. 2001. Molar-incisor hypomineralisation. *Caries Res,* 35**,** 390-1.

WHELTON, H., CROWLEY, E., O'MULLANE, D., HARDING, M., GUINEY, H., CRONIN, M., FLANNERY, E. & KELLEHER, V. 2006. North South Survey of Children's Oral Health in Ireland 2002. *Available at: https://www.lenus.ie/bitstream/handle/10147/119028/OralHealthReport.pdf?sequence=1*

WILLIAM, V., MESSER, L. B. & BURROW, M. F. 2006. Molar incisor hypomineralization: review and recommendations for clinical management. *Pediatr Dent,* 28**,** 224-32.

WORLD HEALTH ORGANIZATION 1997. Oral health surveys : basic methods. 4th ed ed. Geneva: World Health Organization.

WU, X., WANG, J., LI, Y. H., YANG, Z. Y. & ZHOU, Z. 2018. Association of molar incisor hypomineralization with premature birth or low birth weight: systematic review and meta-analysis. *J Matern Fetal Neonatal Med***,** 1-9.

YOUNG, M. A. 1973. *An Epidemiological Study of Enamel Opacities.*PhD Thesis, University of London, England.

ZAKIRULLA, M., ALASIRI, M. A., ALSHAHRANI, M. R., ALKHAIRY, S. I., LAHEQ, M. T., ALTHUQBI, A. A., ASIRI, H. I. A. & ALMALKI, A. Y. 2020. Prevalence of Hypomineralization in Second Primary MOLARS (HSPM) in 7 to 10-Year-Old Saudi Children. *Journal of Research in Medical and Dental Science,* 8**,** 124-127.

7 Appendices

Study 1 - Appendix 1.1: Data Collection form

DATA COLLECTION – SYSTEMATIC REVIEW						
Article ID:	Author					
	Year					
	Country					
	Study Type					
Population Details	Location	School ☐ Portable chair ☐ Dental Clinic ☐ Hospital ☐ Other: _____				
	General/specific	General population ☐ Specific groups: ☐ Details: _____				
	Age range					
	Gender	Mixed ☐ Female only ☐ Male only ☐				
Evaluation	Condition	Wet ☐ Dried with cotton rolls/gauze ☐ Dried with air ☐				
	Cleaned	No ☐ Yes toothbrush ☐ Yes gauze/other ☐				
	Light	Natural ☐ Artificial ☐				
Criteria	Diagnostic criteria	EAPD (Weerheijm et al.., 2003) ☐ MIH/HSPM (Ghanin et al.., 2015) ☐ DDE ☐ Other: _____				
	Reference criteria					
Child Level	Sample size (total n – children)		HSPM (total n - children)		Prevalence children (%)	
Tooth level	Total number of 2nd primary molars examined		Total number of 2nd molars with HSPM		Prevalence teeth (%)	
Extras	White/cream		PEB		Ext <1/3	
	Yellow/brown		Atypical restoration		Ext 1/3-2/3	
	Demarcated opacities (total)		Atypical caries		Ext >2/3	

Study 1 - Appendix 1.2: Risk of Bias Assessment tool

RISK OF BIAS ASSESSMENT		
Section 1 :Selection		**X**
1.1 Representativeness	a) Truly representative of the average in the target population. (all subjects or random sampling)	
	b) Somewhat representative of the average in the target population. (hospitals, schools - non-random sampling)	
	c) Selected group of users (specific groups; ex: asthmatic children)	
	d) No description of the sampling strategy	
1.2 Sample Size	(a) Justified and satisfactory (sample size calculation reported	
	(b) Not justified or not reported	
1.3 Non respondents	(a) Comparability between respondents and non-respondents' characteristics is established, and the response rate is satisfactory (>80%)	
	(b) The response rate is unsatisfactory (<80%), or the comparability between respondents and non-respondents is unsatisfactory	
	(c) No description of the response rate or the characteristics of the responders and the non-responders	
Section 2: Comparability		
(Only for studies that had different study groups)	(a) The study controls for the most important factor (location of recruitment)	
	(b) The study control for any additional factor (age)	
	(c) The study does not control for any factor	
Section 3: Outcome:		
3.1 Criteria	a) Used EAPD HSPM criteria	
	b) Did not use EAPD HSPM criteria	
3.2 Training	a) Training of the examiners described in the manuscript	
	b) Training of the examiner **not** described in the manuscript.	
3.3 Calibration	a) Calibration for the methodology of HSPM, with inter- and intra-agreement values provided **greater** than 0.70	
	b) Calibration for the methodology of HSPM, with inter- and intra-agreement values provided **lower** than 0.70	
	c) Training and calibration for the methodology of assessing HSPM, with inter- or intra-agreement value **not** provided	
	(e) Training and calibration not mentioned	

Study 2 - Appendix 2.1: Ethical approval

Coláiste na Tríonóide, Baile Átha Cliath
Trinity College Dublin
Ollscoil Átha Cliath | The University of Dublin

Dr. Charlotte Mc Carra
C/O Division of Public & Child Dental Health
Dublin Dental University Hospital,
Lincoln Place,
Dublin 2,
D02 F859

27th May 2019

Ref: 190403

Title of Study: Prevalence, characteristics and treatment strategies for Hypomineralised Second Primary Molars (HSPM) in Irish school children

Dear Dr. Mc Carra,

Further to a meeting of the Faculty of Health Sciences Ethics Committee held in April 2019. We are pleased to inform you that the above project has ethical approval to proceed.

As a researcher you must ensure that you comply with other relevant regulations, including DATA PROTECTION and HEALTH AND SAFETY.

Yours sincerely,

Prof. Brian O'Connell
Chairperson
Faculty Research Ethics Committee

Dámh na nEolaíochtaí Sláinte
Foirgneamh na Ceimice,
Coláiste na Tríonóide,
Ollscoil Átha Cliath,
Baile Átha Cliath 2, Éire.

Faculty of Health Sciences
Chemistry Building,
Trinity College Dublin,
The University of Dublin,
Dublin 2, Ireland.

www.healthsciences.tcd.ie

Study 2 - Appendix 2.2: Letter of invitation to school

Coláiste na Tríonóide, Baile Átha Cliath
Trinity College Dublin
Ollscoil Átha Cliath | The University of Dublin

Date

Division of Public and Child Dental Health
Dublin Dental University Hospital
Lincoln Place
Dublin 2

School address

Request for permission to conduct research in school

Dear Board of Directors & Parents Association,

My name is Charlotte Mc Carra and I am a clinical doctorate student in Paediatric Dentistry at the School of Dental Science, Trinity College Dublin. I am writing to extend an invitation for your school to take part in a research study.

Study title: Prevalence, characteristics and treatment strategies for Hypomineralised SPMs (HSPM) in Irish school children

This research study relates to a tooth defect, called 'hypomineralisation' or weak enamel. This condition results in the formation of softer enamel which can lead to discoloration, break-down and an increased risk of dental decay. This softness is thought to be caused by a disturbance at the time these teeth are forming however the exact cause remains unclear. This condition is common in the FPM which erupts into the mouth at around the age of six to seven years. The second baby molar which comes into the mouth from age two to three years can also be affected.
This study aims to investigate how prevalent this condition is in 4-to-6- year old Irish school children and how this condition appears in the mouth. We will also investigate if a link exists between this condition and certain factors such as decay risk. The role of natal/early childhood factors in the development of this condition will be examined.

Ethical approval for this study has been obtained from the Faculty of Health Sciences Research Ethics Committee at Trinity College Dublin

We would like to ask your permission for your school to participate in this study, examining children in Junior and Senior Infants Classes. Your co-operation will also be required to distribute information to parents in relation to the study, recruit participants, and conduct the research study on your premises. We would seek individual parent/guardian permission for each child on written informed consent forms to allow their child to participate in the study.

A team of dentists would like to attend your school at a suitable time to examine the teeth of children aged 4-to -6 years old in Junior and Senior Infants Classes. The exam will take approximately 2 minutes per child. Should a child have any dental decay or other treatment needs an information letter will be provided for the child's parent/guardian. Consenting

parents/guardians will also receive a questionnaire regarding pregnancy and early childhood health.

With due consideration to child protection, we would only conduct these examinations in an open area within the school premises under the supervision of the class teachers or school staff. It would be a pre-requisite for this study that an appropriate space and supervisory resources be available in your school.

Any data provided by parent/guardian and data collected from dental examination will remain confidential. Data collected will be coded. This means that a random number will be assigned to all questionnaires and data recording sheets. This number will be used to identify and analyse data collected during the study. Consent forms will be the only documentation retained that holds personal data relating to children and their parents. These will have an alphabetical code and will be needed for verification at the time of assessment to ensure that appropriate consent has been obtained. A master key (code breaker) will be held only by the research team linking coded data to the participant identity. Linking of numerically coded data to the consent form is necessary for our related future research study. Consent forms will be stored separately to numerically coded data. Records will be securely and safely stored in a restricted-access area of the Dublin Dental Hospital for the duration of the study. It is anticipated that re-examination of the same children will occur in 2nd or 3rd class when the permanent teeth can be examined. (due to the time lapse a separate consent form will be provided at that time).

There is no specific benefit to the child participant, but it is hoped the findings from this study will help children in the future through improved awareness and diagnosis of this condition. If dental needs are identified, parents/guardians will be informed via a proforma letter advising on the need to attend with their own dentist. This research is independent of and has no affiliation to the Health Service Executive (HSE) school dental service.

All examiners are qualified dentists from the Dublin Dental University Hospital (DDUH), and we have all completed Children's First child protection training. We have all obtained Garda clearance in order to work at the DDUH; we are also covered under that hospital's Clinical Indemnity Scheme.

I am enclosing a pack containing the parent/guardian invitation letter and study information leaflet, the parent/guardian questionnaire, the consent form and proforma treatment need sheet.

I am hopeful that you will be happy to accept our invitation to participate in this study. It is hoped by carrying out this research, awareness of this condition will be increased in Ireland. Early diagnosis will allow preventive care to be provided which may reduce tooth breakdown and provide protection for these teeth.
Thank you for taking the time to consider this proposal. If you have any queries in relation to any aspect of this research, please do not hesitate to contact me at:
Charlotte.McCarra@dental.tcd.ie or by phone at 01-6127303.

Kind regards,

Dr. Charlotte Mc Carra
B.A., B.Dent.Sc., MFDS (RCSEd)
D.Ch.Dent. (Paediatric Dentistry) candidate

Study 2 – Appendix 2.3 : Participant Information Leaflet

Coláiste na Tríonóide, Baile Átha Cliath
Trinity College Dublin
Ollscoil Átha Cliath | The University of Dublin

Participant Information Leaflet

Title of study: Prevalence, characteristics and treatment strategies for Hypomineralised SPMs (HSPM) in Irish school children.
Please take the time to read this information sheet. If you have any questions we will be happy to answer them.

Who am I and what this study is about:
I am studying Paediatric Dentistry (dentistry for children) at the School of Dental Science, Trinity College Dublin.
Some baby teeth can be softer than expected because of the way they were formed. These teeth can also be more prone to dental decay. We want to see if your child's teeth have any sign of this condition (called hypomineralisation).
We are interested in knowing just how common weak enamel is in 4-to-6- year olds and how it looks in the mouth. We want to know whether there might be a link between weak enamel and issues like getting decay.

What will taking part involve:
My team and I will attend your child's school on <designated date & time>. We will have a quick look at your child's teeth with a mirror while they are sitting in their chair (see picture below). The exam will be in the presence of their class teacher or other school staff and will take about 2 minutes. Each child will get their own mirror and all mirrors are single use. If your child has any dental issues we will give you a letter explaining this and what to do. All members of our team are qualified dentists who are vetted and indemnified. We will also give out a questionnaire related to pregnancy and your child's health early in life and we will ask you to fill this out at home. If you prefer, we will contact you by phone to answer the questions.

Why have you been invited to take part?
Your child's school have kindly allowed us to carry out our research study. We are examining children between 4-to-6 years. All children have received the same information sheet.

Do you have to take part?
Taking part is entirely voluntary and you and your child are under no obligations to take part.
If you decide to take part in this study, you have the right to withdraw you & your child's participation at any time. You will not be penalised in any way, and you and your child will not lose any benefits you had prior to the study.

What are the benefits of taking part in the study?
There will be no specific benefit to your child, but it is hoped the findings from this study may help future children in Ireland through improved awareness and diagnosis of this condition.

Are there any risks of taking part?
The potential risks are limited. We are simply looking at your child's teeth. We are not providing any treatment.

Will taking part be confidential?

Any information you provide, and information gained from your child's dental check-up will remain confidential and be accessed only by the research team.

How will the information you provide be stored and protected?
All personal data and data from your child's check-up will be stored safely and securely in the Dublin Dental University Hospital, with access available to the research team only.

What will happen to the results of the study?
The results from this study will be written up in a doctoral thesis which will be submitted to Trinity College Dublin. The results will also be published in articles in dental journals and will be presented at international dental conferences. These results will be used for educational and teaching purposes.

What do I need to do to take part in this study?
You may enrol for the study by signing a consent form which will be given to you prior to the examination.
If you have any queries in relation to any aspect of this study prior to consenting to your child's participation, I will be happy to answer them – please feel free to contact me by phone at 01-6127303.

Thank you for taking the time to read this
Yours faithfully,
Dr. Charlotte Mc Carra
B.A., B.Dent.Sc., MFDS (RCSEd)
D.Ch.Dent. (Paediatric Dentistry) candidate

Study 2 - Appendix 2.4: Consent form

CONSENT FORM FOR EXAMINATION **ALPHABETICAL CODE:**

Thank you for taking the time to read the information sheet.
We will be checking your child's teeth for soft enamel. This will take place in their classroom in the presence of their class teacher or other school staff. The exam will take about 2 minutes.
We are happy for you to be present for the exam if you wish.
If your child has dental needs, we will let you know.
This check-up is not related to the Health Service Executive (HSE) school dental service.

Data Protection
Any information you provide, and information gained from your child's dental check-up will remain confidential, stored safely and securely and be accessed only by the research team. Only the research team will be able to link data collected to you and your child's personal information.

If you prefer that your child does not participate, this will have no effect on their position in the school.
Consent:
I have read the above information and the participant information sheet.

Child Name:_____ Date of Birth:_____

Study 2 - Appendix 2.5: Proforma should child have dental needs

Coláiste na Tríonóide, Baile Átha Cliath
Trinity College Dublin
Ollscoil Átha Cliath | The University of Dublin

Date:

Dear Parent/Guardian,
Thank you so much for letting us check your child's teeth, we really appreciate it!

Finding	Present
Dental infection	
Dental decay/cavities	
Tooth eruption disturbance	
Other	

When we looked at their teeth we saw:

Your child should attend with your family dentist for treatment of the above.

Kind regards,

Research team

Study 2 - Appendix 2.6: Permission from school for participation

Coláiste na Tríonóide, Baile Átha Cliath
Trinity College Dublin

29/10/2019

Division of Public and Child Dental Health
Dublin Dental University Hospital
Lincoln Place
Dublin 2

St. John Bosco Junior Boys School
Navan Road
Dublin 7

Confirmation of schools participation in research study:

Prevalence, characteristics and treatment strategies for Hypomineralised Second Primary molars (HSPM) in Irish school children

We wish to confirm our school's participation in the above research study.

Name in capitals: KAREN MC GOLDRICK
Signature: Karen McGoldrick
Date: 6/4/19

Study 2 - Appendix 2.7: Data collection sheet

Dental Examination Sheet

Age: Gender: M F Class: Juniors Seniors

Tooth		16	55	54	64	65	26
MIH/HSPM	Numerical score						
	Extent score						
Caries							

Tooth		46	85	84	74	75	36
MIH/HSPM	Numerical score						
	Extent score						
Caries							

MIH/HSPM Numerical Scores
0 = No visible enamel defect
1= Enamel defect not MIH/HSPM
2a= demarcated opacities (creamy or white)
2b = demarcated opacities (yellow or brown)
3= PEB
4=Atypical restoration
5= Atypical caries
6= Missing due to MIH/HSPM
7a= Cannot be scored
7b=SSC
X= Unerupted/partially erupted

MIH/HSPM Extent Scores
I= Less than 1/3 affected
II=at least 1/3 but less than 2/3
III= at least 2/3

Caries Scores
d= visual caries into dentine
m= missing
f= filled/restored
-- = caries free

Study 3- Appendix 3.1: Ethical approval

DUBLIN DENTAL UNIVERSITY HOSPITAL
OSPIDÉAL DÉADAIGH OLLSCOILE ÁTHA CLIATH

Research Ethics Committee
School of Dental Science &
Dublin Dental University Hospital
Lincoln Place
Dublin 2
Ireland

30st June 2020

RE: A questionnaire study of Dentists' Perception and Clinical Management of Hypomineralised Second Primary Molars

REC Reference: 2020-06-01

Dear Dr Mc Carra,

Thank you for your recent correspondence to the Dental School Research Ethics Committee (DSREC). Your application has been granted ethical approval. Please quote the above reference in all future correspondence.

Yours sincerely,

Prof. Gary Moran
Associate Professor in Microbiology
Chair DSREC
School of Dental Science and
Dublin Dental University Hospital,

Study 3 -Appendix 3.2: HSPM Questionnaire

A questionnaire study of dentist's perception and clinical management of Hypomineralised SPMs (Hypomineralised Es)

1. **How old are you?**
   (a) <25 years
   (b) 26-35 years
   (c) 36-45 years
   (d) 46-55 years
   (e) >55 years

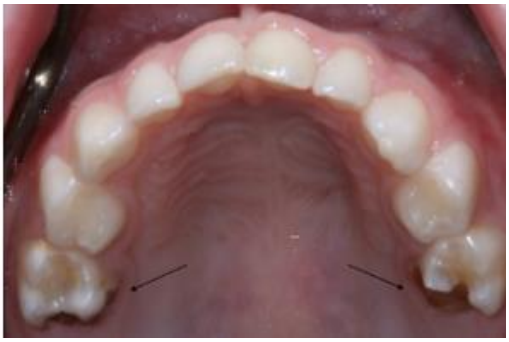
2. **How many years have you been practicing dentistry?**
   (a) <5 years
   (b) 5-10 years
   (c) 10 -15 years
   (d) 15-20 years
   (e) >20 years

3. **Where do you work?**
   (a) Public sector exclusively
   (b) Private practice exclusively
   (c) Public Sector and private practice
   (d) Public Sector and University
   (e) Private practice and University
   (f) University only

4. **Select your area of practice**
   (a) General dentist
   (b) Specialist (Paediatric Dentistry)
   (c) Specialist (other)

5. **Are you aware of a condition known as Hypomineralised SPMs (HSPM) or hypomineralised Es? This condition has a similar presentation to Molar Incisor Hypomineralisation (MIH) but affects the Es instead of the 6s. (see photo below)**

   (a) Yes
   (b) No **(If no survey brings you to Q 12)**



6. **How often do you notice this condition in your practice?**
   (a) Never
   (b) Weekly basis
   (c) Monthly basis
   (d) Yearly basis
   (e) Not sure

7. **How prevalent do you think Hypomineralised Es might be in your community?**
   (a) < 5%
   (b) 5%-10%
   (c) 10%-20%
   (d) >20%
   (e) Not sure

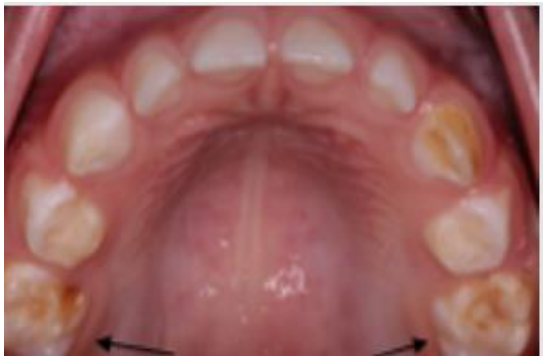
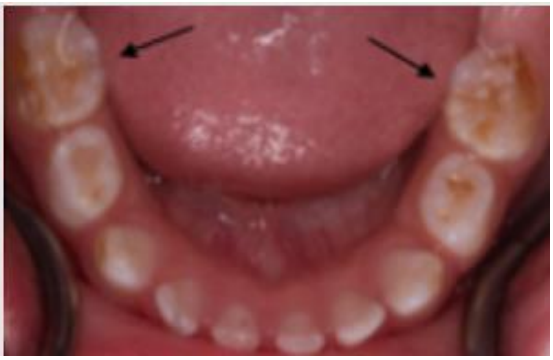
8. **Regarding the severity of the defect; which of the following do you most frequently notice in your practice? (select all that apply)**
   (a) White demarcated opacities
   (b) Yellow/brown opacities
   (c) Post-eruptive breakdown
   (d) Demarcated opacities and post eruptive breakdown

9. **How confident do you feel in diagnosing teeth affected by HSPM (Hypomineralised Es)?**
   (a) Very confident
   (b) Confident
   (c) Unconfident
   (d) Very unconfident

10. **Do you think the pattern (shape, size, location) of caries due to HSPM (Hypomineralised Es) is different from the 'classical caries pattern'?**
   (a) Yes
   (b) No

11. **What type of material do you often use in treating these teeth? (Select all that apply)**
   (a) Glass ionomer
   (b) Resin modified glass ionomer
   (c) Composite
   (d) Compomer
   (e) Preformed crowns (Stainless steel crowns)
   (f) Other (Please specify) _____

Below photos represent a five year old child with hypomineralisation and post eruptive breakdown of all SPMs (Es). All Es are asymptomatic, radiographic findings are normal and the child is very cooperative

12. Would you be comfortable providing restorative care for this child?

(a) Yes
(b) No

13. If no, who would you refer to?

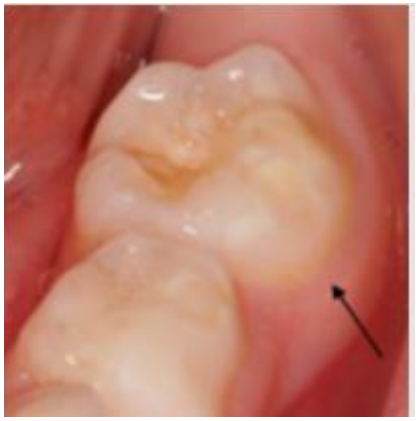
(a) Another General dentist
(b) Paediatric specialist (private)
(c) Hospital setting
(d) Community HSE clinic
(e) Other (please specify) _____

14. Would any of the following be a barrier to you for managing this child? (Select all that apply)

(a) Young age
(b) Child's behaviour
(c) Dental treatment that needs long time to be accomplished
(d) Difficulty deciding how to restore teeth and what materials to use
(e) Repeated failure of restorations
(f) Insufficient training to treat children with this condition
(g) Other (please specify) _____

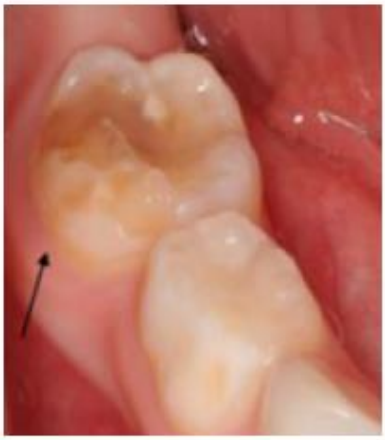
15. Which treatment would you provide for this hypomineralised, caries free SPM (E) with demarcated opacities? The patient is 5 years old, has good oral hygiene and is very cooperative.

(i)	No treatment with preventive advice
(ii)	Fluoride varnish
(iii)	Fissure sealant (glass ionomer)
(iv)	Fissure sealant (resin)
(v)	Glass ionomer restoration
(vi)	Composite restoration
(vii)	Stainless Steel Crown with Hall technique (No LA & No tooth preparation)
(viii)	Conventional Stainless steel crown (With LA & Tooth preparation)
(ix)	Extraction



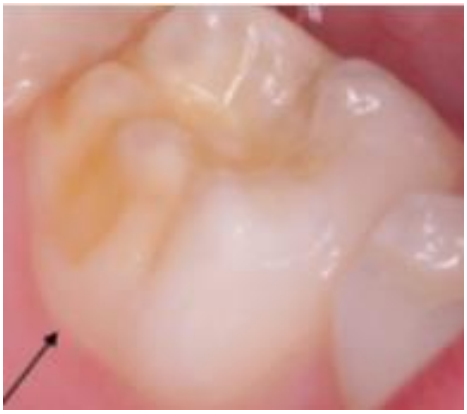
16. Which treatment would you provide for this hypomineralised, asymptomatic SPM (E) with post eruptive breakdown and atypical caries. The patient is five years old, has good oral hygiene and is very cooperative.

(i)	No treatment with preventive advice
(ii)	Fluoride varnish
(iii)	Fissure sealant (glass ionomer)
(iv)	Fissure sealant (resin)
(v)	Glass ionomer restoration
(vi)	Composite restoration
(vii)	Stainless Steel Crown with Hall technique (No LA & No tooth preparation)
(viii)	Conventional Stainless steel crown (With LA & Tooth preparation)
(ix)	Extraction



17. Which treatment would you provide for this caries free, hypomineralised SPM (E) with post eruptive breakdown? The patient is 8 years old, has good oral hygiene and is cooperative.

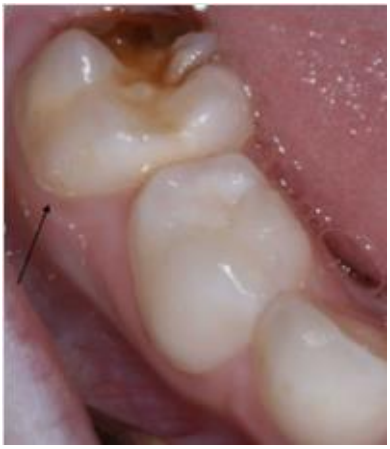
(i)	No treatment with preventive advice
(ii)	Fluoride varnish
(iii)	Fissure sealant (glass ionomer)
(iv)	Fissure sealant (resin)
(v)	Glass ionomer restoration
(vi)	Composite restoration
(vii)	Stainless Steel Crown with Hall technique (No LA & No tooth preparation)
(viii)	Conventional Stainless steel crown (With LA & Tooth preparation)
(ix)	Extraction



18. Which treatment would you provide for this hypomineralised SPM (E) with post eruptive breakdown and atypical caries? The tooth is asymptomatic and there are no signs of clinical or radiographic infection.

The patient is 8 years old, has good oral hygiene and is very cooperative.

(i)	No treatment with preventive advice
(ii)	Fluoride varnish
(iii)	Fissure sealant (glass ionomer)
(iv)	Fissure sealant (resin)
(v)	Glass ionomer restoration
(vi)	Composite restoration
(vii)	Stainless Steel Crown with Hall technique (No LA & No tooth preparation)
(viii)	Conventional Stainless steel crown (With LA & Tooth preparation)
(ix)	Extraction



19. Are you aware that hypomineralised SPMs (Es) may be predictive of Molar Incisor Hypo mineralisation in the FPM teeth (MIH)?

(a) Yes
(b) No

Study 3- Appendix 3.3: Pilot questions

Questionnaire Pilot Phase **Candidate No_____**

Question		Yes	No	Comment
1. Readability	Did the questions and their phrasing make sense?			
2. Clarity	Were all questions expressed clearly and in an easy to understand manner?			
3. Layout	Was the layout easy to follow?			
4. Sequence	Did questions follow a logical sequence?			
5. Relevance and representativeness	Were all questions relevant and representative of the subject being discussed?			
6. Appropriateness	Were all questions appropriate?			

Is there any question you feel would be relevant and was not included in the questionnaire?

No
Yes (describe below)