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Global prevalence and incidence of surgical site infections after appendectomy: a systematic review and meta-analysis protocol

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Keywords:	surgical site infection, appendectomy, prevalence, Incidence

Global prevalence and incidence of surgical site infections after appendectomy: a systematic review and meta-analysis protocol

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Abstract

Introduction

Acute appendicitis is a surgical emergency and the most frequent etiology of surgical acute abdominal pain in developed countries. Its currently recognized treatment is appendectomy. It is estimated that, 300 000 people undergo appendectomy each year in the United States (US). Like all surgical procedures, appendectomy can be associated with many complications like cecal fistulas, persistent ileus, pelvic or abdominal abscess and surgical site infection (SSI). SSI is associated with a prolonged postoperative morbidity and hospitalization stay, a substantial additional healthcare cost, making this complication a serious concern for all surgical teams.

Despite the increasing number of appendectomies done around the world and the problems caused by SSI after appendectomy, there is still scarcity of data concerning the global epidemiology of SSI after appendectomy. The current review aims at providing a summary of the published data on epidemiology of SSI after appendectomy.

Methods and design

We will include cross-sectional studies, randomized controlled trials, case–control and cohort studies. Electronic databases including EMBASE, MEDLINE and ISI Web of Science (Science Citation Index), will be searched for relevant abstracts of studies published between January 1, 2000, and December 30, 2017, without language restriction. The review will be reported according to the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines. After screening of abstracts, study selection, data extraction and assessment of risk of bias, we shall assess the studies individually for clinical and statistical heterogeneity. Appropriate meta-analytic techniques will then be used to pool studies judged to be clinically

homogenous. Visual inspection of Funnel-plots and Egger's test will be used to detect publication bias. Results will be presented by country and continent.

Ethics and dissemination

Since primary data are not collected in this study, ethical approval is not required. This review is expected to provide relevant data to help in quantifying the global burden of SSI after appendectomy. The final report will be published in a peer-reviewed journal.

Systematic review registration: International Prospective Register for Systematic Reviews (PROSPERO) number: CRD42017075257.

Keywords: surgical site infection; appendectomy; prevalence, incidence.

Strengths and limitations of the study

- To the best of our knowledge, this will be the first systematic review summarizing data concerning SSI after appendectomy in the world.
- This review will be conducted with strong and robust methodological processes and statistical analyses to help in providing the highest level of evidence that will help to acquire a better evidence-based decision making on the topic.

Introduction

Defined as an acute inflammation of the appendix, acute appendicitis is the most frequent etiology of surgical acute abdominal pain in developed countries(1). Its currently recognized treatment is appendectomy (2, 3). In the USA, the annual number of people undergoing appendectomy in acute care hospital is estimated at 300 000(4-6).

Appendectomy can be performed through a laparoscopic or an open surgery technique, with laparoscopy being the most recommended method (7-10). This is because it is associated with reduced postoperative pain, a short length of hospital stay with a subsequent earlier return to day-to-day activities, reduced postoperative ileus, and better cosmetic results(7-10). Within the last five decades, the mortality associated with acute appendicitis has significantly dropped from 26% to less than 1% (11, 12).

Like all surgical procedures, appendectomy can be associated with several postoperative complications like persistent ileus, cecal fistula, pelvic or abdominal abscess and surgical site infection (SSI)(13). SSI is associated with a prolonged post operative morbidity, a substantial additional healthcare cost, making this complication a concern for all surgical teams. Some studies done in Brazil, Sweden, China and US report SSI prevalence rates of 7.2%, 5.9%, 6.2% and 2.9% respectively after appendectomy(14). Apart from these isolated studies, there is still scarcity of data concerning the global epidemiology of SSI after appendectomy, despite the increasing number of appendectomies done in the world. The current systematic review and meta-analysis aims at summarizing the available data concerning prevalence and incidence of SSI after appendectomy.

Review questions

1. What is the global prevalence of surgical site infection after appendectomy?
2. What is the global incidence of surgical site infection after appendectomy?

Objectives

This systematic review and meta-analysis aims to:

1. Determine the global prevalence of SSI after appendectomy;
2. Determine the global incidence of SSI after appendectomy.

Methods and design

This systematic review and meta-analysis will be reported in conformity with the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines(15). For the present protocol, the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) for Protocol was used for the reporting(16). An additional file shows the PRISMA for protocol checklist [see Additional File 1].

Criteria for considering studies for the review

Types of studies

We will include cross-sectional studies, randomized controlled trials, case–control and cohort studies. Only studies reporting the used of CDC (Center for Disease Control) terminology and diagnostic criteria for SSI will be considered (17, 18).

Letters, reviews, commentaries and editorials will be excluded.

Types of participants

We will include all participants regardless of their country, age and ethnicity.

Types of outcomes

We will consider studies reporting the following outcomes with enough data to compute these estimates:

- Prevalence of SSI after appendectomy;
- Incidence of SSI after appendectomy.

Studies, in which relevant data on SSI after appendectomy is impossible to extract, will be excluded.

Other criteria

- ✓ All published data between January 1, 2000 and Dcember 30, 2017 will be considered.
- ✓ No language restriction will be applied.
- ✓ For duplicates of studies published in more than one report, the one reporting the largest sample size will be considered.
- ✓ Studies with inaccessible full text either online or from the corresponding author will be excluded.

Search strategy for identifying relevant studies

The search strategy will be conducted in two stages:

Bibliographic database searches

Relevant articles published on SSI after appendectomy will be identified by searching Excerpta Medica Database (EMBASE), MEDLINE through PubMed, and ISI Web of Science (Science Citation Index), between January 1, 2000 and December 30, 2017, without any language restriction. Text words and medical subject heading terms related to SSI and appendicitis will be used (Table 1). When necessary, contact with authors for more information will be made.

Searching for other sources

We will scan the references of all relevant articles for additional data sources missed during our search, and their full-texts will be retrieved. References of pertinent reviews will also be scanned.

Selection of studies for inclusion in the review

Two reviewers (CD and MNT) will independently evaluate the studies obtained from the searches, using an assessment form to ensure that the selection criteria are reliably applied. These reviewers will screen the titles and abstracts of papers obtained, after which the full texts of potentially eligible papers will be retrieved by at least one reviewer. The two reviewers will independently review the full text of each potentially eligible study, compare their results and resolved any discrepancy by the arbitration of a third reviewer (JNT).

Assessment of methodological quality and reporting of data

Methodological quality and risk of bias of included studies will be assessed using an adapted version of the Risk of Bias Tool for Prevalence Studies developed by Hoy *et al*(19). An additional file shows the tool in detail [see Additional file 2]. Since there is no validated study that provides a cut-off score for rating quality of studies; a priori, we will arbitrarily consider 0-4, 5-7, and 8-10 as high, moderate, and low risk of bias respectively.

Data extraction and management

All references identified after implementation of the searched strategy will be imported inside the Endnote software. All records obtained from various databases will be combined in a single Endnote library and the duplicates will be noted and removed. A data extraction form will thereafter be used to collect information on the last name of the first author, year of publication, continent, country, study design, study area (rural versus urban), health care

facility (primary or other center), sample size, mean or median age, gender, specific characteristics of the study population, the surgical method (open surgery or laparoscopy), prevalence and incidence of SSI after appendectomy in the study population. For multinational studies, the prevalence and incidence will be reported for the individual countries. Where it is impossible to disaggregate data of multinational studies by country, the study will be presented as one and the countries in which the study was done will be reported.

Data synthesis and analysis

After data collection, a meta-analysis will be conducted. Unadjusted prevalence and incidence, and standard errors for the study-specific estimates will be recalculated based on the information of crude numerators and denominators provided by individual studies. To keep the effect of studies with extremely small or extremely large prevalence estimates on the overall estimate to a minimum, the variance of the study-specific prevalence/incidence will be stabilized with the Freeman-Tukey double arc-sine transformation(20), before poling the data using a random effects meta-analysis model. Heterogeneity will be assessed using the $\chi 2$ test on Cochrane's Q statistic, and quantified by calculating I^2(21). Values of 25%, 50% and 75% for I^2will represent respectively, low, medium and high heterogeneity. We will assess the presence of publication bias using funnel plots inspection and Egger's test (22). Where substantial heterogeneity will be detected, meta-regression and subgroup analyses will be performed to investigate the possible sources of heterogeneity using the aforementioned variables and the study quality. In case of substantial clinical heterogeneity, a narrative summary of our findings will be done. The inter-rater agreement for study inclusion between investigators will be assessed using Cohen's κ coefficient(23). Data analyses will be done usingthe *'meta'* package of the statistical software R (version 3.2.2 [2014-08-14], The R Foundation for statistical computing, Vienna, Austria).

Presentation and reporting of results

The study selection process will be summarized using a flow diagram. Quantitative data will be presented in tables of individual studies and in summary tables, and forest plots where appropriate. The quality scores and risk of bias for each eligible study will be reported accordingly. This may be tabulated and accompanied by narrative summaries.

Potential amendments

Any amendment in the review process will be reported transparently.

Conclusion

SSI after appendectomy is one of the complications of the surgical treatment of appendicitis. This systematic review aims at providing data of high level of evidence concerning epidemiology of SSI after appendectomy. We hope this review will help to sensitize surgeons to implement effective strategies to prevent SSI in order to scale-down the burden SSI after appendectomy.

Review status:

Preliminary searches.

Abbreviations

MOOSE: Meta-analysis of Observational Studies in Epidemiology.

PRISMA: Preferred Reporting Items for Systematic Review and Meta-Analysis.

SSI: Surgical Site Infection.

Declarations

Acknowledgments

None to declare

Competing interests

The authors declare that they have no competing interests.

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Authors' Contributions

CD had the idea. CD designed and conceived the protocol and drafted the manuscript. MNT, JNT, RNN and JJB participated in the critical revision of the manuscript for methodology and intellectual content. JJB is the guarantor of the review. All authors approved the final version of this manuscript.

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Table 1: Search strategy for PubMed from January 1st, 2000 to Decembre 30th, 2017

Search	Search terms
#1	Appendectomy OR Appendices OR "Appendix Epiploica" OR "Omental Appendix" OR Appendicitis
#2	"Surgical site infection" OR "Surgical wound infection" OR "Surgical wound infections" OR "Surgical site infections" OR "Postoperative Wound Infections" OR "Postoperative Wound Infection"
#3	#1 AND #2

PRISMA-P 2015 Checklist

This checklist has been adapted for use with systematic review protocol submissions to BioMed Central journalsfrom Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews*2015 **4**:1

An Editorial from the Editors-in-Chief of *Systematic Reviews* details why this checklist was adapted -Moher D, Stewart L & Shekelle P: Implementing PRISMA-P: recommendations for prospective authors. *Systematic Reviews*2016**5**:15

Section/topic	#	Checklist item	Information reported		Page number(s)
			Yes	No	
ADMINISTRATIVE INFORMATION					
Title					
Identification	1a	Identify the report as a protocol of a systematic review	☒	☐	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	☐	☒	
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	☒	☐	3
Authors					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	☒	☐	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	☒	☐	10
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	☐	☒	
Support					
Sources	5a	Indicate sources of financial or other support for the review	☒	☐	10
Sponsor	5b	Provide name for the review funder and/or sponsor	☒	☐	10
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	☒	☐	10
INTRODUCTION					

Section/topic	#	Checklist item	Information reported		Page number(s)
			Yes	No	
Rationale	6	Describe the rationale for the review in the context of what is already known	☒	☐	4
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	☒	☐	5
METHODS					
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	☒	☐	5_6
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	☒	☐	6-7
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	☒	☐	6-7
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	☒	☐	7
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	☒	☐	7
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	☒	☐	7
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	☒	☐	5-6
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	☒	☐	6
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	☒	☐	7
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	☒	☐	8
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of	☒	☐	8-9

Section/topic	#	Checklist item	Information reported		Page number(s)
			Yes	No	
		handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2, Kendall's tau)			
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	☒	☐	8-9
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	☒	☐	9
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	☒	☐	8
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	☒	☐	8

Additional File 2. Risk of bias assessment tool for prevalence, incidence and aetiologies outcomes

Risk of Bias Item	Answer: Yes (Low Risk) or No (High risk)
External Validity	
1. Was the study target population a close representation of the national population in relation to relevant variables?	
2. Was the sampling frame a true or close representation of the target population?	
3. Was some form of random selection used to select the sample, OR, was a census undertaken?	
4. Was the likelihood of non-participation bias minimal?	
Internal Validity	
5. Were data collected directly from the subjects (as opposed to medical records)?	
6. Were acceptable case definition of condition used?	
7. Was a reliable and accepted diagnosis method utilized?	
8. Was the same mode of data collection used for all subjects?	
9. Was the length of the shortest prevalence period for the parameter of interest appropriate?	
10. Were the numerator(s) and denominator(s) for the calculation of the prevalence appropriate?	
11. Summary item on the overall risk of study bias LOW RISK OF BIAS: 8 or more "yes" answers. Further research is very unlikely to change our confidence in the estimate. MODERATE RISK OF BIAS: 6 to 7 "yes" answers. Further research is likely to have an important impact on our confidence in the estimate and may change the estimate. HIGH RISK OF BIAS: 5 or fewer "yes" answers. Further research is very likely to have an important impact on our confidence in the estimate and is likely to change the estimate.	

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Primary Subject Heading:	Surgery
Secondary Subject Heading:	Epidemiology, Gastroenterology and hepatology
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Despite the increasing number of appendectomies done around the world and the problems caused by SSI after appendectomy, there is still scarcity of data concerning the global epidemiology of SSI after appendectomy. The current review aims at providing a summary of the published data on epidemiology of SSI after appendectomy.

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Introduction

Defined as an acute inflammation of the appendix, acute appendicitis is the most frequent etiology of surgical acute abdominal pain in developed countries (1). Its currently recognized treatment is appendectomy (2, 3). In the USA, the annual number of people undergoing appendectomy in acute care hospital is estimated at 300 000 (4-6).

Appendectomy can be performed through a laparoscopic or an open surgery technique, with laparoscopy being the most recommended method (7-10). This is because it is associated with reduced postoperative pain, a short length of hospital stay with a subsequent earlier return to day-to-day activities, reduced postoperative ileus, and better cosmetic results (7-10). Within the last five decades, the mortality associated with acute appendicitis has significantly dropped from 26% to less than 1% (11, 12).

Like all surgical procedures, appendectomy can be associated with several postoperative complications like persistent ileus, cecal fistula, pelvic or abdominal abscess and, surgical site infection (SSI) (13). SSI is associated with a prolonged postoperative morbidity, a substantial additional healthcare cost, making this complication a concern for all surgical teams (14, 15). Some studies done in Brazil, Sweden, China and US report SSI prevalence rates of 7.2%, 5.9%, 6.2% and 2.9% respectively after appendectomy (16). Moreover, a recent systematic review on surgical site infections after appendectomy performed in low and middle human development-index countries (LMHDICs) (17) found a high rate of SSI in LMHDICs compared to data of isolated studies done in high Human Development-Index Countries (HHDICs). The aforementioned systematic review differs from the review we plan to do by the fact that, our systematic review will integrate data from developed and developing

countries and, will thus enable to have a global estimation of the burden posed by SSI after appendectomy. In addition, our systematic review will be associated with meta-analysis.

Faced with this gap in the contemporary literature, it is evident that there is still scarcity of data regarding the global epidemiology of SSI after appendectomy, despite the increasing number of appendectomies done in the world. The current systematic review and meta-analysis aims at summarizing the available data concerning prevalence and incidence of SSI after appendectomy.

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1. What is the global prevalence of surgical site infection after appendectomy?
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Studies, in which relevant data on SSI after appendectomy is impossible to extract, will be excluded.

Other criteria

- ✓ All published data between January 1, 2000 and December 30, 2017 will be considered.
- ✓ No language restriction will be applied.
- ✓ For duplicates of studies published in more than one report, the one reporting the largest sample size will be considered.
- ✓ Studies with inaccessible full text either online or from the corresponding author will be excluded.

Search strategy for identifying relevant studies

The search strategy will be conducted in two stages:

Bibliographic database searches

Relevant articles published on SSI after appendectomy will be identified by searching Excerpta Medica Database (EMBASE), MEDLINE through PubMed and, ISI Web of Science (Science Citation Index), between January 1, 2000 and December 30, 2017, without any language restriction. Text words and, medical subject heading terms related to SSI and, appendicitis will be used (Table 1). When necessary, contact with authors for more information will be made.

Searching for other sources

We will scan the references of all relevant articles for additional data sources missed during our search and, their full-texts will be retrieved. References of pertinent reviews will also be scanned.

Selection of studies for inclusion in the review

Two reviewers (CD and MNT) will independently evaluate the studies obtained from the searches, using an assessment form to ensure that the selection criteria are reliably applied. These reviewers will screen the titles and, abstracts of papers obtained, after which the full texts of potentially eligible papers will be retrieved by at least one reviewer. The two reviewers will independently review the full text of each potentially eligible study, compare their results and, resolved any discrepancy by the arbitration of a third reviewer (JNT).

Assessment of methodological quality and reporting of data

Methodological quality and risk of bias of included studies will be assessed using an adapted version of the Risk of Bias Tool for Prevalence Studies developed by Hoy *et al* (22). This tool

will be adapted to the Cochrane's bias assessment tool for the randomized studies (23). An additional file shows the tool in detail [see Additional file 2]. Since there is no validated study that provides a cut-off score for rating quality of studies; a priori, we will arbitrarily consider 0-4, 5-7, and 8-10 as high, moderate, and low risk of bias respectively.

Data extraction and management

All references identified after implementation of the searched strategy will be imported inside the Endnote software. All records obtained from various databases will be combined in a single Endnote library and, the duplicates will be noted and, removed. A data extraction form will thereafter be used to collect information on the last name of the first author, year of publication, continent, country, study design, study area (rural versus urban), age groups (children or adults), high-risk patients for SSI (patients with diabetes mellitus, HIV/AIDS), clinical type of appendicitis (catarrhal, perforated, suppurated, gangrenous), medical interventions before appendectomy (antibiotherapy, analgesics) health care facility (primary or other center), sample size, mean or median age, gender, specific characteristics of the study population, the surgical method (open surgery or laparoscopy), prevalence and, incidence of SSI after appendectomy in the study population. For multinational studies, the prevalence and, incidence will be reported for the individual countries. Where it is impossible to disaggregate data of multinational studies by country, the study will be presented as one and, the countries in which the study was done will be reported.

Data synthesis and analysis

After data collection, a meta-analysis will be conducted. Unadjusted prevalence and, incidence, and standard errors for the study-specific estimates will be recalculated based on the information of crude numerators and, denominators provided by individual studies. To keep the effect of studies with extremely small or extremely large prevalence estimates on the

overall estimate to a minimum, the variance of the study-specific prevalence/incidence will be stabilized with the Freeman-Tukey double arc-sine transformation (24), before poling the data using a random effects meta-analysis model. Heterogeneity will be assessed using the $\chi 2$ test on Cochrane's Q statistic and, quantified by calculating I^2 (25). Values of 25%, 50% and, 75% for I^2will represent respectively, low, medium and, high heterogeneity. We will assess the presence of publication bias using funnel plots inspection and, Egger's test (26). Where substantial heterogeneity will be detected, meta-regression and, subgroup analyses will be performed to investigate the possible sources of heterogeneity using the aforementioned variables and, the study quality. In case of substantial clinical heterogeneity, a narrative summary of our findings will be done. The inter-rater agreement for study inclusion between investigators will be assessed using Cohen's κ coefficient (27). Data analyses will be done using the *'meta'* package of the statistical software R (version 3.2.2 [2014-08-14], The R Foundation for statistical computing, Vienna, Austria). This systematic review protocol is registered under the review number: CRD42017070480 in the International Prospective Register of Systematic Reviews (PROSPERO) (28).

Presentation and reporting of results

The study selection process will be summarized using a flow diagram. Quantitative data will be presented in tables of individual studies and, in summary tables and, forest plots where appropriate. The quality scores and, risk of bias for each eligible study will be reported accordingly. This may be tabulated and, accompanied by narrative summaries.

Patient and Public Involvement

In this study, data will not be collected directly from patients, but in published studies available in main databases.

Potential amendments

Any amendment in the review process will be reported transparently.

Conclusion

SSI after appendectomy is one of the complications of the surgical treatment of appendicitis. This systematic review aims at providing data of high level of evidence concerning epidemiology of SSI after appendectomy. We hope this review will help to sensitize surgeons to implement effective strategies to prevent SSI in order to scale-down the burden SSI after appendectomy.

Strengths and limitations of the study

- To the best of our knowledge, this will be the first global systematic review summarizing data concerning SSI after appendectomy.
- This review will be conducted with strong and, robust methodological processes and, statistical analyses to help in providing the highest level of evidence that will help to acquire a better evidence-based decision making on the topic.
- A limited number of studies on the subject in Low- and middle-income countries could lead to an underestimation of the burden of SSI in this specific part of the world.

Review status:

Preliminary searches.

Abbreviations

MOOSE: Meta-analysis of Observational Studies in Epidemiology.

PRISMA: Preferred Reporting Items for Systematic Review and Meta-Analysis.

SSI: Surgical Site Infection.

Declarations

Acknowledgments

None to declare

Competing interests

The authors declare that they have no competing interests.

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Authors' Contributions

CD had the idea. CD designed and, conceived the protocol and, drafted the manuscript. MNT, JNT, RNN and JJB participated in the critical revision of the manuscript for methodology and, intellectual content. JJB is the guarantor of the review. All authors approved the final version of this manuscript.

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Table 1: Search strategy for PubMed from January 1st, 2000 to Decembre 30th, 2017

Search	Search terms
#1	Appendectomy OR Appendicectomy OR Appendices OR "Appendix Epiploica" OR "Omental Appendix" OR Appendicitis
#2	"Surgical site infection" OR "Surgical wound infection" OR "Surgical wound infections" OR "Surgical site infections" OR "Postoperative Wound Infections" OR "Postoperative Wound Infection"
#3	#1 AND #2 Limits: 01/01/2000 to 30/12/2017 on humans with no language restriction

PRISMA-P 2015 Checklist

This checklist has been adapted for use with systematic review protocol submissions to BioMed Central journalsfrom Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews*2015 **4**:1

An Editorial from the Editors-in-Chief of *Systematic Reviews* details why this checklist was adapted -Moher D, Stewart L & Shekelle P: Implementing PRISMA-P: recommendations for prospective authors. *Systematic Reviews*20165:15

Section/topic	#	Checklist item	Information reported		Page number(s)
			Yes	No	
ADMINISTRATIVE INFORMATION					
Title					
Identification	1a	Identify the report as a protocol of a systematic review	☒	☐	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	☐	☒	
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	☒	☐	3
Authors					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	☒	☐	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	☒	☐	10
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	☐	☒	
Support					
Sources	5a	Indicate sources of financial or other support for the review	☒	☐	10
Sponsor	5b	Provide name for the review funder and/or sponsor	☒	☐	10
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	☒	☐	10
INTRODUCTION					
Rationale	6	Describe the rationale for the review in the context of what is already known	☒	☐	4

Section/topic	#	Checklist item	Information reported		Page number(s)
			Yes	No	
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	☒	☐	5
METHODS					
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	☒	☐	5_6
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	☒	☐	6-7
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	☒	☐	6-7
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	☒	☐	7
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	☒	☐	7
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	☒	☐	7
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	☒	☐	5-6
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	☒	☐	6
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	☒	☐	7
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	☒	☐	8
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2, Kendall's tau)	☒	☐	8-9

Section/topic	#	Checklist item	Information reported		Page number(s)
			Yes	No	
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	☒	☐	8-9
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	☒	☐	9
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	☒	☐	8
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	☒	☐	8

Additional File 2. Risk of bias assessment tool for prevalence, incidence and aetiologies outcomes

Risk of Bias Item	Answer: Yes (Low Risk) or No (High risk)
External Validity	
1. Was the study target population a close representation of the national population in relation to relevant variables?	
2. Was the sampling frame a true or close representation of the target population?	
3. Was some form of random selection used to select the sample, OR, was a census undertaken?	
4. Was the likelihood of non-participation bias minimal?	
Internal Validity	
5. Were data collected directly from the subjects (as opposed to medical records)?	
6. Were acceptable case definition of condition used?	
7. Was a reliable and accepted diagnosis method utilized?	
8. Was the same mode of data collection used for all subjects?	
9. Was the length of the shortest prevalence period for the parameter of interest appropriate?	
10. Were the numerator(s) and denominator(s) for the calculation of the prevalence appropriate?	
11. Summary item on the overall risk of study bias LOW RISK OF BIAS: 8 or more "yes" answers. Further research is very unlikely to change our confidence in the estimate. MODERATE RISK OF BIAS: 6 to 7 "yes" answers. Further research is likely to have an important impact on our confidence in the estimate and may change the estimate. HIGH RISK OF BIAS: 5 or fewer "yes" answers. Further research is very likely to have an important impact on our confidence in the estimate and is likely to change the estimate.	

BMJ Open

Global prevalence and incidence of surgical site infections after appendectomy: a systematic review and meta-analysis protocol

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Date Submitted by the Author:	04-Jun-2018
Complete List of Authors:	Danwang, Celestin; Faculty of Medecine and Biomedical Sciences, Surgery and specialities Mazou, Temgoua Ngou ; Faculty of Medecine and Biomedical Sciences, Internal medicine and specialities Tochie, Joel Noutakdie; Universite de Yaounde I Faculte de Medecine et des Sciences Biomedicales, Nzalie, Rolf ; Ngong District Hospital, North Region, Cameroon Bigna, Jean Joel; Centre Pasteur of Cameroon, Department of Epidemiology and Public Health
Primary Subject Heading:	Surgery
Secondary Subject Heading:	Epidemiology, Gastroenterology and hepatology
Keywords:	surgical site infection, appendectomy, prevalence, Incidence

Global prevalence and incidence of surgical site infections after appendectomy: a systematic review and meta-analysis protocol

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Abstract

Introduction

Acute appendicitis is a surgical emergency, and the most frequent etiology of acute surgical abdominal pain in developed countries. Universally, its widely approved treatment is appendectomy. Like all surgical procedures, appendectomy can be associated with many complications among which are surgical site infections (SSI).

Despite the increasing number of appendectomies done around the world and the associated morbidities related to SSI after appendectomy, there is still scarcity of data concerning the global epidemiology of SSI after appendectomy. The current review aims at providing a summary of the published data on epidemiology of SSI after appendectomy.

Methods and design

We will include randomized controlled trials, cohort studies, case–control and cross-sectional studies. Electronic databases including EMBASE, MEDLINE, and ISI Web of Science (Science Citation Index), will be searched for relevant abstracts of studies published between January 1, 2000, and December 30, 2017, without language restriction. The review will be reported according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines. After screening of abstracts, study selection, data extraction, and assessment of risk of bias, we shall assess the studies individually for clinical and statistical heterogeneity. Appropriate meta-analytic techniques will then be used to pool studies judged to be clinically homogenous. Visual inspection of Funnel-plots, and Egger's test will be used to detect publication bias. Results will be presented by country and continent.

Ethics and dissemination

Since primary data are not collected in this study, ethical approval is not required. This review is expected to provide relevant data to help in quantifying the global burden of SSI after appendectomy. The final report will be published in a peer-reviewed journal.

Systematic review registration: International Prospective Register for Systematic Reviews (PROSPERO) number: CRD42017075257.

Keywords: surgical site infections; appendectomy; prevalence, incidence.

Strengths and limitations of the study

- To the best of our knowledge, this will be the first global systematic review summarizing contemporary data on the occurrence of SSI after appendectomy.
- This review will be conducted with strong and, robust methodological processes and, statistical analyses to help in providing the highest level of evidence that will help to acquire a better evidence-based decision making on this topic.
- A limited number of studies on the subject in low- and middle-income countries could lead to an underestimation of the burden of SSI in this specific part of the world.

Introduction

Defined as an acute inflammation of the appendix, acute appendicitis is the most frequent etiology of acute surgical abdominal pain in developed countries (1). Its currently approved standard of treatment is appendectomy (2, 3). In the USA, the annual number of people undergoing appendectomy in acute care hospital is estimated at 300 000 (4-6).

Appendectomy can be performed through a laparoscopic or an open surgery technique, with laparoscopy being the most recommended method (7-10). This is because, the former is associated with reduced postoperative pain, a short length of hospital stay with a subsequent earlier return to day-to-day activities, reduced postoperative ileus, and better cosmetic results (7-10). Within the last five decades, the mortality associated with acute appendicitis has drastically dropped from 26% to less than 1% (11, 12).

Like all surgical procedures, appendectomy can be associated with several postoperative complications like persistent ileus, cecal fistula, pelvic or abdominal abscess, and surgical site infections (SSI) (13). SSI are associated with a prolonged postoperative morbidity, a substantial additional healthcare cost, making this complication a concern for all surgical teams (14, 15). Some studies done in Brazil, Sweden, China and the USA report SSI prevalence rates of 7.2%, 5.9%, 6.2% and 2.9% respectively after appendectomy (16). Moreover, a recent systematic review on surgical site infections after appendectomy performed in low and middle human development-index countries (LMHDICs) (17) found a high rate of SSI in LMHDICs compared to data of isolated studies done in high Human Development-Index Countries (HHDICs). The aforementioned systematic review differs from the review we plan to do by the fact that, our systematic review will integrate data from

developed and developing countries, hence, this will help provide a global estimation of the burden posed by SSI after appendectomy. In addition, our systematic review will be associated with meta-analysis.

Faced with this gap in the contemporary literature, it is evident that there is still scarcity of data regarding the global epidemiology of SSI after appendectomy, despite the increasing number of appendectomies done in the world. The current systematic review and meta-analysis aim at summarizing the available data concerning prevalence and incidence of SSI after appendectomy.

Review questions

1. What is the global prevalence of surgical site infection after appendectomy?
2. What is the global incidence of surgical site infection after appendectomy?

Objectives

This systematic review and meta-analysis aims to:

1. Determine the global prevalence of SSI after appendectomy;
2. Determine the global incidence of SSI after appendectomy.

Methods and design

This systematic review and meta-analysis will be reported in conformity with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines (18). For the present protocol, the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA-P) for Protocol was used for the reporting (19). An additional file shows the PRISMA-P for protocol checklist [see Additional File 1].

Criteria for considering studies for the review

Types of participants

We will include all participants regardless of their country, age and ethnicity.

Types of studies

We will include randomized controlled trials, cohort studies, case–control and cross-sectional studies. Only studies reporting the used of CDC (Center for Disease Control) terminology and, diagnostic criteria for SSI will be considered (20, 21).

Letters to the editor, narrative reviews, commentaries, perspectives and editorials will be excluded.

Types of outcomes

We will consider studies reporting the following outcomes with enough data to compute these estimates:

- Prevalence of SSI after appendectomy;
- Incidence of SSI after appendectomy.

Studies, in which relevant data on SSI after appendectomy is impossible to extract even after contacting the corresponding author will be excluded.

Other criteria

- ✓ All published data between January 1, 2000 and December 30, 2017 will be considered.
- ✓ No language restriction will be applied.
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Data synthesis and analysis

After data collection, a meta-analysis will be conducted. Unadjusted prevalence, and incidence, and standard errors for the study-specific estimates will be recalculated based on the information of crude numerators, and denominators provided by individual studies. To keep the effect of studies with extremely small or extremely large prevalence estimates on the overall estimate to a minimum, the variance of the study-specific prevalence/incidence will be

stabilized with the Freeman-Tukey double arc-sine transformation (24), before poling the data using a random effects meta-analysis model. Heterogeneity will be assessed using the $\chi 2$ test on Cochrane's Q statistic, and quantified by calculating I^2 (25). Values of 25%, 50% and, 75% for I^2 will respectively represent low, medium and, high heterogeneity. We will assess the presence of publication bias using funnel plots inspection and, Egger's test (26). Where substantial heterogeneity will be detected, meta-regression, and subgroup analyses will be performed to investigate the possible sources of heterogeneity using the aforementioned variables, and the study quality. In case of substantial clinical heterogeneity, a narrative summary of our findings will be done. The inter-rater agreement for study inclusion between investigators will be assessed using Cohen's κ coefficient (27). Data analyses will be done using the *'meta'* package of the statistical software R (version 3.2.2 [2014-08-14], The R Foundation for statistical computing, Vienna, Austria). This systematic review protocol is registered under the review number: CRD42017070480 in the International Prospective Register of Systematic Reviews (PROSPERO) (28).

Presentation and reporting of results

The study selection process will be summarized using a flow diagram. Quantitative data will be presented in tables of individual studies, and in summary tables, and forest plots where appropriate. The quality scores, and risk of bias for each eligible study will be reported accordingly. This may be tabulated, and accompanied by narrative summaries.

Patient and Public Involvement

In this study, data will not be collected directly from patients, but in published studies available in main databases.

Potential amendments

Any amendment in the review process will be reported for transparency.

Conclusion

SSI after appendectomy is one of the complications of the surgical treatment of appendicitis. This systematic review aims at providing high quality evidence on the epidemiology of SSI after appendectomy. We hope this review will help to sensitize surgeons to implement effective strategies to prevent SSI in order to scale-down the burden SSI after appendectomy.

Review status:

Preliminary searches.

Abbreviations

PRISMA: Preferred Reporting Items for Systematic Review and Meta-Analysis.

SSI: Surgical Site Infection.

Declarations

Acknowledgments

None to declare

Competing interests

The authors declare that they have no competing interests.

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Authors' Contributions

CD had the idea. CD designed and, conceived the protocol and, drafted the manuscript. MNT, JNT, RNN and JJB participated in the critical revision of the manuscript for methodology and, intellectual content. CD and JJB are the guarantor of the review. All authors approved the final version of this manuscript.

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Table 1: Search strategy for PubMed from January 1st, 2000 to December 30th, 2017

Search	Search terms
#1	Appendectomy OR Appendicectomy OR Appendices OR "Appendix Epiploica" OR "Omental Appendix" OR Appendicitis
#2	"Surgical site infection" OR "Surgical wound infection" OR "Surgical wound infections" OR "Surgical site infections" OR "Operative site infections" OR "Postoperative Wound Infections" OR "Postoperative Wound Infection"
#3	#1 AND #2 Limits: 01/01/2000 to 30/12/2017 on humans with no language

	restriction

PRISMA-P 2015 Checklist

This checklist has been adapted for use with systematic review protocol submissions to BioMed Central journalsfrom Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews*2015 **4**:1

An Editorial from the Editors-in-Chief of *Systematic Reviews* details why this checklist was adapted -Moher D, Stewart L & Shekelle P: Implementing PRISMA-P: recommendations for prospective authors. *Systematic Reviews*20165:15

Section/topic	#	Checklist item	Information reported		Page number(s)
			Yes	No	
ADMINISTRATIVE INFORMATION					
Title					
Identification	1a	Identify the report as a protocol of a systematic review	☒	☐	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	☐	☒	
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	☒	☐	3
Authors					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	☒	☐	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	☒	☐	10
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	☐	☒	
Support					
Sources	5a	Indicate sources of financial or other support for the review	☒	☐	10
Sponsor	5b	Provide name for the review funder and/or sponsor	☒	☐	10
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	☒	☐	10
INTRODUCTION					
Rationale	6	Describe the rationale for the review in the context of what is already known	☒	☐	4

Section/topic	#	Checklist item	Information reported		Page number(s)
			Yes	No	
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	☒	☐	5
METHODS					
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	☒	☐	5_6
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	☒	☐	6-7
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	☒	☐	6-7
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	☒	☐	7
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	☒	☐	7
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	☒	☐	7
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	☒	☐	5-6
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	☒	☐	6
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	☒	☐	7
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	☒	☐	8
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2, Kendall's tau)	☒	☐	8-9

Section/topic	#	Checklist item	Information reported		Page number(s)
			Yes	No	
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	☒	☐	8-9
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	☒	☐	9
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	☒	☐	8
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	☒	☐	8