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Original articles

Management of a macroscopically normal appendix during surgery for suspected appendicitis: Evidence for clinical practice, healthcare resource use and surgical policy

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Background

Whether a macroscopically normal appendix identified during surgery for suspected acute appendicitis should be removed or left in situ remains controversial. Although unnecessary appendectomy may expose patients to avoidable operative risks and healthcare costs, failure to remove an appendix with occult inflammation may lead to delayed diagnosis, disease progression, and subsequent complications. This systematic review and meta-analysis aimed to determine the incidence of histologically confirmed appendicitis and other clinically significant pathology in macroscopically normal appendices removed during surgery for suspected appendicitis.

Methods

A systematic review was conducted in accordance with the PRISMA 2020 statement and prospectively registered in PROSPERO (CRD42023397449). PubMed, MEDLINE, Scopus, Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Library, the WHO International Clinical Trials Registry Platform, and Google Scholar were systematically searched for eligible studies published up to 1 March 2023. Experimental and observational studies reporting histopathological findings in macroscopically normal appendices removed during surgery for suspected appendicitis were included. Random-effects meta-analysis was performed to estimate the pooled incidence of histologically confirmed appendicitis and overall clinically significant pathology.

Results

Eighteen studies involving 1,780 patients with macroscopically normal appendices removed during diagnostic laparoscopy or open surgery for suspected appendicitis met the inclusion criteria. The pooled incidence of histologically confirmed acute appendicitis was 25% (95% CI 0.15–0.33), while the pooled incidence of overall clinically significant pathology was 28% (95% CI 0.20–0.37). Although appendicitis accounted for the vast majority of abnormal histological findings, other important pathologies, including neuroendocrine tumours and appendiceal neoplasms, were also identified. Considerable between-study heterogeneity was observed.

Conclusions

Macroscopic assessment alone does not reliably exclude appendiceal pathology, with approximately one in four macroscopically normal appendices showing histologically confirmed appendicitis. Appendectomy may therefore be considered when no alternative cause of symptoms is identified, although decisions should be individualised given the heterogeneity and observational nature of the evidence. Clinical guidelines should also consider healthcare capacity, access to follow-up, and the potential resource consequences of both unnecessary surgery and missed disease. Prospective studies incorporating patient-centred outcomes, healthcare utilisation, and economic evaluation are needed to inform context-specific surgical policy.

Registration: PROSPERO CRD42023397449

Acute appendicitis is one of the most common surgical emergencies worldwide and remains a frequent indication for emergency abdominal surgery. Although advances in clinical assessment, laboratory investigations, imaging modalities, and diagnostic algorithms have improved diagnostic accuracy, distinguishing appendicitis from other causes of right lower quadrant pain remains challenging. Consequently, diagnostic laparoscopy continues to play an important role in the evaluation and management of patients with suspected appendicitis, particularly when the diagnosis remains uncertain.

A persistent intraoperative dilemma arises when the appendix appears macroscopically normal during surgery performed for suspected appendicitis. There is currently no universal consensus on whether such an appendix should be removed or left in situ after alternative causes of the patient's symptoms have been excluded.[1] An international survey of surgeons identified the absence of clear clinical guidelines and concern about missing endoluminal or early appendicitis as the principal reasons for performing appendectomy despite a normal macroscopic appearance.[2]

Histopathological diagnosis of acute appendicitis has traditionally relied on the presence of transmural inflammation.[3] However, some pathology departments also recognise isolated mucosal ulceration or mucosal inflammation as evidence of early appendicitis.[4] Consequently, inflammation confined to the mucosa may not be apparent on macroscopic inspection of the serosal surface, raising concerns that a macroscopically normal appendix may harbour clinically significant pathology. Failure to identify and treat occult appendicitis may result in delayed diagnosis, perforation, intra-abdominal abscess, diffuse peritonitis, reoperation, prolonged hospitalisation, and increased healthcare costs.

Conversely, routine removal of all macroscopically normal appendices is not without consequences. Negative appendectomy has been associated with unnecessary exposure to anaesthesia and operative risks, postoperative morbidity, longer hospital stay, and increased healthcare expenditure compared with appendectomy performed for confirmed uncomplicated appendicitis.[5] Unnecessary surgery also imposes avoidable physical, psychological, and economic burdens on patients, families, and healthcare systems.[6] Therefore, the decision to remove or preserve a macroscopically normal appendix requires balancing the risk of missed disease against the harms associated with unnecessary surgery.

Current recommendations reflect this uncertainty. The Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) advises that, after excluding other causes of abdominal pain, removal of a macroscopically normal appendix may be considered on an individual patient basis.[7] Supporting this cautious approach, Lee et al. reported that 13.3% of patients in whom a macroscopically normal appendix was left in situ subsequently required reoperation, of whom 4.17% had histologically confirmed appendicitis.[8] However, the available evidence remains inconsistent and is largely derived from small observational studies with variable definitions of both a macroscopically normal appendix and histological appendicitis.

Although several studies have examined the relationship between intraoperative macroscopic assessment and subsequent histopathological findings, the reported incidence of occult appendicitis varies considerably, and the overall burden of clinically significant pathology remains uncertain. A comprehensive synthesis of the available evidence is therefore needed to inform surgical decision-making, guideline development, and future research.

Accordingly, this systematic review and meta-analysis aimed to determine the pooled incidence of histologically confirmed appendicitis and other clinically significant pathology in macroscopically normal appendices removed during surgery for suspected appendicitis. By quantifying the diagnostic limitations of macroscopic assessment, this review seeks to provide evidence to support clinical decision-making and inform future health policy and research evaluating the balance between unnecessary appendectomy and missed appendiceal disease.

METHODS

PROTOCOL REGISTRATION AND REPORTING

This systematic review and meta-analysis was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO; CRD42023397449) and conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines.[9]

SEARCH STRATEGY

A comprehensive literature search was undertaken in PubMed, MEDLINE, Scopus, the Cochrane Central Register of Controlled Trials (CENTRAL), the Cochrane Library, the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP), and Google Scholar to identify relevant studies published up to 1 March 2023.

The search strategy incorporated combinations of the following keywords and Medical Subject Headings (MeSH), where applicable: *"macroscopically normal appendix"*, *"negative appendectomy"*, *"false negative appendectomy"*, *"appendicitis"*, *"diagnostic laparoscopy"*, *"laparoscopy"*, and *"appendectomy"*. Reference lists of all eligible studies were manually screened to identify additional relevant publications (Appendix 1, **Online Supplementary Document**)

ELIGIBILITY CRITERIA

Published full-text experimental and observational studies evaluating histopathological findings in macroscopically normal appendices removed during surgery for suspected appendicitis were eligible for inclusion. No language restrictions were applied.

Review articles, editorials, letters, conference abstracts, case reports, animal studies, and studies for which the full text could not be retrieved were excluded.

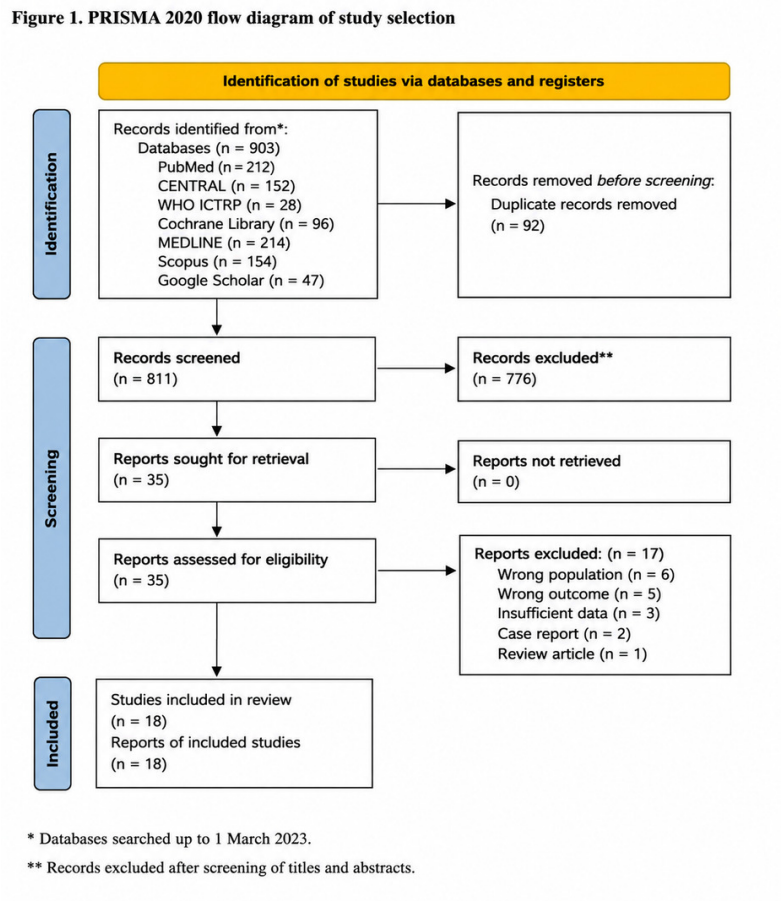

Figure 1. PRISMA 2020 flow diagram of study identification, screening, eligibility assessment, and study inclusion.

STUDY SELECTION

All retrieved records were imported into Covidence software for study management and duplicate removal.

Two reviewers (R.Sh and H.M) independently screened titles and abstracts for eligibility. Potentially relevant studies subsequently underwent full-text assessment by the same reviewers. Disagreements were resolved through discussion, and where consensus could not be reached, a third reviewer (A.A) acted as an adjudicator.

The study selection process is summarised in the PRISMA flow diagram (Figure 1).

DATA EXTRACTION

Data extraction was independently performed by R.Sh and verified by H.M and A.A using a standardized data extraction form.

The following information was extracted from each study:

- year of publication;
- study design;
- study objectives;
- sample size;
- participant characteristics (including age and sex);
- intraoperative findings;
- management of the macroscopically normal appendix;
- histopathological findings; and
- incidence of appendicitis or other significant pathology in macroscopically normal appendices.

QUALITY ASSESSMENT

Methodological quality and risk of bias were independently assessed by two reviewers (R.Sh and H.M), with disagreements resolved by discussion or, when necessary, consultation with a third reviewer (A.A).

Observational studies were assessed using the Modified Newcastle-Ottawa Scale (NOS), a validated tool for evaluating the methodological quality of non-randomized studies (Appendix 2, **Online Supplementary Document**).[10] The assessment considered three domains: selection of study groups, comparability between groups, and ascertainment of the exposure or outcome of interest.

STATISTICAL ANALYSIS

The primary outcome was the pooled incidence of histologically confirmed acute appendicitis in macroscopically normal appendices.

A secondary analysis estimated the pooled incidence of overall clinically significant pathology identified on

histopathological examination despite a macroscopically normal intraoperative appearance.

Pooled incidence estimates were calculated using random-effects meta-analysis and are presented as proportions with corresponding 95% confidence intervals (CIs). Given the anticipated clinical and methodological heterogeneity across the included studies, the DerSimonian-Laird random-effects model was used to estimate between-study variance.

Statistical heterogeneity was quantified using the I^2 statistic, with values of <25%, 25%–50%, and >50% representing low, moderate, and high heterogeneity, respectively.

Publication bias was assessed through visual inspection of funnel plots and Egger's regression test for small-study effects.

All statistical analyses were performed using Stata version 18.0 (StataCorp LLC, College Station, TX, USA).

RESULTS

STUDY SELECTION

The database search identified 903 records, of which 92 duplicate records were removed. Following title and abstract screening, 776 studies were excluded, leaving 35 articles for full-text assessment. Seventeen studies were subsequently excluded for not meeting the eligibility criteria, resulting in 18 studies being included in the final qualitative and quantitative synthesis (Figure 1).

STUDY CHARACTERISTICS

The included studies were published between 1988 and 2021 and comprised two prospective cohort studies,[11,12] one retrospective cross-sectional study,[13] and fifteen retrospective cohort studies. Across all studies, 1,780 patients with a macroscopically normal appendix identified during diagnostic laparoscopy or open surgery for suspected appendicitis underwent appendectomy. Histopathological findings were compared with the intraoperative macroscopic assessment in all included studies. The characteristics of the included studies are summarised in Table 2.

QUALITY ASSESSMENT

The methodological quality of the included studies was assessed using the Modified Newcastle-Ottawa Scale (Table 1). Overall, the studies demonstrated acceptable methodological quality; however, most were retrospective observational studies and therefore remained susceptible to inherent risks of selection bias, information bias, and residual confounding.

HISTOPATHOLOGICAL FINDINGS IN MACROSCOPICALLY NORMAL APPENDICES

Six studies reported the presence of alternative intraoperative pathology that could potentially explain the patient's symptoms despite the appendix appearing macroscopically normal.[13,14,20-22,27] Nevertheless, appendectomy was performed in these patients. Only three of these studies analysed patients with concomitant pathology separately when estimating the incidence of appendicitis.[13,20,27]

Histopathological examination demonstrated substantial discordance between macroscopic appearance and microscopic findings. Acute appendicitis was the predominant abnormal histological diagnosis, accounting for 96.5% of all false-negative macroscopic assessments (Table 3). Other clinically significant pathological findings included nine neuroendocrine tumours (1.7% of all false-negative cases),[11,19,20,24] one appendiceal cystadenoma,[16] and one case of isolated mucosal ulceration without transmural inflammation.[11] Two studies reported additional histopathological abnormalities without specifying their nature or clinical significance.[13,23]

META-ANALYSIS OF HISTOLOGICALLY CONFIRMED ACUTE APPENDICITIS

Across the included studies, the pooled incidence of histologically confirmed acute appendicitis in macroscopically normal appendices was **25%** (95% CI 0.15–0.33) (Figure 2).

Considerable between-study heterogeneity was observed (I^2 = 95%), indicating substantial variability in study populations, operative assessment, histopathological definitions, and study methodology.

META-ANALYSIS OF OVERALL CLINICALLY SIGNIFICANT PATHOLOGY

When all clinically significant histopathological abnormalities were considered, including appendicitis and other important pathological diagnoses, the pooled incidence increased to **28%** (95% CI 0.20–0.37) (Figure 3).

Individual study estimates varied considerably. Tartaglia et al.[20] reported the highest proportion of false-negative macroscopic assessments, with 73% (95% CI 0.66–0.80) of macroscopically normal appendices demonstrating significant histopathological abnormalities. Zarandi et al.[13] reported an overall false-negative rate of 67% (95% CI 0.36–0.97), although only 11% (95% CI 0.00–0.32) represented histologically confirmed acute appendicitis. Chiarugi et al.[14] reported that 58% (95% CI 0.44–0.72) of macroscopically normal appendices demonstrated histopathological evidence of inflammation.

PUBLICATION BIAS

Visual inspection of the funnel plots did not suggest substantial publication bias. Egger's regression test demonstrated no evidence of small-study effects (β = 1.81, standard error = 2.082; z = 0.87; p = 0.384), indicating that publication bias was unlikely to have materially influenced the pooled estimates.

Table 1. Methodological quality assessment of included studies using the Modified Newcastle–Ottawa Scale (NOS).

N	Name	1	2	3	4	5	6	7	Score*
1	Chiarugi, 2001[14]	3	1	2	2	2	3	3	20/21 (95.2%)
2	Grabham, 1999[15]	3	1	1	3	3	2	3	17/21 (81%)
3	Singhal, 2007[16]	3	2	2	2	2	1	2	16/21 (76.1%)
4	Walker, 1995[11]	3	2	3	3	3	3	3	18/21 (85.7%)
5	Thong, 2019[12]	3	3	2	3	3	3	3	19/21 (90.5%)
6	Qin, 2021[17]	3	2	2	3	2	3	3	19/21 (90.5%)
7	Pham, 2015[18]	3	2	2	2	2	3	3	19/21 (90.5%)
8	Strong, 2015[19]	3	2	2	3	3	3	3	18/21 (85.7%)
9	Tartaglia, 2016[20]	3	2	3	2	2	2	3	17/21 (81%)
10	Greason, 1998[21]	3	2	2	2	2	2	3	20/21(95.2%)
11	Roberts, 2008[22]	3	2	2	3	2	3	3	19/21 (90.5%)
12	Shum, 2005[23]	3	2	2	3	3	3	3	20/21 (95.2%)
13	Al-Ghnaniem, 2002[24]	3	2	3	3	2	3	3	17/21(81%)
14	Phillips, 2009[25]	3	2	3	3	2	3	3	16/21 (76.1%)
15	Jones, 1988[26]	3	2	2	2	3	3	3	18/21 (85.7%)
16	A Hussain, 2009[27]	3	2	2	2	2	3	3	19/21 (90.5%)
17	Zarandi, 2014[13]	3	3	3	2	3	3	3	19/21 (90.5%)
18	Kryzauskas, 2016[28]	3	2	2	3	3	3	3	19/21 (90.5%)

DISCUSSION

PRINCIPAL FINDINGS

This systematic review and meta-analysis synthesised the available evidence on the histopathological outcomes of macroscopically normal appendices removed during surgery for suspected appendicitis. The findings demonstrate that macroscopic intraoperative assessment alone is an unreliable predictor of underlying appendiceal pathology. Approximately one-quarter of macroscopically normal appendices (25%) demonstrated histologically confirmed acute appendicitis, while more than one-quarter (28%) contained clinically significant pathology. Although acute appendicitis accounted for most abnormal histological findings, other important diagnoses, including neuroendocrine tumours and appendiceal neoplasms, were also identified. Collectively, these findings suggest that reliance on the gross appearance of the appendix alone may result in missed pathology in a substantial proportion of patients.

COMPARISON WITH PREVIOUS LITERATURE

The diagnosis of acute appendicitis remains challenging despite advances in clinical assessment, laboratory investigations, and imaging. Clinical scoring systems may assist risk stratification but have limited diagnostic accuracy when used in isolation and are often more useful for monitoring disease progression in conservatively managed patients than for making definitive surgical decisions.[29] Similarly, although computed tomography has substantially improved diagnostic performance and reduced negative appendectomy rates, reported diagnostic accuracy remains imperfect and its widespread use is associated with increased healthcare costs, radiation exposure, and variable availability, particularly in emergency settings.[30-33]

Diagnostic laparoscopy therefore continues to play an important role in the evaluation of patients with suspected appendicitis when diagnostic uncertainty persists.[34,35] However, uncertainty frequently remains when the appendix appears macroscopically normal. The pooled findings of this review demonstrate considerable discordance between intraoperative macroscopic appearance and histopathological diagnosis, suggesting that visual inspection alone cannot reliably exclude early or occult appendicitis.

The wide variation observed across individual studies likely reflects differences in patient selection, surgeon experience, operative techniques, histopathological criteria, and definitions of a macroscopically normal appendix. For example, Tartaglia et al.[20] reported the highest proportion of false-negative macroscopic assessments, whereas lower incidences were reported by Zarandi et al.[13] and Chiarugi et al.[14] These differences emphasise the lack of standardised intraoperative criteria and underscore the need for caution when interpreting macroscopic findings in isolation.

CLINICAL IMPLICATIONS

The findings of this review support an individualized approach to intraoperative decision-making rather than routine preservation or routine removal of all macroscopically normal appendices. In patients in whom no alternative explanation for right lower quadrant pain is identified, appendectomy may reduce the risk of missed appendicitis and prevent subsequent complications, including perforation, intra-abdominal abscess, peritonitis, and reoperation.

Table 2. Characteristics of studies included in the systematic review and meta-analysis.

N	Name	Study design	Aim	Study sample size	Grossly normal appendix	Sex	Age	Operative finding	Histopathology of macroscopically normal appendix
1	Chiarugi, 2001[14]	Retrospective cohort	Determine the incidence of appendicitis in grossly normal appendix and its outcomes	48	48	M: 7 F: 41	Range 7-96y	Normal appendix and no other pathology = 34 Normal appendix with other pathology = 14	Normal appendix = 20 Appendicitis = 28
2	Grabham, 1999[15]	Retrospective cohort	Determine the accuracy of laparoscopy in diagnosing an inflamed appendix.	85	37	M: 13 F: 72	Range 15-67y	Normal appendix = 37	Normal appendix = 23 Appendicitis = 14
3	Singhal, 2007[16]	Retrospective cohort	Determine the histopathological diagnosis of grossly normal appendix	190	64	M:15 F:49	Range 12-68y	Normal appendix = 64	Normal appendix = 51 Appendicitis = 12 Other pathology = 1 (Cystadenoma)
4	Walker, 1995[11]	Prospective cohort	Determine diagnosis, treatment and follow-up of patients undergoing emergency appendicectomy	248	66	M:19 F:47	Range 12-68y	Normal appendix = 66	Normal appendix = 56 Appendicitis = 8 Other pathology = 2 (ulceration + neuroendocrine tumor)
5	Thong, 2019[12]	Prospective cohort	Investigate the accuracy of intraoperative macroscopic diagnosis	1169	183	-	-	Normal appendix = 183	Normal appendix = 142 Appendicitis = 41
6	Qin, 2021[17]	Retrospective cohort	Determine the accuracy of intra-operative assessment	420	74	M:191 F:229	>=15y	Normal appendix = 74	Normal appendix = 58 Appendicitis = 16
7	Pham, 2015[18]	Retrospective cohort	Assess accuracy of the intraoperative assessment	303	79	M:27 F:52	Range 15-86y	Normal appendix = 79	Normal appendix = 52 Appendicitis = 27
8	Strong, 2015[19]	Retrospective cohort	Determine the reliability between surgeons and pathologists in patients undergoing appendicectomy	3138	496	-	>=15y	Normal appendix = 496	Normal appendix = 377 Appendicitis = 114 Other pathology = 4 (Neuroendocrine tumor)
9	Tartaglia, 2016[20]	Retrospective cohort	Analyze the microscopical changes in normal appendices removed	164	164	M:20 F:144	Range 4-52y	Normal appendix and no other pathology = 50 Normal appendix with other pathology = 114	Normal appendix = 6 Appendicitis = 43 Other pathology of appendix = 1 (Neuroendocrine tumor) Normal appendix = 38 Appendicitis = 74 Other pathology of appendix = 2 (Neuroendocrine tumor)

N	Name	Study design	Aim	Study sample size	Grossly normal appendix	Sex	Age	Operative finding	Histopathology of macroscopically normal appendix
10	Greason, 1998[21]	Retrospective cohort	Determine the value of incidental laparoscopic appendectomy in right lower pain	44	44	M:8 F:36	Mean 24	Normal appendix and no other pathology = 8 Normal appendix with other pathology = 36	Normal appendix = 42 Appendicitis = 2
11	Roberts, 2008[22]	Retrospective cohort	Investigate macroscopically normal appendix if should be removed	876	156	M:421 F:438	-	Normal appendix and no other pathology = 136 Normal appendix with other pathology = 20	Normal appendix = 102 Appendicitis = 54
12	Shum, 2005[23]	Retrospective cohort	Determine the accuracy of on-table diagnostic	516	75	M:251 F:265	Range 11-90y	Normal appendix = 75	Normal appendix = 59 Appendicitis = 14 Other pathology = 2(not specified)
13	Al-Ghnaniem, 2002[24]	Retrospective cohort	Evaluate the accuracy of operative assessment	387	84	M:199 F:188	Range 3–92y	Normal appendix = 84	Normal appendix = 70 Appendicitis = 13 Other pathology = 1 (Neuroendocrine tumor)
14	Phillips, 2009[25]	Retrospective cohort	Determine the accuracy of intraoperative diagnosis of appendicitis	355	48	-	-	Normal appendix = 48	Normal appendix = 35 Appendicitis = 13
15	Jones, 1988[26]	Retrospective cohort	Investigate the discrepancy between the surgeons' opinion of the appendix at operation	213	40	M:124 F:89	Range 4–83y	Normal appendix = 40	Normal appendix = 40
16	A Hussain, 2009[27]	Retrospective cohort	Correlate the histological, operative, and clinical diagnoses of acute appendicitis	200	61	M:88 F:112	Range 8–83y	Normal appendix and no other pathology = 40 Normal appendix with other pathology = 21	Normal appendix = 30 Appendicitis = 10 Normal appendix = 13 Appendicitis = 8
17	Zarandi, 2014[13]	Retrospective cross-sectional	Evaluate the accuracy of surgeons' intraoperative diagnosis	342	9	M:2 F:7	Range 10-59y	Normal appendix and no other pathology = 3 Normal appendix with other pathology = 6	Normal appendix = 3 Appendicitis = 0 Appendicitis = 1 Other pathology = 5(not specified)
18	Kryzauskas, 2016[28]	Retrospective cohort	Identify factors associated with negative appendectomy	554	52		Range 18-88y	Normal appendix = 52	Normal appendix = 44 Appendicitis = 8

Table 3. Distribution of histopathological diagnoses among macroscopically normal appendices with clinically significant pathology.

Positive pathology in macroscopically normal appendix among total false negative results	Percentage
Acute appendicitis	96.5%
Neuroendocrine tumors	1.7%
Cystadenoma	0.19%
Ulceration of the appendix with no inflammation	0.19%
Unspecified	1.3%

Conversely, routine appendectomy carries its own risks, including operative complications, anaesthetic exposure, postoperative morbidity, and negative appendectomy. The decision should therefore be informed by the overall clinical picture, including preoperative probability of appendicitis, intraoperative findings, patient characteristics, surgeon judgement, and the availability of postoperative observation and follow-up. Rather than relying exclusively on the macroscopic appearance of the appendix, surgeons should integrate all available clinical and operative information when deciding whether appendectomy is warranted.

HEALTH SYSTEM, ECONOMIC AND POLICY IMPLICATIONS

The implications of these findings extend beyond individual patient management and are highly relevant to healthcare resource allocation and surgical policy. The management of a macroscopically normal appendix represents a balance between two competing healthcare risks: unnecessary appendectomy and missed appendicitis.

Routine removal of macroscopically normal appendices may increase operative time, pathology workload, hospital costs, and expose some patients to avoidable surgery. Conversely, failure to remove an appendix containing occult inflammation may result in delayed diagnosis, perforation, emergency reoperation, prolonged hospitalisation, increased healthcare expenditure, and avoidable morbidity. From a health system perspective, these downstream consequences may ultimately consume substantially greater healthcare resources than the initial appendectomy itself.

The optimal management strategy is also likely to vary according to healthcare setting. In high-income countries, widespread access to high-quality imaging, pathology services, specialist surgeons, and structured postoperative follow-up may support more selective preservation of a macroscopically normal appendix. In contrast, many low- and middle-income countries continue to face delayed presentation, limited access to advanced diagnostic imaging, shortages of specialist surgical services, and restricted opportunities for timely re-evaluation. Under these circumstances, the clinical and economic consequences of missed appendicitis may be considerably greater, potentially favouring appendectomy when no alternative pathology is identified.

These findings therefore support the development of context-specific rather than universal clinical guidelines. Future recommendations should consider not only diagnostic accuracy and surgical outcomes but also healthcare capacity, resource availability, patient access to follow-up,

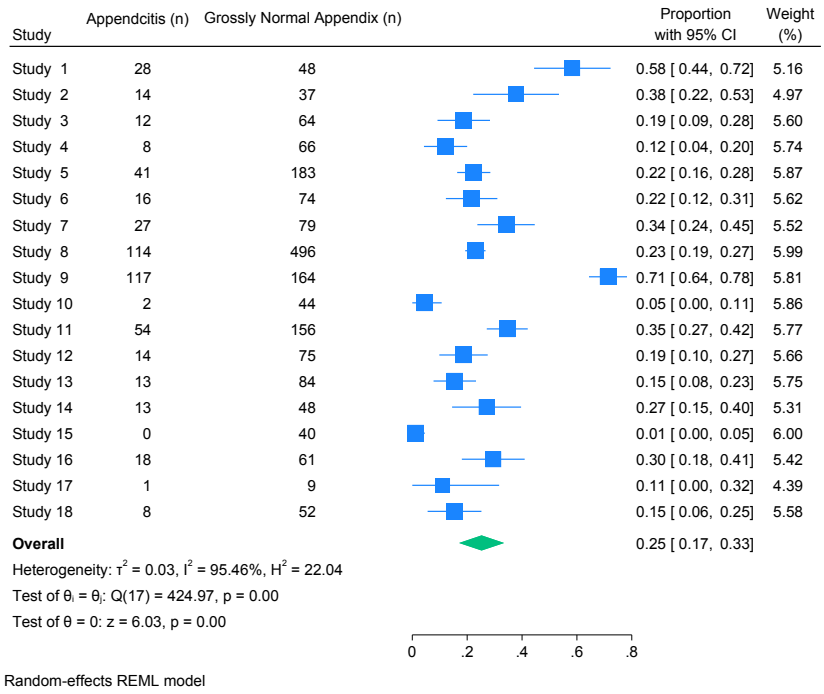

Figure 2. Forest plot showing the pooled incidence of histologically confirmed acute appendicitis in macroscopically normal appendices.

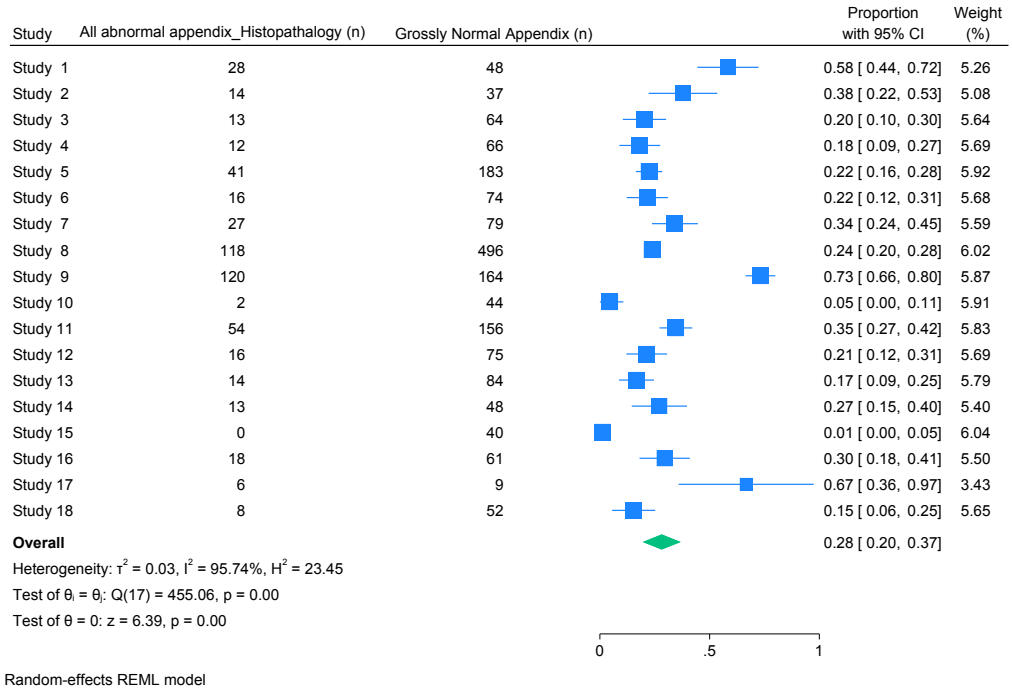

Figure 3. Forest plot showing the pooled incidence of clinically significant histopathological abnormalities in macroscopically normal appendices.

and the economic consequences of both overtreatment and delayed treatment. Incorporating health economic evidence into future guideline development would facilitate more efficient allocation of healthcare resources while maintaining patient safety.

STRENGTHS AND LIMITATIONS

This review represents, to our knowledge, the first systematic review and meta-analysis to quantify the incidence of histologically confirmed appendicitis and other clinically significant pathology in macroscopically normal appendices removed during surgery for suspected appendicitis. A comprehensive literature search, duplicate study selection, standardized quality assessment, and quantitative synthesis strengthen the validity of the findings.

Nevertheless, several limitations should be acknowledged. First, the evidence base consisted entirely of observational studies, most of which were retrospective, limiting causal inference and increasing susceptibility to selection bias and residual confounding. Second, substantial statistical heterogeneity was observed across studies, reflecting differences in patient populations, surgical techniques, definitions of a macroscopically normal appendix, and histopathological diagnostic criteria. Third, the included studies spanned more than three decades, during which imaging modalities, operative practice, and pathological classification have evolved considerably. Finally, important patient-centred outcomes, including postoperative complications, symptom resolution, readmissions, quality of life, and long-term outcomes, were inconsistently reported, precluding quantitative synthesis.

FUTURE RESEARCH

Future research should focus on well-designed prospective multicentre studies using standardized definitions of both macroscopically normal appendix and histological appendicitis. Comparative studies evaluating appendectomy versus observation should incorporate clinically meaningful outcomes, including postoperative complications, quality of life, readmissions, patient-reported outcomes, and long-term morbidity.

Importantly, future investigations should also include formal economic evaluations, such as cost-effectiveness and cost-utility analyses, to determine whether routine or selective appendectomy represents the most efficient use of healthcare resources in different health system contexts. Such evidence would strengthen future clinical guidelines and support evidence-informed policy decisions across both high-income and resource-constrained settings.

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AUTHORSHIP CONTRIBUTIONS

All authors contributed substantially to the conception and design of the study, data acquisition, analysis and interpretation, manuscript drafting and critical revision, approved the final version of the manuscript, and agree to be accountable for all aspects of the work.

COMPETING INTERESTS

The authors have completed the International Committee of Medical Journal Editors (ICMJE) Uniform Disclosure Form and declare that they have no competing interests.

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SUPPLEMENTARY MATERIALS

ONLINE SUPPLEMENTARY DOCUMENT

Download: https://jogh-ep.org/article/166234-management-of-a-macroscopically-normal-appendix-during-surgery-for-suspected-appendicitis-evidence-for-clinical-practice-healthcare-resource-use-and/attachment/357257.docx