Does Retaining Third Molars Result in the Development of Pathology Over Time? A Systematic Review

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Purpose: The present systematic review was conducted to assess the available literature on pathologies associated with third molar retention.

Materials and Methods: A systematic literature search was conducted in MEDLINE (PubMed), Embase, and Cochrane Library and reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines. Relevant reports were selected using predefined inclusion and exclusion criteria. Pathology related to third molar retention included caries, periodontal pathology, second molar external root resorption, and pathologic widening of the third molar pericoronal space. The methodologic quality of each study was reviewed using a pathology-specific tool to assess the risk of bias.

Results: A total of 37 studies were included for qualitative analysis. The available data showed that asymptomatic retained third molars frequently become diseased with increasing age of the patient and increased retention time. Caries and periodontal pathology were most frequently observed, especially in partially erupted third molars and mesially inclined mandibular third molars. Overall, the available data were regarded as medium to fair quality evidence.

Conclusions: The available data have revealed that retained asymptomatic third molars rarely remain disease-free over time. Increasing age and, thus, increasing retention time seemed associated with greater disease prevalence. Well-designed, prospective follow-up studies are needed to substantiate the clinical management of asymptomatic disease-free third molars.

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Conflict of Interest Disclosures: None of the authors have any relevant financial relationship(s) with a commercial interest.

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Received May 8 2020

Accepted June 6 2020

© 2020 American Association of Oral and Maxillofacial Surgeons 0278-2391/20/30588-7

https://doi.org/10.1016/j.joms.2020.06.014

Third molars (wisdom teeth) have often been viewed as "ticking time bombs" that have little to no masticatory function and will often only partially erupt or, even, remain completely unerupted in the dental arch. Thus, removal of third molars has been one of the most commonly performed procedures by oralmaxillofacial surgeons. Failure of a tooth to reach a normal functional position in the occlusion is termed impaction and can result from a lack of space or development of the tooth germ in an abnormal position. The worldwide prevalence of third molar impaction has been estimated to be 24%, greater than that for any other teeth.¹ Although impaction itself is not considered a pathology, it has been associated with several pathologies that might indicate the necessity for the removal of the impacted tooth, such as infection, nonrestorable carious lesions, periodontal pathology, root resorption, pericoronitis, cysts, and tumors. Other surgical indications have included removal before chemotherapy or radiation therapy, removal in the context of orthodontic or prosthodontic treatment, preparation for orthognathic surgery, and cases in which the third molar will be used for tooth autotransplantation.

Clinicians have agreed that for such cases, or when symptoms arise, third molar removal will generally be justified. However, the management of third molars when free of pathology (also denoted as prophylactic removal) has been debated for many decades.² Several international guidelines have been reported on this topic, including the 2000 National Institute for Health and Care Excellence (NICE) guidelines from the United Kingdom, the 2000 Scottish Intercollegiate Guidelines Network (SIGN) guidelines, and the 2012 Belgian Health Care Knowledge Centre (KCE) report.³⁻⁵ Generally, these guidelines have advocated a conservative approach to pathologyfree impacted third molars because it has remained uncertain whether these teeth will eventually develop pathology that would require removal. Given the economic and personal costs involved, it is understandable how the validity of this procedure has been called into question. It is evident that the choice of the clinician should be based on their expertise, the individual needs of the patient, and the best research available. However, it is also evident that the reported studies have not provided a clear answer and that a regular need exists to update current prevailing positions in accordance with the best available research. The present systematic review was conducted to assess the reported data on the pathologies associated with third molar retention.

Materials and Methods

The present systematic review was conducted and reported in accordance with the principles of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) to ensure comprehensiveness.⁶ The review was registered at the Prospective Register of Systematic Reviews (registry no. CRD42018102034).

INFORMATION SOURCES AND SEARCH STRATEGY

The search strategy was designed to determine the pathologies associated with the retention of (asymptomatic) third molars and the quality of the available evidence regarding retention and prophylactic removal. The search strategy was constructed for PubMed (MEDLINE) and adapted for Embase and the Cochrane Library. The reference lists of previous systematic reviews were screened for additional relevant reports. The full search syntax has been provided be in Appendix 1. MeSH or EMTREE terms and keywords were combined to ensure that all relevant studies would be included. The search strategy was constructed to obtain data on third molars and the occurrence of oral pathologies. These were narrowed down during screening to the 4 most common pathologies related to third molars. Only English language studies were included. Duplicate reports were manually checked and removed.

INCLUSION AND EXCLUSION CRITERIA

All identified studies were screened by 2 authors (M.V., D.H.) using the title, abstract, and full-text with reference to the inclusion criteria. In all phases of screening, disagreements were resolved by discussion between the 2 reviewers. When a consensus could not be reached, an experienced third author (R.J.) was consulted.

The inclusion criteria were as follows:

- 1. Studies investigating a human population with the presence of at least 1 third molar in a longitudinal or cross-sectional study design
- Studies investigating the prevalence and/or incidence of pathology related to the presence and/or third molar retention using clinical and/ or radiographic evaluation
- 3. Studies reporting sufficient information to extract data for the measured outcomes

Review articles, case reports, case series, expert opinions, letters, and editorials were excluded from the present analysis.

DATA EXTRACTION

The relevant data were extracted from the reports by 3 authors (C.V., M.V., D.H.). The primary outcome measures were the prevalence, incidence, and relative risks of pathologic conditions. Pathology was defined

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as dental caries of the third molar or the distal portion of the second molar, periodontal pathology (ie, clinical attachment loss, alveolar bone loss) of the third molar or distal to the second molar, external root resorption (ERR) of the second molar, and pathologic widening of the third molar pericoronal space. The extracted data included the study and sample characteristics (ie, authors, year of publication, sample number, sample age, number of third molars, state of eruption), methods (ie, study design, methods of measurement, follow-up time), and outcome measures (ie, investigated pathologies, results, conclusions). *P* values < .05 were considered statistically significant.

ASSESSMENT OF STUDY QUALITY

All included studies were evaluated for methodologic validity using a risk of bias tool inspired by the Cochrane Collaboration's (CC) tool.⁷ We had modified the CC tool to ensure an optimal fit for the included studies. The risk of bias was assessed across 4 domains and 5 topics: selection (study population), detection (standardization and method of measurement), attrition (incomplete data), and reporting (selective reporting). Of the 5 topics, 4 were adopted from the original CC tool. Additionally, we constructed a pathology-specific assessment of the methodologic quality (method of measurement). Every report was assessed for each of the potential biases and scored 2, 1 or 0, indicating a low, medium, and high risk of bias, respectively. For each pathology, the mean quality scores were calculated per the topic of bias. All assessments were performed by 2 authors (C.V., M.V.). Disagreements were resolved by discussion between the 2 authors.

Results

The complete selection process is displayed in a PRISMA flow chart (Fig 1). Searching the MEDLINE, Embase, and Cochrane Library databases identified 8,682, 8,015, and 1,538 records, respectively. After removal of duplicates, 9,163 unique studies were identified. A selection of 151 reports remained after title screening. Additionally, 98 reports were removed because the abstract failed to meet the inclusion criteria. After strictly applying the inclusion and exclusion criteria, 37 reports were selected for analysis and quality assessment.⁸⁻⁴⁴

STUDY CHARACTERISTICS

A detailed overview of the study characteristics is provided in Table 1. The included studies had been reported from 1989 to 2019. Of the 37 studies, 12 were prospective cohort studies, 1 was a retrospective cohort study, and 24 were cross-sectional studies (Table 1). The follow-up time for the prospective

cohort studies was 2.2 to 6.9 years (mean, 4.0 years), with 1 outlier reporting a follow-up period of more than 25 years.³² The retrospective cohort study had a median follow-up time of 7.7 years (mean, not reported).³⁵ Of the 37 studies, 21 collected data from a subsample of a previously conducted prospective cohort study (Table 1), and 15 examined patients from their own department or practice. The remaining study examined the records of British military personnel.³⁵ In 16 studies, the dataset originating from a longitudinal trial at the University of Kentucky and University of North Carolina had been used. 10-13,44 Other datasets used in the present review included the Piedmont 65+ Dental Study, US Department of Veterans Affairs Dental Longitudinal Study, Third National Health and Nutrition Survey (NHANES III), Dental Atherosclerosis Risk in Communities (ARIC) study, Helsinki Aging Study, and Finland Health 2000 Survey. The total number of subjects included in the present review was 47,876 (3,783 in the cohort studies and 44,093 in the cross-sectional studies). However, because several studies used subsamples of the same dataset, the actual total number of unique subjects could not be determined precisely (but was likely \sim 2500 subjects). The overall mean age (mean of the mean) was 36 ± 15 years (range, 13 to 93 years). However, 3 studies had not reported a mean age.^{17,35,40} The mean sample size was $1,294 \pm 2067$ (range, 49 to 6,793). The total number of third molars across all studies was 17,156 (mean, 953 \pm 1,426; range, 84 to 5,665), although the number of unique third molars was, again, likely to be lower because of reused datasets. Also, 19 studies had not reported the number of investigated third molars.

STUDY METHODS AND OUTCOMES

Of the 37 studies, 22 investigated caries of the third or second molar, 24 investigated periodontal pathology of the third or second molar, 9 investigated ERR of the second molar, and 5 investigated pathologic widening of the third molar pericoronal space. Also, 23 studies had investigated only 1 of these pathologies, 9 investigated 2, 1 investigated 3, and 4 investigated 4 pathologies. In 14 studies, the data were collected using both clinical and radiographic examinations. In 11 studies, the data were collected through clinical examination only, and in 12 studies, the data were collected from radiographic examinations only.

DATA RESULTS

The main conclusions drawn from the included reports are summarized in Table 2, with studies with statistically significant findings marked with an asterisk. The study results varied widely owing to variability in the included samples and methods.

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THIRD MOLAR RETENTION AND PATHOLOGY

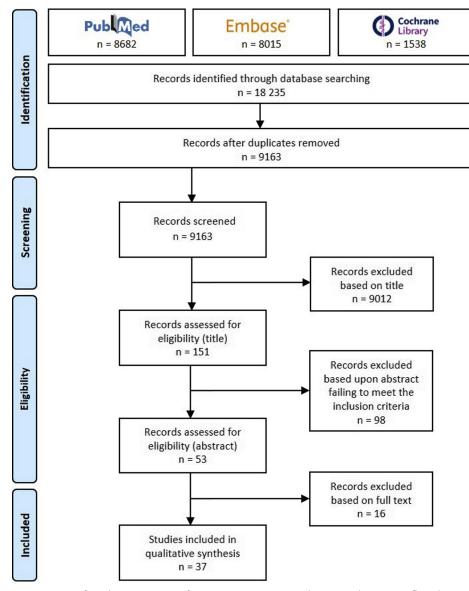


FIGURE 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2009 flow diagram. Vandeplas et al. Third Molar Retention and Pathology. J Oral Maxillofac Surg 2020.

Caries

Caries was by far the most observed pathology in the retained third molars. The prevalence ranged from 24 to 80%, depending on the age of the subjects.^{24,38,41} As demonstrated by Shugars et al³⁹ in 2005, mandibular third molars were significantly more affected by caries than were maxillary third molars. Several prevalence studies also demonstrated that third molars have an increased risk of developing caries in the case of partial third molar eruption (both upper and lower jaws) and in the case of a mesial third molar inclination in the mandible.^{23,27,30,34,38} Moreover, an association was demonstrated between the presence of a third molar and the risk of caries on the distal side of the second molar (M2D). In a 3year follow-up of 416 persons (age, 28 to 76 years), Nunn et al³² found that the presence of an erupted third molar increased the risk of caries on the M2D by 2.5-fold compared with the risk in absence of the third molar. Similar results were reported by Pepper et al,³⁵ who investigated a younger population (age, 17 to 18.9 years). They reported a significant increase in M2D caries prevalence when a partially erupted third molar was present (7%) compared with its absence (3%). Likewise, a split-mouth study by Chou et al¹⁵ of 70 elderly patients showed that caries in the third molar region (M2D and third molar) was significantly more frequent in the third molar group than in the non-third molar group. Chou et al¹⁵ concluded that the presence of a third molar is a risk

Table 1. OVERVIEW OF STUDY CHARACTERISTICS, SAMPLES, AND METHODS

					Sar	nple				Outco	omes	
Design	Investigator	Mean Follow- Up (yr)	Examination Method	Description	Patients (n)	Age (yr) Mean; Range	Third Molars (n)	Eruption Status	Caries	Periodontal Pathology	M2 ERR	Pathologic Widening of M3 Pericoronal Space
Prospective cohort												
	Ahmad et al, ⁸ 2008	5.1	Clinical	University of Kentucky and North Carolina study subsample	49	21; 19-39	100	Erupted and impacted	Yes	Yes	No	No
	Blakey et al, ¹² 2006	2.2	Clinical and radiographic	University of Kentucky and North Carolina study subsample	254	28; 14-45	NA	Erupted	No	Yes	No	No
	Blakey et al, ¹¹ 2007	5.9	Clinical	University of Kentucky and North Carolina study subsample	195	26; 22-34	NA	Erupted	No	Yes	No	No
	Blakey et al, ¹³ 2009	4.1	Clinical and radiographic	University of Kentucky and North Carolina study subsample	106	25; 20-32	NA	Erupted	No	Yes	No	No
	Divaris et al, ¹⁸ 2012	4.6	Clinical	University of Kentucky and North Carolina study subsample	215	26; 14-45	NA	Erupted	Yes	No	No	No
	Fisher et al, ²² 2012	6.9	Clinical and radiographic	University of Kentucky and North Carolina study subsample	179	29; 14-45	NA	Erupted	Yes	Yes	No	No
	Golden et al, ²⁵ 2015	6	Clinical	University of Kentucky and North Carolina study subsample	129	23; 19-28	NA	Erupted	No	Yes	No	No
	Moss et al, ³⁰ 2007	3	Clinical	Piedmont 65+ Dental Study subsample	818	73; >65	NA	Erupted	Yes	Yes	No	No
	Nance et al, ³¹ 2006	2.2	Clinical	University of Kentucky and North Carolina study subsample	237	26; 22-33	948	Erupted	No	Yes	No	No
	Nunn et al, ³² 2013	NA	Clinical and radiographic	US Department of Veterans Affairs Dental Longitudinal Study subsample	416	46; 28-76	344	Erupted and impacted	Yes	Yes	No	No

Table 1. Cont'd

					Sar	nple				Outco	omes	
Design	Investigator	Mean Follow- Up (yr)	Examination Method	Description	Patients (n)	Age (yr) Mean; Range	Third Molars (n)	Eruption Status	Caries	Periodontal Pathology	M2 ERR	Pathologic Widening of M3 Pericoronal Space
	Shugars et al, ³⁹ 2005	2.9	Clinical and radiographic	University of Kentucky and North Carolina study subsample	211	27; 23-33	NA	Erupted	Yes	No	No	No
	White et al, ⁴⁴ 2006	2.2	Clinical	University of Kentucky and North Carolina study subsample	254	28; 18-24	NA	Erupted	No	Yes	No	No
cohort Cross-	Pepper et al, ³⁵ 2017	7.7 (median)	Clinical and radiographic	British military personnel	720	18 (median); 17-18	NA	Erupted and impacted	Yes	No	No	No
sectional	Al Hobail et al, ⁹ 2019	NA	Clinical and radiographic	Riyadh Elm University dental clinic patients	313	32; ≥25	1,252	Erupted and impacted	Yes	No	No	No
	Blakey et al, ¹⁰ 2002	NA	Clinical and radiographic	University of Kentucky and North Carolina study subsample	329	25; 22-32	NA	Erupted	No	Yes	No	No
	Celikoglu et al, ¹⁴ 2010	NA	Radiographic	Department of Orthodontics, University of Ataturk patients	351	23; 20-26	1,161	Impacted	Yes	Yes	Yes	Yes
	Chou et al, ¹⁵ 2017	NA	Clinical and radiographic	Department of Periodontology and Dentistry, Kaohsiung Municipal Ta-Tung Hospital patients	70	45; 26-73	81	Erupted	Yes	Yes	No	No
	Chu et al, ¹⁶ 2003	NA	Clinical and radiographic	Prince Philip Dental Hospital patients	2081	40; 14-89	3,778	Impacted	Yes	Yes	No	No
	Claudia et al, ¹⁷ 2018	NA	Radiographic	Private practice patients, Constana, Romania	55	NA; 20-65	95	Erupted and impacted	Yes	No	No	No
	Eliasson et al, ¹⁹ 1,989	NA	Clinical and radiographic	Department of Oral Radiology patients, Karolinska Institutet, Stockholm	644	43; ≥30	NA	Erupted and impacted	No	Yes	Yes	Yes

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Elter et al, ²¹ 2004	NA	Clinical	Third National Health and Nutrition Survey study subsample	5,831	26; 18-34	NA	Erupted	No	Yes	No	No
Elter et al, ²⁰ 2005	NA	Clinical	Dental ARIC study subsample	6,793	62; 52-74	NA	Erupted	No	Yes	No	No
Garaas et al, ²³ 2011	NA	Clinical	Dental ARIC study subsample	2064	62; 52-74	NA	Erupted	Yes	Yes	No	No
Garaas et al, ²⁴ 2012	NA	Clinical and radiographic	University of Kentucky and North Carolina study subsample	409	25; 22-31	NA	Erupted	Yes	Yes	No	No
Jung et al, ²⁶ 2013	NA	Radiographic	Pusan National University Dental Hospital patients	3,799	50; 25-92	NA	Erupted and impacted	Yes	Yes	Yes	Yes
Li et al, ²⁷ 2019	NA	Radiographic	Hospital of Stomatology, Sun Yat-sen University patients	276	34; 16-81	507	Impacted	No	No	Yes	No
Marques et al, ²⁸ 2017	NA	Radiographic	School of Dentistry, University of Barcelona patients	203	26; 18-45	327	Impacted	Yes	No	No	No
Moss et al, ²⁹ 2009	NA	Clinical	Dental ARIC study subsample	6,793	62; 52-74	NA	Erupted	No	Yes	No	No
Oenning et al, ³³ 2015	NA	Radiographic	Piracicaba Dental School, University of Campinas, São Paulo, patients	116	23; 14-62	174	Impacted	No	No	Yes	No
Özeç et al, ³⁴ 2009	NA	Radiographic	Cumhuriyet University, Turkey, patients	485	25; 18-49	585	Impacted	Yes	No	No	No
Schriber et al, ³⁶ 2019	NA	Radiographic	Department of Oral Surgery and Stomatology, University of Bern, patients	84	34; 17-77	84	Impacted	No	No	Yes	No
Sejfija et al, ³⁷ 2019	NA	Radiographic	University of Dentistry Clinical Center of Kosovo patients	5,515	29; 18-77	1,297	Impacted	Yes	Yes	Yes	Yes
Shugars et al, ³⁸ 2004	NA	Clinical and radiographic	University of Kentucky and North Carolina study subsample	389	27; 22-32	NA	Erupted	Yes	No	No	No
Syed et al, ⁴⁰ 2017	NA	Radiographic	College of Dentistry, King Khalid University, Abha, Kingdom of Saudi Arabia, patients	979	NA; 21-45	333	Impacted	Yes	No	No	No
Ventä et al, ⁴¹ 2015	NA	Radiographic	Helsinki Aging Study	293	79; 76-86	99	Erupted and impacted	Yes	Yes	No	No

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Mean Follow- Design Mean Follow- Follow- Notation Mean Follow- Follow- Follow- Follow- Status Mean Follow- Follow- Follow- Status Mean Follow- Follow- Follow- Status Periodontal Follow- Follow- Status Periodontal Follow-	Mean Follow- Investigator Mean Follow- Follow- Up (yr) Examination Method Patients Age (yr) Third Mean; Periodontal Molars M2 I Ventä et al, ⁴² NA Clinical and Tradiographic Enale (n) Range (n) Status Caries Pathology ER Ventä et al, ⁴³ NA Clinical and Tradiographic Finland Health 2000 6,005 47; 30-93 5,665 Frupted and Yes Yes						Sam	Sample				Outcomes	mes	
NAClinical and radiographicFinland Health 20006,00547; 30-935,665Erupted and impactedYesYesYesNARadiographicSurvey21630; 16-71326ImpactedNoNoYesMaxillofacial Surgery, Nanjing Medical University patients21630; 16-71326ImpactedNoNoYes		Design	Investigator	Mean Follow- Up (yr)	Examination Method	Description	Patients (n)	Age (yr) Mean; Range	Third Molars (n)		Caries	Periodontal Pathology	M2 ERR	Pathologic Widening of M3 Pericoronal Space
NA Radiographic Department of Oral and 216 30; 16-71 326 Impacted No Yes Maxillofacial Surgery, Maxillofacial Surgery, Nanjing Medical University patients			Ventä et al, ⁴² 2019	NA	Clinical and radiographic	Finland Health 2000 Survey	6,005	47; 30-93	5,665	Erupted and impacted	Yes	Yes	Yes	Yes
	Abbreviations: ARIC, Atherosclerosis Risk in Communities; ERR, external root resorption; M2, second molar; M3, third molar; NA, not applicable or not available.		Wang et al, ⁴⁵ 2017	NA	Radiographic	Department of Oral and Maxillofacial Surgery, Nanjing Medical University patients	216	30; 16-71	326	Impacted	No	No	Yes	No

factor that could negatively affect oral health well into later life.

Periodontal Pathology

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Age and, thus, the retention time, appeared to have a significant relationship to periodontal disease prevalence. The series of follow-up studies reported by Blakey et al^{10,12-14} and White et al⁴⁴ showed progressively increasing third molar periodontal probing depths (PDs) over time that exceeded 4 mm. During the 4 years of follow-up, 38% of the patients had PDs of 4 mm or more in the third molar region, even when all PDs had been low or nonexistent at baseline.¹³ Similarly, Ahmad et al⁸ reported a 51% prevalence of third molar PDs of 4 mm or more at baseline in a population aged 18 to 20 years, with a 10% increase found 5 years later. Periodontal disease was observed significantly more often in patients older than 25 years.¹⁰ The overall prevalence of periodontal disease in the included studies ranged from 33 to 61% for the third molar and 17 to 50% for the M2D. Fisher et al^{22} noted that third molars were more affected by periodontal pathology than were first or second molars (56 vs 50%, respectively). In 4 studies, the mandible had been significantly more affected than the maxilla.^{10,11,13,41} Moreover, the periodontal health of the second molar was shown to be negatively affected by retention of the adjacent third molar, in both young and older populations. Two studies by Elter et al^{20,21} examined 5,831 young patients (age range, 18 to 34 years) and 6,793 older patients (age range, 52 to 74 years). They reported that the odds of a PD greater than 5 mm for the second molar were 2 and 1.5 times, respectively, greater when the adjacent third molar was present than when it was absent. The odds increased with increasing age. This association between third molar presence and the occurrence of second molar periodontal disease was also reported by Chou et al¹⁵ and Nunn et al.³² During a follow-up period of more than 25 years, Nunn et al³² found significant differences in the relative risks for second molar pathology in patients with all types of third molar impaction, third molar agenesis, or third molar absence due to earlier removal. Using the absence of the third molars as a reference, the relative risk for an M2D PD greater than 4 mm was 1.87 for erupted third molars, 6.41 for soft tissue impacted third molars, and 1.60 for bony impacted third molars. In addition, the relative risks for 20% or more of M2D alveolar bone loss were 1.49 for erupted third molars, 9.15 for soft tissue impacted third molars, and 3.09 for bony impacted third molars.

Second Molar ERR

Several cross-sectional studies of second molar ERR in the presence of a third molar were available. In general, increasing age, third molar impaction status, and

Outcome	Pathology-Related Results	Reference
Caries	M3 presence or retention related to presence of caries in M3 region	9*, 14, 15*, 16, 18, 22, 26, 27, 32*, 34*, 35*, 38*, 39, 40, 41
	M3 position related to presence of caries in M3 region	9*, 14, 15*, 16, 17, 26, 27*, 32*, 34*, 35*, 40, 41
Periodontal pathology	M3 presence or retention related to presence of periodontal pathology in M3 region	8, 10*, 11, 12*, 14, 15*, 16, 20, 21, 22, 26, 32, 41, 44
	M3 position related to presence of periodontal pathology in M3 region	14, 15*, 16, 26, 31, 32*, 41
M2 ERR	M3 presence or retention related to presence of M2 ERR	14, 27*, 36*, 37, 43*
	M3 position related to presence of M2 ERR	14, 27*, 33, 36*, 43*
Pathologic widening of M3 pericoronal space	M3 presence or retention related to pathologic widening of M3 pericoronal space	42
	M3 position related to pathologic widening of M3 pericoronal space	42

Table 2. MAIN CONCLUSIONS FROM INCLUDED REPORTS STRATIFIED BY PATHOLOGY RELATED TO THIRD MOLAR RETENTION

Abbreviations: ERR, external root resorption; M2, second molar; M3, third molar. * Studies with statistically significant findings.

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impacted depth were significantly associated with prevalence of second molar ERR. Differences in second molar ERR prevalence were observed between the studies that investigated patients with a mean age younger or older than 25 years (40 to $49\%^{14,33}$ vs 0.5 to 50%, ^{19,26,36,37,42} respectively). Also, differences between the maxilla and mandible were reported. Li et al²⁷ concluded that second molar ERR is common and significantly more prevalent in the mandible (53%) than in the maxilla (33%), a finding contradicted by Sejfija et al.³⁷ Sejfija et al³⁷ reported that maxillary second molars showed significantly more severe degrees of resorption. They also reported that the mesial angulation and impaction depth of the third molar were significantly associated with second molar ERR.³⁷ Similar significant findings regarding age and third molar orientation were reported by Schriber et al.³⁶ In their study, 50% of the cases were in the maxilla, and the most significant increase in second molar ERR prevalence was found when the third molar was transversely positioned.³⁶

Pathologic Widening of Third Molar Pericoronal Space

A widely varying range of results were reported on the prevalence of a widened third molar pericoronal space. Studies investigating pericoronal pathology in erupted, partially erupted, and impacted third molars reported a prevalence of 0.7 to 13%.^{14,26,37} These studies included patients ranging in age from 18 to 92 years, and large differences were observed in the cutoff values for defining a widened pericoronal space on panoramic radiographs (range, 2.5 to 4 mm). Sejfija et al³⁷ examined mostly young persons (mean age, 29 years) and reported a prevalence of 1.2% using a 4-mm cutoff on panoramic imaging. In contrast, Eliasson et al,¹⁹ with a very similar study design but of older subjects (mean age, 43 years) and using a 2.5-mm cutoff, reported a prevalence of 4%. Additionally, the latter study reported that mandibular third molars were more affected than were maxillary third molars.¹⁹ Of the included studies, only Ventä et al⁴² attributed the presence of pericoronal pathology to the position of the third molar (aberrant orientation and impaction depth).

ASSESSMENT OF METHODOLOGIC QUALITY

The tool used to assess the methodologic quality of the included studies is presented in Table 3. The corresponding results are listed in Table 4 and shown in Figure 2. The mean scores per topic of risk of bias could range from 0 to 2. A higher score indicates a lower risk of bias. A visual assessment of the studies with good, medium or fair, or poor quality per risk of bias domain and topic stratified by the pathology related to third molar retention is provided in Figure 2. The overall quality was considered fair.

Discussion

Third molars have been widely discussed and have been the topic of more than 10,000 reports in

Table 3. RISK OF BIAS TOOL USED TO EVALUATE METHODOLOGIC QUALITY OF INCLUDED STUDIES Bias Domain and Definition Score Selection bias: study population Study population represented general population 2 Study population did not represent general population 1 Study population did not represent general population and was ill defined 0 Detection bias: standardization of measurement 2 Examiners were calibrated and/or used a protocol Study poorly defined or did not define its examiners 1 0 Examiners were not calibrated nor used a protocol Detection bias: method of measurement Caries Radiographic and clinical assessment using visual and tactile examination 2 Only radiographic or only clinical assessment using visual tactile examination 1 Other methods not considered current clinical standard used 0 Periodontal pathology Radiographic and clinical assessment through pocket probing 2 Only radiographic or only clinical assessment through pocket probing 1 Other methods not considered current clinical standard used 0 M2 ERR CBCT or intraoral radiographic assessment (periapical, bitewing) 2 Panoramic radiographic assessment 1 Other methods not considered current clinical standard used 0 Pathologic widening of M3 pericoronal space CBCT or intraoral radiographic assessment with 2-mm cutoff 2 Panoramic radiographic assessment with 2.5-mm cutoff 1 Other methods not considered current clinical standard used 0 Attrition bias: incomplete data Outcome data for all included subjects complete for entire study duration 2 Outcome data for included subjects not complete but was clearly discussed 1 0 Outcome data clearly missing or inadequately discussed Reporting bias: selective reporting Basic data on results adequately reported as defined in methods 2 Reporting of results raised concerns about data completeness 1 Reported results clearly incomplete or inadequately reported 0

Abbreviations: CBCT, cone-beam computed tomography; ERR, external root resorption; M2, second molar; M3, third molar. *Vandeplas et al. Third Molar Retention and Pathology. J Oral Maxillofac Surg 2020.*

biomedical libraries. However, no consensual guidelines have been developed regarding the clinical management of these teeth. The studies included in the present systematic review covered a period of 30 years, a period in which dental practice and care have evolved tremendously, as have the guidelines for third molar management. Because of the current guidelines discouraging prophylactic removal of third molars, the purpose of the present systematic review was to investigate the occurrence of pathologies associated with the retention of asymptomatic third molars.

The available data revealed that retained asymptomatic third molars will rarely remain disease-free, especially when they have partially erupted. Caries and periodontal disease were by far the most commonly observed pathologic outcomes related to retention of third molars. These pathologies occurred at the third molar itself but were also significantly more prevalent on the M2D when adjacent to a third molar. In accordance with the classic findings by Ash et al,⁴⁵ in 1962, the studies in the present review showed that second molars had more periodontal disease when a third molar was present, and this was also true for caries.

Age also played a significant role. Considering that third molars typically erupt between the ages of 17 and 24 years, it was not surprising that third molar and M2D caries were significantly more prevalent in subjects older than 25 years than in younger subjects and that the prevalence varied widely from 24 to 80% depending on the age of the subjects.^{24,38,41}

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Table 4. RESULTS OF RISK OF BIAS ASSESSMENT EVALUATING METHODOLOGIC QUALITY OF INCLUDED STUDIES

		Ris	sk of Bias Score		
Pathology	Selection Bias: Study Population	Detection Bias: Standardization of Measurement	Detection Bias: Method of Measurement	Attrition Bias: Incomplete Data	Reporting Bias: Selective Reporting
Caries					
Ahmad et al, ⁸ 2008	1	2	1	1	2
Al Hobail et al, ⁹ 2019	1	2	2	1	2
Celikoglu et al, ¹⁴ 2010	1	2	1	1	2
Chou et al, 15 2017	1	2	2	1	1
Chu et al, 16 2003	1	2	1	1	1
Claudia et al, ¹⁷ 2018	1	1	1	1	2
Divaris et al, ¹⁸ 2012	1	2	2	1	2
Fisher et al, ²² 2012	1	1	2	1	2
Garaas et al, ²³ 2011	1	2	1	1	2
Garaas et al, ²⁴ 2012	1	2	2	1	2
Jung et al, ²⁶ 2013	1	1	1	1	2
Marques et al, 28 2017	1	2	1	1	2
Marques et al, 2017 Moss et al, 302007	1	1	1	1	2
Nunn et al, ³² 2013	1	1	1 2	1	2
Özeç et al, ³⁴ 2009	0	2			2
Pepper et al, ³⁵ 2017			1	1	
Sejfija et al, ³⁷ 2019	1	0	1	1	2
	1	2	1	1	2
Shugars et al, ³⁸ 2004	1	2	2	1	2
Shugars et al, 39 2005	1	2	2	1	2
Syed et al, ⁴⁰ 2017 Ventä et al, ⁴¹ 2015	1	1	1	1	2
	1	1	2	1	2
Ventä et al, ⁴² 2019	1	2	2	1	2
Periodontal pathology		2	-	_	
Ahmad et al, ⁸ 2008	1	2	1	1	2
Blakey et al, ¹⁰ 2002	1	2	1	1	2
Blakey et al, ¹² 2006	1	2	1	1	2
Blakey et al, ¹¹ 2007	1	2	2	0	0
Blakey et al, 13 2009	1	2	2	1	2
Celikoglu et al, ¹⁴ 2010	1	2	1	1	2
Chou et al, ¹⁵ 2017	1	2	2	1	1
Chu et al, ¹⁶ 2003	1	2	1	1	1
Eliasson et al, ¹⁹ 1989	1	1	1	1	2
Elter et al, ²¹ 2004	1	2	1	1	2
Elter et al, ²⁰ 2005	1	2	1	1	2
Fisher et al, ²² 2012	1	1	2	1	2
Garaas et al, ²³ 2011	1	2	1	1	2
Garaas et al, ²⁴ 2012	1	2	2	1	2
Golden et al, ²⁵ 2015	1	1	1	0	2
Jung et al, ²⁶ 2013	1	1	1	1	2
Moss et al, ³⁰ 2007	1	1	1	1	2
Moss et al, ²⁹ 2009	1	2	1	1	2
Nance et al, ³¹ 2006	1	2	2	1	2
Nunn et al, ³² 2013	1	1	2	1	2
Sejfija et al, ³⁷ 2019	1	2	1	1	2
Ventä et al, ⁴¹ 2015	1	1	2	1	2
Ventä et al, ⁴² 2019	1	2	2	1	2
White et al, ⁴⁴ 2006	1	2	1	1	2
M2 ERR					
Celikoglu et al, ¹⁴ 2010	1	2	1	1	2
Eliasson et al, ¹⁹ 1989	1	1	1	1	2
Jung et al, ²⁶ 2013	1	1	1	1	2

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		Ri	sk of Bias Score		
Pathology	Selection Bias: Study Population	Detection Bias: Standardization of Measurement	Detection Bias: Method of Measurement	Attrition Bias: Incomplete Data	Reporting Bias: Selective Reporting
127 2010	-	2	2		2
Li et al, ²⁷ 2019	1	2	2	1	2
Oenning et al, ³³ 2015	1	1	2	1	2
Schriber et al, ³⁶ 2019	1	1	2	1	2
Sejfija et al, ³⁷ 2019	1	2	1	1	2
Ventä et al, ⁴² 2019	1	2	1	1	2
Wang et al, ⁴³ 2017	1	1	2	1	2
Pathologic widening of					
M3 pericoronal space	-	2		-	2
Celikoglu et al, ¹⁴ 2010	I	2	1	1	2
Eliasson et al, ¹⁹ 1989	1	1	1	1	2
Jung et al, ²⁶ 2013	1	1	0	1	2
Sejfija et al, ³⁷ 2019	1	2	0	1	2
Ventä et al, ⁴² 2019	1	2	1	1	2

Table 4. Cont'd

Abbreviations: ERR, external root resorption; M2, second molar; M3, third molar.

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Similarly, periodontal disease nearly doubled in those older than 25 years.¹⁰ The prevalence of deep third molar periodontal pockets (PD of \geq 5 mm) was surprisingly greater than would have been be expected from the results from the NHANES III. When examining older ages, fewer than 2% of the subjects aged 52 to 74 years were free of periodontal pathology and caries in the Dental ARIC study.²³

Several studies have reported that third or second molar pathology was dependent on the impaction status of the third molar.^{8,32,38,44} In particular, caries and periodontal pathology were more prevalent in the presence of a third molar and even more so when the third molar had partially erupted. Because caries and periodontal disease are primarily caused by dental plaque, these phenomena can be explained by the difficulties in maintaining oral hygiene distally in the mouth and, consequently, the accumulation of plaque. This can be aggravated when the third molar has only partially erupted, because this position will undermine the second molar's gingival seal.⁴⁶

However, prospective longitudinal studies are lacking on the topics of second molar ERR and pathologic widening of the pericoronal space. The studies that investigated these pathologies were all cross-sectional in design, compromising the opportunity to inquire into the development of these pathologies over time. Nonetheless, several of these cross-sectional studies reported a significant association with older age and the prevalence of second molar ERR. Mesial bony impaction was not only associated with a greater prevalence, but also with more severe resorption.^{27,36,43}

A major limitation of the included studies were the study samples, which were not very generalizable to the overall population. All included prospective studies had used subsamples of longitudinal trials. The data had originally been prospectively collected; thus, the studies analyzing these data were, by definition, also prospective. To the best of our knowledge, no prospective studies using their own original sample data have been reported that would fit the criteria for the present review. By far the most used sample originated from the University of Kentucky and University of North Carolina (10 of 12 prospective studies and 13 of all 37 studies). Thus, it is likely that data from the same subjects were used in multiple of the included reports. Other studies included patients from private practices or academic institution clinical departments or subsamples of various other studies. None of the samples were representative of the general population. Research on third molar pathology has nearly always been performed on a clinical sample of patients visiting the dental department of a hospital seeking advice on one or more oral events. Patients with symptom-free third molars can be difficult to reach. Nevertheless, it is important to state that absence of symptoms does not equal the absence of disease, which was clearly and repeatedly demonstrated by Dodson and Marciani.47-49

Another limitation was the method by which the disease outcomes were measured, especially for caries and periodontal disease. These should ideally be assessed both clinically and radiographically, preferably with visual and tactile assessment (ie, probing) and

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Outcomes	Bias domains	Mean risk of bias score (± SD)	Total scores
	Selection bias: Study population	0.95 ± 0.21	
	Detection bias: Standardization of measurement	1.59 ± 0.59	
Caries	Detection bias: Method of measurement	1.45 ± 0.51	
	Attrition bias: Incomplete data	1.00 ± 0.00	
	Reporting bias: Selective reporting	1.91 ± 0.29	
	Selection bias: Study population	1.00 ± 0.00	
	Detection bias: Standardization of measurement	1.71 ± 0.46	
Periodontal pathology	Detection bias: Method of measurement	1.38 ± 0.49	
Puttionog,	Attrition bias: Incomplete data	0.92 ± 0.28	
	Reporting bias: Selective reporting	1.83 ± 0.48	
	Selection bias: Study population	1.00 ± 0.00	
	Detection bias: Standardization of measurement	1.44 ± 0.53	
M2 External root resorption	Detection bias: Method of measurement	1.44 ± 0.53	
roorroorpion	Attrition bias: Incomplete data	1.00 ± 0.00	
	Reporting bias: Selective reporting	2.00 ± 0.00	
	Selection bias: Study population	1.00 ± 0.00	
Pathologic	Detection bias: Standardization of measurement	1.60 ± 0.55	
widening of the M3 pericoronal	Detection bias: Method of measurement	0.60 ± 0.55	
space	Attrition bias: Incomplete data	1.00 ± 0.00	
	Reporting bias: Selective reporting	2.00 ± 0.00	

FIGURE 2. Visual assessment of the risk of bias of studies stratified by pathology. The overall quality of the included studies was considered medium or fair). Each domain was given a numerical value of 2, 1 or 0, indicating a low, medium, or high risk of bias, respectively. For visual assessment of the risk of bias, the values were given a corresponding color, indicating good (green), medium or fair (yellow), or poor (red) quality. SD, standard deviation.

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intraoral radiography (ie, periapical, bitewing). Most (20 of 35) of the reports studying these pathologies used only one of these methods to measure the disease outcomes. This not only impaired the disease measurements, but also limited the possibility of assessing the position of the impacted third molar. For second molar ERR and pericoronal widening of the third molar pericoronal space, the method of choice has been conebeam computed tomography (CBCT) or intraoral radiography.^{50,51} Panoramic radiographs have been considered a valid, although less suitable, method to accurately assess these pathologies. Thus, the wide variability in the prevalence of second molar ERR (range, 0.5 to 50%) can be attributed to the study by Eliasson et al,¹⁹ which used 2-dimensional panoramic radiographs to assess resorption. In contrast, Schriber et al³⁶ evaluated the 3-dimensional extent of resorption using CBCT. Furthermore, when evaluating widening of the pericoronal space (prevalence range, 0.7 to 13%), the cutoff for the presence of pathology should be set to greater than 2.5 mm for panoramic images and greater than 2 mm for CBCT and intraoral radiographs. However, of the 5 studies that investigated this pathology, 2 used cutoff values greater than 2.5 (Ventä et al,⁴² 3 to 5 mm; Sejfija et al,³⁷ 4 mm).^{37,42} Because of the differences in methods and different age categories examined in the included studies, large variations were found in the disease prevalence. To critically evaluate the quality of the selected methods of measurement, we included an extra category in the risk of bias assessment. Moreover, the reports that failed to describe the distinction between maxillary and mandibular observations might further substantiate the wide variation in results. In these cases, a lower prevalence of a certain pathology in the upper or lower jaw could mask or confound a greater prevalence in the other jaw, and vice versa.^{19,36}

The included studies were classified by 4 main pathologies: caries, periodontal pathology, second molar ERR, and pathologic widening of the third molar pericoronal space. These 4 pathologies associated with the third molars should not be considered exhaustive but, rather, were the most frequently investigated pathologies in the included studies. The present review did not examine the pathologies that have been associated with a widening of the third molar pericoronal space, such as various cysts and tumors^{52,53} or abscesses and systemic inflammation associated with third molar retention.⁵⁴ Mandibular fractures and other complications were also not investigated.⁵² Crowding of the anterior incisors has long been considered a consequence of third molar retention; however, it is now understood that third molars cannot distort the dental alignment to such a degree.⁵⁵⁻⁵⁷

Data on the long-term effects of retaining third molars have remained limited. The average follow-up time was only 4 years, which is arguably insufficient to make accurate predictions on the future development of pathology. Moreover, studies that had followed third molar status reported that the third molars frequently had to be removed during the follow-up period.⁵⁸ This substantiates the hypothesis that third molars will rarely remain disease-free over a lifetime.

To date, no systematic approaches are available to allow for satisfactory predictions regarding third molar disease development, with consideration of impaction status, patient's oral hygiene, and the overall clinical picture. Several international guidelines on the clinical management of third molars have been reported to aid clinicians with treatment decisions. These have included the 2000 NICE guidelines from the United Kingdom, the 2000 SIGN guidelines, and the 2012 KCE report.³⁻⁵ After the publication of these guidelines, the number of surgical third molar removals temporarily decreased for some years; however, they have again increased to a level comparable to that in the mid-1990s.⁵⁹ Thus, patients have been, on average, 6 years older when undergoing this surgery than in the past.^{60,61} This might lead to a reversed effect of increasing the risk of complications associated with older age and unfavorable conditions on surgical removal.^{$62,\overline{63}$} The guidelines have mainly advised against the prophylactic removal of third molars because of the lack of clinical evidence that third molars will eventually develop pathology when retained. With this argumentum ad ignorantiam approach, the guidelines, thus, concluded that retention systematically outperforms extraction, despite providing no evidence to suggest that these teeth would remain free of pathology and symptoms.⁶⁴ In the present ongoing disagreement, clinicians have largely relied on their own expertise and beliefs in their clinical decision making.^{2,65} Thus, great variation has continued to exist among clinicians regarding their evaluation and beliefs regarding the need for third molar removal.

In conclusion, the present systematic review was conducted to explore the current data regarding the pathologies associated with the retention of asymptomatic third molars. The results of our systematic review have shown that medium to fair quality evidence is available that has demonstrated that pathology in these teeth is common and, moreover, that retention of the third molar is significantly associated with an increased risk of pathology in the second molar, especially with partially erupted and/or mesially inclined, mandibular third molars. Well-designed prospective follow-up studies are needed to substantiate the clinical management (removal or retention) of asymptomatic third molars.

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Appendix 1 Search Syntax for Each Database (Search Last Performed April 2, 2020):

SEARCH PubMed:

Domain:

(((*molar, third"[MeSH Terms] OR wisdom teeth[Title/Abstract]) OR wisdom tooth[Title/Abstract]) OR (third molar[Title/Abstract] OR third molars[Title/Abstract])) OR (3rd molar[Title/Abstract] OR 3rd molars[Title/Abstract])

AND Outcome:

(((((((((((((((((((((((((((())) Caries" [Mesh:NoExp]) OR "Osteomyelitis"[Mesh:NoExp]) OR Periodontal Diseases[MeSH Terms]) OR Tooth Resorption[MeSH Terms]) OR Jaw Cysts[MeSH Terms]) OR Odontogenic tumors[MeSH Terms]) OR Jaw Neoplasms[MeSH Terms]) OR Jaw Fractures [MeSH Terms]) OR Tooth Extraction[MeSH Terms]) OR Trigeminal Nerve Injuries[MeSH Terms]) OR caries[Title/Abstract]) OR decay[Title/Abstract]) OR periodontal[Title/ carious[Title/Abstract]) OR Abstract]) OR periodontitis[Title/Abstract]) OR resorption[Title/Abstract]) OR inflammation[Title/Abstract]) OR inflammatory[Title/Abstract]) OR pericoronitis[Title/Abstract]) OR abcess[Title/Abstract]) OR osteomyelitis[Title/Abstract]) OR cvst*[Title/Abstract]) OR tumor*[Title/Abstract]) OR tumour*[Title/Abstract]) OR neoplasm*[Title/Abstract]) OR carcinoma[Title/Abstract]) OR crowding[Title/Abstract]) OR removed[Title/Abstract]) OR removal[Title/Abstract]) OR extraction[Title/Abstract]) OR extracted[Title/Abstract]) OR patholog*[Title/Abstract]) OR symptoms[Title/Abstract]) OR symptomatic[Title/Abstract]) OR disease[Title/Abstract]) OR diseased[Title/Abstract]) OR nerve[Title/Abstract]) OR neural[Title/Abstract]) OR neuro*[Title/Abstract]) OR fracture*[Title/Abstract]

Final:

#domain AND #outcome

SEARCH EMBASE:

#1: 'third molar*':ab,ti OR 'wisdom tooth':ab,ti OR 'wisdom teeth':ab,ti OR '3rd molar*':ab,ti

#2: 'dental caries'/exp OR 'periodontal disease'/exp OR 'tooth abscess'/exp OR 'osteomyelitis'/exp OR 'jaw cyst'/exp OR 'jaw tumor'/exp OR 'jaw

fracture'/exp OR 'crowding (tooth)'/exp OR 'tooth extraction'/exp OR 'trigeminal nerve injury'/exp OR 'caries':ab,ti OR 'carious':ab,ti OR 'decay':ab,ti OR 'periodontal':ab,ti OR 'periodontitis':ab,ti OR 'resorption':ab,ti OR 'inflammation':ab,ti OR 'inflammatory':ab,ti OR 'pericoronitis':ab,ti OR 'osteomyelitis':ab,ti OR 'cyst*':ab,ti OR 'abscess':ab,ti OR 'tumor*':ab,ti OR 'tumour*':ab,ti OR 'carcinoma':ab,ti OR 'neoplasm*':ab,ti OR 'patholog*':ab,ti OR 'symptoms':ab,ti OR 'symptomatic':ab,ti OR 'disease':ab,ti OR 'diseased':ab,ti OR 'extracted':ab,ti OR 'extraction':ab,ti OR 'removed':ab,ti OR 'removal':ab,ti OR 'crowding':ab,ti OR 'nerve':ab,ti OR 'neural':ab,ti OR 'neuro*':ab,ti OR 'fracture':ab,ti

Final:

#1 AND #2

SEARCH COCHRANE LIBRARY:

#1: Mesh term "third molar"

#2: "third molar":ab,ti OR "wisdom tooth":ab,ti OR "wisdom teeth":ab,ti OR "3rd molar":ab,ti

#3: #1 OR #2

- #4: Mesh "dental caries" (NoExp)
- #5: Mesh "Periodontal diseases"
- #6: Mesh "Tooth resorption"
- #7: Mesh "Osteomyelitis" (NoExp)
- #8: Mesh "Jaw cysts"

#9: Mesh "Odontogenic tumors"

#10: Mesh "Jaw neoplasms"

- #11: Mesh "Tooth extraction"
- #12: Mesh "Trigeminal Nerve Injuries"
- #13: Mesh "Jaw Fractures"
- #14: #4 OR ... #13

#15: "caries":ab,ti OR "decay":ab,ti OR "carious":ab,ti OR "periodontal":ab,ti OR "periodontitis":ab,ti OR "resorption":ab,ti OR "inflammation":ab,ti OR "inflammatory":ab,ti OR "pericoronitis":ab,ti OR "osteomyelitis":ab,ti OR "cyst*":ab,ti OR "abscess":ab,ti OR "tumor*":ab,ti OR "cyst*":ab,ti OR "abscess":ab,ti OR "tumor*":ab,ti OR "tumour*":ab,ti OR "neoplasm*":ab,ti OR "carcinoma":ab,ti OR "removed":ab,ti OR "removal":ab,ti OR "extraction":ab,ti OR "extracted":ab,ti OR "patholog*":ab,ti OR "symptoms":ab,ti OR "symptomatic":ab,ti OR "diseased":ab,ti OR "crowding":ab,ti OR "neural":ab,ti OR "neuro*":ab,ti OR "fracture":ab,ti

#16: #14 OR #15 #17: #3 AND #16