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Pulpotomy as treatment option in mature permanent dentition with irreversible pulpitis: A systematic review

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Pulpotomy as treatment option in mature permanent dentition with irreversible pulpitis: A systematic review.

"SYSTEMATIC REVIEW"

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Table of Abbreviations

Abbreviation:	**Meaning:**
CEM	Calcium-Enriched Materia
CH	Calcium Hydroxide
K	Cohen's kappa score statistic
MTA	Mineral Trioxide Aggregate
NSRCT	Non-surgical Root Canal Treatment
OCEBM	Oxford Centre for Evidence-Based Medicine
P	P-value statistic
PRF	Platelet-Rich Fibrin
RT	Radiographic
SD	Standard Deviation
VPT	Vital Pulp Therapy

Abstract

Introduction: Irreversible pulpitis is a widely prevalent disease with very poor prognosis for the tooth if left untreated. Typically for permanent dentition with mature apices, the treatment options have been limited to either non-surgical root canal therapy (NSRCT) or extraction. Unfortunately, both options pose disadvantages, with NSRCT leading to the loss of the pulp vitality, and extraction causing occlusion and functional problems. Recent studies have suggested the possibility of pulpotomy as an alternative treatment option which would allow the pulp of the tooth to remain in the roots, thereby maintaining the biological advantages its retention. This systematic review aims to evaluate if pulpotomy is a viable treatment option in such instances.

Materials and Methods: An electronic search was conducted in four databases (PubMed, EBSCOhost, Scopus and Web of Science) combined with backwards referencing, towards studies conducted for pulpotomy in mature permanent dentition with irreversible pulpitis, until April 2023.

Results: 49 studies from the initial search were identified, with 11 studies included in the final systematic review: 6 randomised control/clinical trials, 3 observational studies, 1 prospective study and 1 pilot feasibility study. 5 pulpotomy agents were used in this study: MTA, CH, Biodentine, CEM and PRF. The weighted mean overall success for VPT at six-months was 79.44%, at one-year 83%, and 77.15% at two-years.

Conclusion: Pulpotomy showed a very high success rate from 6 months to 2 years, with results comparable to NSRCT. MTA appeared to be the most successful pulpotomy agent however further research is needed into the other materials.

Key words*: mature adult dentition, irreversible pulpitis, pulpotomy, endodontic treatment, root canal therapy*

Resumen

Introducción: La pulpitis irreversible es una enfermedad ampliamente prevalente con muy mal pronóstico para el diente si no se trata. Normalmente, en la dentición permanente con ápices maduros, las opciones de tratamiento se han limitado a la endodoncia no quirúrgica o a la extracción. Lamentablemente, ambas opciones presentan desventajas, ya que el tratamiento no quirúrgico del conducto radicular conduce a la pérdida de vitalidad de la pulpa y la extracción causa problemas funcionales y de oclusión. Estudios recientes han sugerido la posibilidad de la pulpotomía como una opción de tratamiento alternativa que permitiría que la pulpa del diente permanezca en las raíces, manteniendo así las ventajas biológicas su retención. Esta revisión sistemática pretende evaluar si la pulpotomía es una opción de tratamiento viable en estos casos.

Materiales y métodos: Se realizó una búsqueda electrónica en cuatro bases de datos (PubMed, EBSCOhost, Scopus y Web of Science) combinada con referencias de estudios dirigidos hacia pulpotomias en dentición permanente madura con pulpitis irreversible, hasta abril del 2023.

Resultados: Se identificaron 49 estudios de la búsqueda inicial, con 11 estudios incluidos en la revisión sistemática final: 6 ensayos controlados aleatorios/clínicos, 3 estudios observacionales, 1 estudio prospectivo y 1 estudio piloto de viabilidad. En este estudio se utilizaron 5 agentes de pulpotomía: MTA, CH, Biodentine, CEM y PRF. La media ponderada del éxito global de la VPT a los seis meses fue del 79,44%, al año del 83% y a los dos años del 77,15%.

Conclusiones: La pulpotomía mostró una tasa de éxito muy elevada entre los 6 meses y los 2 años, con resultados comparables a los del NSRCT. El MTA parecía ser el agente de pulpotomía más exitoso, aunque es necesario seguir investigando los demás materiales.

Palabras claves: *mature adult dentition, irreversible pulpitis, pulpotomy, endodontic treatment, root canal therapy.*

I. Introduction

1.1 General

Dental caries in permanent teeth is the most prevalent disease globally as demonstrated in "The Global Burden of Disease" (GBD) 2017 (1) and are thought to affect 97% of people worldwide during their lifetime(2), with untreated caries affecting 35% global population in 2010 (3). For the patient this can be concerning as failure to treat caries is the leading cause of tooth loss in adults, as well as extreme pain, often as a sequalae of pulpal disease progression(4). Caries bacteria is the major cause of pulpal inflammation and infection (5), and untreated caries can allow the ingress of bacteria and their toxins into the pulpal portion of the tooth, leading to varying degrees of inflammation with varying consequences ranging from asymptomatic to intolerable pain, due to conditions such as pulpitis and other pulpal diseases. Pulpal disease very common, with an estimated prevalence of 16.4% to over 30%. However, irreversible pulpitis, a serious form of pulpitis, oftentimes shows no pain and therefore it is undetected in up 40% of cases(6). Because it can go undetected, as well as the poor prognosis for the associated tooth if left untreated, irreversible pulpitis is particularly ominous.

Traditionally, non-surgical root canal treatment (NSRCT) was the mainstay treatment for carious pulp exposures, particularly in mature permanent teeth, as recommended reputable authorities such as the American Dental Association 2020, European Society of Odontology 2006 (7), and others. However, histological studies have shown that clinical diagnosis does not always coincide with histological evaluation. In addition, pulpal infection may be limited to the coronal portion of the pulp, and pulpectomy may not be necessary.

In the last decade, there has been growing evidence from clinical trials demonstrating the favourable outcomes of vital pulp therapy in cases of irreversible pulpitis. As a result, professional societies have published new position statements on the treatment of teeth with carious pulp exposure and diagnosed with reversible or irreversible pulpitis, with a growing openness towards vital pulp therapies (VPT) for irreversible pulpitis in mature permanent dentition (8).

1.2 Dental Caries

Dental caries is a progressive disease process which may be defined as a biofilm-mediated, diet modulated, multifactorial, non-communicable, dynamic disease resulting in net mineral loss of dental hard tissues, which is determined by biological, behavioural, psychosocial, and environmental factors(9). The disease is initially reversible and its progression can be stopped at any stage, even when a cavitation appears, should sufficient biofilm be eliminated. Dental caries is considered a chronic disease that has a slow progression in the majority of individuals(10).

When the microorganisms from the oral cavity associated with the carious lesion degrade the mineralised tissues of enamel and dentine and invade the dental pulp, pulpal disease such as necrosis and pulpitis can occur. After cavitation, the bacteria and their by-products are able to diffuse along the dentinal tubules, resulting in a pulpal inflammation, pulpitis.(11)

1.3 Pulp, Dentin and the Body's Defence against Caries

The human body is not defenceless to this microbial attack to the dentition and so disease progression is not without resistance. The pulp has sensory and defensive mechanism which are very advanced and well-orchestrated to detect and fight-off the bacteria and their toxins. . The dentin also provides protection in conjunction with the pulp.

Both functionally and anatomically, the dentin and dental pulp are considered a single entity and are often associated as the "dentin-pulp complex" (12). Dentin is the mineralised avascular connective tissue which forms the majority of the tooth's structure. It underlies and provides both support and resilience to the enamel of the crown and the cementum of the roots. The dental pulp is a richly innervated and highly vascularised soft connective tissue(13). It is a very significant structure within a tooth and has multiple functions(14). One of purposes of the dental pulp is that it is responsible for the formation of dentine, which continues throughout the tooth's life and can form secondary dentine circumferentially at a slow rate. The pulp can also form reactionary dentine and reparative dentine in response to adverse stimuli, including caries, bacteria, operative dental procedures, or trauma to the tooth. Reactionary dentine tubules are continuous with the primary dentine and include odontoblastic processes, while reparative dentine is irregular and often missing dentinal

tubules and localized to the site of irritation(14). These harmful noxious stimuli can also lead to the sclerosis of dentin, whereby the odontoblasts secrete hydroxyapatite crystals into the dentinal tubules in order to reduce their permeability and thus retard the ingress of bacteria and their toxins (15).

A unique characteristic of the pulp is that this highly vascular soft tissue is confined with within the ridged area created by its enclosure by calcified dentin walls. As a consequence of this peculiarity, when the pulp is subjected to an inflammation, such that seen when caries lesions approximate the pulp, the subsequent vasodilation and increased blood flow can directly harm the pulp tissue due the inextensible environment. The high vascularity is however very useful as it provides the tooth with immunological defence mechanisms (16). The ridged chamber of dentin, cementum (at the radicular level) and enamel (superficially to the dentin) however offers advantages to the pulp such as providing a strong mechanical support, and protection from the microbial rich oral environment(17).

The nerves of the richly innervated pulp enter via the apical foramen and form the subodontoblastic plexus within the pulp. The few axons which pass into the odotoblast layer extend into the dentinal tubules. In response to fluid changes within the tubule, they are able to provide a warming of the nearby noxious stimuli and imminent or initiating tissue damage. The fluid in the dentinal tubules is produced by ultrafiltration from the pulpal capillaries, and can dilute toxins to reduce their harmful effects. The hydrostatic pressure is greatest at the pulpal end of the tubule, and this outward force helps to limit the entry of microorganisms for a limited time. The pulp requires a blood supply to transport immune cells and inflammatory mediators to the site, and to dilute and remove harmful substances, thereby resisting infection for as long as possible(15).

The enamel is considered the most crucial protective tissue, as it is the outermost layer of the tooth exposed to the oral cavity containing bacteria. If the enamel is damaged, particularly with exposed dentine, bacteria may enter and irritate the pulp. Dentinal tubules can then provide a direct pathway to the pulp for bacteria or endotoxins, potentially causing pulp irritation (18). The major causes of compromise to the ridged tooth structures are caries (17). Bacteria are the most common cause of pulp, root canal, and periradicular diseases

(14). Other major compromising factors of the tooth structure include fractures and leaky restoration margins. If untreated, the infiltrated dentinal tubules will develop into pulpal necrosis and the inflammation may spread to the surrounding alveolar bone and cause periapical pathosis (17).

As the carious lesion comes closer to the pulp tissue, both the innate and adaptive immune responses are activated. The front line of the defence is performed by layer of odontoblasts, which exist on the periphery of the pulp chamber, proximal to the dentine. They act to both produce mineralised tissue and to provide protection by forming a cell barrier. Odontoblasts are also able to recognise pathogens early in the process, secrete antibacterial compounds and neutralise bacterial toxins, initiate the immune response and alert other key players of the host defence. Should the bacteria advance closer to the pulp, additional cell types of the pulp, including fibroblasts, stem and immune cells, but also vascular and neuronal networks, contribute with a variety of specific defence mechanisms and inflammatory mediations which are crucial for pulpal homeostasis (19).

As discussed, immune cells in the healthy human pulp provide protection and surveillance functions. Leukocytes are present but contribute less than 1% to the total cell population. Of the other types of immune cells found, the pulp contains granulocytes/neutrophils (CD16+ CD15+ CD14−) as the major subpopulation, followed by CD3+ T lymphocytes, CD14+ monocytes and dendritic cells. Minor subpopulations include natural killer (NK) cells, B cells and regulatory T cells (T-regs). These immune cells are essential to the initiation of the immunological response of the pulp to oral pathogens and toxins, especially with the coordination between the immune cells and other cells types in the pulp such as odontoblasts, pulp fibroblasts and pulpal stem cells (19).

1.4 Pathogenesis of Pulpitis

The steps from the bacteria's presence into the pulp, and then subsequent necrosis, is a well-documented pathogenesis which must be prevented. At the stage of irreversible pulpitis, the pulp is considered as "incapable of healing" (7). The chain of progression usually follows the inevitable sequence of: Clinically normal pulp, followed by chronic reversible pulpitis, acute reversible pulpitis, chronic irreversible pulpitis, acute irreversible pulpitis, pulp

necrobiosis, pulp necrosis with infection, and then finally a pulpless and infected root canal system (20). This infected root canal system then will go on to infect the periradicular tissues, where a myriad of further complication can arise, with potentially lethal consequences in extreme cases such as untreated facial cellulitis. Figure 1 is a schematic adapted from (14), which illustrates some of such complications should the infected root canal system be allowed to persist without treatment.

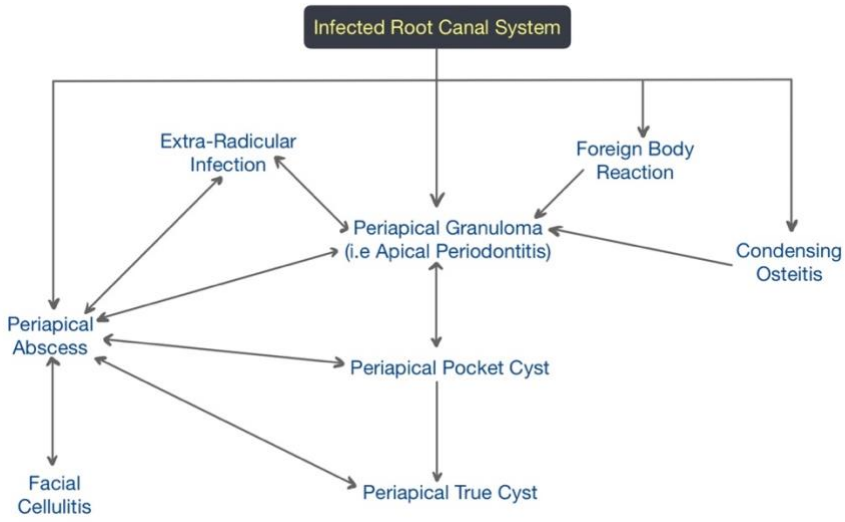


***Figure 1**: schematic adapted from Abbott P et al, 2022* (14)

Patients with apical periodontitis may seek treatment at any point in the disease process, but most commonly present during acute episodes that cause pain. However, some patients may delay seeking treatment and experience subsiding pain as acute inflammation becomes chronic. As the disease progresses, a periapical radiolucency may develop, and the patient may experience occasional episodes of pain from secondary acute apical periodontitis. This cycle may occur multiple times before the patient seeks treatment. In some cases, a chronic apical abscess may develop, and the patient may notice a draining sinus, prompting them to seek treatment (14).

1.5 Definition and Categorisation of Pulpitis and Other Pulpal Diseases

In order to better understand how to prevent and treat pulpal disease, the field of dentistry specifically focused on pulpal diseases and periradicular tissues, namely endodontics, has attempted to create classifications and definitions of pulpal disease. A major pulpal disease is pulpitis, which the American Association of Endodontists (AAE) defines pulpitis as "a

clinical and histologic term denoting inflammation of the dental pulp; clinically described as reversible or irreversible and histologically described as acute, chronic or hyperplastic" (21). The other pulpal disease defined by AAE is pulpal necrosis, which is a clinical diagnostic category indicating death of the dental pulp(4).

Clinically, pulpitis has been categorised/subdivided broadly in a dichotomous way: reversible and irreversible pulpitis (7). AAE defines "reversible pulpitis" as a "clinical diagnosis based on subjective and objective findings indicating that the inflammation should resolve and the pulp return to normal" (7). In contrast, the AAE defines "irreversible pulpitis" (IP) as "a clinical diagnosis based on subjective and objective findings indicating that the vital inflamed pulp is incapable of healing and that root canal treatment is indicated" (7). Irreversible pulpitis is then further subdivided into two clinical forms: symptomatic or asymptomatic irreversible pulpitis. The distinction of the two forms is determined only by their additional descriptors, with symptomatic irreversible pulpitis presenting lingering thermal pain, spontaneous pain, referred pain. Asymptomatic irreversible pulpitis presents clinically with no clinical symptoms, but with inflammation produced by caries, caries excavation, trauma(7).

It is understood however that this classification of pulpitis into irreversible and reversible has its limitations, principally because clinical symptoms and sensibility testing of pulp disease has a poor correlation with the actual pulp status when assessed histologically (3). The pulp itself is very difficult to clinically monitor regarding the stage of inflammation it is currently at, as currently there exists no device available in normal clinical settings which provides an accurate, non-invasive estimation of pulpal inflammation. Clinicians are therefore resorted to reliance upon indirect methods to determine diagnoses, and it should be noted that because of this, both irreversible and reversible pulpitis are not based on true histopathologic conditions(12).

Due to the gap between the actual histopatholoical condition of the pulp and its clinically diagnosed form, there is room for opinion when categorising the type and diagnosis of pulpitis from a clinical perspective. The major shortcoming of such categorisations of pulpitis into simply irreversible and reversible forms, is the lack of clear definition and clinical determination of what separates these stages biologically(6).

Different authors have suggested varying categorisations, with none having universal adoption. The AAE is a very prominent authority when it comes to the categorisation of pulpitis, hence for the proceeding document, their categorisation will be used. However, it is worth noting how other prominent authors and authorities have decided to categorise the different pulpal diseases. Many of such categorisations can be seen in table 1, which is an adaptation of the comparative table published in the Australian Dental Journal in 2007 (22).

Author and year	Normal pulp status	Pulpitis	Pulp necrosis	Pulp degenerations	Additional categorisation
World Health Organisation (1995) (23)	(NOTE: Normal pulp not mentioned)	Initial (hyperaemia) Acute - Suppurative (pulpal abscess) Chronic - Chronic ulcerative - Chronic hyperplastic (pulpal polyp) Other unspecified pulpitis Pulpitis unspecified	Necosis of the pulp	Pulp degenerations: - Denticles - Pulp calcification - Pulpal stones	Abnormal hard tissue formation in pulp - Secondary or irregular dentin
Weine (1989) (24)	(NOTE: Normal pulp not mentioned)	Hyperalgesia (reversible pulpitis) - Hypersensitive dentine - Hyperaemia Painful pulpitis - Acute pulpalgia (acute pulpitis) Chronic pulpalgia (subacute pulpitis) Nonpainful pulpitis Chronic ulcerative pulpitis Chronic pulpitis (no caries) Chronic hyperplastic pulpitis (pulp polyp)	Pulp necrosis	Pulp degeneration: - Atrophy - Dystrophic calcification	Internal resorption
Ingle (1965) (25)	Healthy pulp	Hyper-reactive pulpalgia Hypersensitivity Hyperaemia Acute pulpalgia - Incipient - Moderate - Advanced Chronic pulpalgia Hyperplastic pulposis	Pulp necrosis: Liquefaction Sicca	Pulp degeneration: - Atrophic pulposis - Calcific pulposis	Internal resorption
Seltzer & Bender (1984) (26)	(NOTE: Normal pulp not mentioned)	Incipient form of chronic pulpitis Acute pulpitis Chronic partial pulpitis with partial necrosis Chronic total pulpitis with partial liquefaction necrosis	Pulp necrosis	Pulp degeneration: - Atrophic pulp - Dystrophic Mineralization	

		Chronic partial pulpitis (hyperplastic form)		
Cohen & Burns (1998) (27)	Within normal Limits - Normal pulp - Calcific metamorphosis	Reversible Irreversible - Asymptomatic irreversible pulpitis Hyperplastic pulpitis Internal resorption Canal calcification Symptomatic irreversible pulpitis	Necrosis: - Partial - Complete	
Tronstad (1991) (28)	Healthy pulp	Asymptomatic pulpitis Symptomatic pulpitis	Necrotic pulp	
AAE Glossary (2020) (4)	Normal pulp	Reversible pulpitis Irreversible pulpitis (IP) - Symptomatic IP - Asymptomatic IP	Pulp necrosis	
Harty (1990) (29)	Normal pulp	Reversible pulpitis Irreversible pulpitis	Necrosis	
Walton & Torabinejad (2002) (30)	(NOTE: Normal pulp not mentioned)	Reversible pulpitis Irreversible pulpitis Hyperplastic pulpitis	Pulpal necrosis: - Pulp calcification - Internal (intracanal) resorption	
Grossman (1978) (31)	(NOTE: Normal pulp not mentioned)	Hyperaemia Pulpitides: - Acute pulpitis - Chronic ulcerative pulpitis - Chronic hyperplastic pulpitis	Necrosis	Pulp degeneration: - Calcific - Fibrous - Atrophic - Internal resorption
Castellucci (2004) (32)	Healthy pulp	Hyperaemia Pulpitis irreversible	Necrosis	
Stock (2004) (33)	Normal pulp	Concussed pulp - Reversible pulpitis - Irreversible pulpitis	Pulpal necrosis: Internal resorption	
Bergenholtz (2003) (34)	Pulpa sana	Pulpitis	Necrosis pulpae	

Table 1: Comparison of different categorisations of pulpal disease (22)

Due to these issues in the clinical diagnosis and subsequent treatment decision regarding pulpitis, authors Wolters et al (35) have proposed a newer classification which they believe should be used in, shown in table 2 .

Stage of pulpitis	*Clinical Description*	*Histological Description*	*Therapy*
Initial pulpitis	Heightened but not lengthened response to the cold test Not sensitive to percussion and no spontaneous pain.	Limited local inflammation confined to coronal pulp	Indirect pulp capping
Mild pulpitis	Heightened and lengthened reaction to cold, warmth and sweet stimuli that can last up to 20 s but then subsides, possibly percussion sensitive.	Limited local inflammation confined to coronal pulp	Indirect pulp capping
Moderate pulpitis	Clear symptoms, strong, heightened and prolonged reaction to cold, which can last for minutes Possibly percussion sensitive Spontaneous dull pain that can be more or less suppressed with pain medication.	Extensive local inflammation confined to the crown pulp	Coronal pulpotomy – partly/completely
Severe pulpitis	Severe spontaneous pain and clear pain reaction to warmth and cold stimuli Often, sharp to dull throbbing pain, patients have trouble sleeping because of the pain (gets worse when lying down). Tooth is very sensitive to touch and percussion.	Extensive local inflammation in the crown pulp that possibly extends into the root canals	Full coronal pulpotomy if haemostasis can be achieved. If bleeding from pulp stumps persists, more inflamed tissue is removed from canals. If bleeding still persists, full pulpectomy is done

Table 2: Wolters et al classification (35)

1.6 Current treatment of Irreversible Pulpitis – Non-Surgical Root Canal Therapy

The pulp of a tooth with irreversible pulpitis (IP) is typically considered as "incapable of healing"(7) and therefore the treatment has traditionally been the invasive approach of a complete pulp extirpation (pulpectomy) followed by the completion of the nonsurgical root canal procedure (NSRCT)(7,36) As discussed earlier, the ramifications of leaving irreversible pulpitis untreated warrant a treatment method that must ensure a minimal risk of an infection of the root canal system and peri-radicular tissues. Endodontic treatment such as NSRCT, intends on achieving this securely. It involves the chemo-mechanical preparation of the root canal system to eliminate organic, inorganic and bacterial products, as well as the sealing of the radicular space with a biocompatible material (obturation). Root canal sealers are used in conjunction with the core filling material to establish an adequate three-dimensional seal and induce hard tissue formation in healing outcomes (37). The procedural steps are well-established, and include: cavity preparation into the pulp chamber of the tooth, extirpation of the pulp tissue, complete filling of the pulp space in order to an environment conducive of healing and to prevent future bacterial ingress, followed finally by a definitive restoration of the endodontic cavity and coronal tooth structure (38).

NSRCT has shown a very good success rate, with some studies showing a success rate of 93% at 3 years, and 88% at 5 years (39). For such reasons, NSRCT has been a universally

accepted treatment procedure. However, it is not without issues. The limitations of non-surgical RCT are technical, biological and economical. From a technical perspective, NSRCT is an elaborate treatment procedure which is technique sensitive, oftentimes requiring multiple appointments, a skilled and experienced dental practitioner, and the use of a complex armamentarium. These technical limitations also lend themselves to a high cost that the patient must incur if he/she elects for the procedure (8). For patients who cannot afford NSRCT, or for instances where a sufficiently skilled practitioner is not available, the patient may need to be treated with the traditionally used alternative treatment of tooth extraction. Extractions hinder function and quality of life (38)he limitations of NSRCT from a biological perspective are multifold, but based around the advantages of preserving the pulpal tissue. By removing the pulp, the tooth is unable to maintain pulpal proprioception, immune defence mechanism, and the regenerative potential of the radicular healthy pulp (8). In addition, maintaining pulp vitality would enables continual development of the tooth and dento-alveloar complex when the tooth is still forming (40).

Another factor which bodes poorly for the esteem held for NSRCT as a treatment option for irreversible pulpitis, is that as discussed earlier, the validity of the diagnostic term "irreversible pulpitis" has been questioned following the emerging body of evidence which shows that the clinical diagnosis of IP might not correlate well with the histologic condition of the pulp. Recent evidence suggests that even in situations of advanced pulpal inflammation with irreversible pulpitis, the bacterial infection and micro-abscesses were limited to the coronal portion of the pulp only, with a sound condition in the underlying and/or radicular pulp (41).

The biological limitations of NSRCT lie forgoing the benefits of maintaining pulp vitality. These benefits are significant, and are seemingly becoming more possible with recent developments in biomaterial science such as Bioceramic materials, as well as an increased understanding of the role of dentine and molecular influences on pulpal repair (14). In addition, "minimally invasive dentistry/endodontics" have emerged as a research trend, with a focus being placed on the minimal loss of biological tissues where possible (14). Studies have also shown that Root canal treated teeth have a lower chance of survival compared to teeth that have not undergone root canal treatment. This could be due to poor disinfection

resulting in an ongoing infection or the re-entry of bacteria into the root canal system through leaks in the filling. Furthermore, root canal treated teeth are structurally weaker and are more susceptible to fracture (15). In fact, a study conducted on human teeth has found that those with viable pulp are less susceptible to bacterial invasion into the dentinal tubules compared to teeth with root canal fillings, demonstrating that the pulp plays a crucial role in defending against bacterial invasion (17). As a consequence of these factors, there has been much recent research and gradual adoption of new treatment strategies for pulpitis, most notably being vital pulp therapy (VPT)(14)

1.7 Vital Pulp Therapy

In endodontics, the maintenance of a healthy pulpal tissue whilst preventing the infection of the periodontium, forms the basis of minimally invasive and biologically based vital pulp treatment (VPT). Despite improvements in understanding of the protective abilities of the dentin-pulp complex in both a protective as well as reparative capacity, treatment of deep carious lesions, pulpitis and pulpal exposure has previously been considered as unpredictable and hence why NSRCT has traditionally been the treatment of choice for irreversible pulpitis in mature permanent dentition. Research now shows that it is possible for even symptomatic pulp to recover if managed correctly, even if the caries is extremely deep (14), with other new studies demonstrating that patients presenting with irreversible pulpitis can be definitively treated effectively with a pulpotomy (a form of VPT) (42). If sufficient research proves this to be correct, there will be a resultant paradigm shift in how we manage pulpal disease, and that the current terms used for pulpal disease will be inaccurate (40). Despite of this, a 2017 study shows less invasive procedures are not currently common in places such as France and Germany (43).

As per the British Endodontic Society, Vital pulp therapy/treatment (VPT) is the umbrella term for the following four treatments: (40)

1. *Indirect pulp capping:* The application of a material onto a thin layer of dentine which is close to the pulp with the aim of producing a positive biological response so the pulp can protect itself.
2. *Direct pulp capping:* The application of a material directly onto the pulp with the aim of producing a positive biological response so the pulp can protect itself.

3. *Partial pulpotomy:* The removal of a small portion of superficial coronal pulp tissue followed by the application of a material directly onto the pulp with the aim of producing a positive biological response so the pulp can protect itself.
4. *Full pulpotomy:* Complete removal of the coronal pulp to the root canal orifice level followed by the application of a material directly onto the remaining pulp with the aim of producing a positive biological response so the pulp can protect itself.

1.8 Pulpotomy

This paper attempts to investigate the viability of pulpotomy as a treatment option for mature, permanent dentition, therefore a further look specifically into pulpotomy is very important.

Pulpotomy is the most invasive of the four main VPTs, however it has also been demonstrated to be the most predictable and successful VPT in the management of carious pulp exposures. Pulpotomy has also demonstrated success in permanent teeth, with reports of a success range between 82% to 100% (44). More specifically and perhaps surprisingly, a systematic review from 2017 has shown that even in permanent teeth with a mature apex, coronal pulpotomy may have success rates of 92.7% after three years (45).

This isn't to say that pulpotomy of mature permanent teeth suffering irreversible pulpitis is a definitely recommendable treatment option, superior to the currently recommended NSRCT. Most authors indicate for the need of further research before widespread adaptation, mainly due to the fears of a gap of knowledge surrounding the risk factors involved in such a treatment, which include the correct identification of the preoperative symptoms, sound diagnosis of the pulpal condition, consideration of the stage of root development, and the choice of pulp capping material (41).

In both the minimally invasive VPT and indirect pulp capping, pulpal exposure is not performed and so they are considered less invasive procedures that direct pulp capping and pulpotomy, where pulpal exposure is performed. The question then arises of the required extent of pulpal exposure. The general rule is that if the caries is both deep and the diagnosis of the pulp is irreversible pulpitis, and the response to pulp sensibility testing is beyond

normal limits, pulpal exposure is needed during the VPT. In order to determine the extent of pulpal tissue removal required, the clinician must combine three sources of evidence: pulpal bleeding, the visual condition of the pulp, and preoperative symptoms. Another general rule is that if haemostasis cannot be controlled after 5 minutes, or necrotic tissue is evident visually, further pulp tissue should be removed leading through partial pulpotomy, full pulpotomy, and eventually pulpectomy. To treat irreversible pulpitis, a partial or coronal pulpotomy may be performed to the level of the root canal orifices. Once bleeding has stopped, a pulpotomy agent should be applied directly to the pulp tissue and the tooth should be restored right away (14).

Pulpotomy can be performed as either a partial or a full pulpotomy. Partial pulpotomy is the removal of a limited portion of vital coronal pulp as a means of preserving the remaining coronal and radicular pulp tissues (4). It is also known as “shallow pulpotomy (or “Cvek” pulpotomy if performed after trauma or mechanical exposure), and may be preferred over pulp capping after carious exposure because it allows for physical removal of biofilm and inflamed pulp tissue and creates a cavity for capping material. In cases of extremely deep carious lesions, partial pulpotomy may be preferable to avoid infected dentine chips entering the pulp, but it is technically challenging and requires a skilled operator with magnification. Some studies indicate that partial pulpotomy has a success rate of over 75% after at least 12 months in teeth with (partial) irreversible pulpitis, with improved results when using MTA as the capping agent rather than calcium hydroxide. Partial pulpotomy involved the removal of 2-3 mm of pulp tissue. On the other hand, a full pulpotomy involves removing the entire coronal pulp and placing a biomaterial directly onto the pulp tissue at the level of the root canal orifices (14). Partial pulpotomy is indicated when: “Dentine is lost due to caries, trauma or previous iatrogenic intervention and a cavity exists where the soft tissue of the pulp is exposed and bleeding. The exposed pulp appears to be inflamed/contaminated or it is not possible to get haemostasis. Symptoms may exist” (40).

As for full pulpotomy, according to the British Endodontic Society, the procedure is as follows: “The tooth should be isolated with a rubber dam. The coronal pulp tissue is completely removed to canal orifice level with a high-speed handpiece and bleeding controlled using cotton pellets soaked (removing gross excess) ideally with sodium

hypochlorite (0.5 -5%). If bleeding is not controlled within five minutes further pulp tissue should be removed until haemostasis is achieved or it is determined that a pulpectomy should be carried out. A CSC is placed onto the remaining pulp tissue. However, calcium hydroxide is suitable if an appropriate CSC is not available. If calcium hydroxide is used it should be sealed with glass ionomer cement (GIC) or a resin glass ionomer cement (RMGIC)." (40)

A concern regarding the use of pulpotomy in mature permanent dentition is that although historical success has been shown for the technique, it has been focused on young immature permanent teeth. This is because of a lack of understanding of the pulp's healing capabilities, confounded by the limitation of available materials (8). In the past, calcium hydroxide was commonly used for VPT and aalthough it has some benefits, there are concerns about its long-term effectiveness, as studies have shown lower success rates compared to other materials like mineral trioxide aggregate (MTA) (36,46).

II. Justification, Hypothesis, Objectives

2.1 Justification

Short of extraction, non-surgical root canal treatment (NSRCT) is widely considered the only viable treatment option for adult mature teeth suffering irreversible pulpitis (7,36). However, this treatment is not without its drawbacks; it is very technique sensitive, not very cost-effective and it does not save any vital pulp (8). With that being said, recent publications have indicated that another possible treatment option may be a viable alternative to NSRCT, namely pulpotomy. Traditionally pulpotomy has only been considered possible for adult teeth suffering irreversible pulpitis if the root apex has not yet closed i.e. only in immature adult dentition. Recent publications have now emerged however, which indicate pulpotomy may also be effective in mature adult dentition (42,45). This is very interesting as full pulpotomy offers some clear advantages over NSRCT such as simplifying the management of complex cases, less invasive, less painful, avoiding the need for extraction and reducing the cost and burden of patient referral, as well as attempting to retain some vitality in the tooth. Due to the advantages that pulpotomy offers, it would appear to be a better option if possible and effective. However, the evidence is still emerging and relatively limited. To this end, this study was designed to look at the available publications to determine if pulpotomy is a viable treatment option for mature adult teeth with irreversible pulpitis, and to see how effective it is when compared to the current treatment option for such cases, NSRCT.

2.2 Hypothesis

Null Hypothesis (H_0): Pulpotomy is not an effective treatment option in mature permanent dentition with irreversible pulpitis.

Alternative Hypothesis (H_A): Pulpotomy is an effective treatment option in mature permanent dentition with irreversible pulpitis.

2.3 Objectives

General objective: Evaluate the overall success of pulpotomy as a treatment option in mature adult dentition with irreversible pulpitis.

Specific objective: Identify which materials are most effective for the pulpotomy in mature adult dentition with irreversible pulpitis.

Materials and Methods

3.1 Key words and MeSH terms

In order to identify and collect studies which investigated the effectiveness of pulpotomy as a treatment for irreversible pulpitis in mature permanent dentition, a PICO (Patients Intervention Comparison Outcome) type question was created using MeSH terms (Medical Subject Headings). These MeSH terms were transcribed from DeCS (Descriptors in Health Sciences) vocabulary.

The MeSH keywords included 'mature adult dentition', 'irreversible pulpitis', 'pulpotomy', 'endodontic treatment', 'root canal therapy'. Moreover, Boolean operators such (OR, AND) were used such as 'Mature permanent dentition' OR 'Mature adult dentition' OR 'Mature permanent teeth)'OR 'Mature adult teeth' OR 'Adult closed apex' OR 'Permanent closed apex' AND 'Irreversible pulpitis'. For more about which specific Boolean operators were used, please see *table 1*.

3.2 PICO Question

Using the PICO question "is pulpotomy a treatment option in mature permanent dentition with irreversible pulpitis?", a search was created and subsequent Boolean operators added, which have been included in *table 3*:

P - Population	I - Intervention	C - Comparison	O - Outcome
Patients with mature permanent dentition, with irreversible pulpitis	Pulpotomy of mature permanent dentition	Endodontic treatment	Outcomes of pulpotomy as a treatment option
Boolean used: ((Mature permanent dentition) OR (Mature adult dentition) OR (Mature permanent teeth) OR (Mature adult teeth) OR (Adult	Boolean used: Pulpotomy AND (((Mature permanent dentition) OR (Mature adult dentition) OR (Mature permanent teeth) OR (Mature	Boolean used: ((Endodontic treatment) OR (Root canal treatment) OR Root canal therapy [MeSH] OR (RCTx) OR (RCT)) AND (((Mature	Boolean used: (outcomes pulpotomy) AND ((Mature permanent dentition) OR (Mature adult dentition) OR (Mature permanent teeth) OR

closed apex) OR (Permanent closed apex)) AND (Irreversible pulpitis)	adult teeth) OR (Adult closed apex) OR (Permanent closed apex)) AND (Irreversible pulpitis))	permanent dentition) OR (Mature adult dentition) OR (Mature permanent teeth) OR (Mature adult teeth) OR (Adult closed apex) OR (Permanent closed apex)) AND (Irreversible pulpitis))	(Mature adult teeth) OR (Adult closed apex) OR (Permanent closed apex)) AND (Irreversible pulpitis)

Table 3: PICO Question and Boolean operators

3.3 Databases consulted

The following databases were consulted to obtain relevant studies to this research: PubMed, EBSCO, Scopus, Web of Science. After searching these databases with the Boolean operators and PICO question as a framework as shown in table 2, 88 articles were found: PubMed (n=33), EBSCO (n=5), Scopus (n=8), Web of science (n=42).

3.4 Inclusion and Exclusion Criteria

Inclusion criteria:

- **Type of study:** Randomized controlled clinical trials; quasi experimental studies; studies of prospective and retrospective cohorts and case series; studies on human subjects, number of participants ≥6 patients; transversal studies; publications in English language; published until February 2023, with no limit on the study age.
- **Type of patient:** Patients with adult/permanent dentition with closed apex presenting with irreversible pulpitis in said teeth.

  Type of intervention: Full pulpotomy treatment of said teeth, with the use of appropriate pulpotomy agents (MTA, Biodentin, ferric sulfate, calcium hydroxide, formocresol or others) and pulpotomy techniques.
- **Type of outcome variables**: primary outcomes are lack of clinical and radiographical signs of failure. Secondary outcome variables include healing or resolution of periapical rarefication after pulpotomy. Minimum follow-up of 6 months.

Exclusion criteria:

- **Type of study:** Case reports, case series, or review papers.
- **Type of patient:** Studies reporting on pulpotomy in deciduous teeth or teeth with an immature apex.
- **Type of intervention:** Studies reporting on pulpotomy in teeth with trauma. Studies using lasers in pulpotomy. Studies reporting on other vital pulp therapy procedures such as direct or indirect pulp capping
- **Outcome variable**: Studies not reporting on success rate or where raw data was is unavailable to calculate success rate. Studies where outcomes do not separate irreversible pulpitis from reversible pulpitis

3.5 Search Strategy

The relevant keywords and MeSH (Medical Subject Heading) terms were identified and used in combination through the use of Boolean operators ("AND", "OR", "NOT") in order to obtain 42 articles before screening. In addition, backwards refereeing was used to identify a further 4 articles, making a total of 46 articles initially. No restriction in the way of year of publication was made. Details of the PICO question and Boolean operators used can be seen in table 3.

Selection was then made in multiple stages. Of the initial 46 articles, a preliminary screening of titles and abstracts was conducted, followed by a more rigorous screening of the articles after having obtained the full documents were possible. Details of this can be seen in the PRISMA 2020 flow chart in figure 2.

IV. Results

4.1 Selection of Articles: Prisma Flow Chart

After the initial search using the four selected databases, a total of 88 studies were obtained: PubMed (n=33), EBSCOhost (n=5), SCOPUS (n=8), Web of Science (n=42). Backwards referencing was also used to obtain an initial set of further articles: backward referencing (n=4). Of the initial 88 studies from the four databases, pre-screening duplicate removal lead to the inclusion of 53 studies for title and abstract screening: PubMed (n=33), Web of Science (n=20). Subsequent to article and title screening, 30 studies from database searching were sought for retrieval: PubMed (n=20), Web of Science (n=8). Of these, 24 studies were then obtained and assed for eligibility: Pubmed (n=15), Web of Science (n=9). From the backwards referencing, all 4 studies were sought for retrieval. After final eligibility screening, a total of 11 studies were included in the final review: PubMed (n=8), Web of Science (n=2), backward referencing (n=1).

The k-value for inter-examiner agreement on the inclusion of studies was 0.74 (titles and abstracts) and 1.00 (full-text) indicating " Substantial" and "complete" agreement, respectively, according to Landisy Koch's criteria (47).

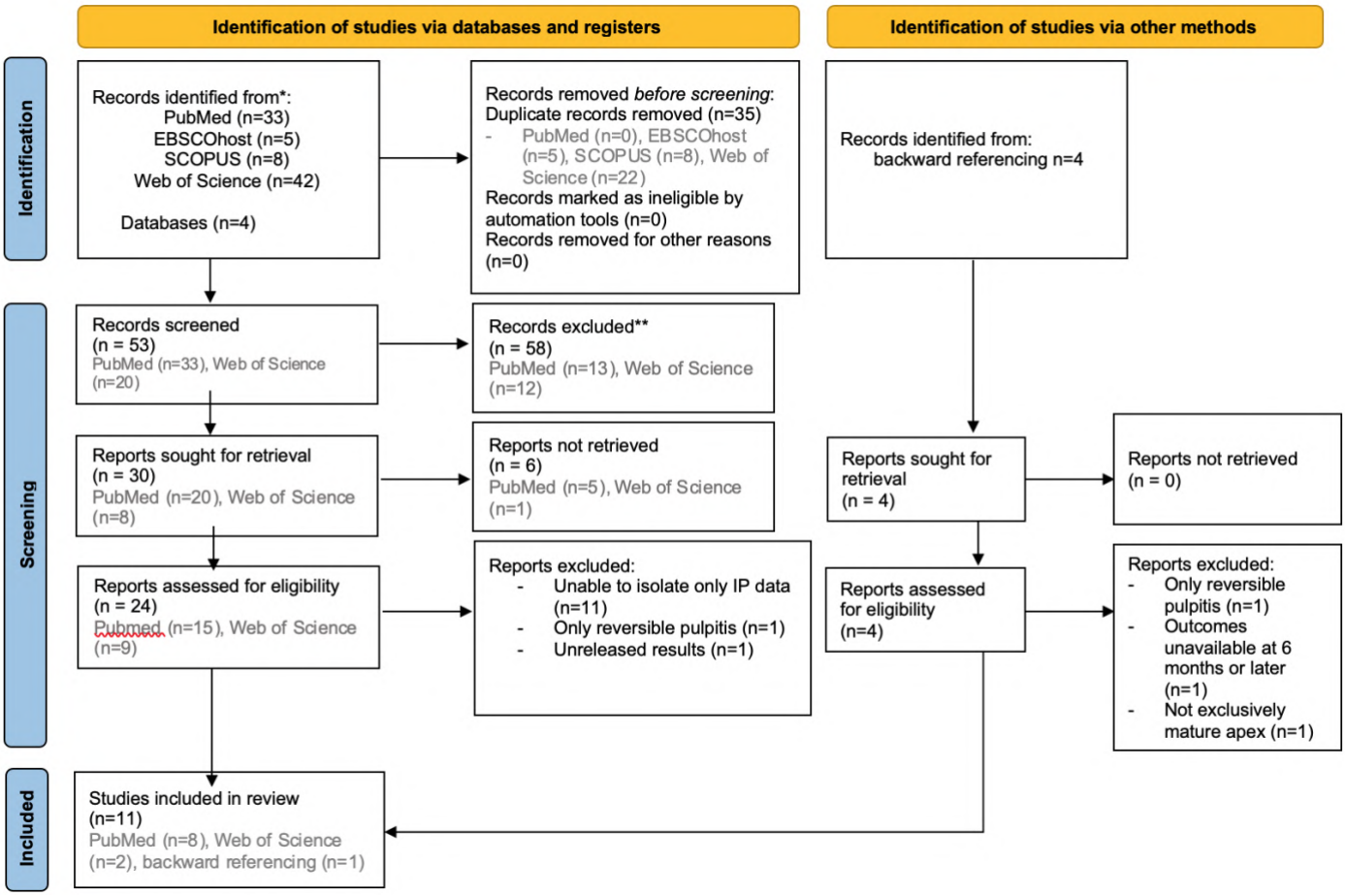


***Figure 2**:* PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources (48).

Annex 1 shows the rationale behind the inclusion/exclusion of the studies selected in this systematic review. It functions as an accompaniment to figure 2.

4.2 Classification of the studies

4.2.1 Classification according to the study type

The studies included in this systematic review were of different types, including 2 randomised control trials (49,50), 4 randomised clinical trials (51–54), 3 observational studies (55–57), 1 prospective study (58), and 1 block-randomised pilot feasibility study (59). Additionally, five different pulpotomy agents were used: MTA, calcium hydroxide (CH), Biodentine, CEM (calcium-enriched mixture) and PRF (platelet-rich fibrin).

Table 4 illustrates the different materials and study types, as well as the reported outcome success in each study, using data only of overall outcome success where possible, and separated into clinical and radiographical success where overall success not stated in the study.

#	Database	Author and year	Type of study	Age range (Mean±SD)	Pulpotomy Agent(s)	Sample size (teeth)	6 month Success (%)	1 year Success (%)	2 year Success (%)	5 year Success (%)
1	PubMed	Taha NA et al. 2017	Randomized Clinical Trial	20 – 52 (30.3±9.6)	MTA	27	84%	83%	85%	-
					CH	23	62%	55%	43%	-
2	PubMed	Sánchez-Lara Y et al. 2022	Pilot Feasibility Study, block randomised	17 - 78 (34.63±15.76)	MTA	41	-	97.5%	-	-
3	PubMed	Koli B et al. 2021	Observational Study	18 - 35 (24.8±5.95)	MTA	30	-	93.3%	-	-
4	PubMed	Taha NA et al. 2018	Observational Study	19 – 69 (33.2)	Biodentine	64	98.40%	Clinical = 100% RT = 98.4%	-	-
5	PubMed	Sharma R et al. 2021	Observational Study	16 -35 years (25.3±6.17)	MTA	40	-	88%	-	-
6	PubMed	Rechithra R et al. 2021	Prospective Clinical Study	16 - 35	MTA	80	-	93.75%	-	-
7	PubMed	Asgary S et al. 2013*	Randomized Clinical Trial	9 - 65	CEM	205	Clinical = 94.4%	Clinical = 97.6%	-	-
8	PubMed	Asgary S et al. 2014*	Randomized Clinical Trial	9 - 65	CEM	205	Clinical = 94.4%)	Clinical = 97.6%*	Clinical = 98.19% RT = 86.1%	-
9	PubMed	Asgary S et al. 2015*	Randomized Clinical Trial	9 – 65	CEM	205	Clinical = 94.4%*	Clinical = 97.6%*	Clinical = 98.19% RT = 86.1%	78.1%
10	Web of Science	Galani M et al. 2017	Randomized Controlled Trial	15 – 36 (20.56±4.38)	MTA	26	-	1.5 year success = 96.67%		-
11	Manual	Kumar V et al. 2016	Randomized Controlled Trial	14 - 23 (17.81)	CH	18	68.75%	37.50%	-	-
				14 - 32 (21.20)	MTA	19	66.70%	44.40%		
				14 - 32 (25.81)	PRF	17	50%	35.70%		

*Asgary S et al 2013, 2014, 2015 are continuations of the same report.

CEM= Calcium-enriched material
CH= Calcium Hydroxide

PRF= Platelet-rich fibrin

RT= Radiorgraphic

Manual database is equivalent to "backward referencing"

Table 4: study characteristics and reported outcome success

Most studies reported the overall success of the treatments investigated (51,54–59), however some studies made note of just the clinical success (52,53). Radiographic success was included, however not appropriately for inclusion in this results table as it was only created as a comparison between one period of time to its changes at another. Some studies included both the clinical and radiographical results, yet made no inclusion on an explicitly stated "overall success" value (53,54,56).

The sample sizes from all of the studies ranged from 17 to 205, and the ages ranged from 9-69 years (49–59).

4.2.2 Classification according to the level of evidence

In order to evaluate the level of evidence of each study, the Jadad Scale was used for randomised control trials and randomised clinical trials (60), with the results demonstrated in table 5. All studies were also evaluated with regards to their level of evidence according to the Oxford scale of scientific evidence Classification of the individual articles, shown in table 6 (61). As for the risk of bias, the non-randomised studies were evaluated using the Cochrane ROBINS-I tool (62) shown in table 7 and figure 3.

Table 5: Jadad Scale for randomised studies (60)

		Randomisation		Blinding		Withdrawals and drop-outs	
Author	**Title**	**Was the study described as randomized?**	**Was the method of randomization appropriate?**	**Was the study described as double-blind?**	**Was the method of blinding appropriate?**	**Were withdrawals and dropouts described?**	**Total Score**
Taha NA et al. 2017	Partial Pulpotomy in Mature Permanent Teeth with Clinical Signs Indicative of Irreversible Pulpitis: A Randomized Clinical Trial	1	1	0	0	0	**2**
Asgary S et al. 2013*	One-year results of vital pulp therapy in permanent molars with irreversible pulpitis: an ongoing multicenter, randomized, non-inferiority clinical trial	1	1	0	0	1	**3**
Asgary S et al. 2014*	Two-year results of vital pulp therapy in permanent molars with irreversible pulpitis: an ongoing multicenter randomized clinical trial	1	1	0	0	1	**3**
Asgary S et al. 2015*	Five-year results of vital pulp therapy in permanent molars with irreversible pulpitis: a non-inferiority multicenter randomized clinical trial	1	1	0	0	1	**3**
Galani M et al. 2017	Comparative Evaluation of Postoperative Pain and Success Rate after Pulpotomy and Root Canal Treatment in Cariously Exposed Mature Permanent Molars: A Randomized Controlled Trial	1	1	0	0	0	**2**
Kumar V et al. 2016	Comparative evaluation of platelet-rich fibrin, mineral trioxide aggregate, and calcium hydroxide as pulpotomy agents in permanent molars with irreversible pulpitis: A randomized controlled trial	1	1	1	1	1	**5**

*Asgary et al 2013, 2014, 2015 are all continuations of the same study, and hence they share the same Jadad Score.

Table 6: Oxford scale of scientific evidence Classification of the individual articles.(61)

No.	Author and Year	Title	Type of Study	OCEBM Evidence level
1	Taha NA et al. 2017	Partial Pulpotomy in Mature Permanent Teeth with Clinical Signs Indicative of Irreversible Pulpitis: A Randomized Clinical Trial	Randomized Clinical Trial	2b
2	Sánchez-Lara Y et al. 2022	A Pilot Feasibility Study to Establish Full Pulpotomy in Mature Permanent Teeth with Symptomatic Irreversible Pulpitis as a Routine Treatment in Mexican Public Healthcare Services	Pilot Feasibility Study, block randomised	4
3	Koli B et al. 2021	Combination of Nonsurgical Endodontic and Vital Pulp Therapy for Management of Mature Permanent Mandibular Molar Teeth with Symptomatic Irreversible Pulpitis and Apical Periodontitis	Observational Study	3b
4	Taha NA et al. 2018	Outcome of full pulpotomy using Biodentine in adult patients with symptoms indicative of irreversible pulpitis	Observational Study	3b
5	Sharma R et al. 2021	Association between concentration of active MMP-9 in pulpal blood and pulpotomy outcome in permanent mature teeth with irreversible pulpitis - a preliminary study	Observational study	3b
6	Rechithra R et al. 2021	Influence of occlusal and proximal caries on the outcome of full pulpotomy in permanent mandibular molar teeth with partial irreversible pulpitis: A prospective study	Prospective Clinical Study	3b
7	Asgary S et al. 2013*	One-year results of vital pulp therapy in permanent molars with irreversible pulpitis: an ongoing multicenter, randomized, non-inferiority clinical trial	Randomized Clinical Trial	2b
8	Asgary S et al. 2014*	Two-year results of vital pulp therapy in permanent molars with irreversible pulpitis: an ongoing multicenter randomized clinical trial	Randomized Clinical Trial	2b
9	Asgary S et al. 2015*	Five-year results of vital pulp therapy in permanent molars with irreversible pulpitis: a non-inferiority multicenter randomized clinical trial	Randomized Clinical Trial	2b
10	Galini M et al. 2017	Comparative Evaluation of Postoperative Pain and Success Rate after Pulpotomy and Root Canal Treatment in Cariously Exposed Mature Permanent Molars: A Randomized Controlled Trial	Randomized control trial	2b
11	Kumar V et al. 2016	Comparative evaluation of platelet-rich fibrin, mineral trioxide aggregate, and calcium hydroxide as pulpotomy agents in permanent molars with irreversible pulpitis: A randomized controlled trial	Randomized Control Trial	2b

Table 7: Cochrane ROBINS-I risk of bias (62)

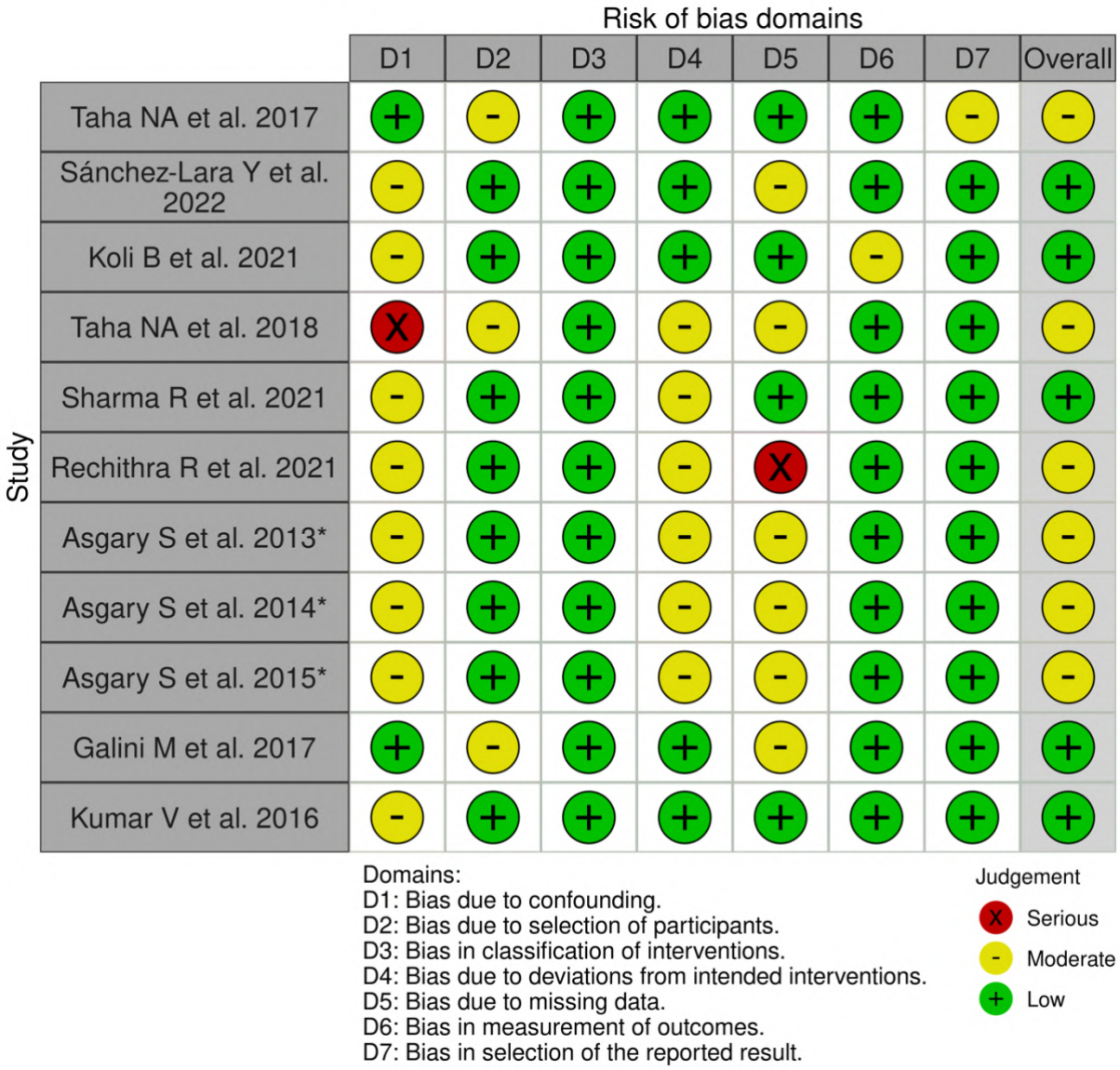
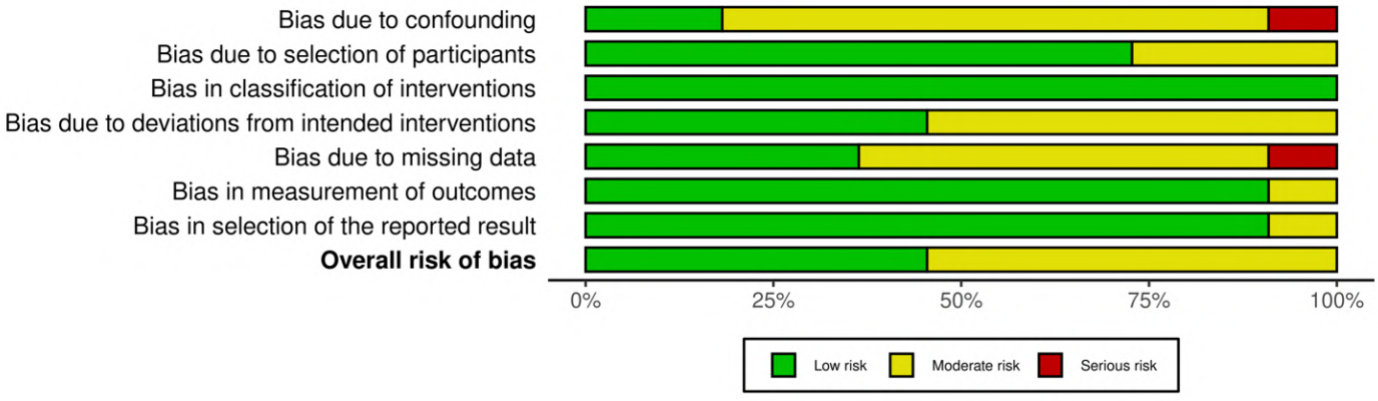


Figure 3: Cochrane ROBINS-I risk of bias diagram



4.3 Critical Analysis of the Results

The results of this systematic review are reported in terms of success of the pulpotomy, either clinically, radiographically or overall, as shown in table 4. Despite the heterogeneity of the results, the weighted mean and standard deviation can be calculated for both different time period and for different materials, the calculations for which can be found in Annex 2. The weighted mean overall success for VPT after six-months was 79.44% with a standard deviation of 0.0302. In this calculation, values from Asgary et al 2013, 2014 and 2015 papers were not included due to their lack of reporting on an overall success rate or both a clinical and radiographical success rate (52–54) At the one-year duration, the weighted mean for overall success was 83% with a standard deviation of 0.0448. This calculation excluded Asgary et al 2013, 2014 and 2015 study for the same reasons as mentioned for the prior mean calculation (52–54), and it also involved creating an overall success percentage for the study by Taha NA et al 2018 (56), by averaging the reported clinical and radiographic success rates . The overall mean two-year success rate was calculated to be 77.15% with a standard deviation of 0.0406. This calculation involved averaging the reported clinical and radiographic success rates for Asgary et al 2015 (54), and did not attempt to include Asgary et al 2014 (53) in order to not double count the same study twice, as both studies are continuations of the same experiment. Additionally, Galani et al 2017 who reported a 96.67% overall success rate, was not incorporated into the any of the mean calculations as the report was unique in providing results at the 1.5-year mark, which was an incompatible duration for the calculations.

Other statistics such as pain levels were thoroughly reported in many of the studies, however they were not relevant outcomes in this systematic review.

V. Discussion

Previous systematic reviews have mainly aimed to focus on the outcomes of pulpotomy in teeth with deep caries (44,63), however very few have been conducted specifically on mature dentition with signs indicating irreversible pulpitis. To this end studies were excluded if they did not clearly detail a sound technique for pulp extirpation, pulpotomy and subsequent restoration. Additionally, the inclusion and exclusion criteria were applied strictly as they were created based on research of other comparable studies and contemplation of the requirements needed to answer the general and secondary objectives of this systematic review. Some studies were excluded due to their lack of differentiation in pulpotomy outcome depending on if the tooth was diagnoses with reversible or irreversible pulpitis (8,64,65).

5.1 Evaluation: Overall success of pulptomy in mature permanent dentition with irreversible pulpitis

The main objective of this systematic review was to evaluate the overall success of pulpotomy as a treatment option in mature adult dentition with irreversible pulpitis. It was found that the mean success after six months 79.44% with a standard deviation of 0.0302, mean one-year success was 83% with a standard deviation of 0.0448, and finally a mean two-year success of 77.15% with a standard deviation of 0.0406. Additionally, the only study which provided a five-year outcome, Asgary S et al. 2015, reported a success of 78.1% (54). Another study also reported at a slightly different outcome time to the other studies, reporting an eighteen-month success of 96.67% (49). These results concur with the few systematic reviews and meta-analysis which report on the same topic and seem to suggest that the overall success of pulpotomy in mature permanent dentition with signs of irreversible pulpitis, is relatively high (38,42,66). The results are also similar to those found in mature permanent dentition with reversible pulpitis as demonstrated by Alqaderi H et al. who found one-year and two-year success at 94% and 92% respectively (67).

In order to further evaluate this question, it may be important to contrast these values of outcome success to those seen in the alternative treatment option, namely non-surgical root canal therapy (NSRCT). By drawing this comparison, further contextual understanding can

be given to the efficacy of pulpotomy in such conditions. NSRCT has shown a very good success rate, with some studies showing a success rate of 93% at 3 years, and 88% at 5 years (39). However other studies have demonstrated a much lower success rate. Interestingly, many of the studies included in this systematic review were studies conducted with one arm for VPT and another study arm for NSRCT (49,52–55,57). This is of particular interest when trying to evaluate the success of pulpotomy in such instances, as comparing both interventions in the same study allows a better control of variables, consistent outcome measurements and internal validity. Koli et al found that the one-year success for NSRCT was 90%, whereas it was 93.3% in the VPT group, demonstrating a very high treatment success in both groups (55). Sharma et al didn't draw a good comparison between VPT and NSRCT since unlike the VPT group, the NSRCT group was diagnosed as not having irreversible pulpitis (57)

Most noteworthy in this direct inter-study comparison of VPT and NSRCT was the randomised control trial conducted over five years by Asgary et al, who had a very large sample size of 407 patients, randomly allocated into a VPT group and a NSRCT group (52–54). They found that the six-month success for VPT and NSRCT was 94.4% and 91.3% respectively, with a p-value of 0.257. At twelve-months, the success was 97.6% and 89.3% for VPT and NSRCT respectively, with a p-value of 0.718 (52,53). Their five-year analysis included a large size of 271 patients (66.6 %; 137 in VPT group and 134 in NSRCT group) who showed no significant differences in follow-up duration according to an independent t test at a p-value 0.27. They found a success rate of 78.1% and 75.3 % for the VPT and NSRCT groups, respectively (P=0.61), and the chi-square test revealed no significant difference in the treatment outcomes (54). This would indicate that even over the extended time period of five years, pulpotomy as a treatment option was a viable option in comparison to NSRCT, without considering the additional advantages that VPT has to offer over NSRCT.

Of the studies included in this systematic review, one showed quite negative outcomes of overall success at the six month and one-year period. This was the randomised control trial conducted by Kumar et al, who found an overall success after six months of 50-69.75%, and a one-year success of 35.7-44.4% (50). These values came from a sample size of fifty-four,

and showed a low success for VPT regardless of which of the three materials they used. However their clinical success at the same outcome periods was very high and comparable to the to the other studies of this review, showing a success of 81.2-92.8% at both six months and one year (50).

5.2 Evaluation: Success of different pulpotomy agents in treating irreversible pulpitis in mature permanent dentition

The secondary objective of this systematic review is to identify which materials are most effective for the pulpotomy in mature adult dentition with mature apex. This is a very important question to investigate because pulpotomy has demonstrated a high success rate comparable to NSRCT in the treatment of irreversible pulpitis in closed apex, permanent teeth, yet concerns due to a lack of understanding take part in its current low adaptation by clinicians. Understanding the pulp biology, pulpotomy agent choices, and their efficacy, can direct clinicians to make a more informed choice when opting for VPT, and it can also help to guide the direction of future research in this area.

In order to maintain a healthy pulp in VPT, the primary objective of any pulp capping agent is to support the normal functions of the tooth and promote the deposition of reactionary or reparative dentine. This will assist in increasing the thickness of dentine between the pulp and the deepest part of the cavity, protecting the pulp from future harmful stimuli. The ideal requirements desired from a pulp capping material in VPT include: Antimicrobial activity, creation of a bacterial tight seal and prevention of microleakage, promotion of tertiary dentinogenesis and control of hard tissue barrier formation, biocompatibility (prevention of 'over'-irritation and avoidance of induction of a severe inflammatory response), radiopacity, clinical ease of handling, resistant to forces of displacement following the subsequent application of a further material over the agent used in VPT, and finally, a lack of induction of tooth discolouration. However, no single material is able to satisfy each of these desires (68).

Traditionally, calcium hydroxide (CH) has been conventionally used pulp capping material in VPT, however CH as a pulp capping agent has shown instability, susceptibility to microleakage, as well as poor insolubility and ineffective dentinal adhesion. Fortunately,

research has now improved on newer materials such as bioceramics, with studies suggesting much more favourable outcomes and characteristics (69).

The success rate of endodontic procedures has been improved since the early 1990s with the use of MTA due to its exceptional biocompatibility, ability to seal, ability to tolerate moisture, and features that promote bone growth (8). MTA is a Portland cement, with common suppliers including Dentsply-Tulsa Dental in Johnson City, USA. It has been widely accepted as the most effective bioceramic material for various clinical applications and is the been the most thoroughly researched among the bioceramic cements (69). Although MTA has consistently shown a high success rate in various clinical studies, it's drawbacks include the possibility of causing discoloration, long setting time, and difficult handling. Consequently, clinicians and researchers have been continuously searching for superior materials (8).

More recently, newer bioceramic materials have been introduced, including as Biodentin and Calcium Enriched Mixture (CEM) (69). This is very welcome as some authors have raised issues regarding the initial cytotoxicity and reduction in the size of pulp chamber due to the formation of reparative dentin deeper to CH or MTA (50). Biodentine (Septodont) is composed of tricalcium silicate, dicalcium silicate, calcium carbonate, zirconium oxide, iron oxide, bismuth oxide (insoluble radiopacifier) and calcium chloride. Marketed as a dentin substitute, it offers a shorter and better setting time, 10-12 minutes, then ProRoot MTA. Additionally, it is both biocompatible, with a comparable sealing ability to MTA. By forming needle-like cystals, it is able to adhere well to the underlying dentin, leading to a similar hard-tissue layer as that formed by MTA. MTA has shown success in direct pulp capping as well as in partial and full pulpotmies (8).

Calcium enriched mixture (CEM) is promising pulp-capoping agent made of calcium oxide, sulfur trioxide, phosphorous pentoxide, silicon dioxide as major components and other minor compoents. Upon mixture with a water-based solution, CEM forms a bioactive calcium and phosphate enriched mixture with physical propoties comparable to MTA (69).

Rutherford and Fitzgerald interestingly suggested a therapeutic approach permitting the induction of a predetermined and controlled amount of reparative dentin. They believed that

there was a possibility of creating fibrous connective tissue which would lie superficial to the pulpal tissue and not as a replacement at the expense of it. This layer would then promise to mineralises to form reparative dentin (70). The discovery of such a biological pulpotomy agent, which attenuates inflammation and promotes regeneration, has lead to the study of Platelet-rich fibrin (PRF). PRF is solely autologous and therefore indicated a very high biocompatibility with limited pulpal inflammatory response when directly placed onto the amputated pulp. PRF also could offer pulpal healing support by moderating pulpal inflammation, and has been successful used in the management of a mature molar with irreversible pulpitis, however, evidence is very limited in its use in the long term especially (50,71).

Despite the improved understanding of pulpal biology, improvements in material choices, evidences of VPTs efficacy and the shift in desires towants minimally invasive endodontics, pulpotomy in irreversible pulpitis has not been widely adopted. A recent review paper by Henry Duncan summarised this lack of adaptation to four main factors: a lack of consensus in decision-making when managing deep caries and the inflamed pulp, diagnostic issues when assessing and treating the inflamed pulp, a need for further clinical outcome evaluation for VPT in relation to the inflamed pulp, and finally further understanding needed on the importance of tissue handling, VPT materials and visual inspection after carious exposure (71).

The eleven studies included in this systematic review reported on five different pulpotomy agents: MTA, calcium hydroxide (CH), Biodentine, CEM (calcium-enriched mixture) and PRF (platelet-rich fibrin). MTA was incorporated in seven studies (49,50,55–59), with ProRoot White MTA being utilised by six studies (49–51,55,57,58) and only Sánchez-Lara et al utilising a different MTA (White MTA by Angelus) (59). The two studies which used CH, used different manufacturers, with Taha NA et al using CH by Dycal, and Kuman et al using CH by Prevest Denpro (50,51). As for Biodentine and PRF, only one study utilised each (but neither used both in the same study) (50,56).

The results obtained allowed the calculation of weighted mean success associated with each pulpotomy agent, however heterogeneity in outcomes provided certain difficulties in these

calculations (see annex 3 for more detailed calculations). With regards to MTA, only one study by Taha NA et al reported a six-month outcome, reporting an overall success of 84% (51). The overall weighted mean success for MTA at one-year was 92% with a standard deviation of 0.0447. Again the same study by Taha NA et al was the only to report a two-year outcome for MTA, which was found to be 85% (51). Gilani et al reported a 1.5-year success for MTA of 96.67% (49). Overall, MTA appears to be a very successful material for VPT in mature adult dentition with irreversible pulpitis, and it was also the most well-studied material in this review, with a total sample size of 218 across six different studies (49,51,55,57–59).

Calcium hydroxide (CH) appeared to demonstrate less favourable outcome results as a pulpotomy agent. The weighted mean success at six-months was 64.96% with a standard deviation of 0.0335, and a considerably low one-year mean success of 47.32% with a standard deviation of 0.0868 (50,51). The outcome at 2-years was reported only by one study, Taha Na et al, with an overall success for CH at low 43%. A total sample size of 41was reported on for CH across two studies (50,51). This is a low sample size, and when combined with the low success rates and lack of 5-year study, perhaps further research is needed before CH should be considered recommendable as the pulpotomy agent of choice.

CEM had just one study to report, split over 3 publications for different time released and slightly different commentary (52–54). The results on CEM at 6-months and 1-year are a clinical success of 94.4% and 97.6% respectively. The five-year success overall was reported at 78.% (54). A total sample size of 205 was included which is very large with the drawback that external validity of these results is unknown as it is drawn from only one study. However, this was a five-year study and it demonstrated a respectable Jadad score of 3, OCEM of 2b and ROBINS-I was moderate.

Finally, biodentin was also reported by just one single study by Taha NA et al 2018 (56). The six-month success was 98.4%, and the 1-year success was clinically 100% and radiographically 98.4%. These are very high success rates, however again the external validity is questionable due to a singlular study. The sample size was less than for CEM, at 64, and the study was evaluated to have a OCEM of 3b and a moderate ROBINS-I score.

5.3 Limitations

The limitations of this systematic review are mainly due to the heterogeneity of the outcomes measured, making it difficult to conduct further statistical analysis or attempt a meta-analysis.

The first study of the review by Taha and Khazali had the issues of a relatively limited sample size of 50, which may restrict the external validity of the findings. It had a moderate JADAD score of 2, suggesting some limitations in study quality, such as the potential for bias or incomplete reporting of study methods. This could affect the overall reliability of the results (51).

The second study was conducted by Sanchez-Lara et al as a Pilot feasibility study with block-randomisation. Again, the sample size of 41 is not very large. This study was considered a low 4 on the OCEBM scale for quality of evidence, however the low risk of bias according to ROBINS-I adds some credibility to the findings (59).

The third study of this review was from Koli et al, which also suffered from a small sample size, at 30 teeth. It was regarded as an OCEBM 3b which is quite respectable, and it had a low risk of bias according to ROBINS-I. Unfortunately the study only reported overall outcome at the 1-year mark and didn't provide information at 6-months or later than a year (55).

Study number four was conducted by Taha and Abdelkhader. A limitation of this study was the limited follow-up period of just 1-year, although unlike the previous study, it did report a 6-month outcome. The one-year outcome was not very easy to interpret however, as it reported both clinical and radiographic success, but not overall success. Akin to the previous study, it also scored an OCEBM of 3b, however it was not helped by the ROBINS-I evaluation for risk of bias for which it was graded as moderate (56).

The study by Sharma et al was a preliminary study had a small sample size of 40. Additionally, it only reported the one-year success and didn't provide any outcomes at 6 months or later than one year. Additionally, the concentration of the study on MMP-9 meant

in some areas of interest to this systematic review, it was slightly lacking in description. It is an OCEBM 3b, and it has a low risk of bias according to ROBINS-I (57).

Rechithra R et al's study provided a more respectable sample size of 80, however this is not considered high. A larger sample would provide more robust evidence and enhance the reliability of the findings. It suffered from the exact same limitations as the previous study in that it only reported outcomes at 1-year, and not at 6 months or later that a year. Additionally, Rechithra R et al included an interesting breakdown of the influence of caries location on the success outcome, however this was not of interest in this particular systematic review. The study has a ROBINS-I moderate risk of bias, and is also recognized as a 3b on the OCEBM classification scale (58).

Asgary et al produced three reports of the same study, all three of which were included in this systematic review (52–54). This itself could have posed issues had they been counted as separate studies in the mean calculations. The studies were created as non-inferiority clinical trial design, aiming to demonstrate that vital pulp therapy is not inferior to conventional root canal treatment. However, non-inferiority trials have inherent limitations and potential sources of bias that need to be considered when interpreting the findings. All three of them received an OCEBM level of 2b, with Jadad scores of 3 and a ROBINS-I of moderate risk of bias. The studies also only reported clinical success at 6 months and 1 year, meaning their resuts couldn't be incorporated into the weighted mean which looked to consider only overall success (52–54). The 2014 and 2015 papers however at least reported both clinical and radiographic success at 2 years and 5 years, making it possible to calculate an average overall success (53,54). With regards to Asgary et al 2015 reporting of CEM, despite the very large size of the study, external validity could be low considering it was the only study to report on CEM as a pulpotomy agent in this systematic review (54). In addition, it also was very difficult to interpret the outcomes as they were often reported in comparison to earlier reported success rates for example, five-year treatment outcomes were compared to 1-year treatment outcomes (54).

Galani et al provided a limited sample size of 26. However, the major limitation of this study was in its lack of clear methodology for the diagnosis of irreversible pulpitis, casting doubt

on the reliability of the diagnosis and therefore the results themselves. Outcomes were also not reported at early intervals like six months, and were difficult to compare to other studies as it was the only one to report only at 18 months and not at 6 months, 1 year, 2 years or later. It had a high OCEBM 2b and a low ROBINS-I risk of bias, however a relatively low Jadad score of 2 (49).

The final study included in this systematic review was by Kumar et al 2016 (50). The moderate sample size of 54 was distributed into three groups, which offered a good understanding of how effective different pulpotomy agents are, however lead to a small sample size in each group of 18, 19 and 17 for CH, MTA and PRF respectively. This study proved to be an outlier in that the overall success showed to be much lower than other studies for the same material and time period. Confusingly, clinical and radiographic success was reported as very high in some instances like for example MTA at 6 months had a radiographic success of 84.6% and clinical success of 81.2%, yet the overall success was considered to be only 68.75%, with the authors not explaining well how this much lower overall was derived from such high clinical and radiographic success. OCEBM was 2b for this study, was a perfect Jadad of 5 and a low risk of bias according to ROBINS-I, meaning that despite the areas of confusion, it appeared to be a very reliable study (50).

VI. Conclusion

To conclude, this systematic review indicates that pulpotomy is a viable treatment option in permanent dentition with irreversible pulpitis, with outcome success very comparable or better than NSRCT. When considering the other benefits of VPT over NSRCT, the viability of VPT in such instances is further remarkable.

With regards to pulpotomy agents, MTA in particular appear to be most effective. However due to limited study sizes, it would not be possible to recommend any other material in particular. Areas of further research, particularly in the use Biodentin, CEM, PRF, appears recommendable.

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IV. ANNEX

Annex 1: Table of inclusion and exclusion of all articles considered in this systematic review.

PUBMED

33 results	Article	Author	Year	Sample size	INCLUSION / EXCLUSION reason
1 d	Outcomes of root canal therapy or full pulpotomy using two endodontic biomaterials in mature permanent teeth: a randomized controlled trial	Asgary, Saeed; Eghbal, Mohammad Jafar; Shahravan, Arash; Saberi, Eshaghali; Baghban, Alireza Akbarzadeh; Parhizkar, Ardavan	2022	157 carious pulp exposed teeth Randomised control trial	EXCLUDE not about irreversible Pulpitis
2	Vital Pulp Therapy in Permanent Mature Posterior Teeth with Symptomatic Irreversible Pulpitis: A Systematic Review of Treatment Outcomes	Santos JM, Pereira JF, Marques A, Sequeira DB, Friedman S.	2021	142 articles, of which 9 randomized controlled trials and 3 prospective cohort studies were selected for review.	EXCLUDE because systematic review
3	Success of Coronal Pulpotomy in Permanent Teeth with Irreversible Pulpitis: An Evidence-based Review	Sadaf D.	2020	14 articles	EXCLUDE because evidence
4	Pulpotomy for mature carious teeth with symptoms of irreversible pulpitis: A systematic review	Cushley S, Duncan HF, Lappin MJ, Tomson PL, Lundy FT, Cooper P, Clarke M, El Karim IA.	2019	8 articles	EXCLUDE because systematic
5	Partial Pulpotomy in Mature Permanent Teeth with Clinical Signs Indicative of Irreversible Pulpitis: A Randomized Clinical Trial	Taha NA, Khazali MA.	2017	50 patients all >20 years old	INCLUDE
6	Comparative evaluation of complete and partial pulpotomy in mature permanent teeth with symptomatic irreversible pulpitis: A randomized clinical trial	Ramani A, Sangwan P, Tewari S, Duhan J, Mittal S, Kumar V.	2022	106 permanent molars initial, 101 follow-up All age 18-40 years	Exclude because cannot access
7	Combination of Nonsurgical Endodontic and Vital Pulp Therapy for Management of Mature Permanent Mandibular Molar Teeth with Symptomatic Irreversible Pulpitis and Apical Periodontitis	Koli B, Chawla A, Logani A, Kumar V, Sharma S.	2021	Mandibular molar teeth (N = 60)	INCLUDE
8	Treatment Outcomes of 4 Vital Pulp Therapies in Mature Molars	Asgary S, Hassanizadeh R, Torabzadeh H, Eghbal MJ.	2018	Blinded participants (N = 302) were randomly allocated to 4 study arms.	EXCLUDE because not exclusivley IP
9	Outcome of full pulpotomy in mature permanent molars using 3 calcium silicate-based materials: A parallel, double blind, randomized controlled trial	Taha NA, Al-Rawash MH, Imran ZA.	2022	n=164 teeth (in 146 patients) Block randomization technique: (50 MTA, 50 Biodentine and 64 TotalFill).	EXCLUDE because not exclusivley IP
10	Is pulpotomy an effective therapeutic option for the management of acute irreversible pulpitis in mature permanent teeth?	Madurantakam P.	2022	4 studies	EXCLUDE because comprehensive literature
11	Outcome of pulpotomy in permanent teeth with irreversible pulpitis: a systematic review and meta-analysis	Ather A, Patel B, Gelfond JAL, Ruparel NB.	2022	n=11 studies A total of 1,116 records were retrieved and 11 studies were included in the quantitative analysis.	EXCLUDE because systematic review and meta analysis
12	Long-term Pulpal and Restorative Outcomes of Pulpotomy in Mature Permanent Teeth	Tan SY, Yu VSH, Lim KC, Tan BCK, Neo CLJ, Shen L, Messer HH.	2020	61 teeth (52 patients)	EXCLUDE because not exclusivley IP
13	Factors that influence the outcome of pulpotomy in permanent teeth	Duncan HF, El-Karim I, Dummer PMH, Whitworth J, Nagendrababu V.	2022		EXCLUDE because evidence
14	Minimally invasive endodontics: a new era for pulpotomy in mature permanent teeth	Philip, Nebu; Suneja, Bharat	2022		EXCLUDE because narrative
15	Factors affecting the outcome of full pulpotomy in permanent posterior teeth diagnosed with reversible or irreversible pulpitis	Zhang M, Xiong Y, Wang X, Wang Y, Cai Y, Xu J, Zhang C, Li J.	2022	105 permanent posterior teeth (92 patiets) CANNOT seem to find breakdown of reversible vs irreversible	EXCLUDE because not exclusivley IP
16	A Pilot Feasibility Study to Establish Full Pulpotomy in Mature Permanent Teeth with Symptomatic Irreversible Pulpitis as a Routine Treatment in Mexican Public Healthcare Services	Sánchez-Lara Y Tajonar RG, Vergara-Tinoco JV, Dammaschke T, Domínguez-Pérez RA.	2022	n=41 teeth and 41 patients	INCLUDE
17	Long-term outcomes of pulpotomy in permanent teeth with irreversible pulpitis: A multi-center randomized controlled trial	Asgary S, Eghbal MJ, Bagheban AA.	2017	412 patients met the inclusion criteria. 344 and 304 subjects were available for 2- and 5-year follow-ups	EXCLUDE because not exclusivley IP
18	Health Technology Assessment of CEM Pulpotomy in Permanent Molars with Irreversible Pulpitis	Yazdani S, Jadidfard MP, Tahani B, Kazemian A, Dianat O, Alim Marvasti L.	2014	384 teeth (203 maxillary, 181 mand) 232 with Irreversible Pulpitis (60.4%)	EXCLUDE because not exclusivley IP
19	Evaluation of Complete Pulpotomy With Biodentine on Mature Permanent Molars With Signs and Symptoms of Symptomatic Irreversible Pulpitis: 12-months Follow-up	Anta S, Diouma N, Ousmane NS, Fatou LB, Florence F, Babacar T.	2022	n=68 molars (in 68 patients) A total of 66 patients received complete pulpotomy (diagnosed with symptomatic irreversible pulpitis in 68 patients aged 20 years and older)	Cannot access
20	Association between concentration of active MMP-9 in pulpal blood and pulpotomy outcome in permanent mature teeth with irreversible pulpitis - a preliminary study	Sharma R, Kumar V, Logani A, Chawla A, Mir RA, Sharma S, Kalaivani M.	2021	n=40 permanent molars	INCLUDE
21	Outcome of Mineral Trioxide Aggregate Pulpotomy for Mature Permanent Molars with Symptoms Indicative of Irreversible Pulpitis	Hussain MI, Bashar AM.	2022	n=20 permanent mature third molars in 20 patients	Cannot access
22	Influence of occlusal and proximal caries on the outcome of full pulpotomy in permanent mandibular molar teeth with partial irreversible pulpitis: A prospective study	R R, Aravind A, Kumar V, Sharma S, Chawla A, Logani A.	2021	n=80 mandibular molar teeth (with clinical and radiographic diagnosis of symptomatic partial irreversible pulpitis without periapical rarefaction) occlusal (n = 40) and proximal caries groups (n = 40).	INCLUDE
23	Assessment of Mineral Trioxide Aggregate pulpotomy in mature permanent teeth with carious exposures	Taha NA, Ahmad MB, Ghanim A.	2017	n=52 permanent molar teeth with fully developed roots and vital pulps in 43 patients Clinical signs and symptoms suggestive of irreversible pulpitis were established in 44/52 teeth,	EXCLUDE because not exclusivley IP
24	Outcome of full pulpotomy using Biodentine in adult patients with symptoms indicative of irreversible pulpitis	Taha NA, Abdelkhader SZ.	2018	n=64 permanent molar teeth with symptomatic vital pulps in 52 patients (aged 19-69 years)	INCLUDE
25	A clinical trial of pulpotomy vs. root canal thera	Asgary S, Eghbal MJ.	2010	ARTICLE WAS RETRAC	because retracted
26	Which procedures and materials could be applied for full pulpotomy in permanent mature teeth? A systematic review	Zanini M, Hennequin M, Cousson PY.	2019	53 publications	EXCLUDE because systematic
27	Outcome of partial and full pulpotomy in cariously exposed mature molars with symptoms indicative of irreversible pulpitis: A randomized controlled trial	Jassal A, Nawal RR, Yadav S, Talwar S, Yadav S, Duncan HF.	2023	n=50 mature permanent molar teeth with carious exposures with symptoms indicative of irreversible pulpitis were randomly allocated equally into two groups.	Cannot access
28	Miniature Pulpotomy of Symptomatic Mature Permanent Teeth: A Report of Two Cases	Asgary S, Nourzadeh M, Eghbal MJ	2016	2 clinical cases	EXCLUDE because small case
29	One-year results of vital pulp therapy in permanent molars with irreversible pulpitis: an ongoing multicenter, randomized, non-inferiority clinical trial	Asgary S, Eghbal MJ, Ghoddusi J, Yazdani S.	2013	407 patients spread over 23 healthcare centers Randomly allocated into two study arms including one-visit RCT (reference treatment; n = 202) and VPT/CEM (alternative treatment; n = 205).	INCLUDE
30	Two-year results of vital pulp therapy in permanent molars with irreversible pulpitis: an ongoing multicenter randomized clinical trial	Asgary S, Eghbal MJ, Ghoddusi J.	2014	multicenter (n = 23), non-inferiority clinical trial, 407 patients were randomized to either one-visit RCT (n = 202) or VPT/CEM (n = 205) for 27 months.	INCLUDE
31	Treatment Outcomes of Full Pulpotomy as an Alternative to Tooth Extraction in Molars with Hyperplastic/Irreversible Pulpitis: A Case Report	Asgary S, Verma P, Nosrat A.	2017	1 patient, 2 teeth	EXCLUDE because small case report
32	Vital Pulp Therapy of a Mature Molar with Concurrent Hyperplastic Pulpitis, Internal Root Resorption and Periradicular Periodontitis: A Case Report	Asgary S, Kemal Çalışkan M.	2015	1 patient, 1 tooth	EXCLUDE because small case report
33	Outcome of vital pulp therapy in deeply carious molars affected with molar incisor hypomineralisation (MIH) defects: a randomized clinical trial	Al-Batayneh OB, Abdelghani IM.	2022	n = 50 children with deeply carious young PFM affected with MIH, and diagnosed with reversible or irreversible pulpitis were randomized into 2 groups: indirect pulp treatment (IPT) and pulpotomy (partial or complete).	EXCLUDE because not about IP

EBSCO

	Article	Author	Year	Sample size	INCLUSION/EXCLUSION
5 results					
1	Association between concentration of active MMP-9 in pulpal blood and pulpotomy outcome in permanentmature teeth with irreversible pulpitis - a preliminary study.	Sharma R, Kumar V, Logani A, Chawla A, Mir RA, Sharma S, Kalaivani M.	2021	REPEAT OF PUBMED	REPEAT of PUBMED #20
2	Treatment Outcomes of Full Pulpotomy as an Alternative to Tooth Extraction in Molars with Hyperplastic/Irreversible Pulpitis: A Case Report.	Asgary S, Verma P, Nosrat A.	2017	REPEAT OF PUBMED	REPEAT OF PUBMED #31
3	Minimally invasive endodontics: a new era for pulpotomy in mature permanent teeth	Philip, Nebu; Suneja, Bharat	2022	REPEAT OF PUBMED	REPEAT OF PUBMED #14
4	Outcome of Mineral Trioxide Aggregate Pulpotomy for Mature Permanent Molars with Symptoms Indicative of Irreversible Pulpitis	Hussain MI, Bashar AM.	2022	REPEAT OF PUBMED	REPEAT OF PUBMED #21
5	Success of Coronal Pulpotomy in Permanent Teeth with Irreversible Pulpitis: An Evidence-based Review	Sadaf D.	2020	REPEAT OF PUBMED	REPEAT OF PUBMED #3

SCOPUS

	Article	Author	Year	Sample size	INCLUSION/EXCLUSION
8 results					
1	Minimally invasive endodontics: a new era for pulpotomy in mature permanent teeth	Philip N, Suneja B.	2022	REPEAT OF PUBMED	REPEAT OF PUBMED #14
2	Outcomes of root canal therapy or full pulpotomy using two endodontic biomaterials in mature permanent teeth: a randomized controlled trial	Asgary S, Eghbal MJ, Shahravan A, Saberi E, Baghban AA, Parhizkar A.	2022	REPEAT OF PUBMED	REPEAT OF PUBMED #1
3	Treatment Outcomes of Full Pulpotomy as an Alternative to Tooth Extraction in Molars with Hyperplastic/Irreversible Pulpitis: A Case Report.	Asgary S, Verma P, Nosrat A.	2017	REPEAT OF PUBMED	REPEAT OF PUBMED #31
4	Miniature Pulpotomy of Symptomatic Mature Permanent Teeth: A Report of Two Cases	Asgary S, Nourzadeh M, Eghbal MJ	2016	REPEAT OF PUBMED	REPEAT OF PUBMED #28
5	Two-year results of vital pulp therapy in permanent molars with irreversible pulpitis: an ongoing multicenter randomized clinical trial	Asgary S, Eghbal MJ, Ghoddusi J.	2014	REPEAT OF PUBMED	REPEAT OF PUBMED #30
6	Health Technology Assessment of CEM Pulpotomy in Permanent Molars with Irreversible Pulpitis	Yazdani S, Jadidfard MP, Tahani B, Kazemian A, Dianat O, Alim Marvasti L.	2014	REPEAT OF PUBMED	REPEAT OF PUBMED #18
7	One-year results of vital pulp therapy in permanent molars with irreversible pulpitis: an ongoing multicenter, randomized, non-inferiority clinical trial	Asgary S, Eghbal MJ, Ghoddusi J, Yazdani S.	2013	REPEAT OF PUBMED	REPEAT OF PUBMED #29
8	A clinical trial of pulpotomy vs. root canal thera	Asgary S, Eghbal MJ.	2010	REPEAT OF PUBMED	REPEAT OF PUBMED #25

Manual findings

	Article	Author	Year	Sample size	INCLUSION/CLUSION
4 results					
1	Treatment outcomes of pulpotomy in permanent molars with irreversible pulpitis using biomaterials: A multi-center randomized controlled trial	Asgary, S., & Eghbal, M. J.	2013	n=413 patients MTA pulpotomy (PMTA: n = 208) and CEM pulpotomy (PCEM: n = 205).	EXCLUDE because no exclusivley mature ape
2	MTA pulpotomy of human permanent molars with irreversible pulpitis	Eghbal MJ, Asgary S, Baglue RA, Parirokh M, Ghoddusi J.	2009	n=14	EXLCUDE because les than 6m
3	MTA pulpotomy as an alternative to root canal treatment in children's permanent teeth in a dental public health setting.	Alqaderi HE, Al-Mutawa SA, Qudeimat MA	2014		EXCLUDE because no about IP
4	Comparative evaluation of platelet-rich fibrin, mineral trioxide aggregate, and calcium hydroxide as pulpotomy agents in permanent molars with irreversible pulpitis: A randomized controlled trial	Kumar V, Juneja R, Duhan J, Sangwan P, Tewari S.	2016	n=54	INCLUDE

"manual finding" refers to the articles identifies through backwards referencing

Web of Science

42 results	Article	Author	Year	Sample size	INCLUSION/EXCLUSION
1	The treatment of mature permanent teeth with irreversible pulpitis by cervical pulpotomy: A systematic review	Skitioui, M (Skitioui, Mohamed); Seck, A (Seck, Anta); Niang, SO (Niang, Seydina Ousmane); Fikhar, A (Fikhar, Anass); Toure, B (Toure, Babacar)	2022	4 articles	EXCLUDE because systematic review
2	Pulpotomy for the Management of Irreversible Pulpitis in Mature Teeth (PIP): a feasibility study	Hamilton, Alice; Clarkson, Jan E.; Ramsay, Craig R.; Mannocci, Francesco; Jarad, Fadi; Albadri, Sondos; Ricketts, David; Tait, Carol; Banerjee, Avijit; Deery, Chris; Boyers, Dwayne; Marshman, Zoe; Goulao, Beatriz; Hamilton, Alice R.; Banister, Katie; Bell, Rosanne; Brown, Lori; Conway, David, I; Donaldson, Pina; Duncan, Anne; Dunn, Katharine; Fee, Patrick; Forrest, Mark; Glenny, Anne-Marie; Gouck, Jill; Gupta, Ekta; Jacobsen, Elisabet; Kettle, Jennifer; Maclennan, Graeme; Macpherson, Lorna; McGuff, Tina; Mitchell, Fiona; van der Pol, Marjon; Moazzez, Rebecca; Roberston, Douglas; Wojewodka, Gabriella; Young, Linda; Lamont, Thomas	2022	The feasibility study will recruit and train 10 primary care dentists in the full pulpotomy technique. Dentists will recruit and provide full pulpotomy to 40 participants (four per practice) with indications of partial irreversible pulpitis. Since this is a feasibility study and its aim is not to estimate a treatment effect, a sample size calculation was not performed. We will recruit 530 patient participants from 50 general dental practices in Scotland and England.	EXCLUDE because unreleased results
3	Vital pulp therapy of mature permanent teet with irreversible pulpitis from the perspective of pulp biology	Lin, Louis M.; Ricucci, Domenico; Saoud, Tarek M.; Sigurdsson, Asgeir; Kahler, Bill	2020	N/A	EXCLUDE because narrative reviw paper
4	Pulpotomy for mature carious teeth with symptoms of irreversible pulpitis: A systematic review	Cushley S, Duncan HF, Lappin MJ, Tomson PL, Lundy FT, Cooper P, Clarke M, El Karim IA.	2019	REPEAT OF PUBMED	REPEAT OF PUBMED #4
5	Success of Coronal Pulpotomy in Permanent Teeth with Irreversible Pulpitis: An Evidence-based Review	Sadaf D.	2020	REPEAT OF PUBMED	REPEAT OF PUBMED #3
6	Evaluation of Complete Pulpotomy With Biodentine on Mature Permanent Molars With Signs and Symptoms of Symptomatic Irreversible Pulpitis: 12-months Follow-up	Anta S, Diouma N, Ousmane NS, Fatou LB, Florence F, Babacar T.	2022	REPEAT OF PUBMED	REPEAT OF PUBMED #19
7	Outcome of full pulpotomy using Biodentine in adult patients with symptoms indicative of irreversible pulpitis	Taha NA, Abdelkhader SZ.	2018	REPEAT OF PUBMED	REPEAT OF PUBMED #24
8	Vital Pulp Therapy in Permanent Mature Posterior Teeth with Symptomatic Irreversible Pulpitis: A Systematic Review of Treatment Outcomes	Santos JM, Pereira JF, Marques A, Sequeira DB, Friedman S.	2021	REPEAT OF PUBMED	REPEAT OF PUBMED #2
9	Association between concentration of active MMP-9 in pulpal blood and pulpotomy outcome in permanent mature teeth with irreversible pulpitis - a preliminary study	Sharma R, Kumar V, Logani A, Chawla A, Mir RA, Sharma S, Kalaivani M.	2021	REPEAT OF PUBMED	REPEAT of PUBMED #20
10	A Pilot Feasibility Study to Establish Full Pulpotomy in Mature Permanent Teeth with Symptomatic Irreversible Pulpitis as a Routine Treatment in Mexican Public Healthcare Services	Sánchez-Lara Y Tajonar RG, Vergara-Tinoco JV, Dammaschke T, Domínguez-Pérez RA.	2022	REPEAT OF PUBMED	REPEAT OF PUBMED #16
11	Coronal pulpotomy for cariously exposed permanent posterior teeth with close d apices: A systematic review and meta-analysis	Alqaderi, Hend; Lee, Chun-Teh; Borzangy, Sary; Pagonis, Tom C.	2016	Out of 299 articles, six studies were included for the analysis of one-year WSR, and five studies were included in the analysis of two-year WSR	EXCLUDE because systematic review and meta analysis
12	Combination of Nonsurgical Endodontic and Vital Pulp Therapy for Management of Mature Permanent Mandibular Molar Teeth with Symptomatic Irreversible Pulpitis and Apical Periodontitis	Koli B, Chawla A, Logani A, Kumar V, Sharma S.	2021	REPEAT OF PUBMED	REPEAT OF PUBMED #7
13	Comparative evaluation of complete and partial pulpotomy in mature permanent teeth with symptomatic irreversible pulpitis: A randomized clinical trial	Ramani A, Sangwan P, Tewari S, Duhan J, Mittal S, Kumar V.	2022	REPEAT OF PUBMED	REPEAT OF PUBMED #6
14	Vital Pulp Therapy of Permanent Teeth with Reversible or Irreversible Pulpitis: An Overview of the Literature	Iaculli, Flavia; Rodriguez-Lozano, Francisco Javier; Briseno-Marroquin, Benjamin; Wolf, Thomas Gerhard; Spagnuolo, Gianrico; Rengo, Sandro	2022	N/A	EXCLUDE because literature review
15	Outcomes of root canal therapy or full pulpotomy using two endodontic biomaterials in mature permanent teeth: a randomized controlled trial	Asgary, Saeed; Eghbal, Mohammad Jafar; Shahravan, Arash; Saberi, Eshaghali; Baghban, Alireza Akbarzadeh; Parhizkar, Ardavan	2022	REPEAT OF PUBMED	REPEAT OF PUBMED #1
16	Outcome of partial and full pulpotomy in cariously exposed mature molars with symptoms indicative of irreversible pulpitis: A randomized controlled trial	Jassal A, Nawal RR, Yadav S, Talwar S, Yadav S, Duncan HF.	2023	REPEAT OF PUBMED	REPEAT OF PUBMED #27
17	Assessment of Mineral Trioxide Aggregate pulpotomy in mature permanent teeth with carious exposures	Taha NA, Ahmad MB, Ghanim A.	2017	REPEAT OF PUBMED	REPEAT OF PUBMED #23
18	Which procedures and materials could be applied for full pulpotomy in permanent mature teeth? A systematic review	Zanini M, Hennequin M, Cousson PY.	2019	REPEAT OF PUBMED	REPEAT OF PUBMED #26
19	Outcome of full pulpotomy in mature permanent molars using 3 calcium silicate-based materials: A parallel, double blind, randomized controlled trial	Taha NA, Al-Rawash MH, Imran ZA.	2022	REPEAT OF PUBMED	REPEAT OF PUBMED #9
20	Influence of occlusal and proximal caries on the outcome of full pulpotomy in permanent mandibular molar teeth with partial irreversible pulpitis: A prospective study	R R, Aravind A, Kumar V, Sharma S, Chawla A, Logani A.	2021	REPEAT OF PUBMED	REPEAT OF PUBMED #22
21	Outcome of pulpotomy in permanent teeth with irreversible pulpitis: a systematic review and meta-analysis	Ather A, Patel B, Gelfond JAL, Ruparel NB.	2022	REPEAT OF PUBMED	REPEAT OF PUBMED #11
22	Two-year results of vital pulp therapy in permanent molars with irreversible pulpitis: an ongoing multicenter randomized clinical trial	Asgary S, Eghbal MJ, Ghoddusi J.	2014	REPEAT OF PUBMED	REPEAT OF PUBMED #30
23	Conservative Management of Mature Permanent Teeth with Carious Pulp Exposure	Taha, NA (Taha, Nesrin A.); About, I (About, Imad); Sedgley, CM (Sedgley, Christine M.); Messer, HH (Messer, Harold H.)	2020	N/A	EXCLUDE because Article / Proceedings
24	4-Year Follow-up of Full Pulpotomy in Symptomatic Mature Permanent Teeth with Carious Pulp Exposure Using a Stainproof Calcium Silicate- based Material	Taha, NA (Taha, Nesrin A.) ; Al-khatib, H (Al-khatib, Hanan)	2022	109 teeth in 90 patients with an age range of 14-60 years (mean 5 25 years). The study sample available for follow-up was 100 teeth in 86 patients with a recall rate above 90%. Preoperative pulp diagnosis was reversible pulpitis in 39 teeth and irreversible pulpitis in 61 teeth.	EXCLUDE because not exclusivley IP
25	Factors that influence the outcome of pulpotomy in permanent teeth	Duncan HF, El-Karim I, Dummer PMH, Whitworth J, Nagendrababu V.	2022	REPEAT OF PUBMED	REPEAT OF PUBMED #13
26	Long-term Pulpal and Restorative Outcomes of Pulpotomy in Mature Permanent Teeth	Tan SY, Yu VSH, Lim KC, Tan BCK, Neo CLJ, Shen L, Messer HH.	2020	REPEAT OF PUBMED	REPEAT OF PUBMED #12
27	One-year results of vital pulp therapy in permanent molars with irreversible pulpitis: an ongoing multicenter, randomized, non-inferiority clinical trial	Asgary S, Eghbal MJ, Ghoddusi J, Yazdani S.	2013	REPEAT OF PUBMED	REPEAT OF PUBMED #29
28	Five-year results of vital pulp therapy in permanent molars with irreversible pulpitis: a non-inferiority multicenter randomized clinical trial	Asgary, Saeed; Eghbal, Mohammad Jafar; Fazlyab, Mahta; Baghban, Alireza Akbarzadeh; Ghoddusi, Jamileh	2015	407 patients were blindly allocated into two treatment groups [group 1 (VPT/CEM, n = 205) and group 2 (RCT, n = 202)] treated in 23 health-care centers by calibrated dentists. The treatment outcomes were assessed after 60 months.	INCLUDE
29	Evaluation of Success of Pulpotomy in Mature Permanent Teeth with Carious exposure using Mineral Trioxide Aggregate	Alqaderi, Hend; Lee, Chun-Teh; Borzangy, Sary; Pagonis, Tom C.	2021	75 cases	EXCLUDE because article paper

30	Outcome of Vital Pulp Therapy in Permanent Teeth with Carious Pulp Exposure: A Series of Successfully Treated Teeth	Kadhem, Majeed; Yusuf, Ahmed; Altajer, Faten; Hadi, Alaa S.; Alwadaei, Manal	2021	Eleven patients were included of both categories (mature n=3 and immature n=8 roots) with established preoperative pulpal diagnosis for irreversible (n=8)/reversible pulpitis (n=3).	EXCLUDE because small case report
31	Coronal Pulpotomy Technique Analysis as an Alternative to Pulpectomy for Preserving the Tooth Vitality, in the Context of Tissue Regeneration: A Correlated Clinical Study across 4 Adult Permanent Molars	Solomon, Raji Viola; Faizuddin, Umrana; Karunakar, Parupalli; Sarvani, Grandhala Deepthi; Soumya, Sevvana Sree	2015	Vital pulpotomy was performed on 5 carious involved, permanent molars diagnosed with acute irreversible pulpitis in 17 to 22-year-old patients.	EXCLUDE because small case report
32	Treatment Outcomes of 4 Vital Pulp Therapies in Mature Molars	Asgary S, Hassanizadeh R, Torabzadeh H, Eghbal MJ.	2018	REPEAT OF PUBMED	REPEAT OF PUBMED #8
33	Comparative Evaluation of Postoperative Pain and Success Rate after Pulpotomy and Root Canal Treatment in Cariously Exposed Mature Permanent Molars: A Randomized Controlled Trial	Galani, Mohit; Tewari, Sanjay; Sangwan, Pankaj; Mittal, Shweta; Kumar, Vinay; Duhan, Jigyasa	2017	54 permanent teeth with carious exposures were randomly divided equally into 2 groups.	INCLUDE
34	Long-term outcomes of pulpotomy in permanent teeth with irreversible pulpitis: A multi-center randomized controlled trial	Asgary S, Eghbal MJ, Bagheban AA.	2017	REPEAT OF PUBMED	REPEAT OF PUBMED #17
35	Postendodontic Pain after Pulpotomy or Root Canal Treatment in Mature Teeth with Carious Pulp Exposure: A Multicenter Randomized Controlled Trial	Eghbal, Mohammad Jafar; Haeri, Ali; Shahravan, Arash; Kazemi, Ali; Moazami, Fariborz; Mozayeni, Mohammad Ali; Saberi, Eshaghali; Samiei, Mohammad; Vatanpour, Mehdi; Akbarzade Baghban, Alireza; Fazlyab, Mahta; Parhizkar, Ardavan; Ahmadi, Mahboobe; Akbarian Rad, Nazila; Bijari, Shima; Bineshmarvasti, Delaram; Davoudi, Paria; Dehghan, Roya; Dehghani, Mandana; Ebrahimi, Habibollah; Emami, Nafiseh; Farajian, Nafiseh; Fereidooni, Rahim; Ghobadi, Gelareh; Ghodrati, Mostafa; Gohari, Atefeh; Hashemi, Azadeh; Hosseini, Mohammadreza; Karami, Elham; Kheirabadi, Nasir; Kozegari, Sepideh; Labaf Ghasemi, Hadi; Majidi, Alireza; Malekzadeh, Parastu; Mehrabi, Vahid; Mohammadi, Mehrnush; Moradi Eslami, Leila; Noghani, Atefeh; Omatali, Negin; Pourhatami, Negar; Rahbani Nobar, Behnam; Rahmani, Saeid; Shafaq, Parviz; Sooflabadi, Sara; Teimoori, Somaye; Vatandoost, Farzaneh; Asgary, Saeed	2020	seven academic centers, 550 cariously exposed pulps were included and randomly allocated into PMTA (n = 188), PCEM (n = 194), or RCT (n = 168) arms.	EXCLUDE because not exclusivley IP
36	Success rates of coronal and partial pulpotomies in mature permanent molars: a systematic review and single-arm meta-analysis	Lin, Galvin Sim Siang; Hisham, Abdul Rauf Badrul; Cher, Chia Yee; Cheah, Kah Kei; Ghani, Nik Rozainah Nik Abdul; Noorani, Tahir Yusuf	2021	Eleven studies were included in the analysis of 1-year success rates, whereas five studies were included in the analyses of 2-year and > 2-year success rates for coronal pulpotomy.	EXCLUDE because systematic review and meta-analysis
37	Present status and future directions-Vital pulp treatment and pulp preservation strategies	Duncan, Henry F.	2022	N/A	EXCLUDE because review paper
38	Clinical guidelines for vital pulp therapy	Bogen, George	2019	N/A	EXCLUDE because
39	Vital pulp therapy: histopathology and histobacteriology-based guidelines to treat teeth with deep caries and pulp exposure	Ricucci, Domenico; Siqueira Jr, Jose F.; Li, Yuanyuan; Tay, Franklin R.	2019	Two hundred and sixty-four carious, unrestored and VPT-treated human teeth, which were extracted for reasons not related to the present study. The teeth were processed for histological and histobacteriological examination. Other 757 clinical cases that received different VPT procedures were followed-up to identify success rates, with the longest observational period of 30 years.	EXCLUDE because not relevent enough
40	Periapical Healing After Direct Pulp Capping With Calcium-enriched Mixture Cement: A Case Report	Asgary, S.; Nosrat, A.; Homayounfar, N.	2012	1 successful direct pulp capping of a mature symptomatic mandibular second molar in a 14-year-old girl.	EXCLUDE because not relevent enough
41	European Society of Endodontology position statement: Management of deep caries and the exposed pulp	Dummer, P. M. H.; Franco, V; Gambarini, G.; Orstavik, D.; Tjaderhane, L.; Whitworth, J.; Duncan, H. F.; Galler, K. M.; Tomson, P. L.; Simon, S.; El-Karim, I.; Kundzina, R.; Krastl, G.; Dammaschke, T.; Fransson, H.; Markvart, M.; Zehnder, M.; Bjorndal, L.	2019	N/A	EXCLUDE because not relevent enough
42	AAE Position Statement on Vital Pulp Therapy	[Anonymous]	2021	N/A	EXCLUDE because not

Annex 2: Weighted mean and standard deviation calculations for outcome success % at different durations (weighted means and standard deviations highlighted in yellow)

#	Sample size	6 month success	6m Weighted success (n*success)	Squared deviation	Multiply each squared difference by its correspondi ng weight
1	27	0.840	22.68	478.978237	12932.4124
	23	0.620	14.26	181.321614	4170.39712
4* (Took average of clincal and radiographic)	64	0.984	62.976	3866.54783	247459.061
11	18	0.688	12.375	134.109635	2413.97342
	19	0.667	12.673	141.100459	2680.90872
	17	0.500	8.5	59.375831	1009.38913
SUM	168		133.464		270666.142
Weighted mean			0.79442857		
Divide the sum of the weighted squared differences by the sum of the weights					1611.10799
SUM prod method					0.03020283

#	Sample size	1 year success	1 year Weighted success (n*success)	Squared deviation	Multiply each squared difference by its correspondi ng weight
1	27	0.8300	22.41	465.69664	12573.8093
	23	0.5500	12.65	139.712532	3213.38823
2	41	0.9750	39.975	1532.33146	62825.5899
3	30	0.9330	27.99	737.665903	22129.9771
4	64	0.9920	63.488	3926.02566	251265.642
5	40	0.8800	35.2	1181.29728	47251.8913
6	80	0.9375	75	5501.18973	440095.178
11	18	0.3750	6.75	45.5625	820.125
	19	0.4440	8.436	57.8513207	1099.17509
	17	0.3570	6.069	27.4471794	466.602049
SUM	359		297.968		841741.378
Weighted mean			0.82999443		
Divide the sum of the weighted squared differences by the sum of the weights					2344.68351
SUM prod method					0.04482787

#	Sample size	2 year success	2 year Weighted success (n*success)	Squared deviation	Multiply each squared difference by its correspondi ng weight
1	27	0.85000	22.95	491.88	13280.8795
	23	0.43000	9.89		0
9* (Took average of clincal and radiographic)	41	0.91145	37.36945		0
SUM	91		70.20945		13280.8795
Weighted mean			0.77153242		
Divide the sum of the weighted squared differences by the sum of the weights					145.94373
SUM prod method					0.04057465

Annex 3: Weighted mean and standard deviation calculations for outcome success % for different pulpotomy agents (weighted means and standard deviations highlighted in yellow)

#	Pulpotomy Agent(s)	Sample size (teeth)	6 month Success (%)	1 year Success (%)	2 year Success (%)	5 year Success (%)	6m Weighted success (n*success)	1 year Weighted success (n*success)	2 year Weighted success (n*success)	(x_i - mean)^2 * n_i @ 6m	(x_i - mean)^2 * n_i @ 1 year	(x_i - mean)^2 * n_i @ 2 year
1	MTA	27	84%	83%	85%	-	22.68	22.41	22.95	14.62433354	0.21903453	14.9746046
2	MTA	41	-	97.5%	-	-	-	39.975	-		0.12371487	
3	MTA	30	-	93.3%	-	-	-	27.99	-		0.00501647	
5	MTA	40	-	88%	-	-	-	35.2	-		0.06422037	
6	MTA	80	-	93.75%	-	-	-	75	-		0.02430772	
10	MTA	26	-	1.5 year success = 96.67%		-	-	-	-		-	
						SUM of weighted success	22.68	200.575	22.95			
						SUM of sample size	218	218	218			
						Overall weighted mean success	0.1040367	0.92006881	0.10527523			
						Σ[(x_i - mean)^2 * n_i]				14.62433354	0.43629397	14.9746046
						Σ[(x_i - mean)^2 * n_i] / Σn_i				0.067084099	0.00200135	0.06869085
						SD				0.259005982	0.04473643	0.26208939

#	Pulpotomy Agent(s)	Sample size (teeth)	6 month Success (%)	1 year Success (%)	2 year Success (%)	5 year Success (%)	6m Weighted success (n*success)	1 year Weighted success (n*success)	2 year Weighted success (n*success)	(x_i - mean)^2 * n_i @ 6m	(x_i - mean)^2 * n_i @ 1 year	(x_i - mean)^2 * n_i @ 2 year
1	CH	23	62%	55%	43%	-	14.26	12.65	9.89	0.0201982	0.13576294	0.81967567
11	CH	18	68.75%	37.50%	-	-	12.375	6.75	-	0.025808812	0.17347487	
						SUM of weighted success	26.635	19.4	9.89			
						SUM of sample size	41	41	41			
					SUM of weighted means / SUM of sample size =	Overall weighted mean success	0.64963415	0.47317073	0.24121951			
						Σ[(x_i - mean)^2 * n_i]				0.046007012	0.3092378	0.81967567
						Σ[(x_i - mean)^2 * n_i] / Σn_i				0.001122122	0.00754239	0.01999209
						SD				0.033498093	0.08684691	0.14139339

#	Pulpotomy Agent(s)	Sample size (teeth)	6 month Success (%)	1 year Success (%)	2 year Success (%)	5 year Success (%)
9	CEM	205	Clinical = 94.4%*	Clinical = 97.6%*	Clinical = 98.19% RT = 86.1%	78.1%
#	Pulpotomy Agent(s)	Sample size (teeth)	6 month Success (%)	1 year Success (%)	2 year Success (%)	5 year Success (%)
4	Biodentine	64	98.40%	Clinical = 100% RT = 98.4%	-	-

PULPOTOMY AS A TREATMENT OPTION IN MATURE PERMANENT DENTITION WITH IRREVERSIBLE PULPITIS: A SYSTEMATIC REVIEW

AUTHOR

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INTRODUCTION

Irreversible pulpitis is a widely prevalent disease with very poor prognosis for the tooth if left untreated.

Typically for permanent dentition with mature apices, the treatment options have been limited to either non-surgical root canal therapy (**NSRCT**) or extraction. Unfortunately, both options pose disadvantages, with NSRCT leading to the loss of the pulp vitality, and extraction causing occlusion and functional problems.

Recent studies have suggested the possibility of **pulpotomy** as an alternative treatment option which would allow the pulp of the tooth to remain in the roots, thereby maintaining the **biological advantages** its retention. This systematic review aims to evaluate if pulpotomy is a viable treatment option in such instances

OBJECTIVES

General objective:
Evaluate the overall success of pulpotomy as a treatment option in mature adult dentition with irreversible pulpitis.

Specific objective:
Identify which materials are most effective for the pulpotomy in mature adult dentition with irreversible pulpitis.

HYPOTHESIS

Null Hypothesis (H0):
Pulpotomy is not an effective treatment option in mature permanent dentition with irreversible pulpitis.

Alternative Hypothesis (HA):
Pulpotomy is an effective treatment option in mature permanent dentition with irreversible pulpitis.

MATERIALS AND METHODS

Databases used: PubMed, EBSCO, Scopus, Web of Science, backwards reference searching.

Tools for Risk of Bias and Evidence Level: ROBINS-I, Jadad, OCEBM

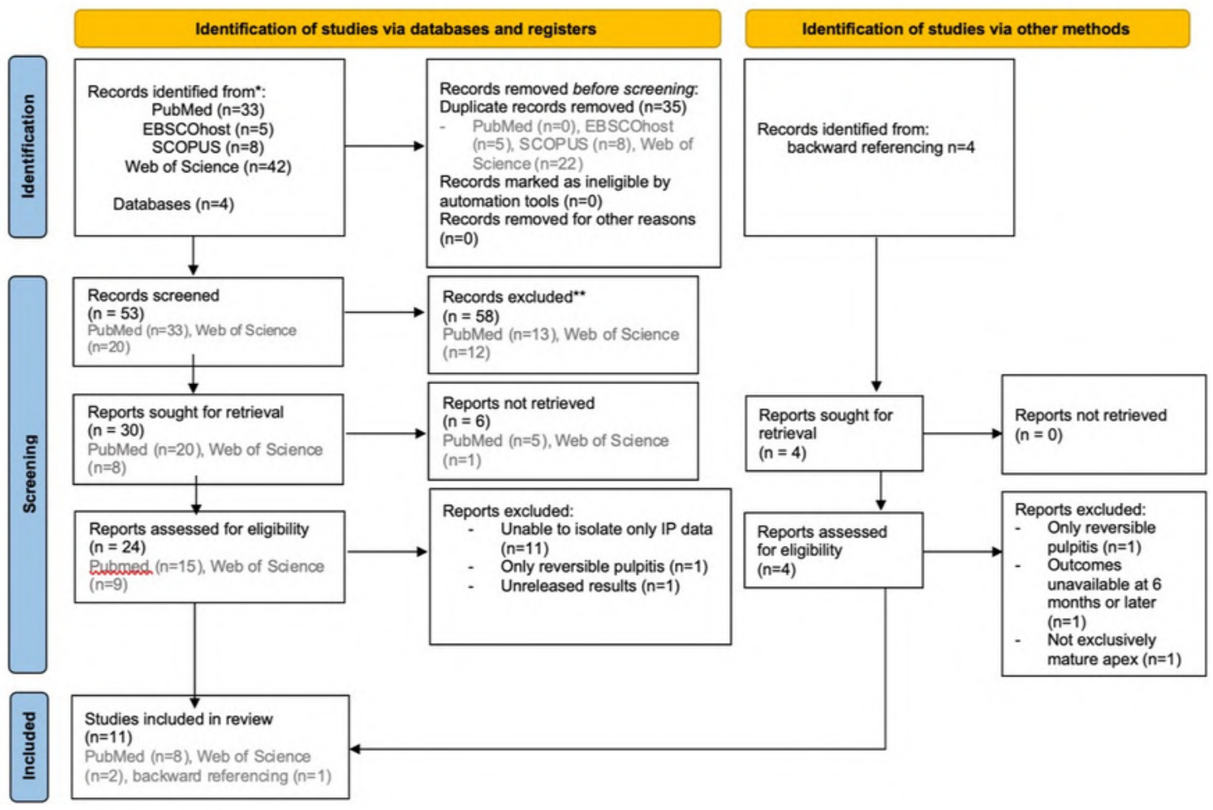

Figure 1: PRISMA 2020 flow-diagram showing selection process of included articles

P - Population	I - Intervention	C - Comparison	O - Outcome
Patients with mature permanent dentition, with irreversible pulpitis	Pulpotomy of mature permanent dentition	Endodontic treatment	Outcomes of pulpotomy as a treatment option

Figure 2: PICO question breakdown

RESULTS

49 studies from the initial search were identified, with 11 studies included in the final systematic review: 6 randomised control/clinical trials, 3 observational studies, 1 prospective study and 1 pilot feasibility study. 5 pulpotomy agents were used in this study: 7 studies with MTA, 2 with CH, 1 with Biodentine, 1 with CEM and 1 with PRF. This is demonstrated in figure 3.

<u>The weighted mean overall success for VPT:</u>

- **six-months: 79.44%** (SD 0.0302)
- **one-year: 83%** (SD 0.0448)
- **two-years 77.15%** (SD 0.0406)

VPT showed to be comparable and at times superior to NSRCT at comparable timeframes.

<u>The weighted mean overall success for different pulpotomy agents:</u>

- **MTA at one-year: 92%** (SD 0.0447)
- **CH at six-months: 64.96%** (SD 0.0335)
- **CH at one-year: 47.32%** (SD 0.0868)

MTA showed to be very effective but it is unclear as to which material was best due to limitations in sample size.

#	Database	Author and year	Type of study	Age range (Mean±SD)	Pulpotomy Agent(s)	Sample size (teeth)	6 month Success (%)	1 year Success (%)	2 year Success (%)	5 year Success (%)
1	PubMed	Taha NA et al. 2017	Randomized Clinical Trial	20 – 52 (30.3±9.6)	MTA	27	84%	83%	85%	-
					CH	23	62%	55%	43%	-
2	PubMed	Sánchez-Lara Y et al. 2022	Pilot Feasibility Study, block randomised	17 - 78 (34.63±15.76)	MTA	41	-	97.5%	-	-
3	PubMed	Koli B et al. 2021	Observational Study	18 - 35 (24.8±5.95)	MTA	30	-	93.3%	-	-
4	PubMed	Taha NA et al. 2018	Observational Study	19 – 69 (33.2)	Biodentine	64	98.40%	Clinical = 100% RT = 98.4%	-	-
5	PubMed	Sharma R et al. 2021	Observational Study	16 -35 years (25.3±6.17)	MTA	40	-	88%	-	-
6	PubMed	Rechithra R et al. 2021	Prospective Clinical Study	16 - 35	MTA	80	-	93.75%	-	-
7	PubMed	Asgary S et al. 2013*	Randomized Clinical Trial	9 - 65	CEM	205	Clinical = 94.4%	Clinical = 97.6%	-	-
8	PubMed	Asgary S et al. 2014*	Randomized Clinical Trial	9 - 65	CEM	205	Clinical = 94.4%)	Clinical = 97.6%*	Clinical = 98.19% RT = 86.1%	-
9	PubMed	Asgary S et al. 2015*	Randomized Clinical Trial	9 – 65	CEM	205	Clinical = 94.4%*	Clinical = 97.6%*	Clinical = 98.19% RT = 86.1%	78.1%
10	Web of Science	Galani M et al. 2017	Randomized Controlled Trial	15 – 36 (20.56±4.38)	MTA	26	-	1.5 year success = 96.67%		-
11	Manual	Kumar V et al. 2016	Randomized Controlled Trial	14 - 23 (17.81)	CH	18	68.75%	37.50%	-	-
				14 - 32 (21.20)	MTA	19	66.70%	44.40%		
				14 - 32 (25.81)	PRF	17	50%	35.70%		

*Asgary S et al 2013, 2014, 2015 are continuations of the same report.

CEM= Calcium-enriched material
CH= Calcium Hydroxide
PRF= Platelet-rich fibrin
RT= Radiorgraphic

Manual database is equivalent to "backward referencing".

Figure 3: table of results from the 11 articles included in the review

DISCUSSION

- Success of pulptomy objectivley compared to NSRCT shows it is a viable option. This is without considering the additional benefits to VPT.
- **Limitations**: small sample sizes, limited number of studies included, heterogenous outcome measurements

CONCLUSION

- Pulpotomy showed a very high success rate from 6-months to 2-years, with results comparable to NSRCT.
- MTA appeared to be the most successful pulpotomy agent however further research is needed into the other materials.

BIBLIOGRAPHY

Bibliography