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Complete List of Authors:	Danwang, Celestin; Universite Libre de Bruxelles, School Of Public Health; Bigna, Jean Joel; Centre Pasteur of Cameroon, Department of Epidemiology and Public Health Tochie, Joel Noutakdie; Universite de Yaounde I Faculte de Medecine et des Sciences Biomedicales, Mbonda, Aimé; Djohong District Hospital, Department of General Medicine Mbanga, Clarence; Mankon Sub-divisional Hospital Nzalie, Rolf ; Ngong District Hospital, North Region, Cameroon Guifo, Marc Leroy ; Universite de Yaounde I Faculte de Medecine et des Sciences Biomedicales Essomba, Arthur ; Universite de Yaounde I Faculte de Medecine et des Sciences Biomedicales

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Global prevalence of surgical-site infection after appendectomy: a systematic review and meta-analysis

Celestin Danwang, MD[1,2], Jean Joel Bigna, MD[3,4*], Joel Noutakdie Tochie, MD[1], Aime Mbonda, MD[5], Clarence Mvalo Mbanga, MD[6], Rolf Nyah Tuku Nzalie, MD[7], Marc Leroy Guifo, MD[1], Arthur Essomba, MD[1]

1. Department of Surgery and Specialties, Faculty of Medicine and Biomedical Sciences, University of Yaoundé I, Yaoundé, Cameroon.
2. School of Public Health, Université Libre de Bruxelles, Brussels, Belgium.
3. Department of Epidemiology and Public Health, Centre Pasteur of Cameroon, Yaoundé, Cameroon.
4. School of Public Health, Faculty of Medicine, University of Paris Sud XI, Le Kremlin-Bicêtre, Paris, France.
5. Department of General Medicine, Djohong District Hospital, Djohong, Cameroon.
6. Department of General Medicine, Mankon Sub-Divisional Hospital, Bamenda, Cameroon.
7. Department of General Medicine, Ngong District Hospital, Ngong, Cameroon.

*Corresponding author: Dr. Jean Joel Bigna, MD, MPH

Department of Epidemiology and Public Health, Centre Pasteur of Cameroon, Yaoundé, Cameroon. E-Mail: bignarimjj@yahoo.fr

E-mail addresses:

CD: danram07@yahoo.fr; JJB: bignarimjj@yahoo.fr; JNT: joeltochie@gmail.com; AM: aimembonda@yahoo.fr; CMM: mbangaclarence@gmail.com; RNN: nzalierolf@yahoo.com; GML: marcleroyguifo@gmail.com; AE: artgessomba@gmail.com

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Abstract

Objectives: Although surgical-site infection (SSI) is one of the most studied healthcare-associated infections, the global burden of SSI after appendectomy remains unknown. Hence, we estimated the incidence of SSI after appendectomy at global and regional levels.

Design: Systematic review and meta-analysis.

Participants: Global population of patients with appendectomy.

Data sources: EMBASE, Medline, and Web of Science were searched to identify observational studies, published between January 1, 2000 and December 30, 2018 and reporting on the incidence of the SSI after appendectomy with no language restriction. A random-effect models meta-analysis served to obtain the pooled incidence of SSI after 100 surgical procedures in patients with appendicitis.

Results: In total, 226 studies (729,434 participants from 49 countries) were included in the meta-analysis. Concerning the methodological quality, 59 (26.1%) studies had a low risk, 147 (65.0%) a moderate risk, and 20 (8.8%) a high risk of bias. We found an overall incidence of SSIs of 7.0 per 100 surgical procedures (95% prediction interval: 1.0-17.6) for appendectomy varying from 0 to 37.4 per 100 surgical procedures. Subgroup analysis for identifying sources of heterogeneity showed that the incidence varied from 5.8 in Europe to 12.6 per 100 surgical procedures in Africa, $p < 0.0001$. The incidence of SSI after appendectomy increased when the level of income decreased; from 6.2 in high-income countries to 11.1 per 100 surgical procedures in low-income countries ($p = 0.015$). Open appendectomy (11.0 per 100 surgical procedures) was found to have a higher incidence of SSI compared to laparoscopy (4.6 per 100 surgical procedures), $p = 0.0002$.

Conclusion: This study suggests a high burden of SSIs after appendectomy in some regions (especially Africa) and in low-income countries. Strategies are needed to implement and vulgarize WHO guidelines to decrease the burden of SSI after appendectomy in these regions.

Registration: PROSPERO, CRD42017075257.

Keywords:

Surgical wound infection; Global Health; Hospital infections; Cross infection; Healthcare associated infection

Strengths and limitations of this study

- This systematic review with the meta-analysis is the first figuring-out a comprehensive global summary of the existing knowledge on the incidence of SSIs after appendectomy.
- It is also the first to summarize the burden of SSIs after appendectomy by all World Health Organization (WHO) regions and by country level of income.
- Using strong and robust methodological and statistical procedures, we found an overall high incidence of SSIs, seven per 100 surgical procedures, with substantial heterogeneity according to WHO regions and country level of income.
- WHO Afro region had the highest incidence. The incidence also increased with decreasing country level of income.
- All sources of heterogeneity for the variation in the incidence of SSI after appendectomy were not identified.

Introduction

Defined as an acute inflammation of the vermiform appendix (1), evidence abounds that acute appendicitis is the most common abdominal surgical emergency (2), with an incidence of almost 100 per 100,000 person-years reported in Australia, Europe and North America (3,4). Evidence suggests appendectomy, a surgical remove of the vermiform appendix as first-line treatment for acute appendicitis, although antibiotic therapy may be efficacious for a selected group of patients with uncomplicated acute appendicitis (5,6). Appendectomy is a relatively safe surgical intervention with a case fatality rate of 2.1 - 2.4 per 1000 patients as reported in studies conducted in Europe (7,8).

Innovations in appendectomy, especially with the advent of minimally invasive or laparoscopic surgery in 1983 (9), which has replaced the traditional open appendectomy in most of high-income countries, has led to a drastic reduction in the morbidity and mortality related to appendectomy (10–12). Laparoscopic appendectomy is now recognized as the gold standard surgical approach for uncomplicated acute appendicitis owing to its merits over open surgery; due to less postoperative pain, reduced postoperative ileus, shorter hospital stay, rapid postoperative recovery, and better aesthetic scars (13–17).

However, regardless of the surgical technique (laparoscopic or open surgery), appendectomy remains a sceptical surgical intervention associated with a substantial risk of surgical-site infections (SSIs). SSIs after appendectomy are postoperative nosocomial infections affecting the incision site, deep tissues, organs at the operative site within 30 days after the surgical procedure (18–21). SSI following appendectomy is a serious post-operative medical concern that increases the financial burden for both healthcare systems and patient, and also have a negative impact on the patients' health related quality of life (22–27).

SSI is both the most frequently studied and the leading healthcare-associated infections reported hospital-wide in low- and middle-income countries (28). A recently published prospective international multicentre cohort study suggested a high burden of SSIs after any gastrointestinal surgery in low-income countries compared to high-income countries (29). Actually, there is no global systematic review with meta-analysis reporting the burden of SSI after appendectomy or comparing the burden between regions and between country level of income. It would be interesting to have such accurately estimated data to construct efficient strategies to curb globally the burden of SSIs after appendectomy. In an effort to fill this gap, the current systematic review and meta-analysis aimed at summarizing contemporary data on the occurrence of SSIs after appendectomy.

Methods

Search strategy and selection criteria

We searched EMBASE, Medline, and Web of Science (Web of Science Core Collection, Current Contents Connect, KCI-Korean Journal Database, SciELO Citation Index, Russian Science Citation Index) to identify observational studies, published between January 1, 2000 and December 30, 2018 and reporting data on the incidence of SSIs after appendectomy. No language restriction was applied. The initial search strategy was designed for EMBASE and was adapted for the use in others databases. The search strategy as illustrated in the study protocol (30), was based on the combination of relevant text words and medical subject headings related to SSIs. Moreover, the references of all relevant articles found were scrutinized for potential additional data sources. When a full text was not available, it was requested via the corresponding author by email. For duplicates or studies published in more than one report, the one reporting the largest sample size was considered. We excluded letters, reviews, commentaries and editorials, studies lacking key data and/or explicit method description as well as studies in which relevant data on SSIs after appendectomy was impossible to extract even after contacting the corresponding author.

Two reviewers (CD and AM) independently screened the titles and abstract of articles for eligibility. Full texts of potentially eligible articles were retrieved and screened for final inclusion. Disagreements between the two reviewers were solved by discussion and when a consensus was not reached, a third reviewer (JNT) resolved discrepancies.

Data analysis

A standardized and pretested data extraction form was used by five reviewers (CD, JNT, AM, RNZ, CMM) to independently extract data from individual studies. A sixth reviewer (JJB) independently extracted data for accuracy. The last name of the first author, year of publication, country, study design, age groups, sample size, mean or median age, proportion of males, specific conditions of the study population, the surgical method (open surgery or laparoscopy), and incidence of SSIs after appendectomy in the study population (or enough data to compute this estimate). For multinational studies, data was disaggregated, with the results shown within individual country.

A meta-analysis was used to summarize data concerning incidence of SSIs, by pooling together data of studies reporting the incidence of SSIs. Study-specific estimates were then pooled through a Dersimonian and Laird random-effects meta-analysis model to obtain an overall summary estimate of the incidence across studies, after stabilizing the variance of individual studies using the Freeman-Tukey double arc-sine transformation (31). Incidence was expressed by 100 surgical procedures with their 95% confidence interval and 95% prediction interval. Heterogeneity was evaluated by the χ^2 test on Cochrane's Q statistic (32) which is quantified by I^2 values, assuming that I^2 values of 25%, 50% and 75% represent low, medium and high heterogeneity respectively (33). Where substantial heterogeneity ($I^2 > 50\%$) was detected, a subgroup analysis was performed to detect its possible sources using the following grouping variables: type of surgery (laparoscopy or open), World Health Organization regions, and country level of income. A *p* value <0.05 was indicative of significant difference. The meta-regression analysis was performed to estimate the explained heterogeneity of each covariate included in the subgroup analysis. Inter-rater agreement for study inclusion was assessed using Cohen's κ coefficient (34). Funnel plots analysis and Egger's test ($p < 0.10$) were performed to detect the presence of publication bias (35). Since we believe that the incidence estimates of interest would likely be published even if substantially different from previously reported estimates, we have not reported adjusted incidence estimate in the case of publication bias.

To assess the methodological quality of each study, two reviewers (CD and CMM) used an adapted version of the tool of bias assessment for prevalence studies developed by Hoy and colleagues (36).

This review was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number CRD42017075257. The protocol has been published in a peer-review journal (30).

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination of our research.

Results

Overall, 619 records were initially identified. After removal of duplicates, screening of study titles, abstracts, and full texts; 226 studies including 729,434 patients were finally retained for meta-analysis **(**Supplementary Figure 1**)**. The full list of included studies is in the Appendix. Concerning the methodological quality, 59 (26.1%) studies had a low risk, 147 (65.0%) a moderate risk and 20 (8.8%) a high risk of bias. Supplementary Table 1 presents characteristics of included studies. Among the included studies, 154 were done in high-income, 36 upper-middle, 27 lower-middle, and nine in low-income countries. Overall, most of studies were from Europe (n = 68) and Americas (n = 67). SSIs were defined according to Center of Disease

Control and Prevention criteria in 50 studies while 25 studies used other criteria. The definition of SSIs was not clearly given in 151 studies.

The overall incidence of SSI after appendectomy was 7.0 per 100 surgical procedures (95% prediction interval: 1.0-17.6) varying from 0% to 37.4% with substantial heterogeneity and publication bias. The sensitive analysis including only studies with low risk of bias yielded a very close incidence to crude analysis (Table 1).

According to country level of income (Figure 1), the incidence of SSI after appendectomy increased when the level of income decreased; from 6.2 in high income countries to 11.1 per 100 surgical procedures in low income countries ($p = 0.015$) (Table 1).

The incidence varied widely across WHO regions (Figure 2). The incidence varied from 5.8 in Europe to 12.6 per 100 surgical procedures in Africa, $p < 0.0001$ (Table 1). Two regions (Europe and Americas) had an incidence < 6 per 100 surgical procedures, three an incidence between 6-10 per 100 procedures (South-East Asia, Eastern Mediterranean, and Western Pacific), and one an incidence > 10 per 100 procedures (Africa) (Table 1). The incidence also varied widely in different regions. The incidence varied from 0.2 to 32.0 in Africa, from 1.9 to 37.4 in Western Pacific, from 1.3 to 33.8 in Eastern Mediterranean, from 1.2 to 25.8 in South-East Asia, from 0.1 to 37.4 in Americas, and from 0 to 20.0 per 100 surgical procedures in Europe (Figure 2).

Open appendectomy with an incidence of 11.0 (95% prediction interval: 0.0-39.3) per 100 surgical procedures was found to have a higher incidence of SSI compared to laparoscopic appendectomy with an incidence of 4.6 (95% prediction interval: 0.0-14.3) per 100 surgical procedures, $p = 0.0002$ (Figure 3).

Heterogeneity of the overall incidence of SSI after appendectomy was explained by WHO regions (17.1%), country level of income (11.1%), and type of surgical procedure (0.1%).

Discussion

This first systematic review and meta-analysis of data of 729434 surgical procedures in 226 studies from 49 countries found an overall incidence of SSIs of 7.0 per 100 surgical procedures for appendectomy varying from 0 to 37.4 per 100 surgical procedures with substantial heterogeneity according to WHO regions, country level of income, and type of surgical procedure. The incidence increased with decreasing country level of income and was higher when using open surgery compared to laparoscopy. The incidence significantly varied by WHO regions with Africa having the highest burden followed by Western Pacific, Eastern-Mediterranean, and South-East Asia.

Health care-associated infections are acquired by patients when receiving care and are the most frequent adverse event affecting patient safety worldwide. This includes SSIs after appendectomy (37). As reported in a systematic review and meta-analysis, SSIs were the leading infection in hospitals in developed countries (28). The high incidence we found in this study suggests that SSIs after appendectomy remains a global public concern. WHO reported that of every 100 hospitalized patients at any given time, seven in developed and 15 in developing countries will acquire at least one health care-associated infection (37). SSIs are mainly caused by micro-organisms resistant to commonly-used antimicrobials, which can be multidrug-resistant. Indeed, more than 50% of SSIs can be antibiotic-resistant (38). The leading micro-organisms identified in SSIs are *Staphylococcus aureus*, coagulase-negative staphylococci, and *Escherichia coli* as reported by National Healthcare Safety Network (38). It is important to worry since *Staphylococcus aureus* and *Escherichia coli* are the micro-organisms with highest proportion of antibiotic resistance, respectively resistant to oxacillin/methicillin in 43% of cases and to fluoroquinolones in 25% of cases (38). A recent international prospective cohort study shown that 21.6% of patients with SSI after any gastrointestinal surgery had an infection that was resistant to the prophylactic antibiotic used

(29). There are many factors that can favour SSI including patient-related and procedural-related variable (39). These factors can be classified in two categories; non-modifiable like age and sex and modifiable including nutritional status, tobacco use, correct use of antibiotics, obesity, diabetes, prolonged surgery duration, pre-surgery hospital stay of at least two days, lower volume of hospital and surgeons, and the intraoperative techniques (37). Strategies to curb the burden of SSIs should therefore focus on addressing these identified factors.

In our present study looking at specifically SSI after appendectomy, we also found that SSI was higher in low income countries. Interestingly, there was a trend with increasing incidence when the country income decreased. The WHO Africa region essentially constituted with sub-Saharan Africa was the region with highest incidence in this study. The WHO estimates that the endemic burden of health care-associated infections is two to three time significantly higher in low- and middle-income countries than in high-income nations (37). The highest burden found in Africa may be associated with the fact most of countries in this continent are low income countries compared to other regions. Indeed, factors associated with increased risk of SSI after appendectomy may be higher in low-income settings. The burden of diabetes, obesity, and undernutrition are increasing in low-income countries (40,41). There is also inadequate use of antimicrobial in low- and middle-income countries (42,43) and micro-organisms are more resistant to prophylactic antibiotics used to prevent SSI in low-income countries compared to high-income countries (29). Lower level income is also associated with lower volume of surgeon and hospital, factors recognised as associated increased risk of SSIs (37). The higher incidence found in low income countries may also be explained by the fact open surgery is the most used surgical procedure in this setting. Indeed, we found as in other studies that open surgery is associated with higher incidence of SSIs compared to laparoscopy (44,45). Laparoscopy is generally indicated for uncomplicated appendicitis where the dissemination of micro-organism is lower compared open surgery indicated for perforated appendicitis with peritonitis for example. Moreover, only few low-income countries have the necessary infrastructure to carry out laparoscopy procedures compared to high-income countries (46–48). Our findings have important implications for healthcare providers and health policy makers. SSIs are among the most preventable healthcare-associated infections (49,50). They still represent a significant burden in terms of patient morbidity and mortality and additional costs for healthcare systems (37). The prevention of SSI has received considerable attention from surgeons, infection control professionals, health policy makers, the media and the public since there is a perception among the public that SSIs may reflect a poor quality of care (51). However, special attention is needed for low-income countries and Africa. Strategy to curb the burden of SSIs after appendectomy as for other surgery procedures should be focused on strategies than can help to address factors associated with increased risk of SSIs. Therefore, strategies should be a package including how to address the factors cited above. The 26 WHO recommendations to avoid SSIs should be vulgarized and implemented (37), especially in low-income countries. Strengthening the healthcare systems of low-income countries and of countries in WHO Afro region is also a paramount by education of healthcare providers and skilling them on the use of very less invasive surgical procedures.

This study should however be interpreted in the context of some drawbacks. Firstly, the same definition of SSIs was not used by all the included studies. This may lead to an overestimation or underestimation of the SSIs incidence by individual studies (depending on the definition used). Secondly, few studies reported on the associated conditions of the study population since this can modify the risk for developing SSIs. We were not therefore able to measure the impact on our outcome of interest. Thirdly, only a quarter of studies had low risk of bias, however our analysis including only studies with low risk of bias yielded an estimate close to the crude incidence. Fourth, the various geographic regions and countries were variably represented, with some countries with only one study or even no study, which could affect the generalizability of our findings.

Despite these limitations, this is the first systematic review and meta-analysis providing a global estimate of the burden of SSIs after appendectomy. A protocol had been published before, and we used rigorous methodological and statistical procedures to obtain and pool data. Furthermore, subgroup analyses were conducted to investigate the various factors likely affecting our estimate.

This systematic review and meta-analysis compiled data from more than 700,000 people with appendicitis in 49 countries and pointed a high incidence of SSIs after appendectomy, at 7 per 100 surgical procedures. This estimate seemed higher in some WHO regions (especially Africa) and in low-income countries. These data suggest that less invasive procedure is associated with low incidence of SSIs after appendectomy. Strategies are needed to implement already known guidelines to decrease the burden of SSI after appendectomy. However, in low-income countries which have weak health systems, cost-effectiveness studies are needed to inform policies regarding the best strategies for decreasing the burden of SSI after appendectomy.

Contributors

CD and JJB conceived the idea of the study and developed the protocol. JJB, CD, and JNT did the literature search. CD, AM, and JNT selected the studies, CD, JNT, RNZ, AM, CMM, JJB extracted the relevant information. CD, JJB, and CMM synthesized the data. CD, JNT, CMM, and JJB wrote the first draft of the paper. CD, JJB, JNT, AB, RNZ, CMM, GML, and AE critically revised successive drafts of the paper and approved the final version. GML and AE supervised the overall work, CD and JJB are the guarantors of the review.

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Competing interests

We declare no competing interests.

Patient consent

Not applicable.

Data sharing statement

All data generated for this study are in the manuscript and its supporting files.

Figures Legend

Figure 1. Global incidence of SSI (surgical site infection) after appendectomy by level of country income

Figure 2. Global incidence of SSI (surgical site infection) after appendectomy by WHO regions

Figure 3. Global incidence of SSI (surgical site infection) after appendectomy by type of surgical procedures

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Table 1. Summary statistics of meta-analysis incidence of surgery site infections after appendectomy

	Incidence per 100 surgical procedures (95%CI)	95% Prediction interval	N studies	N participants	H (95%CI)	I² (95%CI)	P heterogeneity	P Egger test	P difference
Global	7.0 (6.4-7.7)	1.0-17.7	226	729,434	8.9 (8.7-9.1)	98.7 (98.7-98.8)	< 0.0001	< 0.0001	-
- Low risk of bias	6.9 (6.0-7.9)	1.6-15.2	59	204,450	6.7 (6.3-7.1)	97.7 (97.4-98.0)	< 0.0001	< 0.0001	-
By Level of income									
- Low	11.1 (5.5-18.2)	0.0-42.2	9	1,496	3.8 (3.0-4.8)	93.1 (89.0-95.6)	< 0.0001	0.735	0.015
- Lower-middle	9.2 (6.3-12.6)	0.0-31.6	27	10,379	5.1 (4.6-5.7)	96.2 (95.3-96.9)	< 0.0001	0.960	
- Upper-middle	8.5 (6.5-10.8)	0.3-25.3	36	26,557	5.4 (2.9-5.9)	96.6 (95.9-97.1)	< 0.0001	0.392	
- High	6.2 (5.6-6.9)	0.9-15.3	154	691,002	9.5 (9.2-9.8)	98.9 (98.8-99.0)	< 0.0001	< 0.0001	
By WHO regions									
- Africa	12.6 (3.3-26.4)	0.0-72.5	8	3,001	9.1 (7.9-10.5)	98.8 (98.4-99.1)	< 0.0001	0.628	< 0.0001
- Western Pacific	9.6 (8.1-11.2)	2.3-20.8	43	30,822	3.8 (3.5-4.2)	93.2 (91.7-94.4)	< 0.0001	0.150	
- Eastern Mediterranean	8.2 (6.4-10.2)	1.7-18.6	23	7,779	2.6 (2.2-3.1)	85.3 (79.1-89.6)	< 0.0001	0.515	
- South-East Asia	7.6 (4.7-11.1)	0.0-24.6	16	5,782	3.8 (3.2-4.5)	93.0 (90.1-95.0)	< 0.0001	0.0001	
- Americas	5.9 (5.2-6.6)	1.9-11.7	67	401,931	7.5 (7.1-7.9)	98.2 (98.0-98.4)	< 0.0001	0.0004	
- Europe	5.8 (4.6-7.0)	0.0-19.1	68	276,793	10.4 (10.0-10.8)	99.1 (99.0-99.1)	< 0.0001	< 0.0001	

By type of surgical procedure									
- Laparoscopy with open surgery	4.6 (2.5-7.2)	0.0-15.6	10	4,892	3.2 (2.6-4.2)	90.7 (85.0-94.2)	< 0.0001	0.942	0.0002
- Laparoscopy	4.6 (3.4-5.9)	0.0-14.3	40	33,873	4.4 (4.0-4.8)	94.7 (93.6-95.7)	< 0.0001	0.0002	
- Open surgery	11.0 (7.9-14.4)	0.0-39.3	44	13,120	5.7 (5.2-6.1)	96.9 (96.4-97.3)	< 0.0001	0.077	

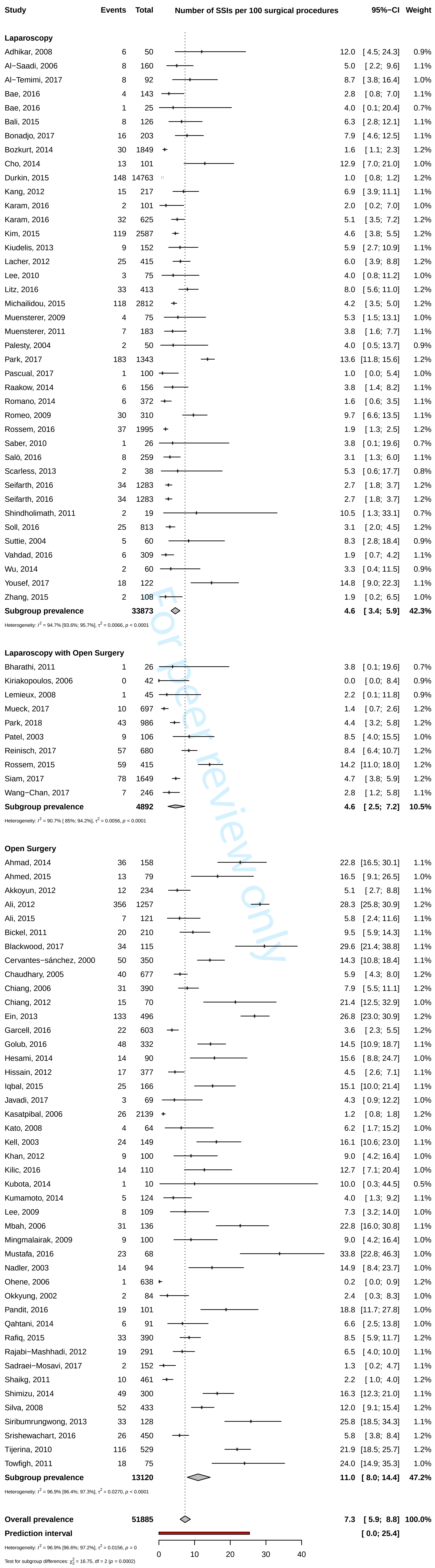
WHO: World Health Organization

Study	Events	Total	95%−CI		Weight
1. Low					
Adhikar, 2008	6	50	12.0	[4.5; 24.3]	0.3%
Al−Saadi, 2006	8	160	5.0	[2.2; 9.6]	0.4%
Asefa, 2002	64	200	32.0	[25.6; 38.9]	0.4%
Asefa, 2014	61	322	18.9	[14.8; 23.7]	0.5%
Batajoo, 2012	18	226	8.0	[4.8; 12.3]	0.4%
Bharathi, 2011	1	26	3.8	[0.1; 19.6]	0.2%
Giiti, 2010	4	199	2.0	[0.6; 5.1]	0.4%
Kumar, 2016	19	212	9.0	[5.5; 13.6]	0.4%
Pandit, 2016	19	101	18.8	[11.7; 27.8]	0.4%
Subgroup prevalence		**1496**	**11.1**	**[5.5; 18.2]**	**3.6%**
Heterogeneity: I^2 = 93.1% [89%; 95.6%], τ^2 = 0.0209, p < 0.0001					
2. Lower−Middle					
Adejumo, 2015	7	141	5.0	[2.0; 10.0]	0.4%
Ahmad, 2014	36	158	22.8	[16.5; 30.1]	0.4%
Ahmed, 2015	13	79	16.5	[9.1; 26.5]	0.4%
Ali, 2012	356	1257	28.3	[25.8; 30.9]	0.5%
Ali, 2015	7	121	5.8	[2.4; 11.6]	0.4%
Chaudhary, 2005	40	677	5.9	[4.3; 8.0]	0.5%
Choudhary, 2014	7	92	7.6	[3.1; 15.1]	0.4%
Hung, 2016	53	752	7.0	[5.3; 9.1]	0.5%
Iqbal, 2015	25	166	15.1	[10.0; 21.4]	0.4%
Khan, 2012	9	100	9.0	[4.2; 16.4]	0.4%
Khan, 2014	18	270	6.7	[4.0; 10.3]	0.5%
Khiria, 2011	18	497	3.6	[2.2; 5.7]	0.5%
Kumar, 2008	10	100	10.0	[4.9; 17.6]	0.4%
Mahmood, 2016	11	200	5.5	[2.8; 9.6]	0.4%
Mbah, 2006	31	136	22.8	[16.0; 30.8]	0.4%
Memon, 2017	16	227	7.0	[4.1; 11.2]	0.4%
Mustafa, 2016	23	68	33.8	[22.8; 46.3]	0.3%
Ohene, 2006	1	638	0.2	[0.0; 0.9]	0.5%
Patel, 2003	9	106	8.5	[4.0; 15.5]	0.4%
Pishori, 2003	281	3304	8.5	[7.6; 9.5]	0.5%
Rafiq, 2015	33	390	8.5	[5.9; 11.7]	0.5%
Rooh−ul−Muqim, 2010	13	165	7.9	[4.3; 13.1]	0.4%
Saha, 2010	8	60	13.3	[5.9; 24.6]	0.3%
Shaikg, 2011	10	461	2.2	[1.0; 4.0]	0.5%
Shindholimath, 2011	2	19	10.5	[1.3; 33.1]	0.2%
Singh, 2017	4	44	9.1	[2.5; 21.7]	0.3%
Yagnik, 2010	7	151	4.6	[1.9; 9.3]	0.4%
Subgroup prevalence		**10379**	**9.2**	**[6.3; 12.6]**	**11.2%**
Heterogeneity: I^2 = 96.2% [95.3%; 96.9%], τ^2 = 0.0183, p < 0.0001					
3. Upper−Middle					
Akkoyun, 2012	12	234	5.1	[2.7; 8.8]	0.5%
Álvarez−Moreno, 2014	37	947	3.9	[2.8; 5.3]	0.5%
Bali, 2015	8	126	6.3	[2.8; 12.1]	0.4%
Biçakci, 2011	40	279	14.3	[10.4; 19.0]	0.5%
Bozkurt, 2014	30	1849	1.6	[1.1; 2.3]	0.5%
Cao, 2015	1102	12586	8.8	[8.3; 9.3]	0.5%
Cervantes−sánchez, 2000	50	350	14.3	[10.8; 18.4]	0.5%
Chamisa, 2009	82	324	25.3	[20.7; 30.4]	0.5%
CHEN, 2010	2	69	2.9	[0.4; 10.1]	0.3%
Garcell, 2016	22	603	3.6	[2.3; 5.5]	0.5%
Golub, 2016	48	332	14.5	[10.9; 18.7]	0.5%
Hamzaoglu, 2004	8	100	8.0	[3.5; 15.2]	0.4%
Javadi, 2017	3	69	4.3	[0.9; 12.2]	0.3%
Kasatpibal, 2005	28	1487	1.9	[1.3; 2.7]	0.5%
Kasatpibal, 2006	26	2139	1.2	[0.8; 1.8]	0.5%
Kilic, 2016	14	110	12.7	[7.1; 20.4]	0.4%
Li, 2005	11	160	6.9	[3.5; 12.0]	0.4%
Li, 2017	46	398	11.6	[8.6; 15.1]	0.5%
Liu, 2017	9	112	8.0	[3.7; 14.7]	0.4%
Mickovic, 2015	9	218	4.1	[1.9; 7.7]	0.4%
Ming, 2009	40	173	23.1	[17.1; 30.1]	0.4%
Mingmalairak, 2009	9	100	9.0	[4.2; 16.4]	0.4%
Rajabi−Mashhadi, 2012	19	291	6.5	[4.0; 10.0]	0.5%
Rios, 2004	23	104	22.1	[14.6; 31.3]	0.4%
Romel Hilaire, 2014	57	720	7.9	[6.1; 10.1]	0.5%
Romeo, 2009	30	310	9.7	[6.6; 13.5]	0.5%
Sadraei−Mosavi, 2017	2	152	1.3	[0.2; 4.7]	0.4%
Shang, 2017	45	398	11.3	[8.4; 14.8]	0.5%
Siribumrungwong, 2013	33	128	25.8	[18.5; 34.3]	0.4%
Sozutek, 2013	5	75	6.7	[2.2; 14.9]	0.3%
Srishewachart, 2016	26	450	5.8	[3.8; 8.4]	0.5%
Tijerina, 2010	116	529	21.9	[18.5; 25.7]	0.5%
Wong, 2015	10	352	2.8	[1.4; 5.2]	0.5%
Wu, 2014	2	60	3.3	[0.4; 11.5]	0.3%
Wu, 2017	43	115	37.4	[28.5; 46.9]	0.4%
Zhang, 2015	2	108	1.9	[0.2; 6.5]	0.4%
Subgroup prevalence		**26557**	**8.5**	**[6.5; 10.8]**	**15.8%**
Heterogeneity: I^2 = 96.6% [95.9%; 97.1%], τ^2 = 0.0122, p < 0.0001					
4. High					
Aguillo, 2005	41	792	5.2	[3.7; 7.0]	0.5%
Al−Temimi, 2017	8	92	8.7	[3.8; 16.4]	0.4%
Almström, 2016	172	2756	6.2	[5.4; 7.2]	0.5%
Anderson, 2014	777	169896	0.5	[0.4; 0.5]	0.5%
Andert, 2017	52	2136	2.4	[1.8; 3.2]	0.5%
Aranda−Narváez, 2010	6	30	20.0	[7.7; 38.6]	0.2%
Aranda−Narvaez, 2014	116	868	13.4	[11.2; 15.8]	0.5%
Arthur, 2017	23	1189	1.9	[1.2; 2.9]	0.5%
Bae, 2016	1	25	4.0	[0.1; 20.4]	0.2%
Bae, 2016	4	143	2.8	[0.8; 7.0]	0.4%
Baek, 2011	10	77	13.0	[6.4; 22.6]	0.4%
Banghu, 2013	203	3326	6.1	[5.3; 7.0]	0.5%
Bansal, 2012	11	187	5.9	[3.0; 10.3]	0.4%
Bickel, 2011	20	210	9.5	[5.9; 14.3]	0.4%
blackwood, 2017	34	115	29.6	[21.4; 38.8]	0.4%
Blakely, 2011	49	131	37.4	[29.1; 46.3]	0.4%
Bonadjo, 2017	16	203	7.9	[4.6; 12.5]	0.4%
Boomer, 2014	71	1388	5.1	[4.0; 6.4]	0.5%
Boomer, 2016	34	1338	2.5	[1.8; 3.5]	0.5%
Brandt, 2008	264	10969	2.4	[2.1; 2.7]	0.5%
Brummer, 2009	279	14209	2.0	[1.7; 2.2]	0.5%
Cairo, 2017	318	20981	1.5	[1.4; 1.7]	0.5%
Cameron, 2017	25	1389	1.8	[1.2; 2.6]	0.5%
Chen, 2012	8	117	6.8	[3.0; 13.0]	0.4%
Chen, 2015	47	236	19.9	[15.0; 25.6]	0.5%
Chiang, 2006	31	390	7.9	[5.5; 11.1]	0.5%
Chiang, 2012	15	70	21.4	[12.5; 32.9]	0.3%
Cho, 2014	13	101	12.9	[7.0; 21.0]	0.4%
Clyde, 2008	95	1198	7.9	[6.5; 9.6]	0.5%
Coakley, 2011	61	728	8.4	[6.5; 10.6]	0.5%
Crandall, 2009	9	176	5.1	[2.4; 9.5]	0.4%
Dede, 2008	31	273	11.4	[7.8; 15.7]	0.5%
Dhiman, 2013	1	1250	0.1	[0.0; 0.4]	0.5%
Dimitriou, 2013	37	404	9.2	[6.5; 12.4]	0.5%
Durkin, 2015	148	14763	1.0	[0.8; 1.2]	0.5%
Ein, 2013	133	496	26.8	[23.0; 30.9]	0.5%
Fukuda, 2016	90	2074	4.3	[3.5; 5.3]	0.5%
Gandaglia, 2014	1983	97780	2.0	[1.9; 2.1]	0.5%
Ghnnam, 2011	6	63	9.5	[3.6; 19.6]	0.3%
Giesen, 2017	42	637	6.6	[4.8; 8.8]	0.5%
Gross, 2016	186	2585	7.2	[6.2; 8.3]	0.5%
Gurien, 2016	13	484	2.7	[1.4; 4.5]	0.5%
Harmon, 2016	23	411	5.6	[3.6; 8.3]	0.5%
Helling, 2017	31	611	5.1	[3.5; 7.1]	0.5%
Helmer, 2002	28	438	6.4	[4.3; 9.1]	0.5%
Hesami, 2014	14	90	15.6	[8.8; 24.7]	0.4%
Hissain, 2012	17	377	4.5	[2.6; 7.1]	0.5%
Horvath, 2016	40	1516	2.6	[1.9; 3.6]	0.5%
Hughes, 2013	25	266	9.4	[6.2; 13.6]	0.5%
Inigo, 2006	46	721	6.4	[4.7; 8.4]	0.5%
Jenkins, 2016	422	12410	3.4	[3.1; 3.7]	0.5%
Kang, 2012	15	217	6.9	[3.9; 11.1]	0.4%
Kapischke, 2013	4	159	2.5	[0.7; 6.3]	0.4%
Karam, 2016	32	625	5.1	[3.5; 7.2]	0.5%
Karam, 2016	2	101	2.0	[0.2; 7.0]	0.4%
Kato, 2008	4	64	6.2	[1.7; 15.2]	0.3%
Kell, 2003	24	149	16.1	[10.6; 23.0]	0.4%
Khan, 2007	8	134	6.0	[2.6; 11.4]	0.4%
Kim, 2011	48	3335	1.4	[1.1; 1.9]	0.5%
Kim, 2015	119	2587	4.6	[3.8; 5.5]	0.5%
Kim, 2016	33	207	15.9	[11.2; 21.7]	0.4%
Kiriakopoulos, 2006	0	42	0.0	[0.0; 8.4]	0.3%
Kirshtein, 2009	21	1435	1.5	[0.9; 2.2]	0.5%
Kiudelis, 2013	9	152	5.9	[2.7; 10.9]	0.4%
Kleif, 2017	90	1151	7.8	[6.3; 9.5]	0.5%
Koizumi, 2014	16	185	8.6	[5.0; 13.7]	0.4%
Kubota, 2014	1	10	10.0	[0.3; 44.5]	0.1%
Kumamoto, 2014	5	124	4.0	[1.3; 9.2]	0.4%
Lacher, 2012	25	415	6.0	[3.9; 8.8]	0.5%
Le, 2009	56	507	11.0	[8.5; 14.1]	0.5%
Lee, 2009	8	109	7.3	[3.2; 14.0]	0.4%
Lee, 2010	19	264	7.2	[4.4; 11.0]	0.5%
Lee, 2010	166	2462	6.7	[5.8; 7.8]	0.5%
Lee, 2010	3	75	4.0	[0.8; 11.2]	0.3%
Lee, 2011	287	7650	3.8	[3.3; 4.2]	0.5%
Lemieux, 2008	1	45	2.2	[0.1; 11.8]	0.3%
Levy, 2013	34	312	10.9	[7.7; 14.9]	0.5%
Lim, 2011	5	60	8.3	[2.8; 18.4]	0.3%
Lima, 2007	7	300	2.3	[0.9; 4.7]	0.5%
Lin, 2006	62	229	27.1	[21.4; 33.3]	0.4%
Litz, 2016	33	413	8.0	[5.6; 11.0]	0.5%
Martinez, 2012	9	75	12.0	[5.6; 21.6]	0.3%
Menezes, 2008	13	118	11.0	[6.0; 18.1]	0.4%
Merenda, 2013	19	317	6.0	[3.6; 9.2]	0.5%
Michailidou, 2015	118	2812	4.2	[3.5; 5.0]	0.5%
Michailidou, 2015	10	264	3.8	[1.8; 6.9]	0.5%
Miyano, 2010	4	23	17.4	[5.0; 38.8]	0.2%
Moazzez, 2013	53	2060	2.6	[1.9; 3.4]	0.5%
Monge Jodra, 2003	459	5780	7.9	[7.3; 8.7]	0.5%
Mueck, 2017	10	697	1.4	[0.7; 2.6]	0.5%
Muensterer, 2009	4	75	5.3	[1.5; 13.1]	0.3%
Muensterer, 2011	7	183	3.8	[1.6; 7.7]	0.4%
Nadler, 2003	14	94	14.9	[8.4; 23.7]	0.4%
Nataraja, 2010	15	191	7.9	[4.5; 12.6]	0.4%
Nataraja, 2012	47	1205	3.9	[2.9; 5.2]	0.5%
Obayashi, 2015	29	485	6.0	[4.0; 8.5]	0.5%
Obinwa, 2015	38	1037	3.7	[2.6; 5.0]	0.5%
Okkyung, 2002	2	84	2.4	[0.3; 8.3]	0.4%
Onieva, 2017	21	294	7.1	[4.5; 10.7]	0.5%
Page, 2010	631	17199	3.7	[3.4; 4.0]	0.5%
Palesty, 2004	2	50	4.0	[0.5; 13.7]	0.3%
Parcells, 2009	151	1063	14.2	[12.2; 16.4]	0.5%
Park, 2017	183	1343	13.6	[11.8; 15.6]	0.5%
Park, 2018	43	986	4.4	[3.2; 5.8]	0.5%
Pascual, 2017	1	100	1.0	[0.0; 5.4]	0.4%
Pearcy, 2017	12	2903	0.4	[0.2; 0.7]	0.5%
Putnam, 2016	84	410	20.5	[16.7; 24.7]	0.5%
Qahtani, 2014	6	91	6.6	[2.5; 13.8]	0.4%
Quezada, 2015	10	227	4.4	[2.1; 8.0]	0.4%
Raakow, 2014	6	156	3.8	[1.4; 8.2]	0.4%
Reinisch, 2017	57	680	8.4	[6.4; 10.7]	0.5%
Romano, 2014	6	372	1.6	[0.6; 3.5]	0.5%
Romy, 2008	176	2468	7.1	[6.1; 8.2]	0.5%
Rossem, 2015	59	415	14.2	[11.0; 18.0]	0.5%
Rossem, 2016	37	1995	1.9	[1.3; 2.5]	0.5%
Rotermann, 2004	3108	80867	3.8	[3.7; 4.0]	0.5%
Saar, 2016	19	266	7.1	[4.4; 10.9]	0.5%
Saber, 2010	1	26	3.8	[0.1; 19.6]	0.2%
Sahm, 2010	28	1710	1.6	[1.1; 2.4]	0.5%
Sahm, 2015	880	12570	7.0	[6.6; 7.5]	0.5%
Salö, 2016	8	259	3.1	[1.3; 6.0]	0.5%
Sanchez−Santana, 2017	43	930	4.6	[3.4; 6.2]	0.5%
Sauvain, 2016	58	2559	2.3	[1.7; 2.9]	0.5%
Scarborough, 2012	1650	39122	4.2	[4.0; 4.4]	0.5%
Scarless, 2013	2	38	5.3	[0.6; 17.7]	0.3%
Seifarth, 2016	34	1283	2.7	[1.8; 3.7]	0.5%
Seifarth, 2016	34	1283	2.7	[1.8; 3.7]	0.5%
Senekjan, 2013	2240	61830	3.6	[3.5; 3.8]	0.5%
Seo, 2002	20	129	15.5	[9.7; 22.9]	0.4%
Sesia, 2011	3	265	1.1	[0.2; 3.3]	0.5%
Shimizu, 2014	49	300	16.3	[12.3; 21.0]	0.5%
Siam, 2017	78	1649	4.7	[3.8; 5.9]	0.5%
Silva, 2008	52	433	12.0	[9.1; 15.4]	0.5%
Sivrikoz, 2015	230	4844	4.7	[4.2; 5.4]	0.5%
Soll, 2016	25	813	3.1	[2.0; 4.5]	0.5%
Staszewicz, 2014	407	6383	6.4	[5.8; 7.0]	0.5%
Suttie, 2004	5	60	8.3	[2.8; 18.4]	0.3%
Svensson, 2016	105	1745	6.0	[4.9; 7.2]	0.5%
Taguchi, 2015	24	81	29.6	[20.0; 40.8]	0.4%
Tanaka, 2007	13	95	13.7	[7.5; 22.3]	0.4%
Toro Pablo, 2017	40	600	6.7	[4.8; 9.0]	0.5%
Towfigh, 2011	18	75	24.0	[14.9; 35.3]	0.3%
Troillet, 2017	609	15439	3.9	[3.6; 4.3]	0.5%
Tsioplis, 2013	122	1439	8.5	[7.1; 10.0]	0.5%
Vahdad, 2016	6	309	1.9	[0.7; 4.2]	0.5%
Van Rossem, 2014	30	267	11.2	[7.7; 15.7]	0.5%
Van Rossem, 2016	111	1378	8.1	[6.7; 9.6]	0.5%
Wang−Chan, 2017	7	246	2.8	[1.2; 5.8]	0.5%
Watanabe, 2011	101	903	11.2	[9.2; 13.4]	0.5%
Willis, 2016	64	313	20.4	[16.1; 25.3]	0.5%
Wu, 2006	185	1795	10.3	[8.9; 11.8]	0.5%
Wu, 2011	114	1366	8.3	[6.9; 9.9]	0.5%
Yaghoubian, 2010	252	4325	5.8	[5.1; 6.6]	0.5%
Yousef, 2017	18	122	14.8	[9.0; 22.3]	0.4%
Subgroup prevalence		**691002**	**6.2**	**[5.6; 6.9]**	**69.5%**
Heterogeneity: I^2 = 98.9% [98.8%; 99%], τ^2 = 0.0055, p = 0					
Overall prevalence		**729434**	**7.0**	**[6.4; 7.7]**	**100.0%**
Prediction interval				**[1.0; 17.6]**	

Heterogeneity: I^2 = 98.7% [98.7%; 98.8%], τ^2 = 0.0067, p = 0

Test for subgroup differences: χ^2_3 = 10.50, df = 3 (p = 0.0148)

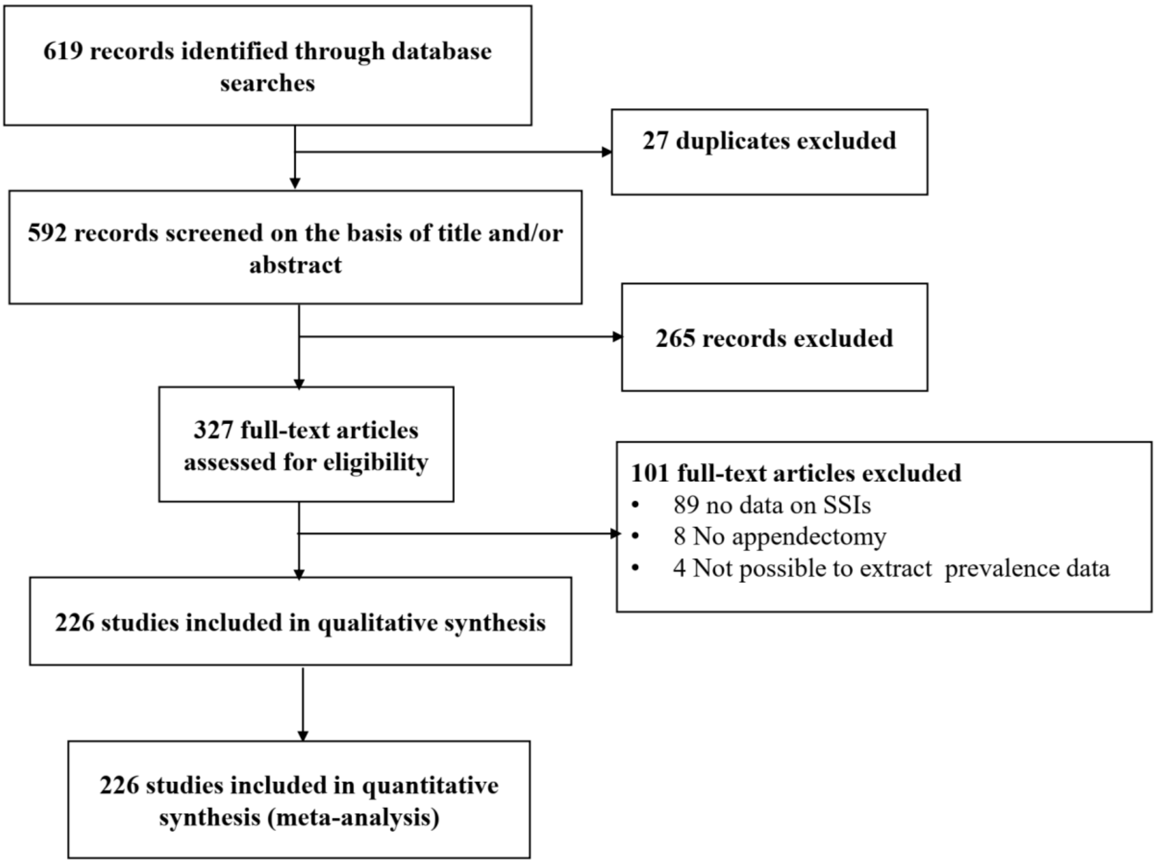

Study Events Total Number of SSIs per 100 surgical procedures 95%−CI Weight
Africa
Adejumo, 2015 7 141 5.0 [2.0; 10.0] 0.4%
Ali, 2012 356 1257 28.3 [25.8; 30.9] 0.5%
Asefa, 2002 64 200 32.0 [25.6; 38.9] 0.4%
Chamisa, 2009 82 324 25.3 [20.7; 30.4] 0.5%
Giiti, 2010 4 199 2.0 [0.6; 5.1] 0.4%
Mbah, 2006 31 136 22.8 [16.0; 30.8] 0.4%
Ohene, 2006 1 638 0.2 [0.0; 0.9] 0.5%
Patel, 2003 9 106 8.5 [4.0; 15.5] 0.4%
Subgroup prevalence 3001 12.6 [3.3; 26.4] 3.6%
Heterogeneity: I^2 = 98.8% [98.4%; 99.1%], τ^2 = 0.0629, p < 0.0001
Americas
Al−Temimi, 2017 8 92 8.7 [3.8; 16.4] 0.4%
Álvarez−Moreno, 2014 37 947 3.9 [2.8; 5.3] 0.5%
Bae, 2016 4 143 2.8 [0.8; 7.0] 0.4%
Blackwood, 2017 34 115 29.6 [21.4; 38.8] 0.4%
Blakely, 2011 49 131 37.4 [29.1; 46.3] 0.4%
Bonadjo, 2017 16 203 7.9 [4.6; 12.5] 0.4%
Boomer, 2014 71 1388 5.1 [4.0; 6.4] 0.5%
Boomer, 2016 34 1338 2.5 [1.8; 3.5] 0.5%
Cairo, 2017 318 20981 1.5 [1.4; 1.7] 0.5%
Cameron, 2017 25 1389 1.8 [1.2; 2.6] 0.5%
Cervantes−sánchez, 2000 50 350 14.3 [10.8; 18.4] 0.5%
Clyde, 2008 95 1198 7.9 [6.5; 9.6] 0.5%
Coakley, 2011 61 728 8.4 [6.5; 10.6] 0.5%
Crandall, 2009 9 176 5.1 [2.4; 9.5] 0.4%
Dhiman, 2013 1 1250 0.1 [0.0; 0.4] 0.5%
Durkin, 2015 148 14763 1.0 [0.8; 1.2] 0.5%
Ein, 2013 133 496 26.8 [23.0; 30.9] 0.5%
Gandaglia, 2014 1983 97780 2.0 [1.9; 2.1] 0.5%
Garcell, 2016 22 603 3.6 [2.3; 5.5] 0.5%
Gross, 2016 186 2585 7.2 [6.2; 8.3] 0.5%
Gurien, 2016 13 484 2.7 [1.4; 4.5] 0.5%
Harmon, 2016 23 411 5.6 [3.6; 8.3] 0.5%
Helling, 2017 31 611 5.1 [3.5; 7.1] 0.5%
Helmer, 2002 28 438 6.4 [4.3; 9.1] 0.5%
Jenkins, 2016 422 12410 3.4 [3.1; 3.7] 0.5%
Karam, 2016 32 625 5.1 [3.5; 7.2] 0.5%
Karam, 2016 2 101 2.0 [0.2; 7.0] 0.4%
Kim, 2011 48 3335 1.4 [1.1; 1.9] 0.5%
Lacher, 2012 25 415 6.0 [3.9; 8.8] 0.5%
Le, 2009 56 507 11.0 [8.5; 14.1] 0.5%
Lee, 2009 8 109 7.3 [3.2; 14.0] 0.4%
Lee, 2010 166 2462 6.7 [5.8; 7.8] 0.5%
Lee, 2011 287 7650 3.8 [3.3; 4.2] 0.5%
Lemieux, 2008 1 45 2.2 [0.1; 11.8] 0.3%
Levy, 2013 34 312 10.9 [7.7; 14.9] 0.5%
Litz, 2016 33 413 8.0 [5.6; 11.0] 0.5%
Michailidou, 2015 10 264 3.8 [1.8; 6.9] 0.5%
Michailidou, 2015 118 2812 4.2 [3.5; 5.0] 0.5%
Moazzez, 2013 53 2060 2.6 [1.9; 3.4] 0.5%
Mueck, 2017 10 697 1.4 [0.7; 2.6] 0.5%
Muensterer, 2009 4 75 5.3 [1.5; 13.1] 0.4%
Muensterer, 2011 7 183 3.8 [1.6; 7.7] 0.4%
Nadler, 2003 14 94 14.9 [8.4; 23.7] 0.4%
Page, 2010 631 17199 3.7 [3.4; 4.0] 0.5%
Palesty, 2004 2 50 4.0 [0.5; 13.7] 0.3%
Parcells, 2009 151 1063 14.2 [12.2; 16.4] 0.5%
Pearcy, 2017 12 2903 0.4 [0.2; 0.7] 0.5%
Putnam, 2016 84 410 20.5 [16.7; 24.7] 0.5%
Quezada, 2015 10 227 4.4 [2.1; 8.0] 0.5%
Rios, 2004 23 104 22.1 [14.6; 31.3] 0.4%
Romano, 2014 6 372 1.6 [0.6; 3.5] 0.5%
Romel Hilaire, 2014 57 720 7.9 [6.1; 10.1] 0.5%
Romeo, 2009 30 310 9.7 [6.6; 13.5] 0.5%
Rotermann, 2004 3108 80867 3.8 [3.7; 4.0] 0.5%
Saber, 2010 1 26 3.8 [0.1; 19.6] 0.2%
Scarborough, 2012 1650 39122 4.2 [4.0; 4.4] 0.5%
Seifarth, 2016 34 1283 2.7 [1.8; 3.7] 0.5%
Seifarth, 2016 34 1283 2.7 [1.8; 3.7] 0.5%
Senekjan, 2013 2240 61830 3.6 [3.5; 3.8] 0.5%
Silva, 2008 52 433 12.0 [9.1; 15.4] 0.5%
Sivrikoz, 2015 230 4844 4.7 [4.2; 5.4] 0.5%
Tijerina, 2010 116 529 21.9 [18.5; 25.7] 0.5%
Towfigh, 2011 18 75 24.0 [14.9; 35.3] 0.4%
Willis, 2016 64 313 20.4 [16.1; 25.3] 0.5%
Wong, 2015 10 352 2.8 [1.4; 5.2] 0.5%
Yaghoubian, 2010 252 4325 5.8 [5.1; 6.6] 0.5%
Yousef, 2017 18 122 14.8 [9.0; 22.3] 0.4%
Subgroup prevalence 401931 5.9 [5.2; 6.6] 31.4%
Heterogeneity: I^2 = 98.2% [98%; 98.4%], τ^2 = 0.0026, p = 0
Eastern Mediterranean
Ahmad, 2014 36 158 22.8 [16.5; 30.1] 0.4%
Ahmed, 2015 13 79 16.5 [9.1; 26.5] 0.4%
Al−Saadi, 2006 8 160 5.0 [2.2; 9.6] 0.4%
Ali, 2015 7 121 5.8 [2.4; 11.6] 0.4%
Chaudhary, 2005 40 677 5.9 [4.3; 8.0] 0.5%
Ghnnam, 2011 6 63 9.5 [3.6; 19.6] 0.3%
Hesami, 2014 14 90 15.6 [8.8; 24.7] 0.4%
Hissain, 2012 17 377 4.5 [2.6; 7.1] 0.5%
Iqbal, 2015 25 166 15.1 [10.0; 21.4] 0.4%
Javadi, 2017 3 69 4.3 [0.9; 12.2] 0.3%
Khan, 2012 9 100 9.0 [4.2; 16.4] 0.4%
Khan, 2014 18 270 6.7 [4.0; 10.3] 0.5%
Kumar, 2008 10 100 10.0 [4.9; 17.6] 0.4%
Mahmood, 2016 11 200 5.5 [2.8; 9.6] 0.4%
Memon, 2017 16 227 7.0 [4.1; 11.2] 0.5%
Mustafa, 2016 23 68 33.8 [22.8; 46.3] 0.3%
Pishori, 2003 281 3304 8.5 [7.6; 9.5] 0.5%
Qahtani, 2014 6 91 6.6 [2.5; 13.8] 0.4%
Rafiq, 2015 33 390 8.5 [5.9; 11.7] 0.5%
Rajabi−Mashhadi, 2012 19 291 6.5 [4.0; 10.0] 0.5%
Rooh−ul−Muqim, 2010 13 165 7.9 [4.3; 13.1] 0.4%
Sadraei−Mosavi, 2017 2 152 1.3 [0.2; 4.7] 0.4%
Shaikg, 2011 10 461 2.2 [1.0; 4.0] 0.5%
Subgroup prevalence 7779 8.2 [6.4; 10.2] 9.7%
Heterogeneity: I^2 = 85.3% [79.1%; 89.6%], τ^2 = 0.0051, p < 0.0001
Europe
Aguillo, 2005 41 792 5.2 [3.7; 7.0] 0.5%
Akkoyun, 2012 12 234 5.1 [2.7; 8.8] 0.5%
Almström, 2016 172 2756 6.2 [5.4; 7.2] 0.5%
Anderson, 2014 777 169896 0.5 [0.4; 0.5] 0.5%
Andert, 2017 52 2136 2.4 [1.8; 3.2] 0.5%
Aranda−Narváez, 2010 6 30 20.0 [7.7; 38.6] 0.2%
Aranda−Narvaez, 2014 116 868 13.4 [11.2; 15.8] 0.5%
Asefa, 2014 61 322 18.9 [14.8; 23.7] 0.5%
Bali, 2015 8 126 6.3 [2.8; 12.1] 0.4%
Bansal, 2012 11 187 5.9 [3.0; 10.3] 0.4%
Biçakci, 2011 40 279 14.3 [10.4; 19.0] 0.5%
Bickel, 2011 20 210 9.5 [5.9; 14.3] 0.4%
Bozkurt, 2014 30 1849 1.6 [1.1; 2.3] 0.5%
Brandt, 2008 264 10969 2.4 [2.1; 2.7] 0.5%
Brummer, 2009 279 14209 2.0 [1.7; 2.2] 0.5%
Dede, 2008 31 273 11.4 [7.8; 15.7] 0.5%
Dimitriou, 2013 37 404 9.2 [6.5; 12.4] 0.5%
Giesen, 2017 42 637 6.6 [4.8; 8.8] 0.5%
Golub, 2016 48 332 14.5 [10.9; 18.7] 0.5%
Hamzaoglu, 2004 8 100 8.0 [3.5; 15.2] 0.4%
Horvath, 2016 40 1516 2.6 [1.9; 3.6] 0.5%
Hughes, 2013 25 266 9.4 [6.2; 13.6] 0.5%
Inigo, 2006 46 721 6.4 [4.7; 8.4] 0.5%
Kapischke, 2013 4 159 2.5 [0.7; 6.3] 0.4%
Kell, 2003 24 149 16.1 [10.6; 23.0] 0.4%
Khan, 2007 8 134 6.0 [2.6; 11.4] 0.4%
Kilic, 2016 14 110 12.7 [7.1; 20.4] 0.4%
Kiriakopoulos, 2006 0 42 0.0 [0.0; 8.4] 0.3%
Kirshtein, 2009 21 1435 1.5 [0.9; 2.2] 0.5%
Kiudelis, 2013 9 152 5.9 [2.7; 10.9] 0.4%
Kleif, 2017 90 1151 7.8 [6.3; 9.5] 0.5%
Lima, 2007 7 300 2.3 [0.9; 4.7] 0.5%
Martinez, 2012 9 75 12.0 [5.6; 21.6] 0.4%
Menezes, 2008 13 118 11.0 [6.0; 18.1] 0.4%
Merenda, 2013 19 317 6.0 [3.6; 9.2] 0.5%
Mickovic, 2015 9 218 4.1 [1.9; 7.7] 0.4%
Monge Jodra, 2003 459 5780 7.9 [7.3; 8.7] 0.5%
Nataraja, 2010 15 191 7.9 [4.5; 12.6] 0.4%
Nataraja, 2012 47 1205 3.9 [2.9; 5.2] 0.5%
Obinwa, 2015 38 1037 3.7 [2.6; 5.0] 0.5%
Onieva, 2017 21 294 7.1 [4.5; 10.7] 0.5%
Pascual, 2017 1 100 1.0 [0.0; 5.4] 0.4%
Raakow, 2014 6 156 3.8 [1.4; 8.2] 0.4%
Reinisch, 2017 57 680 8.4 [6.4; 10.7] 0.5%
Romy, 2008 176 2468 7.1 [6.1; 8.2] 0.5%
Rossem, 2015 59 415 14.2 [11.0; 18.0] 0.5%
Rossem, 2016 37 1995 1.9 [1.3; 2.5] 0.5%
Saar, 2016 19 266 7.1 [4.4; 10.9] 0.5%
Sahm, 2010 28 1710 1.6 [1.1; 2.4] 0.5%
Sahm, 2015 880 12570 7.0 [6.6; 7.5] 0.5%
Salö, 2016 8 259 3.1 [1.3; 6.0] 0.5%
Sanchez−Santana, 2017 43 930 4.6 [3.4; 6.2] 0.5%
Sauvain, 2016 58 2559 2.3 [1.7; 2.9] 0.5%
Scarless, 2013 2 38 5.3 [0.6; 17.7] 0.3%
Sesia, 2011 3 265 1.1 [0.2; 3.3] 0.5%
Siam, 2017 78 1649 4.7 [3.8; 5.9] 0.5%
Soll, 2016 25 813 3.1 [2.0; 4.5] 0.5%
Sozutek, 2013 5 75 6.7 [2.2; 14.9] 0.4%
Staszewicz, 2014 407 6383 6.4 [5.8; 7.0] 0.5%
Suttie, 2004 5 60 8.3 [2.8; 18.4] 0.3%
Svensson, 2016 105 1745 6.0 [4.9; 7.2] 0.5%
Toro Pablo, 2017 40 600 6.7 [4.8; 9.0] 0.5%
Troillet, 2017 609 15439 3.9 [3.6; 4.3] 0.5%
Tsioplis, 2013 122 1439 8.5 [7.1; 10.0] 0.5%
Vahdad, 2016 6 309 1.9 [0.7; 4.2] 0.5%
Van Rossem, 2014 30 267 11.2 [7.7; 15.7] 0.5%
Van Rossem, 2016 111 1378 8.1 [6.7; 9.6] 0.5%
Wang−Chan, 2017 7 246 2.8 [1.2; 5.8] 0.5%
Subgroup prevalence 276793 5.8 [4.6; 7.0] 31.4%
Heterogeneity: I^2 = 99.1% [99%; 99.1%], τ^2 = 0.0106, p = 0
South−East Asia
Adhikar, 2008 6 50 12.0 [4.5; 24.3] 0.3%
Batajoo, 2012 18 226 8.0 [4.8; 12.3] 0.5%
Bharathi, 2011 1 26 3.8 [0.1; 19.6] 0.2%
Choudhary, 2014 7 92 7.6 [3.1; 15.1] 0.4%
Kasatpibal, 2005 28 1487 1.9 [1.3; 2.7] 0.5%
Kasatpibal, 2006 26 2139 1.2 [0.8; 1.8] 0.5%
Khiria, 2011 18 497 3.6 [2.2; 5.7] 0.5%
Kumar, 2016 19 212 9.0 [5.5; 13.6] 0.4%
Mingmalairak, 2009 9 100 9.0 [4.2; 16.4] 0.4%
Pandit, 2016 19 101 18.8 [11.7; 27.8] 0.4%
Saha, 2010 8 60 13.3 [5.9; 24.6] 0.3%
Shindholimath, 2011 2 19 10.5 [1.3; 33.1] 0.2%
Singh, 2017 4 44 9.1 [2.5; 21.7] 0.3%
Siribumrungwong, 2013 33 128 25.8 [18.5; 34.3] 0.4%
Srishewachart, 2016 26 450 5.8 [3.8; 8.4] 0.5%
Yagnik, 2010 7 151 4.6 [1.9; 9.3] 0.4%
Subgroup prevalence 5782 7.6 [4.7; 11.1] 6.2%
Heterogeneity: I^2 = 93% [90.1%; 95%], τ^2 = 0.0110, p < 0.0001
Western Pacific
Arthur, 2017 23 1189 1.9 [1.2; 2.9] 0.5%
Bae, 2016 1 25 4.0 [0.1; 20.4] 0.2%
Baek, 2011 10 77 13.0 [6.4; 22.6] 0.4%
Cao, 2015 1102 12586 8.8 [8.3; 9.3] 0.5%
Chen, 2010 2 69 2.9 [0.4; 10.1] 0.3%
Chen, 2012 8 117 6.8 [3.0; 13.0] 0.4%
Chen, 2015 47 236 19.9 [15.0; 25.6] 0.5%
Chiang, 2006 31 390 7.9 [5.5; 11.1] 0.5%
Chiang, 2012 15 70 21.4 [12.5; 32.9] 0.3%
Cho, 2014 13 101 12.9 [7.0; 21.0] 0.4%
Fukuda, 2016 90 2074 4.3 [3.5; 5.3] 0.5%
Hung, 2016 53 752 7.0 [5.3; 9.1] 0.5%
Kang, 2012 15 217 6.9 [3.9; 11.1] 0.4%
Kato, 2008 4 64 6.2 [1.7; 15.2] 0.3%
Kim, 2015 119 2587 4.6 [3.8; 5.5] 0.5%
Kim, 2016 33 207 15.9 [11.2; 21.7] 0.4%
Koizumi, 2014 16 185 8.6 [5.0; 13.7] 0.4%
Kubota, 2014 1 10 10.0 [0.3; 44.5] 0.1%
Kumamoto, 2014 5 124 4.0 [1.3; 9.2] 0.4%
Lee, 2010 3 75 4.0 [0.8; 11.2] 0.4%
Lee, 2010 19 264 7.2 [4.4; 11.0] 0.5%
Li, 2005 11 160 6.9 [3.5; 12.0] 0.4%
Li, 2017 46 398 11.6 [8.6; 15.1] 0.5%
Lim, 2011 5 60 8.3 [2.8; 18.4] 0.3%
Lin, 2006 62 229 27.1 [21.4; 33.3] 0.5%
Liu, 2017 9 112 8.0 [3.7; 14.7] 0.4%
Ming, 2009 40 173 23.1 [17.1; 30.1] 0.4%
Miyano, 2010 4 23 17.4 [5.0; 38.8] 0.2%
Obayashi, 2015 29 485 6.0 [4.0; 8.5] 0.5%
Okkyung, 2002 2 84 2.4 [0.3; 8.3] 0.4%
Park, 2017 183 1343 13.6 [11.8; 15.6] 0.5%
Park, 2018 43 986 4.4 [3.2; 5.8] 0.5%
Seo, 2002 20 129 15.5 [9.7; 22.9] 0.4%
Shang, 2017 45 398 11.3 [8.4; 14.8] 0.5%
Shimizu, 2014 49 300 16.3 [12.3; 21.0] 0.5%
Taguchi, 2015 24 81 29.6 [20.0; 40.8] 0.4%
Tanaka, 2007 13 95 13.7 [7.5; 22.3] 0.4%
Watanabe, 2011 101 903 11.2 [9.2; 13.4] 0.5%
Wu, 2006 185 1795 10.3 [8.9; 11.8] 0.5%
Wu, 2011 114 1366 8.3 [6.9; 9.9] 0.5%
Wu, 2014 2 60 3.3 [0.4; 11.5] 0.3%
Wu, 2017 43 115 37.4 [28.5; 46.9] 0.4%
Zhang, 2015 2 108 1.9 [0.2; 6.5] 0.4%
Subgroup prevalence 30822 9.6 [8.1; 11.2] 17.8%
Heterogeneity: I^2 = 93.2% [91.7%; 94.4%], τ^2 = 0.0058, p < 0.0001
Overall prevalence 726108 7.0 [6.4; 7.7] 100.0%
Prediction interval [1.0; 17.6]
Heterogeneity: I^2 = 98.7% [98.7%; 98.8%], τ^2 = 0.0067, p = 0
Test for subgroup differences: χ^2_5 = 31.10, df = 5 (p < 0.0001)
0 10 20 30 40


Study Events Total Number of SSIs per 100 surgical procedures 95%−CI Weight
Laparoscopy
Adhikar, 2008 6 50 12.0 [4.5; 24.3] 0.9%
Al−Saadi, 2006 8 160 5.0 [2.2; 9.6] 1.1%
Al−Temimi, 2017 8 92 8.7 [3.8; 16.4] 1.0%
Bae, 2016 4 143 2.8 [0.8; 7.0] 1.1%
Bae, 2016 1 25 4.0 [0.1; 20.4] 0.7%
Bali, 2015 8 126 6.3 [2.8; 12.1] 1.1%
Bonadjo, 2017 16 203 7.9 [4.6; 12.5] 1.1%
Bozkurt, 2014 30 1849 1.6 [1.1; 2.3] 1.2%
Cho, 2014 13 101 12.9 [7.0; 21.0] 1.0%
Durkin, 2015 148 14763 1.0 [0.8; 1.2] 1.2%
Kang, 2012 15 217 6.9 [3.9; 11.1] 1.1%
Karam, 2016 2 101 2.0 [0.2; 7.0] 1.0%
Karam, 2016 32 625 5.1 [3.5; 7.2] 1.2%
Kim, 2015 119 2587 4.6 [3.8; 5.5] 1.2%
Kiudelis, 2013 9 152 5.9 [2.7; 10.9] 1.1%
Lacher, 2012 25 415 6.0 [3.9; 8.8] 1.2%
Lee, 2010 3 75 4.0 [0.8; 11.2] 1.0%
Litz, 2016 33 413 8.0 [5.6; 11.0] 1.2%
Michailidou, 2015 118 2812 4.2 [3.5; 5.0] 1.2%
Muensterer, 2009 4 75 5.3 [1.5; 13.1] 1.0%
Muensterer, 2011 7 183 3.8 [1.6; 7.7] 1.1%
Palesty, 2004 2 50 4.0 [0.5; 13.7] 0.9%
Park, 2017 183 1343 13.6 [11.8; 15.6] 1.2%
Pascual, 2017 1 100 1.0 [0.0; 5.4] 1.0%
Raakow, 2014 6 156 3.8 [1.4; 8.2] 1.1%
Romano, 2014 6 372 1.6 [0.6; 3.5] 1.1%
Romeo, 2009 30 310 9.7 [6.6; 13.5] 1.1%
Rossem, 2016 37 1995 1.9 [1.3; 2.5] 1.2%
Saber, 2010 1 26 3.8 [0.1; 19.6] 0.7%
Salö, 2016 8 259 3.1 [1.3; 6.0] 1.1%
Scarless, 2013 2 38 5.3 [0.6; 17.7] 0.8%
Seifarth, 2016 34 1283 2.7 [1.8; 3.7] 1.2%
Seifarth, 2016 34 1283 2.7 [1.8; 3.7] 1.2%
Shindholimath, 2011 2 19 10.5 [1.3; 33.1] 0.7%
Soll, 2016 25 813 3.1 [2.0; 4.5] 1.2%
Suttie, 2004 5 60 8.3 [2.8; 18.4] 0.9%
Vahdad, 2016 6 309 1.9 [0.7; 4.2] 1.1%
Wu, 2014 2 60 3.3 [0.4; 11.5] 0.9%
Yousef, 2017 18 122 14.8 [9.0; 22.3] 1.1%
Zhang, 2015 2 108 1.9 [0.2; 6.5] 1.0%
Subgroup prevalence 33873 4.6 [3.4; 5.9] 42.3%
Heterogeneity: I^2 = 94.7% [93.6%; 95.7%], τ^2 = 0.0066, p < 0.0001
Laparoscopy with Open Surgery
Bharathi, 2011 1 26 3.8 [0.1; 19.6] 0.7%
Kiriakopoulos, 2006 0 42 0.0 [0.0; 8.4] 0.9%
Lemieux, 2008 1 45 2.2 [0.1; 11.8] 0.9%
Mueck, 2017 10 697 1.4 [0.7; 2.6] 1.2%
Park, 2018 43 986 4.4 [3.2; 5.8] 1.2%
Patel, 2003 9 106 8.5 [4.0; 15.5] 1.0%
Reinisch, 2017 57 680 8.4 [6.4; 10.7] 1.2%
Rossem, 2015 59 415 14.2 [11.0; 18.0] 1.2%
Siam, 2017 78 1649 4.7 [3.8; 5.9] 1.2%
Wang−Chan, 2017 7 246 2.8 [1.2; 5.8] 1.1%
Subgroup prevalence 4892 4.6 [2.5; 7.2] 10.5%
Heterogeneity: I^2 = 90.7% [85%; 94.2%], τ^2 = 0.0056, p < 0.0001
Open Surgery
Ahmad, 2014 36 158 22.8 [16.5; 30.1] 1.1%
Ahmed, 2015 13 79 16.5 [9.1; 26.5] 1.0%
Akkoyun, 2012 12 234 5.1 [2.7; 8.8] 1.1%
Ali, 2012 356 1257 28.3 [25.8; 30.9] 1.2%
Ali, 2015 7 121 5.8 [2.4; 11.6] 1.1%
Bickel, 2011 20 210 9.5 [5.9; 14.3] 1.1%
Blackwood, 2017 34 115 29.6 [21.4; 38.8] 1.1%
Cervantes−sánchez, 2000 50 350 14.3 [10.8; 18.4] 1.1%
Chaudhary, 2005 40 677 5.9 [4.3; 8.0] 1.2%
Chiang, 2006 31 390 7.9 [5.5; 11.1] 1.2%
Chiang, 2012 15 70 21.4 [12.5; 32.9] 1.0%
Ein, 2013 133 496 26.8 [23.0; 30.9] 1.2%
Garcell, 2016 22 603 3.6 [2.3; 5.5] 1.2%
Golub, 2016 48 332 14.5 [10.9; 18.7] 1.1%
Hesami, 2014 14 90 15.6 [8.8; 24.7] 1.0%
Hissain, 2012 17 377 4.5 [2.6; 7.1] 1.1%
Iqbal, 2015 25 166 15.1 [10.0; 21.4] 1.1%
Javadi, 2017 3 69 4.3 [0.9; 12.2] 1.0%
Kasatpibal, 2006 26 2139 1.2 [0.8; 1.8] 1.2%
Kato, 2008 4 64 6.2 [1.7; 15.2] 1.0%
Kell, 2003 24 149 16.1 [10.6; 23.0] 1.1%
Khan, 2012 9 100 9.0 [4.2; 16.4] 1.0%
Kilic, 2016 14 110 12.7 [7.1; 20.4] 1.0%
Kubota, 2014 1 10 10.0 [0.3; 44.5] 0.5%
Kumamoto, 2014 5 124 4.0 [1.3; 9.2] 1.1%
Lee, 2009 8 109 7.3 [3.2; 14.0] 1.0%
Mbah, 2006 31 136 22.8 [16.0; 30.8] 1.1%
Mingmalairak, 2009 9 100 9.0 [4.2; 16.4] 1.0%
Mustafa, 2016 23 68 33.8 [22.8; 46.3] 1.0%
Nadler, 2003 14 94 14.9 [8.4; 23.7] 1.0%
Ohene, 2006 1 638 0.2 [0.0; 0.9] 1.2%
Okkyung, 2002 2 84 2.4 [0.3; 8.3] 1.0%
Pandit, 2016 19 101 18.8 [11.7; 27.8] 1.0%
Qahtani, 2014 6 91 6.6 [2.5; 13.8] 1.0%
Rafiq, 2015 33 390 8.5 [5.9; 11.7] 1.2%
Rajabi−Mashhadi, 2012 19 291 6.5 [4.0; 10.0] 1.1%
Sadraei−Mosavi, 2017 2 152 1.3 [0.2; 4.7] 1.1%
Shaikg, 2011 10 461 2.2 [1.0; 4.0] 1.2%
Shimizu, 2014 49 300 16.3 [12.3; 21.0] 1.1%
Silva, 2008 52 433 12.0 [9.1; 15.4] 1.2%
Siribumrungwong, 2013 33 128 25.8 [18.5; 34.3] 1.1%
Srishewachart, 2016 26 450 5.8 [3.8; 8.4] 1.2%
Tijerina, 2010 116 529 21.9 [18.5; 25.7] 1.2%
Towfigh, 2011 18 75 24.0 [14.9; 35.3] 1.0%
Subgroup prevalence 13120 11.0 [8.0; 14.4] 47.2%
Heterogeneity: I^2 = 96.9% [96.4%; 97.3%], τ^2 = 0.0270, p < 0.0001
Overall prevalence 51885 7.3 [5.9; 8.8] 100.0%
Prediction interval [0.0; 25.4]
Heterogeneity: I^2 = 96.9% [96.6%; 97.2%], τ^2 = 0.0156, p = 0
Test for subgroup differences: χ^2_2 = 16.75, df = 2 (p = 0.0002)
0
10
20
30
40

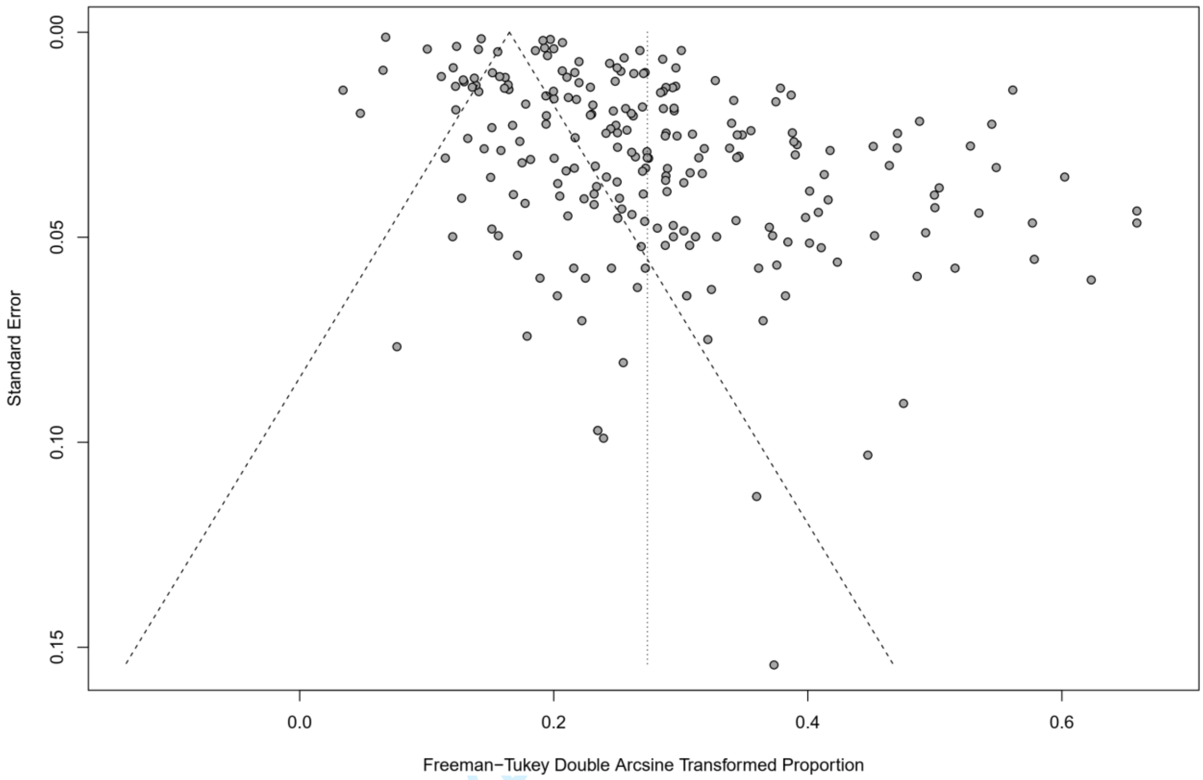
Global burden of surgical-site infection after appendectomy: a systematic review and meta-analysis

APPENDIX

Celestin **Danwang**, Jean Joel **Bigna**, Joel Noutakdie **Tochie**, Aime **Mbonda**, Clarence Mvalo **Mbanga**, Rolf Nyah Tuku **Nzalie**, Marc Leroy **Guifo**, Arthur **Essomba**



Supplementary Figure 1. Study flow



Supplementary Figure 2. Funnel plot for publication bias

Supplementary Table 1 : Characteristics of included studies

Characteristics	**N = 226**
Year of publication, range	2000-2018
%Male, range	0-100 (n = 195)
Mean/median age, range	7-74 (n = 186)
%HIV	0-13.1 (n = 2)
%Diabetes	0-95.7 (n = 34)
%Obesity	0-7.4 (n = 18)
Design, n	
- Cross sectional	120
- Cohort study	99
- Case control	7
WHO regions, n	
- Africa	8
- Americas	67
- Eastern Mediterranean	23
- Europe	68
- Multiregional	1
- South-East Asia	16
- Western Pacific	43
Level of income, n	
- Low	9
- Lower-middle	27
- Upper-middle	36
- High	154
Timing of data collection	
- Retrospective	123
- Prospective	101
- Unclear	2
Sampling	
- Consecutive	131
- Systematic	37
- Random	32
- Exhaustive	11
- Unclear	15
Number of sites	
- Multisite	51
- One site	170
- Unclear	5
Pattern of appendicitis, range	
- %Catarrhal	0-100 (n = 84)
- %Perforated	0-100 (n = 110)
- %Suppurated	0-100 (n = 70)
- %Gangrenous	0-46.7 (n = 89)
%With administered antibiotics	24.1-100 (n = 109)
%With administered analgesics	64.5-100 (n = 20)
%With diet > 6 or 8 hours	50-100 (n = 3)
Type of surgery	
- %Open surgery	0-100 (n = 134)

- %Laparoscopy	0-100 (n = 187)
Mean/median time to complete the intervention (in hours), range	0.1-2.2 (n = 106)
Type of anesthesia, n	
- General	118
- Spinal and general	2
- Unclear	106
SSI definition, n	
- CDC-NNIS criteria	50
- Other criteria	25
- Not reported/Unclear	151

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5-6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	8
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7-8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7-8

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7-8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	8
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	8-9
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	8-9
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	8-9
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	9
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	12
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	14

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Complete List of Authors:	Danwang, Celestin; Universite Libre de Bruxelles, School of Public Health; University of Yaoundé I, Department of Surgery and Specialties, Faculty of Medicine and Biomedical Sciences Bigna, Jean Joel; Centre Pasteur of Cameroon, Department of Epidemiology and Public Health Tochie, Joel Noutakdie; University of Yaoundé I, Department of Anesthesiology and Critical Care Medicine, Faculty of Medicine and Biomedical Sciences Mbonda, Aimé; Djohong District Hospital, Department of General Medicine Mbanga, Clarence; Mankon Sub-divisional Hospital Nzalie, Rolf ; Ngong District Hospital, North Region, Cameroon Guifo, Marc Leroy ; University of Yaoundé I, Department of Surgery and Specialties, Faculty of Medicine and Biomedical Sciences Essomba, Arthur ; University of Yaoundé I, Department of Surgery and Specialties, Faculty of Medicine and Biomedical Sciences

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Global incidence of surgical-site infection after appendectomy: a systematic review and meta-analysis

Celestin Danwang[1,2], Jean Joel Bigna[3*], Joel Noutakdie Tochie[4], Aime Mbonda[5], Clarence Mvalo Mbanga[6], Rolf Nyah Tuku Nzalie[7], Marc Leroy Guifo[1], Arthur Essomba[1]

1. Department of Surgery and Specialties, Faculty of Medicine and Biomedical Sciences, University of Yaoundé I, Yaoundé, Cameroon.
2. School of Public Health, Université Libre de Bruxelles, Brussels, Belgium.
3. Department of Epidemiology and Public Health, Centre Pasteur of Cameroon, Yaoundé, Cameroon.
4. Department of Anesthesiology and Critical Care Medicine, Faculty of Medicine and Biomedical Sciences, University of Yaoundé I, Yaoundé, Cameroon.
5. Department of General Medicine, Djohong District Hospital, Djohong, Cameroon.
6. Department of General Medicine, Mankon Sub-Divisional Hospital, Bamenda, Cameroon.
7. Department of General Medicine, Ngong District Hospital, Ngong, Cameroon.

*Corresponding author: Dr. Jean Joel Bigna, MD, MPH

Department of Epidemiology and Public Health, Centre Pasteur of Cameroon, Yaoundé, Cameroon. E-Mail: bignarimjj@yahoo.fr

E-mail addresses:

CD: danram07@yahoo.fr; JJB: bignarimjj@yahoo.fr; JNT: joeltochie@gmail.com; AM: aimembonda@yahoo.fr; CMM: mbangaclarence@gmail.com; RNN: nzalierolf@yahoo.com; GML: marcleroyguifo@gmail.com; AE: artgessomba@gmail.com

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Abstract

Objectives: Although surgical-site infection (SSI) is one of the most studied healthcare-associated infections, the global burden of SSI after appendectomy remains unknown. Hence, we estimated the incidence of SSI after appendectomy at global and regional levels.

Design: Systematic review and meta-analysis.

Participants: Patients with appendectomy.

Data sources: EMBASE, PubMed, and Web of Science were searched to identify observational studies and clinical trials, published between January 1, 2000 and December 30, 2018 and reporting on the incidence of the SSI after appendectomy; with no language restriction. A random-effect models meta-analysis served to obtain the pooled incidence of SSI after 100 surgical procedures in patients with appendectomy.

Results: In total, 226 studies (729,434 participants from 49 countries) were included in the meta-analysis. Concerning the methodological quality, 59 (26.1%) studies had a low risk, 147 (65.0%) a moderate risk, and 20 (8.8%) a high risk of bias. We found an overall incidence of SSIs of 7.0 per 100 surgical procedures (95% prediction interval: 1.0-17.6) for appendectomy varying from 0 to 37.4 per 100 surgical procedures. Subgroup analysis for identifying sources of heterogeneity showed that the incidence varied from 5.8 in Europe to 12.6 per 100 surgical procedures in Africa, $p < 0.0001$. The incidence of SSI after appendectomy increased when the level of income decreased; from 6.2 in high-income countries to 11.1 per 100 surgical procedures in low-income countries ($p = 0.015$). Open appendectomy (11.0 per 100 surgical procedures) was found to have a higher incidence of SSI compared to laparoscopy (4.6 per 100 surgical procedures), $p = 0.0002$.

Conclusion: This study suggests a high burden of SSIs after appendectomy in some regions (especially Africa) and in low-income countries. Strategies are needed to implement and vulgarize WHO guidelines to decrease the burden of SSI after appendectomy in these regions.

Registration: PROSPERO, CRD42017075257.

Keywords:

Surgical wound infection; Global Health; Hospital infections; Cross infection; Healthcare associated infection

Strengths and limitations of this study

- This meta-analysis is the first to summarize the global incidence of SSIs after appendectomy.
- We investigated WHO regions, level of income, and surgical procedure as sources of heterogeneity.
- We were not able to investigate all sources of heterogeneity because of missing information in the original studies.
- There were few studies from low income countries and from Africa.

Introduction

Defined as an acute inflammation of the vermiform appendix,[1] evidence abounds that acute appendicitis is the most common abdominal surgical emergency,[2] with an incidence of almost 100 per 100,000 person-years reported in Australia, Europe and North America.[3 4] Evidence suggests appendectomy, a surgical remove of the vermiform appendix as first-line treatment for acute appendicitis, although antibiotic therapy may be efficacious for a selected group of patients with uncomplicated acute appendicitis.[5-7] Appendectomy is a relatively safe surgical intervention with a case fatality rate of 2.1 - 2.4 per 1000 patients as reported in studies conducted in Europe.[8 9]

Innovations in appendectomy, especially with the advent of minimally invasive or laparoscopic surgery in 1983,[10] which has replaced the traditional open appendectomy in most of high-income countries, has led to a drastic reduction in the morbidity and mortality related to appendectomy.[11-13] Laparoscopic appendectomy is now recognized as the gold standard surgical approach for uncomplicated acute appendicitis owing to its merits over open surgery; due to less postoperative pain, reduced postoperative ileus, shorter hospital stay, rapid postoperative recovery, and better aesthetic scars.[14-19]

However, regardless of the surgical technique (laparoscopic or open surgery), appendectomy remains a sceptical surgical intervention associated with a substantial risk of surgical-site infections (SSIs). SSIs after appendectomy are postoperative nosocomial infections affecting the incision site, deep tissues, organs at the operative site within 30 days after the surgical procedure.[20-22] SSI following appendectomy is a serious post-operative medical concern that increases the financial burden for both healthcare systems and patient, and also have a negative impact on the patients' health related quality of life.[23-28]

SSI is both the most frequently studied and the leading healthcare-associated infections reported hospital-wide in low- and middle-income countries.[29] A recently published prospective international multicentre cohort study suggested a high burden of SSIs after any gastrointestinal surgery in low-income countries compared to high-income countries.[30] Actually, there is no global systematic review with meta-analysis reporting the burden of SSI after appendectomy or comparing the burden between regions and between country level of income. It would be interesting to have such accurately estimated data to construct efficient strategies to curb globally the burden of SSIs after appendectomy. In an effort to fill this gap, the current systematic review and meta-analysis aimed at summarizing contemporary data on the occurrence of SSIs after appendectomy.

Methods

Design

This systematic review and meta-analysis was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number CRD42017075257. The protocol has been published in a peer-review journal.[31]

Eligibility criteria

We considered observational studies (cross-sectional, case-control, and cohort) and clinical trials of patients with appendectomy. Outcome of interest was incidence of SSI of enough data (number of cases of SSI and sample size) to compute this estimate. We excluded letters, reviews, commentaries and editorials, and studies lacking key data and/or explicit method description as well as studies in which relevant data on SSIs after appendectomy was impossible to extract even after contacting the corresponding author.

Search strategy

We searched EMBASE, PubMed, and Web of Science (Web of Science Core Collection, Current Contents Connect, KCI-Korean Journal Database, SciELO Citation Index, Russian

Science Citation Index) to identify observational studies, published between January 1, 2000 and December 30, 2018. No language restriction was applied. The initial search strategy was designed for EMBASE and was adapted for the use in others databases. The search strategy as illustrated in the Supplementary Table 1 and in the study protocol,[31] was based on the combination of relevant text words and medical subject headings related to SSIs. Moreover, the references of all relevant articles found were scrutinized for potential additional data sources. When a full text was not available, it was requested via the corresponding author by email. For duplicates or studies published in more than one report, the one reporting the largest sample size was considered.

Study selection

Two reviewers (CD and AM) independently screened the titles and abstract of articles for eligibility. Full texts of potentially eligible articles were retrieved and screened for final inclusion. Disagreements between the two reviewers were solved by discussion and when a consensus was not reached, a third reviewer (JNT) resolved discrepancies. Studies in other languages than French, English, and Spanish were translated using Google Translate.

Data extraction and management

A standardized and pretested data extraction form was used by five reviewers (CD, JNT, AM, RNZ, CMM) to independently extract data from individual studies. A sixth reviewer (JJB) independently extracted data for accuracy. The last name of the first author, year of publication, country, study design, age groups, sample size, mean or median age, proportion of males, specific conditions of the study population, the surgical method (open surgery or laparoscopy), and incidence of SSIs after appendectomy in the study population (or enough data to compute this estimate) were extracted.

To assess the methodological quality of each study, two reviewers (CD and CMM) used an adapted version of the tool of bias assessment for prevalence studies developed by Hoy and colleagues.[32]

Data synthesis and analysis

A meta-analysis was used to summarize data concerning incidence of SSIs, by pooling together data of studies reporting the incidence of SSIs. Study-specific estimates were then pooled through a Dersimonian and Laird random-effects meta-analysis model to obtain an overall summary estimate of the incidence across studies, after stabilizing the variance of individual studies using the Freeman-Tukey double arc-sine transformation.[33] Incidence was expressed by 100 surgical procedures with their 95% confidence interval and 95% prediction interval. Heterogeneity was evaluated by the χ^2 test on Q statistic which is quantified by I^2 values,[34] assuming that I^2 values of 25%, 50% and 75% represent low, medium and high heterogeneity respectively.[35] Where substantial heterogeneity ($I^2 > 50\%$) was detected, a subgroup analysis was performed to detect its possible sources using the following grouping variables: type of surgery (laparoscopy or open), World Health Organization regions, and country level of income. A p value <0.05 was indicative of significant difference. The meta-regression analysis was performed to estimate the explained heterogeneity of each covariate included in the subgroup analysis. Inter-rater agreement for study inclusion was assessed using Cohen's κ coefficient.[36] Funnel plots analysis and Egger's test ($p < 0.10$) were performed to detect the presence of publication bias.[37] Since we believe that the incidence estimates of interest would likely be published even if substantially different from previously reported estimates, we have not reported adjusted incidence estimate in the case of publication bias. Data were analysed using the '*meta*' package in R, version 3.6.1.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination of our research.

Results

Study selection and characteristics

Overall, 619 records were initially identified. After removal of duplicates, screening of study titles, abstracts, and full texts; 226 studies including 729,434 patients were finally retained for meta-analysis **(**Supplementary Figure 1**)**. The full list of included studies is in the Appendix. Concerning the methodological quality, 59 (26.1%) studies had a low risk, 147 (65.0%) a moderate risk and 20 (8.8%) a high risk of bias. Supplementary Table 2 presents characteristics of included studies. Among the included studies, 154 were done in high-income, 36 upper-middle, 27 lower-middle, and nine in low-income countries. Overall, most of studies were from Europe (n = 68) and Americas (n = 67). SSIs were defined according to Center of Disease Control and Prevention criteria in 50 studies while 25 studies used other criteria. The definition of SSIs was not clearly given in 151 studies.

Overall prevalence

The overall incidence of SSI after appendectomy was 7.0 per 100 surgical procedures (95% prediction interval: 1.0-17.6) varying from 0% to 37.4% with substantial heterogeneity and publication bias (Supplementary Figure 2). The sensitive analysis including only studies with low risk of bias yielded a very close incidence to crude analysis (Table 1).

Sources of heterogeneity

According to country level of income (Figure 1), the incidence of SSI after appendectomy increased when the level of income decreased; from 6.2 in high income countries to 11.1 per 100 surgical procedures in low income countries ($p = 0.015$) (Table 1).

The incidence varied widely across WHO regions (Figure 2). The incidence varied from 5.8 in Europe to 12.6 per 100 surgical procedures in Africa, $p < 0.0001$ (Table 1). Two regions (Europe and Americas) had an incidence < 6 per 100 surgical procedures, three an incidence between 6-10 per 100 procedures (South-East Asia, Eastern Mediterranean, and Western Pacific), and one an incidence > 10 per 100 procedures (Africa) (Table 1). The incidence also varied widely in different regions. The incidence varied from 0.2 to 32.0 in Africa, from 1.9 to 37.4 in Western Pacific, from 1.3 to 33.8 in Eastern Mediterranean, from 1.2 to 25.8 in South-East Asia, from 0.1 to 37.4 in Americas, and from 0 to 20.0 per 100 surgical procedures in Europe (Figure 2).

Open appendectomy with an incidence of 11.0 (95% prediction interval: 0.0-39.3) per 100 surgical procedures was found to have a higher incidence of SSI compared to laparoscopic appendectomy with an incidence of 4.6 (95% prediction interval: 0.0-14.3) per 100 surgical procedures, $p = 0.0002$ (Figure 3).

Heterogeneity of the overall incidence of SSI after appendectomy was explained by WHO regions (17.1%), country level of income (11.1%), and type of surgical procedure (4.9%). In the meta-regression analysis of 119 studies reporting the information of the use of antibiotics, there was no association between the variation of SSI incidence and proportion of patients with the use of antibiotics (coefficient: 0.0010 [95%CI: -0.0004; 0.0023]; $p = 0.170$). however, most (79.5%) of these studies reported using antibiotics for all patients.

Discussion

This first systematic review and meta-analysis of data of 729,434 surgical procedures in 226 studies from 49 countries found an overall incidence of SSIs of 7.0 per 100 surgical procedures for appendectomy varying from 0 to 37.4 per 100 surgical procedures with substantial heterogeneity according to WHO regions, country level of income, and type of surgical procedure. The incidence increased with decreasing country level of income and was higher when using open surgery compared to laparoscopy. The incidence significantly varied by WHO regions with Africa having the highest burden followed by Western Pacific, Eastern-Mediterranean, and South-East Asia. We found no association between SSI incidence and proportion of using antibiotics.

Health care-associated infections are acquired by patients when receiving care and are the most frequent adverse event affecting patient safety worldwide. This includes SSIs after appendectomy.[38] As reported in a previous systematic review and meta-analysis, SSIs were the leading infection in hospitals in developed countries.[29] The high incidence we found in this study suggests that SSIs after appendectomy remains a global public concern. WHO reported that of every 100 hospitalized patients at any given time, seven in developed and 15 in developing countries will acquire at least one health care-associated infection.[38] SSIs are mainly caused by micro-organisms resistant to commonly-used antimicrobials, which can be multidrug-resistant. Indeed, more than 50% of SSIs can be antibiotic-resistant.[39] The leading micro-organisms identified in SSIs are *Staphylococcus aureus*, coagulase-negative staphylococci, and *Escherichia coli* as reported by National Healthcare Safety Network.[39] It is important to worry since *Staphylococcus aureus* and *Escherichia coli* are the micro-organisms with highest proportion of antibiotic resistance, respectively resistant to oxacillin/methicillin in 43% of cases and to fluoroquinolones in 25% of cases.[39] A recent international prospective cohort study shown that 21.6% of patients with SSI after any gastrointestinal surgery had an infection that was resistant to the prophylactic antibiotic used.[30] There are many factors that can favour SSI including patient-related and procedural-related variable.[40] These factors can be classified in two categories; non-modifiable like age and sex and modifiable including nutritional status, tobacco use, correct use of antibiotics, obesity, diabetes, prolonged surgery duration, pre-surgery hospital stay of at least two days, lower volume of hospital and surgeons, and the intraoperative techniques.[38] Strategies to curb the burden of SSIs should therefore focus on addressing these identified factors. However, we were not able to find an association between SSI with the use antibiotics, may be due to the low variability in the proportion of antibiotics in the original studies.

In our present study looking at specifically SSI after appendectomy, we also found that SSI was higher in low income countries. Interestingly, there was a trend with increasing incidence when the country income decreased. The WHO Africa region essentially constituted with sub-Saharan Africa was the region with highest incidence in this study. The WHO estimates that the endemic burden of health care-associated infections is two to three time significantly higher in low- and middle-income countries than in high-income nations.[38] The highest burden found in Africa may be associated with the fact most of countries in this continent are low income countries compared to other regions. Indeed, factors associated with increased risk of SSI after appendectomy may be higher in low-income settings. The burden of diabetes, obesity, and undernutrition are increasing in low-income countries.[41 42] There is also inadequate use of antimicrobial in low- and middle-income countries and micro-organisms are more resistant to prophylactic antibiotics used to prevent SSI in low-income countries compared to high-income countries.[30 43 44] Lower level income is also associated with lower volume of surgeon and hospital, factors recognised as associated increased risk of SSIs.[38] The higher incidence found in low income countries may also be explained by the fact open surgery is the most used surgical procedure in this setting. Indeed, we found as in other studies that open surgery is associated with higher incidence of SSIs compared to laparoscopy.[45 46] Laparoscopy is generally indicated for uncomplicated appendicitis where the dissemination of micro-organism is lower compared open surgery indicated for perforated appendicitis with peritonitis for example. Moreover, only few low-income countries have the necessary infrastructure to carry out laparoscopy procedures compared to high-income countries.[47-49]

Our findings have important implications for healthcare providers and health policy makers. SSIs are among the most preventable healthcare-associated infections.[50 51] They still represent a significant burden in terms of patient morbidity and mortality and additional costs for healthcare systems.[38] The prevention of SSI has received considerable attention from surgeons, infection control professionals, health policy makers, the media and the public since there is a perception among the public that SSIs may reflect a poor quality of care.[52] However, special attention is needed for low-income countries and Africa. Strategy to curb the burden of SSIs after appendectomy as for other surgery procedures should be focused on strategies than can help to address factors associated with increased risk of SSIs. Therefore, strategies should be a package including how to address the factors cited above. The 26 WHO recommendations to avoid SSIs should be vulgarized and implemented,[38] especially in low-income countries. Strengthening the healthcare systems of low-income countries and of countries in WHO Afro region is also a paramount by education of healthcare providers and skilling them on the use of very less invasive surgical procedures.

This study should however be interpreted in the context of some drawbacks. Firstly, the same definition of SSIs was not used by all the included studies. This may lead to an overestimation or underestimation of the SSIs incidence by individual studies (depending on the definition used). Secondly, few studies reported on the participants' characteristics and details on the surgical procedure since this can modify the risk for developing SSIs. We were not therefore able to measure the impact on our outcome of interest. Thirdly, only a quarter of studies had low risk of bias, however our analysis including only studies with low risk of bias yielded an estimate close to the crude incidence. Fourth, the various geographic regions and countries were variably represented, with some countries with only one study or even no study, which could affect the generalizability of our findings.

Despite these limitations, this is the first systematic review and meta-analysis providing a global estimate of the burden of SSIs after appendectomy. A protocol had been published before, and we used rigorous methodological and statistical procedures to obtain and pool data. Furthermore, subgroup analyses were conducted to investigate the various factors likely affecting our estimate.

Conclusion

This systematic review and meta-analysis compiled data from more than 700,000 people with appendicitis in 49 countries and pointed a high incidence of SSIs after appendectomy, at 7 per 100 surgical procedures. This estimate seemed higher in some WHO regions (especially Africa) and in low-income countries. These data suggest that less invasive procedure is associated with low incidence of SSIs after appendectomy. Strategies are needed to implement already known guidelines to decrease the burden of SSI after appendectomy. However, in low-income countries which have weak health systems, cost-effectiveness studies are needed to inform policies regarding the best strategies for decreasing the burden of SSI after appendectomy.

Contributors

CD and JJB conceived the idea of the study and developed the protocol. JJB, CD, and JNT did the literature search. CD, AM, and JNT selected the studies, CD, JNT, RNZ, AM, CMM, JJB extracted the relevant information. CD, JJB, and CMM synthesized the data. CD, JNT, CMM, and JJB wrote the first draft of the paper. CD, JJB, JNT, AB, RNZ, CMM, GML, and AE critically revised successive drafts of the paper and approved the final version. GML and AE supervised the overall work, CD and JJB are the guarantors of the review.

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Competing interests

We declare no competing interests.

Patient consent

Not applicable.

Data sharing statement

All data generated for this study are in the manuscript and its supporting files.

Figures Legend

Figure 1. Global incidence of SSI (surgical site infection) after appendectomy by level of country income

Figure 2. Global incidence of SSI (surgical site infection) after appendectomy by WHO regions

Figure 3. Global incidence of SSI (surgical site infection) after appendectomy by type of surgical procedures

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Table 1. Summary statistics of meta-analysis incidence of surgery site infections after appendectomy

	Incidence per 100 surgical procedures (95%CI)	95% Prediction interval	N studies	N participants	H (95%CI)	I^2 (95%CI)	P heterogeneity	P Egger test	P difference
Global	7.0 (6.4-7.7)	1.0-17.7	226	729,434	8.9 (8.7-9.1)	98.7 (98.7-98.8)	< 0.0001	< 0.0001	-
- Low risk of bias	6.9 (6.0-7.9)	1.6-15.2	59	204,450	6.7 (6.3-7.1)	97.7 (97.4-98.0)	< 0.0001	< 0.0001	-
By Level of income									
- Low	11.1 (5.5-18.2)	0.0-42.2	9	1,496	3.8 (3.0-4.8)	93.1 (89.0-95.6)	< 0.0001	0.735	0.015
- Lower-middle	9.2 (6.3-12.6)	0.0-31.6	27	10,379	5.1 (4.6-5.7)	96.2 (95.3-96.9)	< 0.0001	0.960	
- Upper-middle	8.5 (6.5-10.8)	0.3-25.3	36	26,557	5.4 (2.9-5.9)	96.6 (95.9-97.1)	< 0.0001	0.392	
- High	6.2 (5.6-6.9)	0.9-15.3	154	691,002	9.5 (9.2-9.8)	98.9 (98.8-99.0)	< 0.0001	< 0.0001	
By WHO regions									
- Africa	12.6 (3.3-26.4)	0.0-72.5	8	3,001	9.1 (7.9-10.5)	98.8 (98.4-99.1)	< 0.0001	0.628	< 0.0001
- Western Pacific	9.6 (8.1-11.2)	2.3-20.8	43	30,822	3.8 (3.5-4.2)	93.2 (91.7-94.4)	< 0.0001	0.150	
- Eastern Mediterranean	8.2 (6.4-10.2)	1.7-18.6	23	7,779	2.6 (2.2-3.1)	85.3 (79.1-89.6)	< 0.0001	0.515	
- South-East Asia	7.6 (4.7-11.1)	0.0-24.6	16	5,782	3.8 (3.2-4.5)	93.0 (90.1-95.0)	< 0.0001	0.0001	
- Americas	5.9 (5.2-6.6)	1.9-11.7	67	401,931	7.5 (7.1-7.9)	98.2 (98.0-98.4)	< 0.0001	0.0004	
- Europe	5.8 (4.6-7.0)	0.0-19.1	68	276,793	10.4 (10.0-10.8)	99.1 (99.0-99.1)	< 0.0001	< 0.0001	
By type of surgical procedure									
- Laparoscopy with open surgery	4.6 (2.5-7.2)	0.0-15.6	10	4,892	3.2 (2.6-4.2)	90.7 (85.0-94.2)	< 0.0001	0.942	0.0002
- Laparoscopy	4.6 (3.4-5.9)	0.0-14.3	40	33,873	4.4 (4.0-4.8)	94.7 (93.6-95.7)	< 0.0001	0.0002	
- Open surgery	11.0 (7.9-14.4)	0.0-39.3	44	13,120	5.7 (5.2-6.1)	96.9 (96.4-97.3)	< 0.0001	0.077	

WHO: World Health Organization; CI: confidence interval; H: H statistics

Author, Year	Sample	Incidence	[95% C.I.]
Level of income = 1. Low			
Adhikar, 2008	50	12.0	[4.5; 24.3]
Al-Saadi, 2006	160	5.0	[2.2; 9.6]
Asefa, 2002	200	32.0	[25.6; 38.9]
Asefa, 2014	322	18.9	[14.8; 23.7]
Batajoo, 2012	226	8.0	[4.8; 12.3]
Bharathi, 2011	26	3.8	[0.1; 19.6]
Giiti, 2010	199	2.0	[0.6; 5.1]
Kumar, 2016	212	9.0	[5.5; 13.6]
Pandit, 2016	101	18.8	[11.7; 27.8]
Subgroup Incidence	**1496**	**11.1**	**[5.5; 18.2]**
Heterogeneity: I^2 = 93.1% [89%; 95.6%], τ^2 = 0.0209, p = 0			
Level of income = 2. Lower-Middle			
Adejumo, 2015	141	5.0	[2.0; 10.0]
Ahmad, 2014	158	22.8	[16.5; 30.1]
Ahmed, 2015	79	16.5	[9.1; 26.5]
Ali, 2012	1257	28.3	[25.8; 30.9]
Ali, 2015	121	5.8	[2.4; 11.6]
Chaudhary, 2005	677	5.9	[4.3; 8.0]
Choudhary, 2014	92	7.6	[3.1; 15.1]
Hung, 2016	752	7.0	[5.3; 9.1]
Iqbal, 2015	166	15.1	[10.0; 21.4]
Khan, 2012	100	9.0	[4.2; 16.4]
Khan, 2014	270	6.7	[4.0; 10.3]
Khiria, 2011	497	3.6	[2.2; 5.7]
Kumar, 2008	100	10.0	[4.9; 17.6]
Mahmood, 2016	200	5.5	[2.8; 9.6]
Mbah, 2006	136	22.8	[16.0; 30.8]
Memon, 2017	227	7.0	[4.1; 11.2]
Mustafa, 2016	68	33.8	[22.8; 46.3]
Ohene, 2006	638	0.2	[0.0; 0.9]
Patel, 2003	106	8.5	[4.0; 15.5]
Pishori, 2003	3304	8.5	[7.6; 9.5]
Rafiq, 2015	390	8.5	[5.9; 11.7]
Rooh-ul-Muqim, 2010	165	7.9	[4.3; 13.1]
Saha, 2010	60	13.3	[5.9; 24.6]
Shaikg, 2011	461	2.2	[1.0; 4.0]
Shindholimath, 2011	19	10.5	[1.3; 33.1]
Singh, 2017	44	9.1	[2.5; 21.7]
Yagnik, 2010	151	4.6	[1.9; 9.3]
Subgroup Incidence	**10379**	**9.2**	**[6.3; 12.6]**
Heterogeneity: I^2 = 96.2% [95.3%; 96.9%], τ^2 = 0.0183, p < 0.0001			
Level of income = 3. Upper-Middle			
Akkoyun, 2012	234	5.1	[2.7; 8.8]
Álvarez-Moreno, 2014	947	3.9	[2.8; 5.3]
Bali, 2015	126	6.3	[2.8; 12.1]
Bıçakcı, 2011	279	14.3	[10.4; 19.0]
Bozkurt, 2014	1849	1.6	[1.1; 2.3]
Cao, 2015	12586	8.8	[8.3; 9.3]
Cervantes-sánchez, 2000	350	14.3	[10.8; 18.4]
Chamisa, 2009	324	25.3	[20.7; 30.4]
Chen, 2010	69	2.9	[0.4; 10.1]
Garcell, 2016	603	3.6	[2.3; 5.5]
Golub, 2016	332	14.5	[10.9; 18.7]
Hamzaoglu, 2004	100	8.0	[3.5; 15.2]
Javadi, 2017	69	4.3	[0.9; 12.2]
Kasatpibal, 2005	1487	1.9	[1.3; 2.7]
Kasatpibal, 2006	2139	1.2	[0.8; 1.8]
Kilic, 2016	110	12.7	[7.1; 20.4]
Li, 2005	160	6.9	[3.5; 12.0]
Li, 2017	398	11.6	[8.6; 15.1]
Liu, 2017	112	8.0	[3.7; 14.7]
Mickovic, 2015	218	4.1	[1.9; 7.7]
Ming, 2009	173	23.1	[17.1; 30.1]
Mingmalairak, 2009	100	9.0	[4.2; 16.4]
Rajabi-Mashhadi, 2012	291	6.5	[4.0; 10.0]
Rios, 2004	104	22.1	[14.6; 31.3]
Romel Hilaire, 2014	720	7.9	[6.1; 10.1]
Romeo, 2009	310	9.7	[6.6; 13.5]
Sadraei-Mosavi, 2017	152	1.3	[0.2; 4.7]
Shang, 2017	398	11.3	[8.4; 14.8]
Siribumrungwong, 2013	128	25.8	[18.5; 34.3]
Sozutek, 2013	75	6.7	[2.2; 14.9]
Srishewachart, 2016	450	5.8	[3.8; 8.4]
Tijerina, 2010	529	21.9	[18.5; 25.7]
Wong, 2015	352	2.8	[1.4; 5.2]
Wu, 2014	60	3.3	[0.4; 11.5]
Wu, 2017	115	37.4	[28.5; 46.9]
Zhang, 2015	108	1.9	[0.2; 6.5]
Subgroup Incidence	**26557**	**8.5**	**[6.5; 10.8]**
Heterogeneity: I^2 = 96.6% [95.9%; 97.1%], τ^2 = 0.0122, p < 0.0001			
Level of income = 4. High			
Aguillo, 2005	792	5.2	[3.7; 7.0]
Al-Temimi, 2017	92	8.7	[3.8; 16.4]
Almström, 2016	2756	6.2	[5.4; 7.2]
Anderson, 2014	169896	0.5	[0.4; 0.5]
Andert, 2017	2136	2.4	[1.8; 3.2]
Aranda-Narváez, 2010	30	20.0	[7.7; 38.6]
Aranda-Narvaez, 2014	868	13.4	[11.2; 15.8]
Arthur, 2017	1189	1.9	[1.2; 2.9]
Bae, 2016	25	4.0	[0.1; 20.4]
Bae, 2016	143	2.8	[0.8; 7.0]
Baek, 2011	77	13.0	[6.4; 22.6]
Banghu, 2013	3326	6.1	[5.3; 7.0]
Bansal, 2012	187	5.9	[3.0; 10.3]
Bickel, 2011	210	9.5	[5.9; 14.3]
Blackwood, 2017	115	29.6	[21.4; 38.8]
Blakely, 2011	131	37.4	[29.1; 46.3]
Bonadjo, 2017	203	7.9	[4.6; 12.5]
Boomer, 2014	1388	5.1	[4.0; 6.4]
Boomer, 2016	1338	2.5	[1.8; 3.5]
Brandt, 2008	10969	2.4	[2.1; 2.7]
Brummer, 2009	14209	2.0	[1.7; 2.2]
Cairo, 2017	20981	1.5	[1.4; 1.7]
Cameron, 2017	1389	1.8	[1.2; 2.6]
Chen, 2012	117	6.8	[3.0; 13.0]
Chen, 2015	236	19.9	[15.0; 25.6]
Chiang, 2006	390	7.9	[5.5; 11.1]
Chiang, 2012	70	21.4	[12.5; 32.9]
Cho, 2014	101	12.9	[7.0; 21.0]
Clyde, 2008	1198	7.9	[6.5; 9.6]
Coakley, 2011	728	8.4	[6.5; 10.6]
Crandall, 2009	176	5.1	[2.4; 9.5]
Dede, 2008	273	11.4	[7.8; 15.7]
Dhiman, 2013	1250	0.1	[0.0; 0.4]
Dimitriou, 2013	404	9.2	[6.5; 12.4]
Durkin, 2015	14763	1.0	[0.8; 1.2]
Ein, 2013	496	26.8	[23.0; 30.9]
Fukuda, 2016	2074	4.3	[3.5; 5.3]
Gandaglia, 2014	97780	2.0	[1.9; 2.1]
Ghnnam, 2011	63	9.5	[3.6; 19.6]
Giesen, 2017	637	6.6	[4.8; 8.8]
Gross, 2016	2585	7.2	[6.2; 8.3]
Gurien, 2016	484	2.7	[1.4; 4.5]
Harmon, 2016	411	5.6	[3.6; 8.3]
Helling, 2017	611	5.1	[3.5; 7.1]
Helmer, 2002	438	6.4	[4.3; 9.1]
Hesami, 2014	90	15.6	[8.8; 24.7]
Hissain, 2012	377	4.5	[2.6; 7.1]
Horvath, 2016	1516	2.6	[1.9; 3.6]
Hughes, 2013	266	9.4	[6.2; 13.6]
Inigo, 2006	721	6.4	[4.7; 8.4]
Jenkins, 2016	12410	3.4	[3.1; 3.7]
Kang, 2012	217	6.9	[3.9; 11.1]
Kapischke, 2013	159	2.5	[0.7; 6.3]
Karam, 2016	101	2.0	[0.2; 7.0]
Karam, 2016	625	5.1	[3.5; 7.2]
Kato, 2008	64	6.2	[1.7; 15.2]
Kell, 2003	149	16.1	[10.6; 23.0]
Khan, 2007	134	6.0	[2.6; 11.4]
Kim, 2011	3335	1.4	[1.1; 1.9]
Kim, 2015	2587	4.6	[3.8; 5.5]
Kim, 2016	207	15.9	[11.2; 21.7]
Kiriakopoulos, 2006	42	0.0	[0.0; 8.4]
Kirshtein, 2009	1435	1.5	[0.9; 2.2]
Kiudelis, 2013	152	5.9	[2.7; 10.9]
Kleif, 2017	1151	7.8	[6.3; 9.5]
Koizumi, 2014	185	8.6	[5.0; 13.7]
Kubota, 2014	10	10.0	[0.3; 44.5]
Kumamoto, 2014	124	4.0	[1.3; 9.2]
Lacher, 2012	415	6.0	[3.9; 8.8]
Le, 2009	507	11.0	[8.5; 14.1]
Lee, 2009	109	7.3	[3.2; 14.0]
Lee, 2010	75	4.0	[0.8; 11.2]
Lee, 2010	264	7.2	[4.4; 11.0]
Lee, 2010	2462	6.7	[5.8; 7.8]
Lee, 2011	7650	3.8	[3.3; 4.2]
Lemieux, 2008	45	2.2	[0.1; 11.8]
Levy, 2013	312	10.9	[7.7; 14.9]
Lim, 2011	60	8.3	[2.8; 18.4]
Lima, 2007	300	2.3	[0.9; 4.7]
Lin, 2006	229	27.1	[21.4; 33.3]
Litz, 2016	413	8.0	[5.6; 11.0]
Martinez, 2012	75	12.0	[5.6; 21.6]
Menezes, 2008	118	11.0	[6.0; 18.1]
Merenda, 2013	317	6.0	[3.6; 9.2]
Michailidou, 2015	2812	4.2	[3.5; 5.0]
Michailidou, 2015	264	3.8	[1.8; 6.9]
Miyano, 2010	23	17.4	[5.0; 38.8]
Moazzez, 2013	2060	2.6	[1.9; 3.4]
Monge Jodra, 2003	5780	7.9	[7.3; 8.7]
Mueck, 2017	697	1.4	[0.7; 2.6]
Muensterer, 2009	75	5.3	[1.5; 13.1]
Muensterer, 2011	183	3.8	[1.6; 7.7]
Nadler, 2003	94	14.9	[8.4; 23.7]
Nataraja, 2010	191	7.9	[4.5; 12.6]
Nataraja, 2012	1205	3.9	[2.9; 5.2]
Obayashi, 2015	485	6.0	[4.0; 8.5]
Obinwa, 2015	1037	3.7	[2.6; 5.0]
Okkyung, 2002	84	2.4	[0.3; 8.3]
Onieva, 2017	294	7.1	[4.5; 10.7]
Page, 2010	17199	3.7	[3.4; 4.0]
Palesty, 2004	50	4.0	[0.5; 13.7]
Parcells, 2009	1063	14.2	[12.2; 16.4]
Park, 2017	1343	13.6	[11.8; 15.6]
Park, 2018	986	4.4	[3.2; 5.8]
Pascual, 2017	100	1.0	[0.0; 5.4]
Pearcy, 2017	2903	0.4	[0.2; 0.7]
Putnam, 2016	410	20.5	[16.7; 24.7]
Qahtani, 2014	91	6.6	[2.5; 13.8]
Quezada, 2015	227	4.4	[2.1; 8.0]
Raakow, 2014	156	3.8	[1.4; 8.2]
Reinisch, 2017	680	8.4	[6.4; 10.7]
Romano, 2014	372	1.6	[0.6; 3.5]
Romy, 2008	2468	7.1	[6.1; 8.2]
Rossem, 2015	415	14.2	[11.0; 18.0]
Rossem, 2016	1995	1.9	[1.3; 2.5]
Rotermann, 2004	80867	3.8	[3.7; 4.0]
Saar, 2016	266	7.1	[4.4; 10.9]
Saber, 2010	26	3.8	[0.1; 19.6]
Sahm, 2010	1710	1.6	[1.1; 2.4]
Sahm, 2015	12570	7.0	[6.6; 7.5]
Salö, 2016	259	3.1	[1.3; 6.0]
Sanchez-Santana, 2017	930	4.6	[3.4; 6.2]
Sauvain, 2016	2559	2.3	[1.7; 2.9]
Scarborough, 2012	39122	4.2	[4.0; 4.4]
Scarless, 2013	38	5.3	[0.6; 17.7]
Seifarth, 2016	1283	2.7	[1.8; 3.7]
Seifarth, 2016	1283	2.7	[1.8; 3.7]
Senekjan, 2013	61830	3.6	[3.5; 3.8]
Seo, 2002	129	15.5	[9.7; 22.9]
Sesia, 2011	265	1.1	[0.2; 3.3]
Shimizu, 2014	300	16.3	[12.3; 21.0]
Siam, 2017	1649	4.7	[3.8; 5.9]
Silva, 2008	433	12.0	[9.1; 15.4]
Sivrikoz, 2015	4844	4.7	[4.2; 5.4]
Soll, 2016	813	3.1	[2.0; 4.5]
Staszewicz, 2014	6383	6.4	[5.8; 7.0]
Suttie, 2004	60	8.3	[2.8; 18.4]
Svensson, 2016	1745	6.0	[4.9; 7.2]
Taguchi, 2015	81	29.6	[20.0; 40.8]
Tanaka, 2007	95	13.7	[7.5; 22.3]
Toro Pablo, 2017	600	6.7	[4.8; 9.0]
Towfigh, 2011	75	24.0	[14.9; 35.3]
Troillet, 2017	15439	3.9	[3.6; 4.3]
Tsioplis, 2013	1439	8.5	[7.1; 10.0]
Vahdad, 2016	309	1.9	[0.7; 4.2]
Van Rossem, 2014	267	11.2	[7.7; 15.7]
Van Rossem, 2016	1378	8.1	[6.7; 9.6]
Wang-Chan, 2017	246	2.8	[1.2; 5.8]
Watanabe, 2011	903	11.2	[9.2; 13.4]
Willis, 2016	313	20.4	[16.1; 25.3]
Wu, 2006	1795	10.3	[8.9; 11.8]
Wu, 2011	1366	8.3	[6.9; 9.9]
Yaghoubian, 2010	4325	5.8	[5.1; 6.6]
Yousef, 2017	122	14.8	[9.0; 22.3]
Subgroup Incidence	**691002**	**6.2**	**[5.6; 6.9]**
Heterogeneity: I^2 = 98.9% [98.8%; 99%], τ^2 = 0.0055, p < 0.0001			
Overall Incidence	**729434**	**7.0**	**[6.4; 7.7]**
Prediction interval			**[1.0; 17.6]**

Per 100 surgical procedure

Heterogeneity: I^2 = 98.7% [98.7%; 98.8%], τ^2 = 0.0067, p = 0
Residual heterogeneity: I^2 = 98.6% [98.5%; 98.6%], p = 0
Test for subgroup differences: χ^2_3 = 10.50, df = 3 (p = 0.0148)

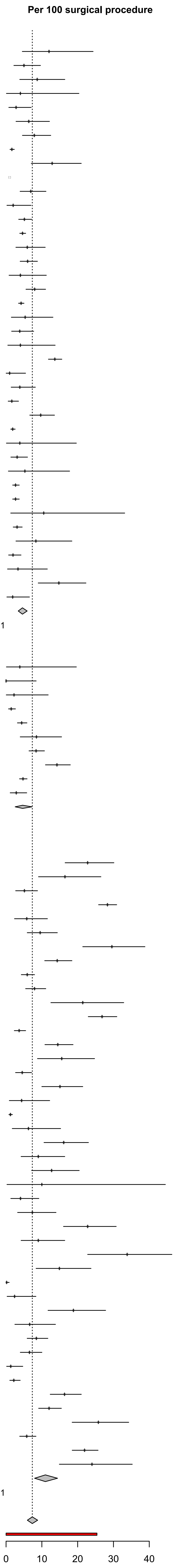
Author, Year	Sample	Incidence	[95% C.I.]
WHO Region = Africa			
Adejumo, 2015	141	5.0	[2.0; 10.0]
Ali, 2012	1257	28.3	[25.8; 30.9]
Asefa, 2002	200	32.0	[25.6; 38.9]
Chamisa, 2009	324	25.3	[20.7; 30.4]
Giiti, 2010	199	2.0	[0.6; 5.1]
Mbah, 2006	136	22.8	[16.0; 30.8]
Ohene, 2006	638	0.2	[0.0; 0.9]
Patel, 2003	106	8.5	[4.0; 15.5]
Subgroup Incidence	**3001**	**12.6**	**[3.3; 26.4]**
Heterogeneity: I^2 = 98.8% [98.4%; 99.1%], τ^2 = 0.0629, p = 0			
WHO Region = Americas			
Al-Temimi, 2017	92	8.7	[3.8; 16.4]
Álvarez-Moreno, 2014	947	3.9	[2.8; 5.3]
Bae, 2016	143	2.8	[0.8; 7.0]
Blackwood, 2017	115	29.6	[21.4; 38.8]
Blakely, 2011	131	37.4	[29.1; 46.3]
Bonadjo, 2017	203	7.9	[4.6; 12.5]
Boomer, 2014	1388	5.1	[4.0; 6.4]
Boomer, 2016	1338	2.5	[1.8; 3.5]
Cairo, 2017	20981	1.5	[1.4; 1.7]
Cameron, 2017	1389	1.8	[1.2; 2.6]
Cervantes-sánchez, 2000	350	14.3	[10.8; 18.4]
Clyde, 2008	1198	7.9	[6.5; 9.6]
Coakley, 2011	728	8.4	[6.5; 10.6]
Crandall, 2009	176	5.1	[2.4; 9.5]
Dhiman, 2013	1250	0.1	[0.0; 0.4]
Durkin, 2015	14763	1.0	[0.8; 1.2]
Ein, 2013	496	26.8	[23.0; 30.9]
Gandaglia, 2014	97780	2.0	[1.9; 2.1]
Garcell, 2016	603	3.6	[2.3; 5.5]
Gross, 2016	2585	7.2	[6.2; 8.3]
Gurien, 2016	484	2.7	[1.4; 4.5]
Harmon, 2016	411	5.6	[3.6; 8.3]
Helling, 2017	611	5.1	[3.5; 7.1]
Helmer, 2002	438	6.4	[4.3; 9.1]
Jenkins, 2016	12410	3.4	[3.1; 3.7]
Karam, 2016	101	2.0	[0.2; 7.0]
Karam, 2016	625	5.1	[3.5; 7.2]
Kim, 2011	3335	1.4	[1.1; 1.9]
Lacher, 2012	415	6.0	[3.9; 8.8]
Le, 2009	507	11.0	[8.5; 14.1]
Lee, 2009	109	7.3	[3.2; 14.0]
Lee, 2010	2462	6.7	[5.8; 7.8]
Lee, 2011	7650	3.8	[3.3; 4.2]
Lemieux, 2008	45	2.2	[0.1; 11.8]
Levy, 2013	312	10.9	[7.7; 14.9]
Litz, 2016	413	8.0	[5.6; 11.0]
Michailidou, 2015	2812	4.2	[3.5; 5.0]
Michailidou, 2015	264	3.8	[1.8; 6.9]
Moazzez, 2013	2060	2.6	[1.9; 3.4]
Mueck, 2017	697	1.4	[0.7; 2.6]
Muensterer, 2009	75	5.3	[1.5; 13.1]
Muensterer, 2011	183	3.8	[1.6; 7.7]
Nadler, 2003	94	14.9	[8.4; 23.7]
Page, 2010	17199	3.7	[3.4; 4.0]
Palesty, 2004	50	4.0	[0.5; 13.7]
Parcells, 2009	1063	14.2	[12.2; 16.4]
Pearcy, 2017	2903	0.4	[0.2; 0.7]
Putnam, 2016	410	20.5	[16.7; 24.7]
Quezada, 2015	227	4.4	[2.1; 8.0]
Rios, 2004	104	22.1	[14.6; 31.3]
Romano, 2014	372	1.6	[0.6; 3.5]
Romel Hilaire, 2014	720	7.9	[6.1; 10.1]
Romeo, 2009	310	9.7	[6.6; 13.5]
Rotermann, 2004	80867	3.8	[3.7; 4.0]
Saber, 2010	26	3.8	[0.1; 19.6]
Scarborough, 2012	39122	4.2	[4.0; 4.4]
Seifarth, 2016	1283	2.7	[1.8; 3.7]
Seifarth, 2016	1283	2.7	[1.8; 3.7]
Senekjan, 2013	61830	3.6	[3.5; 3.8]
Silva, 2008	433	12.0	[9.1; 15.4]
Sivrikoz, 2015	4844	4.7	[4.2; 5.4]
Tijerina, 2010	529	21.9	[18.5; 25.7]
Towfigh, 2011	75	24.0	[14.9; 35.3]
Willis, 2016	313	20.4	[16.1; 25.3]
Wong, 2015	352	2.8	[1.4; 5.2]
Yaghoubian, 2010	4325	5.8	[5.1; 6.6]
Yousef, 2017	122	14.8	[9.0; 22.3]
Subgroup Incidence	**401931**	**5.9**	**[5.2; 6.6]**
Heterogeneity: I^2 = 98.2% [98%; 98.4%], τ^2 = 0.0026, p = 0			
WHO Region = Eastern Mediterranean			
Ahmad, 2014	158	22.8	[16.5; 30.1]
Ahmed, 2015	79	16.5	[9.1; 26.5]
Al-Saadi, 2006	160	5.0	[2.2; 9.6]
Ali, 2015	121	5.8	[2.4; 11.6]
Chaudhary, 2005	677	5.9	[4.3; 8.0]
Ghnnam, 2011	63	9.5	[3.6; 19.6]
Hesami, 2014	90	15.6	[8.8; 24.7]
Hissain, 2012	377	4.5	[2.6; 7.1]
Iqbal, 2015	166	15.1	[10.0; 21.4]
Javadi, 2017	69	4.3	[0.9; 12.2]
Khan, 2012	100	9.0	[4.2; 16.4]
Khan, 2014	270	6.7	[4.0; 10.3]
Kumar, 2008	100	10.0	[4.9; 17.6]
Mahmood, 2016	200	5.5	[2.8; 9.6]
Memon, 2017	227	7.0	[4.1; 11.2]
Mustafa, 2016	68	33.8	[22.8; 46.3]
Pishori, 2003	3304	8.5	[7.6; 9.5]
Qahtani, 2014	91	6.6	[2.5; 13.8]
Rafiq, 2015	390	8.5	[5.9; 11.7]
Rajabi-Mashhadi, 2012	291	6.5	[4.0; 10.0]
Rooh-ul-Muqim, 2010	165	7.9	[4.3; 13.1]
Sadraei-Mosavi, 2017	152	1.3	[0.2; 4.7]
Shaikg, 2011	461	2.2	[1.0; 4.0]
Subgroup Incidence	**7779**	**8.2**	**[6.4; 10.2]**
Heterogeneity: I^2 = 85.3% [79.1%; 89.6%], τ^2 = 0.0051, p < 0.0001			
WHO Region = Europe			
Aguillo, 2005	792	5.2	[3.7; 7.0]
Akkoyun, 2012	234	5.1	[2.7; 8.8]
Almström, 2016	2756	6.2	[5.4; 7.2]
Anderson, 2014	169896	0.5	[0.4; 0.5]
Andert, 2017	2136	2.4	[1.8; 3.2]
Aranda-Narváez, 2010	30	20.0	[7.7; 38.6]
Aranda-Narvaez, 2014	868	13.4	[11.2; 15.8]
Asefa, 2014	322	18.9	[14.8; 23.7]
Bali, 2015	126	6.3	[2.8; 12.1]
Bansal, 2012	187	5.9	[3.0; 10.3]
Bıçakcı, 2011	279	14.3	[10.4; 19.0]
Bickel, 2011	210	9.5	[5.9; 14.3]
Bozkurt, 2014	1849	1.6	[1.1; 2.3]
Brandt, 2008	10969	2.4	[2.1; 2.7]
Brummer, 2009	14209	2.0	[1.7; 2.2]
Dede, 2008	273	11.4	[7.8; 15.7]
Dimitriou, 2013	404	9.2	[6.5; 12.4]
Giesen, 2017	637	6.6	[4.8; 8.8]
Golub, 2016	332	14.5	[10.9; 18.7]
Hamzaoglu, 2004	100	8.0	[3.5; 15.2]
Horvath, 2016	1516	2.6	[1.9; 3.6]
Hughes, 2013	266	9.4	[6.2; 13.6]
Inigo, 2006	721	6.4	[4.7; 8.4]
Kapischke, 2013	159	2.5	[0.7; 6.3]
Kell, 2003	149	16.1	[10.6; 23.0]
Khan, 2007	134	6.0	[2.6; 11.4]
Kilic, 2016	110	12.7	[7.1; 20.4]
Kiriakopoulos, 2006	42	0.0	[0.0; 8.4]
Kirshtein, 2009	1435	1.5	[0.9; 2.2]
Kiudelis, 2013	152	5.9	[2.7; 10.9]
Kleif, 2017	1151	7.8	[6.3; 9.5]
Lima, 2007	300	2.3	[0.9; 4.7]
Martinez, 2012	75	12.0	[5.6; 21.6]
Menezes, 2008	118	11.0	[6.0; 18.1]
Merenda, 2013	317	6.0	[3.6; 9.2]
Mickovic, 2015	218	4.1	[1.9; 7.7]
Monge Jodra, 2003	5780	7.9	[7.3; 8.7]
Nataraja, 2010	191	7.9	[4.5; 12.6]
Nataraja, 2012	1205	3.9	[2.9; 5.2]
Obinwa, 2015	1037	3.7	[2.6; 5.0]
Onieva, 2017	294	7.1	[4.5; 10.7]
Pascual, 2017	100	1.0	[0.0; 5.4]
Raakow, 2014	156	3.8	[1.4; 8.2]
Reinisch, 2017	680	8.4	[6.4; 10.7]
Romy, 2008	2468	7.1	[6.1; 8.2]
Rossem, 2015	415	14.2	[11.0; 18.0]
Rossem, 2016	1995	1.9	[1.3; 2.5]
Saar, 2016	266	7.1	[4.4; 10.9]
Sahm, 2010	1710	1.6	[1.1; 2.4]
Sahm, 2015	12570	7.0	[6.6; 7.5]
Salö, 2016	259	3.1	[1.3; 6.0]
Sanchez-Santana, 2017	930	4.6	[3.4; 6.2]
Sauvain, 2016	2559	2.3	[1.7; 2.9]
Scarless, 2013	38	5.3	[0.6; 17.7]
Sesia, 2011	265	1.1	[0.2; 3.3]
Siam, 2017	1649	4.7	[3.8; 5.9]
Soll, 2016	813	3.1	[2.0; 4.5]
Sozutek, 2013	75	6.7	[2.2; 14.9]
Staszewicz, 2014	6383	6.4	[5.8; 7.0]
Suttie, 2004	60	8.3	[2.8; 18.4]
Svensson, 2016	1745	6.0	[4.9; 7.2]
Toro Pablo, 2017	600	6.7	[4.8; 9.0]
Troillet, 2017	15439	3.9	[3.6; 4.3]
Tsioplis, 2013	1439	8.5	[7.1; 10.0]
Vahdad, 2016	309	1.9	[0.7; 4.2]
Van Rossem, 2014	267	11.2	[7.7; 15.7]
Van Rossem, 2016	1378	8.1	[6.7; 9.6]
Wang-Chan, 2017	246	2.8	[1.2; 5.8]
Subgroup Incidence	**276793**	**5.8**	**[4.6; 7.0]**
Heterogeneity: I^2 = 99.1% [99%; 99.1%], τ^2 = 0.0106, p < 0.0001			
WHO Region = Multiregional			
Banghu, 2013	3326	6.1	[5.3; 7.0]
Subgroup Incidence	**3326**	**6.1**	**[5.3; 6.9]**
Heterogeneity: not applicable			
WHO Region = South-East Asia			
Adhikar, 2008	50	12.0	[4.5; 24.3]
Batajoo, 2012	226	8.0	[4.8; 12.3]
Bharathi, 2011	26	3.8	[0.1; 19.6]
Choudhary, 2014	92	7.6	[3.1; 15.1]
Kasatpibal, 2005	1487	1.9	[1.3; 2.7]
Kasatpibal, 2006	2139	1.2	[0.8; 1.8]
Khiria, 2011	497	3.6	[2.2; 5.7]
Kumar, 2016	212	9.0	[5.5; 13.6]
Mingmalairak, 2009	100	9.0	[4.2; 16.4]
Pandit, 2016	101	18.8	[11.7; 27.8]
Saha, 2010	60	13.3	[5.9; 24.6]
Shindholimath, 2011	19	10.5	[1.3; 33.1]
Singh, 2017	44	9.1	[2.5; 21.7]
Siribumrungwong, 2013	128	25.8	[18.5; 34.3]
Srishewachart, 2016	450	5.8	[3.8; 8.4]
Yagnik, 2010	151	4.6	[1.9; 9.3]
Subgroup Incidence	**5782**	**7.6**	**[4.7; 11.1]**
Heterogeneity: I^2 = 93% [90.1%; 95%], τ^2 = 0.0110, p = NA			
WHO Region = Western Pacific			
Arthur, 2017	1189	1.9	[1.2; 2.9]
Bae, 2016	25	4.0	[0.1; 20.4]
Baek, 2011	77	13.0	[6.4; 22.6]
Cao, 2015	12586	8.8	[8.3; 9.3]
Chen, 2010	69	2.9	[0.4; 10.1]
Chen, 2012	117	6.8	[3.0; 13.0]
Chen, 2015	236	19.9	[15.0; 25.6]
Chiang, 2006	390	7.9	[5.5; 11.1]
Chiang, 2012	70	21.4	[12.5; 32.9]
Cho, 2014	101	12.9	[7.0; 21.0]
Fukuda, 2016	2074	4.3	[3.5; 5.3]
Hung, 2016	752	7.0	[5.3; 9.1]
Kang, 2012	217	6.9	[3.9; 11.1]
Kato, 2008	64	6.2	[1.7; 15.2]
Kim, 2015	2587	4.6	[3.8; 5.5]
Kim, 2016	207	15.9	[11.2; 21.7]
Koizumi, 2014	185	8.6	[5.0; 13.7]
Kubota, 2014	10	10.0	[0.3; 44.5]
Kumamoto, 2014	124	4.0	[1.3; 9.2]
Lee, 2010	75	4.0	[0.8; 11.2]
Lee, 2010	264	7.2	[4.4; 11.0]
Li, 2005	160	6.9	[3.5; 12.0]
Li, 2017	398	11.6	[8.6; 15.1]
Lim, 2011	60	8.3	[2.8; 18.4]
Lin, 2006	229	27.1	[21.4; 33.3]
Liu, 2017	112	8.0	[3.7; 14.7]
Ming, 2009	173	23.1	[17.1; 30.1]
Miyano, 2010	23	17.4	[5.0; 38.8]
Obayashi, 2015	485	6.0	[4.0; 8.5]
Okkyung, 2002	84	2.4	[0.3; 8.3]
Park, 2017	1343	13.6	[11.8; 15.6]
Park, 2018	986	4.4	[3.2; 5.8]
Seo, 2002	129	15.5	[9.7; 22.9]
Shang, 2017	398	11.3	[8.4; 14.8]
Shimizu, 2014	300	16.3	[12.3; 21.0]
Taguchi, 2015	81	29.6	[20.0; 40.8]
Tanaka, 2007	95	13.7	[7.5; 22.3]
Watanabe, 2011	903	11.2	[9.2; 13.4]
Wu, 2006	1795	10.3	[8.9; 11.8]
Wu, 2011	1366	8.3	[6.9; 9.9]
Wu, 2014	60	3.3	[0.4; 11.5]
Wu, 2017	115	37.4	[28.5; 46.9]
Zhang, 2015	108	1.9	[0.2; 6.5]
Subgroup Incidence	**30822**	**9.6**	**[8.1; 11.2]**
Heterogeneity: I^2 = 93.2% [91.7%; 94.4%], τ^2 = 0.0058, p < 0.0001			
Overall Incidence	**729434**	**7.0**	**[6.4; 7.7]**
Prediction interval			**[1.0; 17.6]**

Heterogeneity: I^2 = 98.7% [98.7%; 98.8%], τ^2 = 0.0067, p = 0

Residual heterogeneity: I^2 = 98.2% [98.1%; 98.3%], p = 0

Test for subgroup differences: χ^2_6 = 33.60, df = 6 (p < 0.0001)

Author, Year	Sample	Incidence	[95% C.I.]
Procedure = Laparoscopy			
Adhikar, 2008	50	12.0	[4.5; 24.3]
Al-Saadi, 2006	160	5.0	[2.2; 9.6]
Al-Temimi, 2017	92	8.7	[3.8; 16.4]
Bae, 2016	25	4.0	[0.1; 20.4]
Bae, 2016	143	2.8	[0.8; 7.0]
Bali, 2015	126	6.3	[2.8; 12.1]
Bonadjo, 2017	203	7.9	[4.6; 12.5]
Bozkurt, 2014	1849	1.6	[1.1; 2.3]
Cho, 2014	101	12.9	[7.0; 21.0]
Durkin, 2015	14763	1.0	[0.8; 1.2]
Kang, 2012	217	6.9	[3.9; 11.1]
Karam, 2016	101	2.0	[0.2; 7.0]
Karam, 2016	625	5.1	[3.5; 7.2]
Kim, 2015	2587	4.6	[3.8; 5.5]
Kiudelis, 2013	152	5.9	[2.7; 10.9]
Lacher, 2012	415	6.0	[3.9; 8.8]
Lee, 2010	75	4.0	[0.8; 11.2]
Litz, 2016	413	8.0	[5.6; 11.0]
Michailidou, 2015	2812	4.2	[3.5; 5.0]
Muensterer, 2009	75	5.3	[1.5; 13.1]
Muensterer, 2011	183	3.8	[1.6; 7.7]
Palesty, 2004	50	4.0	[0.5; 13.7]
Park, 2017	1343	13.6	[11.8; 15.6]
Pascual, 2017	100	1.0	[0.0; 5.4]
Raakow, 2014	156	3.8	[1.4; 8.2]
Romano, 2014	372	1.6	[0.6; 3.5]
Romeo, 2009	310	9.7	[6.6; 13.5]
Rossem, 2016	1995	1.9	[1.3; 2.5]
Saber, 2010	26	3.8	[0.1; 19.6]
Salö, 2016	259	3.1	[1.3; 6.0]
Scarless, 2013	38	5.3	[0.6; 17.7]
Seifarth, 2016	1283	2.7	[1.8; 3.7]
Seifarth, 2016	1283	2.7	[1.8; 3.7]
Shindholimath, 2011	19	10.5	[1.3; 33.1]
Soll, 2016	813	3.1	[2.0; 4.5]
Suttie, 2004	60	8.3	[2.8; 18.4]
Vahdad, 2016	309	1.9	[0.7; 4.2]
Wu, 2014	60	3.3	[0.4; 11.5]
Yousef, 2017	122	14.8	[9.0; 22.3]
Zhang, 2015	108	1.9	[0.2; 6.5]
Subgroup Incidence	**33873**	**4.6**	**[3.4; 5.9]**
Heterogeneity: I^2 = 94.7% [93.6%; 95.7%], τ^2 = 0.0066, p < 0.0001			
Procedure = Laparoscopy with Open Surgery			
Bharathi, 2011	26	3.8	[0.1; 19.6]
Kiriakopoulos, 2006	42	0.0	[0.0; 8.4]
Lemieux, 2008	45	2.2	[0.1; 11.8]
Mueck, 2017	697	1.4	[0.7; 2.6]
Park, 2018	986	4.4	[3.2; 5.8]
Patel, 2003	106	8.5	[4.0; 15.5]
Reinisch, 2017	680	8.4	[6.4; 10.7]
Rossem, 2015	415	14.2	[11.0; 18.0]
Siam, 2017	1649	4.7	[3.8; 5.9]
Wang-Chan, 2017	246	2.8	[1.2; 5.8]
Subgroup Incidence	**4892**	**4.6**	**[2.5; 7.2]**
Heterogeneity: I^2 = 90.7% [85%; 94.2%], τ^2 = 0.0056, p < 0.0001			
Procedure = Open Surgery			
Ahmad, 2014	158	22.8	[16.5; 30.1]
Ahmed, 2015	79	16.5	[9.1; 26.5]
Akkoyun, 2012	234	5.1	[2.7; 8.8]
Ali, 2012	1257	28.3	[25.8; 30.9]
Ali, 2015	121	5.8	[2.4; 11.6]
Bickel, 2011	210	9.5	[5.9; 14.3]
Blackwood, 2017	115	29.6	[21.4; 38.8]
Cervantes-sánchez, 2000	350	14.3	[10.8; 18.4]
Chaudhary, 2005	677	5.9	[4.3; 8.0]
Chiang, 2006	390	7.9	[5.5; 11.1]
Chiang, 2012	70	21.4	[12.5; 32.9]
Ein, 2013	496	26.8	[23.0; 30.9]
Garcell, 2016	603	3.6	[2.3; 5.5]
Golub, 2016	332	14.5	[10.9; 18.7]
Hesami, 2014	90	15.6	[8.8; 24.7]
Hissain, 2012	377	4.5	[2.6; 7.1]
Iqbal, 2015	166	15.1	[10.0; 21.4]
Javadi, 2017	69	4.3	[0.9; 12.2]
Kasatpibal, 2006	2139	1.2	[0.8; 1.8]
Kato, 2008	64	6.2	[1.7; 15.2]
Kell, 2003	149	16.1	[10.6; 23.0]
Khan, 2012	100	9.0	[4.2; 16.4]
Kilic, 2016	110	12.7	[7.1; 20.4]
Kubota, 2014	10	10.0	[0.3; 44.5]
Kumamoto, 2014	124	4.0	[1.3; 9.2]
Lee, 2009	109	7.3	[3.2; 14.0]
Mbah, 2006	136	22.8	[16.0; 30.8]
Mingmalairak, 2009	100	9.0	[4.2; 16.4]
Mustafa, 2016	68	33.8	[22.8; 46.3]
Nadler, 2003	94	14.9	[8.4; 23.7]
Ohene, 2006	638	0.2	[0.0; 0.9]
Okkyung, 2002	84	2.4	[0.3; 8.3]
Pandit, 2016	101	18.8	[11.7; 27.8]
Qahtani, 2014	91	6.6	[2.5; 13.8]
Rafiq, 2015	390	8.5	[5.9; 11.7]
Rajabi-Mashhadi, 2012	291	6.5	[4.0; 10.0]
Sadraei-Mosavi, 2017	152	1.3	[0.2; 4.7]
Shaikg, 2011	461	2.2	[1.0; 4.0]
Shimizu, 2014	300	16.3	[12.3; 21.0]
Silva, 2008	433	12.0	[9.1; 15.4]
Siribumrungwong, 2013	128	25.8	[18.5; 34.3]
Srishewachart, 2016	450	5.8	[3.8; 8.4]
Tijerina, 2010	529	21.9	[18.5; 25.7]
Towfigh, 2011	75	24.0	[14.9; 35.3]
Subgroup Incidence	**13120**	**11.0**	**[8.0; 14.4]**
Heterogeneity: I^2 = 96.9% [96.4%; 97.3%], τ^2 = 0.0270, p < 0.0001			
Overall Incidence	**51885**	**7.3**	**[5.9; 8.8]**
Prediction interval			**[0.0; 25.4]**



Heterogeneity: I^2 = 96.9% [96.6%; 97.2%], τ^2 = 0.0156, p = 0
Residual heterogeneity: I^2 = 95.9% [95.4%; 96.4%], p = 0
Test for subgroup differences: χ^2_2 = 16.75, df = 2 (p = 0.0002)

MOOSE Checklist for Meta-analyses of Observational Studies

Item No	Recommendation	Reported on Page No
Reporting of background should include		
1	Problem definition	5
2	Hypothesis statement	6
3	Description of study outcome(s)	5
4	Type of exposure or intervention used	NA
5	Type of study designs used	5-6
6	Study population	5-6
Reporting of search strategy should include		
7	Qualifications of searchers (eg, librarians and investigators)	13
8	Search strategy, including time period included in the synthesis and key words	6; Suppl. Table 1
9	Effort to include all available studies, including contact with authors	6
10	Databases and registries searched	6
11	Search software used, name and version, including special features used (eg, explosion)	6
12	Use of hand searching (eg, reference lists of obtained articles)	6
13	List of citations located and those excluded, including justification	8, Suppl. Fig 1, Suppl. References
14	Method of addressing articles published in languages other than English	7
15	Method of handling abstracts and unpublished studies	7
16	Description of any contact with authors	6
Reporting of methods should include		
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	6
18	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	6-7
19	Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	6-7
20	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	8
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	8
22	Assessment of heterogeneity	7
23	Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	7-8
24	Provision of appropriate tables and graphics	Table 1; Fig 1-3
Reporting of results should include		
25	Graphic summarizing individual study estimates and overall estimate	Fig 1-3
26	Table giving descriptive information for each study included	Suppl. Table 1
27	Results of sensitivity testing (eg, subgroup analysis)	9; Table 1

28	Indication of statistical uncertainty of findings	9; Table 1; Fig 1-3

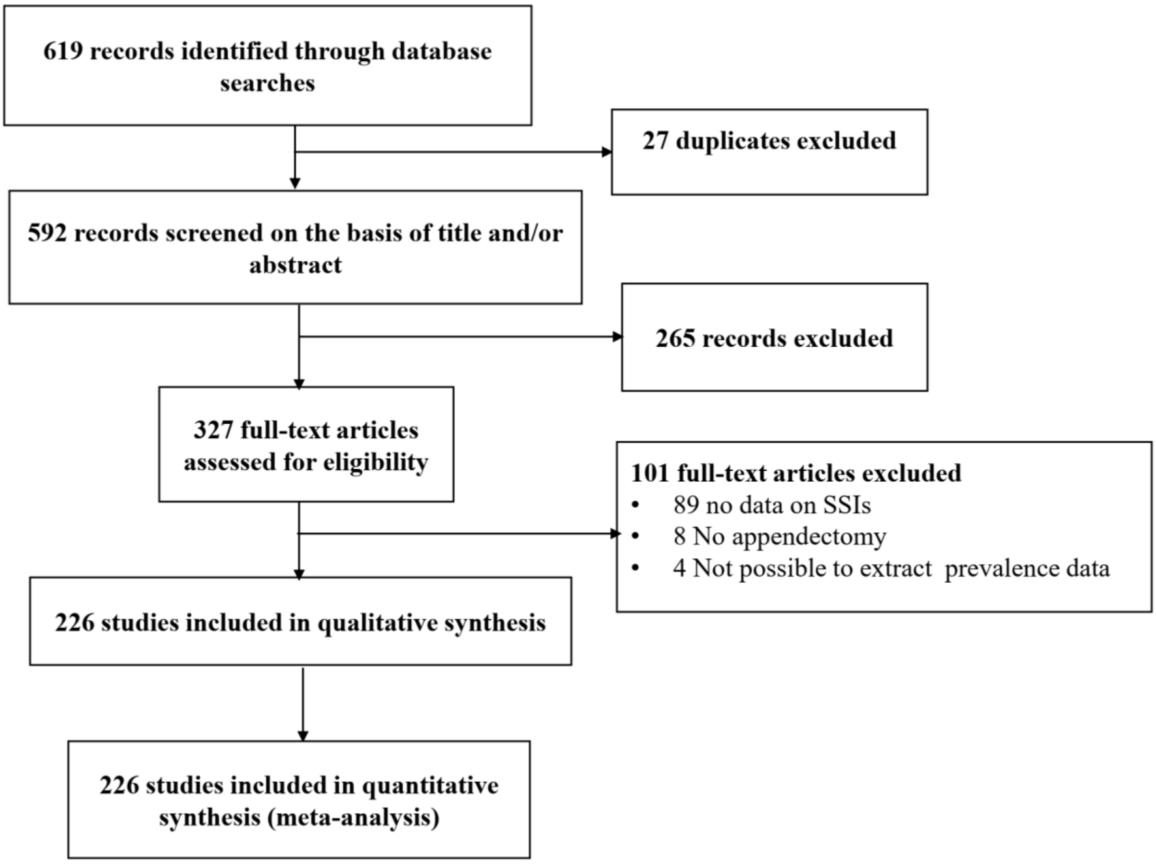
Item No	Recommendation	Reported on Page No
Reporting of discussion should include		
29	Quantitative assessment of bias (eg, publication bias)	12-13
30	Justification for exclusion (eg, exclusion of non-English language citations)	12-13
31	Assessment of quality of included studies	12-13
Reporting of conclusions should include		
32	Consideration of alternative explanations for observed results	13
33	Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	13
34	Guidelines for future research	13
35	Disclosure of funding source	14

From: Stroup DF, Berlin JA, Morton SC, et al, for the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) Group. Meta-analysis of Observational Studies in Epidemiology. A Proposal for Reporting. *JAMA*. 2000;283(15):2008-2012. doi: 10.1001/jama.283.15.2008.

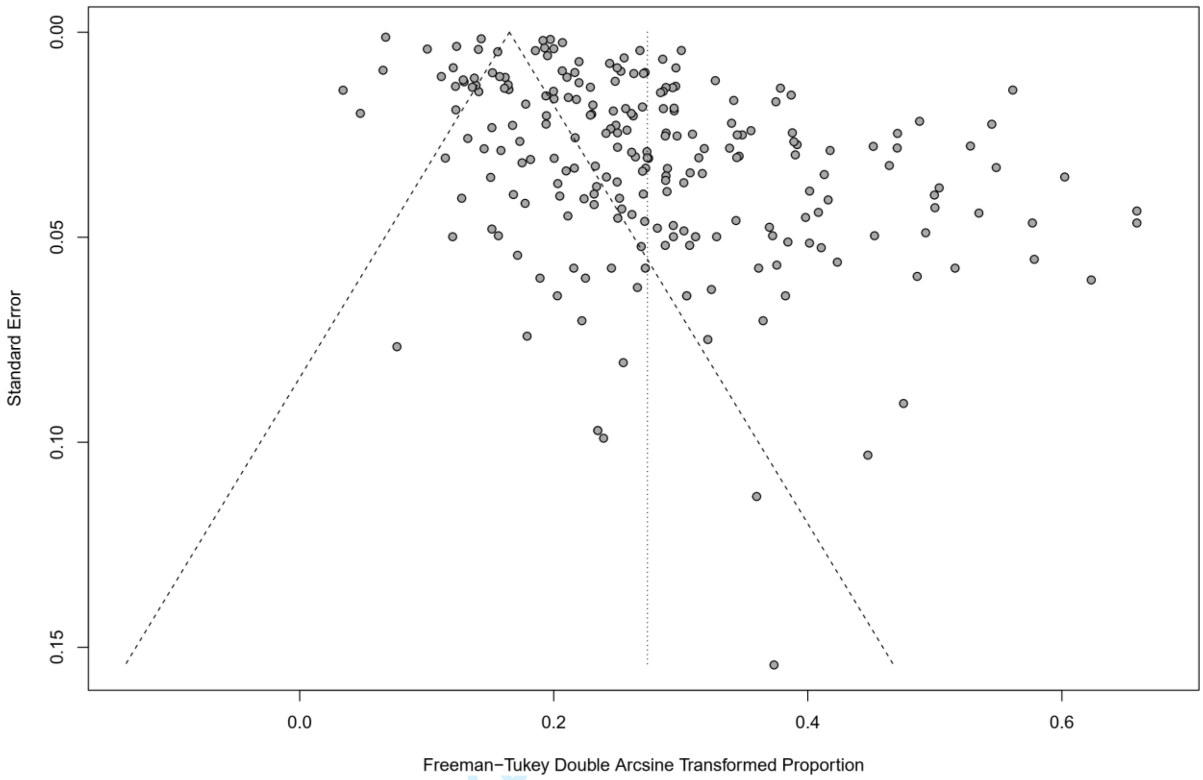
Global incidence of surgical-site infection after appendectomy: a systematic review and meta-analysis

APPENDIX

Celestin **Danwang**, Jean Joel **Bigna**, Joel Noutakdie **Tochie**, Aime **Mbonda**, Clarence Mvalo **Mbanga**, Rolf Nyah Tuku **Nzalie**, Marc Leroy **Guifo**, Arthur **Essomba**



Supplementary Figure 1. Study flow



Supplementary Figure 2. Funnel plot for publication bias

Supplementary Table 1. Search strategy in EMBASE

	Search terms
#1	'appendectomy'/exp OR appendectomy OR 'appendicectomy'/exp OR appendicectomy OR appendices OR 'appendix epiploica' OR 'omental appendix' OR 'appendicitis'/exp OR appendicitis
#2	'surgical site infection'/exp OR 'surgical site infection' OR 'surgical wound infection'/exp OR 'surgical wound infection' OR 'surgical wound infections'/exp OR 'surgical wound infections' OR 'surgical site infections' OR 'operative site infections' OR 'postoperative wound infections'/exp OR 'postoperative wound infections' OR 'postoperative wound infection'/exp OR 'postoperative wound infection'
#3	[2000-2018]/py
#4	#1 AND #2 AND #3

Supplementary Table 2 : Characteristics of included studies

Characteristics	N = 226
Year of publication, range	2000-2018
%Male, range	0-100 (n = 195)
Mean/median age, range	7-74 (n = 186)
%HIV	0-13.1 (n = 2)
%Diabetes	0-95.7 (n = 34)
%Obesity	0-7.4 (n = 18)
Design, n	
- Cross sectional	120
- Cohort study	99
- Case control	7
WHO regions, n	
- Africa	8
- Americas	67
- Eastern Mediterranean	23
- Europe	68
- Multiregional	1
- South-East Asia	16
- Western Pacific	43
Level of income, n	
- Low	9
- Lower-middle	27
- Upper-middle	36
- High	154
Timing of data collection	
- Retrospective	123
- Prospective	101
- Unclear	2
Sampling	
- Consecutive	131
- Systematic	37
- Random	32
- Exhaustive	11
- Unclear	15
Number of sites	
- Multisite	51
- One site	170
- Unclear	5
Pattern of appendicitis, range	
- %Catarrhal	0-100 (n = 84)
- %Perforated	0-100 (n = 110)
- %Suppurated	0-100 (n = 70)
- %Gangrenous	0-46.7 (n = 89)
%With administered antibiotics	24.1-100 (n = 109)
%With administered analgesics	64.5-100 (n = 20)
%With diet > 6 or 8 hours	50-100 (n = 3)
Type of surgery	
- %Open surgery	0-100 (n = 134)

- %Laparoscopy	0-100 (n = 187)
Mean/median time to complete the intervention (in hours), range	0.1-2.2 (n = 106)
Type of anesthesia, n	
- General	118
- Spinal and general	2
- Unclear	106
SSI definition, n	
- CDC-NNIS criteria	50
- Other criteria	25
- Not reported/Unclear	151

Supplementary Table 3. *Individual characteristics of included studies*

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Adejumo	2015	Moderate	Cohort	Nigeria	Retrospective	Consecutive	One site	2007-2014	Adults	39	26	NR	Catarrhal, Perforated, Suppurated, Gangrenous	48.9	NR	NR	NR	100	NR	NR	NR	NR	141
Adhikar	2008	Moderate	Cohort	Nepal	Prospective	Consecutive	One site	2005-2006	Children, Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy	0.5	General	NR	50
Aguillo	2005	Moderate	Cohort	Spain	Prospective	Consecutive	Unclear	NR	Children, Adolescents, Adults, Elderly	63.1	NR	NR	Unclear	NR	NR	NR	NR	100	NR	NR	NR	NR	792
Ahmad	2014	Moderate	Clinical trial	Pakistan	Prospective	Consecutive	One site	2012	Adults	35.4	27.4	NR	Perforated	0	100	0	0	100	Open Surgery	NR	General	NR	158
Ahmed	2015	Moderate	Cross sectional	Pakistan	Retrospective	Consecutive	One site	2009-2010	Children, Adolescents	51.89	10.1	NR	Unclear	NR	NR	NR	NR	100	Open Surgery	NR	NR	NR	79
Akkoyun	2012	Moderate	Case control	Turkey	Retrospective	Consecutive	One site	1998-2011	Children	64.5	8.9	NR	Perforated	0	100	0	0	100	Open Surgery	0.6	General	NR	234
Ali	2015	Moderate	Cross sectional	Pakistan	Prospective	Consecutive	One site	2014	Adults	46.3	27.4	NR	Unclear	NR	NR	NR	NR	100	Open Surgery	NR	General	NR	121
Ali	2012	Moderate	Cohort	Nigeria	Prospective	Consecutive	One site	2002-2009	Children, Adolescents, Adults, Elderly	33.9	32	NR	Catarrhal, Perforated, Suppurated, Gangrenous	NR	23.47	NR	NR		Open Surgery	NR	NR	NR	1257
Almström	2016	Moderate	Cohort	Sweden	Retrospective	Systematic	One site	2006-2013	Children, Adolescents	59.5	NR	NR	Perforated, Non Perforated 76%	NR	24	NR	NR		Laparoscopy or Open Surgery	0.8	NR	NR	2756
Al-Saadi	2006	Moderate	Cohort	Yemen	Retrospective	Consecutive	One site	2003-2005	Children, Adolescents, Adults	75	NR	NR	Catarrhal, Perforated, Suppurated, Gangrenous	NR	60	NR	13	100	Laparoscopy	NR	NR	NR	160
Al-Temimi	2017	Low	Cohort	USA	Prospective	Systematic	One site	2016	Children, Adolescents, Adults, Elderly	40.2	30	NR	Catarrhal, Perforated, Suppurated, Gangrenous, Normal	73	17.4	3.3	3.3		Laparoscopy	0.6	NR	NR	92
Álvarez-Moreno	2014	Low	Cohort	Colombia	Prospective	Systematic	Multisite	2008-2010	Children, Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR		NR	NR	NR	According to CDC-NNIS diagnostic criteria	947
Anderson	2014	Moderate	Cohort	Sweden	Retrospective	Exhaustive	Multisite	1992-2008	Adults	54	NR	NR	Perforated, Not perforated	NR	19.4	0	0		Laparoscopy or Open Surgery	NR	NR	NR	169896
Andert	2017	Moderate	Cohort	Germany	Retrospective	Consecutive	One site	2003-2014	Adults	48.6	30.5	NR	Catarrhal, Perforated, Suppurated, Gangrenous	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	NR	NR	Local signs of inflammation	2136
Aranda-Narvaez	2014	Moderate	Cohort	Spain	Not reported/Unclear	Not clear	One site	2007-2010	Adults	57	29	NR	Catarrhal, Perforated, Suppurated, Gangrenous	65.8	NR	NR	NR	62.00	Laparoscopy or Open Surgery	0.92	NR	According to CDC-NNIS diagnostic Criteria	868
Aranda-Narváez	2010	Low	Cohort	Spain	Retrospective	Random	One site	1997-2009	Children, Adolescents, Adults, Elderly	63.3	35	NR	Suppurated, Gangrenous	0	0	53.3	46.7	100	Laparoscopy or Open Surgery	NR	General	According to CDC-NNIS diagnostic Criteria	30

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Arthur	2017	Low	Cross sectional	Australia	Prospective	Systematic	Multisite	2016	Children, Adolescents, Adults, Elderly	49.5	31.4	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	1	NR	NR	1189
Asefa	2014	Moderate	Cross sectional	Ethopia	Retrospective	Consecutive	One site	2006-2010	Children	62.1	10	NR	Catarrhal, Perforated, Suppurated, Gangrenous	32.3	59.6	6.2	1.9		NR	NR	NR	NR	322
Asefa	2002	High	Cross sectional	Ethopia	Retrospective	Consecutive	One site	1997-1999	Adults	79.5	25.6	NR	Catarrhal, Perforated	45.4	44	0	0		NR	NR	NR	NR	200
Bae	2016	Low	Cross sectional	Korea	Prospective	Systematic	One site	2014-2016	Adults	52	62	NR	Perforated, Suppurated, Gangrenous	NR	4	72	24	100	Laparoscopy	1.2	General	According to CDC-NNIS diagnostic criteria	25
Bae	2016	Moderate	Cross sectional	USA	Retrospective	Systematic	One site	2010-2013	Children, Adolescents, Adults	NR	32	NR	Unclear	NR	NR	NR	NR	36.4	Laparoscopy	NR	NR	According to CDC-NNIS diagnostic criteria	143
Baek	2011	Moderate	Cross sectional	Korea	Retrospective	Exhaustive	One site	2007-2009	Elderly	45.5	68.2	NR	Catarrhal, Perforated, Suppurated, Gangrenous	22.1	29.9	32.5	15.6	100	Laparoscopy or Open Surgery	1.05	General	NR	77
Bali	2015	Moderate	Cohort	Turkey	Prospective	Consecutive	One site	2009-2013	Adults	35.7	32.33	NR	Unclear	NR	NR	NR	NR		Laparoscopy	1	NR	NR	126
Banghu	2013	Low	Cohort	UK, Spain, Japan, Hong Kong, Australia, New Zealand	Prospective	Consecutive	Multisite	2012	Children, Adolescents, Adults, Elderly	51.1	NR	NR	Unclear	NR	NR	NR	NR	96.9	Laparoscopy or Open Surgery	NR	NR	According to CDC-NNIS diagnostic criteria	3326
Bansal	2012	Low	Cohort	Switzerland	Prospective	Consecutive	One site	NR	Children	62	9.8	NR	Catarrhal, Perforated	74.3	25.7	NR	NR	49.2	Laparoscopy or Open Surgery	1.0	NR	According to CDC-NNIS diagnostic Criteria	187
Batajoo	2012	Moderate	Cross sectional	Nepal	Retrospective	Consecutive	One site	2009-2012	Children, Adolescents, Adults, Elderly	45.6	29.6	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	0.8	NR	NR	226
Bharathi	2011	Moderate	Cohort	Nepal	Prospective	Consecutive	One site	2008-2009	Children, Adolescents, Adults, Elderly	50	22.9	NR	Catarrhal, Perforated, Suppurated, Gangrenous	80	NR	NR	NR	100	Laparoscopy with Open Surgery	0.5	NR	NR	26
Bıçakcı	2011	High	Cross sectional	Turkey	Retrospective	Systematic	Unclear	2006-2009	Children, Adolescents	64.5	10	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	NR	279
Bickel	2011	Moderate	Clinical trial	Israel	Prospective	Random	One site	2006-2009	Adults	73	28	NR	Catarrhal, Gangrenous, Phlegmonous 58.6 , Normal 4.3%	17	NR	NR	20.5	100	Open Surgery	0.5	General	NR	210
Blackwood	2017	Moderate	Cross sectional	USA	Retrospective	Random	One site	2010-2015	Children	55.6	10.4	29.6	Unclear	NR	NR	NR	NR		Open Surgery	2	General	According to CDC-NNIS diagnostic Criteria	115
Blakely	2011	Low	Clinical trial	USA	Prospective	Random	One site	2006-2009	Children, Adolescents	55.7	10.2	NR	Perforated	0	100	0	0	100	Laparoscopy or Open Surgery	1.9	NR	NR	131

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Bonadjo	2017	Moderate	Cross sectional	USA	Retrospective	Consecutive	One site	2008-2015	Children, Adolescents	56.2	8.4	NR	Perforated	0	100	0	0	100	Laparoscopy	NR	General	NR	203
Boomer	2016	Low	Cross sectional	USA	Retrospective	Systematic	Multisite	2010-2012	Children, Adolescents	60.3	11.0	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	According to CDC-NNIS diagnostic criteria	1338
Boomer	2014	Low	Cohort	USA	Retrospective	Consecutive	One site	2010-2012	Children, Adolescents	61.1	10.9	NR	Catarrhal, Perforated, Gangrenous	66.2	NR	NR	NR	97.8	Laparoscopy or Open Surgery	NR	General	Wound infection or abdominal/pelvic abscess	1388
Bozkurt	2014	Moderate	Case control	Turkey	Retrospective	Consecutive	One site	2008-2012	Children, Adolescents, Adults, Elderly	54	30.4	NR	Catarrhal	100	0	0	0		Laparoscopy	0.8	General	NR	1849
Brandt	2008	Moderate	Cross sectional	Germany	Retrospective	Systematic	Multisite	2000-2004	Children, Adolescents, Adults, Elderly	NR	NR	NR	NR	NR	NR	NR	NR		NR	NR	NR	According to CDC-NNIS diagnostic criteria	10969
Brummer	2009	Moderate	Cohort	Germany	Retrospective	Consecutive	Multisite	2004-2007	Children, Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	According to CDC-NNIS diagnostic Criteria	14209
Cairo	2017	Moderate	Cohort	USA	Retrospective	Consecutive	Multisite	2012-2015	Children, Adolescents	61.3	11.0	29.9	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	NR	20981
Cameron	2017	Low	Cohort	USA	Retrospective	Systematic	Multisite	2012-2015	Children, Adolescents	60.4	11	11.7	Unclear	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	NR	NR	According to CDC-NNIS diagnostic criteria	1389
Cao	2015	Moderate	Cohort	China	Retrospective	Consecutive	Multisite	2011-2013	Adults	54.2	37.3	12.4	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	0.8	General	NR	12586
Cervantes-sánchez	2000	Low	Clinical trial	Mexico	Prospective	Random	One site	1994-1995	Children, Adults	53.4	28	NR	Unclear	NR	NR	NR	NR		Open Surgery	NR	General	Pus or a positive bacteriologic culture from a wound discharge	350
Chamisa	2009	High	Cross sectional	South Africa	Retrospective	Exhaustive	One site	2002-2004	Children, Adolescents, Adults, Elderly	78.4	NR	NR	Catarrhal, Perforated, Gangrenous, Normal	53	30.5	NR	10.2		Laparoscopy or Open Surgery	NR	NR	NR	324
Chaudhary	2005	Moderate	Clinical trial	Pakistan	Prospective	Random	One site	1999-2003	Children, Adolescents, Adults, Elderly	45.4	NR	NR	Catarrhal	NR	0	0	0		Open Surgery	NR	NR	NR	677
Chen	2015	Moderate	Cohort	Taiwan	Retrospective	Consecutive	One site	2010-2012	Adults	43.6	42.5	NR	Catarrhal, Perforated	87.3	12.7	0	0		Laparoscopy or Open Surgery	NR	NR	NR	236
Chen	2012	High	Cross sectional	Taiwan	Prospective	Consecutive	One site	2010	Adults	60	38	NR	Unclear	NR	NR	NR	NR	73	Laparoscopy or Open Surgery	NR	General	NR	117
Chen	2010	High	Cross sectional	China	Prospective	Systematic	One site	2008-2009	Adults	NR	NR	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	0.8	Spinal and General	NR	69
Chiang	2006	Moderate	Cross sectional	Taiwan	Retrospective	Exhaustive	One site	2002-2004	Adults	59.7	35	NR	Catarrhal, Perforated	68	17	0	0	100	Open Surgery	1.1	General	NR	390

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Chiang	2012	Moderate	Cohort	Taiwan	Prospective	Consecutive	One site	2008-2009	Adults	58.6	37.8	10	Unclear	NR	NR	NR	NR	100	Open Surgery	NR	General	Presence of gross or purulent discharge at the incision site with or without a positive bacterial culture	70
Cho	2014	Low	Cross sectional	Korea	Prospective	Consecutive	One site	2011-2012	Adults	53	38.7	18.8	Unclear	NR	NR	NR	NR		Laparoscopy	NR	General	According to CDC-NNIS diagnostic Criteria	101
Choudhary	2014	Moderate	Cross sectional	India	Prospective	Random	One site	2010-2013	Adults	67	NR	NR	Appendicular mass	0	0	0	0		NR	NR	NR	NR	92
Clyde	2008	High	Cross sectional	USA	Retrospective	Systematic	One site	2002-2007	Children, Adolescents, Adults, Elderly	52	35	NR	Catarrhal, Perforated, Unclear	77	14	0	0		Laparoscopy or Open Surgery	NR	NR	NR	1198
Coakley	2011	Low	Cohort	USA	Retrospective	Exhaustive	One site	2005-2010	Adults	47.3	28.7	NR	Catarrhal, Perforated, Suppurated, Gangrenous	38.3	1.2	47.1	9.8	100	Laparoscopy or Open Surgery	1.0	NR	According to CDC-NNIS diagnostic Criteria	728
Crandall	2009	High	Cross sectional	USA	Retrospective	Not clear	One site	2004-2005	Adults	54	32.5	NR	NR	NR	74	NR	NR		Laparoscopy or Open Surgery	0.9	General	NR	176
Dede	2008	Moderate	Cohort	Hungary	Prospective	Consecutive	One site	2005-2007	Children, Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	NR	273
Dhiman	2013	High	Cross sectional	USA	Retrospective	Not clear	Multisite	2003-2009	Adults	58	30.1	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	NR	1250
Dimitriou	2013	Moderate	Cohort	Germany	Retrospective	Consecutive	One site	2007-2010	Children, Adolescents, Adults, Elderly	53.5	34.9	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	1	NR	NR	404
Durkin	2015	Moderate	Cohort	USA	Retrospective	Consecutive	Multisite	2007-2012	Adults	NR	NR	NR	Unclear	NR	NR	NR	NR		Laparoscopy	NR	NR	NR	14763
Ein	2013	Moderate	Cross sectional	Canada	Retrospective	Consecutive	One site	1969-2003	Children	70	7	NR	Perforated	0	100	0	0	78.8	Open Surgery	NR	General	1.Wound infection=pus draining from between the stitches or staples 2.Intra-abdominal abscess=presence of fever, abdominal pain and or gastrointestinal dysfunction and confirmed by radiologic evidence of intra-abdominal fluid collection	496

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Fukuda	2016	Moderate	Cohort	Japan	Retrospective	Consecutive	Multisite	2007-2011	Children, Adolescents, Adults	54.4	64.5	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	1.3	General	NR	2074
Gandaglia	2014	Low	Cohort	USA	Prospective	Consecutive	Multisite	2005-2011	Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	NR	General	According to CDC-NNIS diagnostic Criteria	97780
Garcell	2016	Low	Cohort	Cuba	Prospective	Consecutive	One site	2013-2015	Children, Adolescents, Adults, Elderly	95.3	30.7	2.1	Unclear	NR	NR	NR	NR		Open Surgery	NR	NR	According to CDC-NNIS diagnostic Criteria	603
Ghnnam	2011	Moderate	Cross sectional	Saudi Arabia	Retrospective	Not clear	One site	2007-2010	Adults	63.4	49.0	NR	Perforated, Unclear	NR	38.1	NR	NR		NR	NR	NR	NR	63
Giesen	2017	Moderate	Cohort	Netherlands	Retrospective	Consecutive	Multisite	2014-2015	Children, Adults	54.3	31	NR	Catarrhal, Perforated, Suppurated, Gangrenous	48.2	17.3	23.2	11.3	100	Laparoscopy or Open Surgery	0.52	NR	According to CDC-NNIS diagnostic criteria	637
Giiti	2010	Moderate	Cross sectional	Tanzania	Prospective	Systematic	One site	2008-2009	Children, Adolescents, Adults, Elderly	44.7	27	NR	Catarrhal, Perforated, Suppurated, Mass	87.4	7.0	1.5	0		NR	NR	NR	NR	199
Golub	2016	Moderate	Cohort	Russia	Retrospective	Consecutive	Multisite	2012	Adolescents, Adults	NR	34.8	NR	Unclear	NR	NR	NR	NR	100	Open Surgery	NR	General	NR	332
Gross	2016	Moderate	Cross sectional	USA	Retrospective	Consecutive	Multisite	2012-2013	Children, Adolescents	60.1	NR	17.8	Perforated	0	100	0	0		Laparoscopy or Open Surgery	NT	General	NR	2585
Gurien	2016	Moderate	Cohort	USA	Retrospective	Consecutive	One site	2009-2012	Children, Adolescents	62	10.5	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	NR	General	Wound infections or intra abdominal abscesses	484
Hamzaoglu	2004	Low	Cross sectional	Turkey	Prospective	Consecutive	One site	1999-2001	Adults	57	46.7	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	NR	100
Harmon	2016	Low	Cohort	USA	Retrospective	Systematic	One site	2007-2012	Children, Adolescents, Adults, Elderly	47.4	39.7	NR	Non perforated	0	0	0	0		Laparoscopy or Open Surgery	NR	NR	According to CDC-NNIS diagnostic criteria	411
Helling	2017	Low	Cross sectional	USA	Retrospective	Systematic	One site	2009-2014	Adults	64.3	34.4	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	NR	NR	According to CDC-NNIS diagnostic criteria	611
Helmer	2002	Low	Cross sectional	USA	Retrospective	Systematic	One site	1998-1999	Children, Adolescents, Adults, Elderly	NR	NR	NR	Perforated, Non perforated	NR	19.4	NR	NR	100	NR	NR	NR	A surgical wound infection was defined as purulent drainage from the wound, cellulitis requiring antibiotics, or the opening of a closed wound. An intra-abdominal abscess was defined as an intraabdominal fluid collection that contained purulent material.	438
Hesami	2014	Low	Clinical trial	Iran	Prospective	Random	Unclear	2010-2011	Children, Adolescents, Adults	58.9	27	NR	Unclear	NR	NR	NR	NR	100	Open Surgery	NR	NR	1..wound unfection=Purulent discharge, redness, inflammation, and the need to reooen	90

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
																						the wound 2...intra-abdominal abscess=abdominal pain, fullness, fever and confirmed by ecography	
Hissain	2012	Moderate	Clinical trial	Saudi Arabia	Prospective	Consecutive	One site	2010-2011	Adults	NR	32.2	NR	Catarrhal	100	0	0	0	100	Open Surgery	NR	NR	1..SSI=Pus discharge from wound needing its opening and drainage 2..Intra-abdominal collection=fluid collection inside the peritoneal cavity confirmed by ultrasound or CT scan that required drainage	377
Horvath	2016	Moderate	Cross sectional	Germany	Retrospective	Consecutive	One site	2005-2013	Adults	47	28.6	NR	Perforated, phelgmonous	NR	52	NR	NR		Laparoscopy or Open Surgery	1.0	General	According to CDC-NNIS diagnostic Criteria	1516
Hughes	2013	Moderate	Cross sectional	United Kingdom	Retrospective	Systematic	One site	2009-2010	Adults	55.6	30	NR	Unclear, simple and complicated	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	NR	General	NR	266
Hung	2016	Moderate	Cross sectional	Vietnam	Prospective	Systematic	Multisite	2008-2010	Adults	45	41.6	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	1	General	NR	752
Inigo	2006	Low	Cohort	Spain	Prospective	Consecutive	One site	1998-2002	Adults	NR	NR	NR	Unclear	NR	NR	NR	NR		NR	0.7	NR	According to CDC-NNIS diagnostic Criteria	721
Iqbal	2015	Low	Clinical trial	Pakistan	Prospective	Random	One site	2011	Adolescents, Adults, Elderly	66.3	26	NR	Catarrhal	100	0	0	0	100	Open Surgery	NR	General	According to Southampton criteria. Southampton grade 2 and above was considered as surgical site infection.	166
Javadi	2017	Moderate	Clinical trial	Iran	Prospective	Random	One site	2016	Children, Adolescents, Adults	65	19.3	NR	Catarrhal, Suppurated, Gangrenous	NR	0	NR	NR		Open Surgery	0.5	General	NR	69
Jenkins	2016	Low	Cohort	USA	Prospective	Systematic	Multisite	2006-2011	Children, Adolescents, Adults, Elderly	51.3	40.1	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	According to CDC-NNIS diagnostic criteria	12410
Kang	2012	Moderate	Case control	Korea	Retrospective	Random	One site	2010-2012	Adults	54.4	31.7	NR	Catarrhal, Perforated, Suppurated, Gangrenous	NR	5.1	NR	NR	100	Laparoscopy	1.1	General	NR	217
Kapischke	2013	Low	Case control	Germany	Retrospective	Consecutive	One site	1999-2001	Children, Adolescents	47.8	11.5	NR	Catarrhal, Perforated	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	0.6	General	According to CDC-NNIS diagnostic criteria	159
Karam	2016	Moderate	Cross sectional	USA	Retrospective	Not clear	One site	2010-2015	Children	62	12	NR	Perforated, Gangrenous	NR	20.6	NR	6.2		Laparoscopy	NR	General	NR	625
Karam	2016	Moderate	Cross sectional	USA	Retrospective	Consecutive	One site	2010-2015	Children, Adolescents	63	NR	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy	1	General	NR	101
Kasatpibal	2005	Low	Cross sectional	Thailand	Prospective	Systematic	Multisite	2003-2004	Children, Adolescents, Adults, Elderly	26.6	37.2	NR	Unclear	NR	NR	NR	NR	24.1	NR	0.8	NR	According to CDC-NNIS diagnostic criteria	1487
Kasatpibal	2006	Moderate	Cohort	Thailand	Prospective	Not clear	Multisite	2003-2004	Children, Adolescents, Adults, Elderly	46.9	26	NR	Catarrhal	100	NR	NR	NR	92.2	Open Surgery	0.97	NR	According to CDC-NNIS diagnostic criteria	2139

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Kato	2008	Low	Cohort	Japan	Prospective	Systematic	One site	2004-2006	Children	NR	9.4	NR	Perforated, Non perforated 75%	NR	25	NR	NR	100	Open Surgery	NR	NR	NR	64
Kell	2003	Moderate	Cohort	Ireland	Prospective	Consecutive	Unclear	NR	Children, Adolescents, Adults, Elderly	75.2	20.7	NR	Unclear	NR	NR	NR	NR	100	Open Surgery	NR	General	Defined based on clinical and microbiological criteria	149
Khan	2007	Low	Cohort	United Kingdom	Prospective	Consecutive	One site	2006	Children, Adolescents, Adults, Elderly	47.0	24	NR	Catarrhal, Perforated	63.4	20.1	0	0	100	Laparoscopy or Open Surgery	0.9	General	According to CDC-NNIS diagnostic Criteria	134
Khan	2012	Moderate	Clinical trial	Pakistan	Prospective	Random	Multisite	2006-2009	Adults	69	33.3	NR	Unclear	NR	NR	NR	NR	100	Open Surgery	0.6	General	NR	100
Khan	2014	Moderate	Clinical trial	Pakistan	Prospective	Random	Multisite	2013-2014	Children, Adolescents, Adults, Elderly	56.7	24	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	Observation of pain, redness, tenderness and purulent discharge	270
Khiria	2011	Moderate	Cross sectional	India	Retrospective	Consecutive	One site	1999-2009	Adults	66	33.4	NR	Perforated, Gangrenous	NR	14.3	NR	5.2		Laparoscopy or Open Surgery	1.2	General	Any evidence of infection(erythema, purulent discharge, induration...) and requiring suture removal, antibiotic treatment, or evidence of dehiscence	497
Kilic	2016	Moderate	Cross sectional	Turkey	Retrospective	Consecutive	One site	2004-2010	Children	62.1	9.5	NR	Perforated	0	100	0	0	100	Open Surgery	NR	NR	According to CDC-NNIS diagnostic Criteria	110
Kim	2015	Low	Cross sectional	Korea	Retrospective	Systematic	One site	2008-2013	Children, Adolescents, Adults, Elderly	47.8	32.6	NR	Perforated, Suppurated, Gangrenous, Normal	6	13.8	64.5	7.1		Laparoscopy	0.7	NR	According to CDC-NNIS diagnostic criteria	2587
Kim	2011	Moderate	Cross sectional	USA	Prospective	Consecutive	One site	2005-2008	Elderly	48.1	73.4	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	According to CDC-NNIS diagnostic Criteria	3335
Kim	2016	Moderate	Cohort	Korea	Retrospective	Consecutive	One site	2005-2012	Adults	59	NR	NR	Perforated, Gangrenous	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	1.9	General	NR	207
Kiriakopoulos	2006	Moderate	Cross sectional	Greece	Retrospective	Consecutive	One site	2000-2004	Adults	73.8	42.3	NR	Perforated, Suppurated, Generalized peritonitis	0	61.9	9.5	0	100	Laparoscopy with Open Surgery	1.1	General	NRR	42
Kirshtein	2009	Moderate	Cross sectional	Israel	Retrospective	Consecutive	One site	2000-2007	Adults	31.9	70.1	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	0.7	General	NR	1435
Kiudelis	2013	Moderate	Cross sectional	Lithuania	Prospective	Consecutive	One site	2004-2009	Adults	46.3	32.3	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy	1.1	General	NR	152
Kleif	2017	Moderate	Cross sectional	Denmark	Retrospective	Not clear	Multisite	2012-2014	Adults	53	47	NR	Suppurated, Gangrenous	NR	NR	NR	NR	98	Laparoscopy or Open Surgery	NR	General	NR	1151
Koizumi	2014	Moderate	Cross sectional	Japan	Prospective	Consecutive	One site	2010	Adults	57.9	39.8	NR	Catarrhal, Perforated, Gangrenous, phelmong	6.4	6.4	NR	25 4		Laparoscopy or Open Surgery	0.9	General	NR	185
Kubota	2014	Low	Clinical trial	Japan	Prospective	Random	One site	2008-2012	Children	63.6	NR	NR	Unclear	NR	NR	NR	NR	100	Open Surgery	NR	General	According to CDC-NNIS diagnostic Criteria	10

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Kumamoto	2014	Low	Cohort	Japan	Prospective	Consecutive	One site	1997-2011	Adults	0	28	NR	Catarrhal, Gangrenous, Phlegmonous	21.8	NR	NR	33.4	100	Open Surgery	0.7	General	NR	124
Kumar	2016	Moderate	Cohort	Nepal	Prospective	Consecutive	One site	2015-2016	Adolescents, Adults	49	33.9	NR	Catarrhal, Perforated, Suppurated, Gangrenous, Normal	88.6	4.7	1.9	2.4		Laparoscopy or Open Surgery	0.7	General	According to CDC-NNIS diagnostic Criteria	212
Kumar	2008	Moderate	Cohort	Pakistan	Prospective	Consecutive	One site	1997-2000	Children, Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR	50	Laparoscopy or Open Surgery	0.7	NR	NR	100
Lacher	2012	Moderate	Cohort	USA	Prospective	Consecutive	One site	2009-2011	Children, Adolescents	64.1	10.9	22.4	Catarrhal, Perforated	71.8	19	NR	NR	100	Laparoscopy	0.7	General	NR	415
Le	2009	Moderate	Cross sectional	USA	Retrospective	Systematic	One site	1997-2007	Children, Adolescents, Adults, Elderly	52.1	31.8	NR	Catarrhal, Perforated, Gangrenous, Normal Appendix	92.9	2	0	2.2	86	Laparoscopy or Open Surgery	0.9	NR	According to CDC-NNIS diagnostic criteria	507
Lee	2009	Low	Clinical trial	USA	Prospective	Random	One site	2006-2008	Children, Adolescents, Adults, Elderly	64.2	34.2	NR	Catarrhal, Perforated, Suppurated, Gangrenous	46.8	26.6	16.5	10.1	100	Open Surgery	NR	NR	Any significant subcutaneous SSI necessitating wound opening or treatment with antibiotics. This also included any subject who was prescribed a separate course of antibiotics after discharge from the hospital.	109
Lee	2010	Moderate	Cross sectional	Taiwan	Prospective	Consecutive	One site	2006-2008	Children	58	11.1	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	2	General	NR	264
Lee	2010	Moderate	Cross sectional	Korea	Retrospective	Consecutive	One site	2008-2009	Adults	49.3	26.7	NR	Perforated, Suppurated	0	26.7	73.3	0		Laparoscopy	1.0	General	NR	75
Lee	2010	Moderate	Cohort	USA	Retrospective	Consecutive	Multisite	1998-2007	Children, Adolescents	61.5	11	NR	Perforated, Non perforated	NR	25.7	NR	NR		Laparoscopy or Open Surgery	NR	General	NR	2462
Lee	2011	Moderate	Cohort	USA	Retrospective	Systematic	Multisite	1998-2007	Children, Adolescents	61	11.6	NR	Perforated, Non perforated 70.8%	NR	29.2	NR	NR		Laparoscopy or Open Surgery	NR	NR	NR	7650
Lemieux	2008	Moderate	Cohort	Canada	Retrospective	Consecutive	One site	1997-2007	Adults	0	28.8	NR	Perforated	NR	NR	NR	NR		Laparoscopy with Open Surgery	0.8	NR	NR	45
Levy	2013	Moderate	Cohort	USA	Retrospective	Consecutive	One site	2010-2011	Children	NR	NR	NR	Catarrhal, Perforated, Suppurated, Gangrenous	56.4	32.7	4.2	6.7		Laparoscopy or Open Surgery	NR	NR	NSQIP criteria	312

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Li	2005	Moderate	Cohort	China	Prospective	Consecutive	One site	2002-2004	Children, Adolescents	71.3	7.9	NR	Catarrhal, Suppurated, Gangrenous	11.0	0	69.4	19.7	100	Laparoscopy or Open Surgery	0.65	General	NR	160
Li	2017	Moderate	Cohort	China	Retrospective	Consecutive	One site	2005-2016	Children	58.8	5.2	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	1	NR	Erythema, swelling and pus at the site of operation	398
Lim	2011	Low	Cohort	Korea	Retrospective	Consecutive	One site	2009-2011	Adults	47.8	50.8	NR	Perforated, Gangrenous	0	61.6	NR	18.3	100	Laparoscopy or Open Surgery	1.3	General	Any evidence of infection (e.g., erythema, purulent discharge, induration, etc) requiring suture removal, antibiotics or dehiscence.	60
Lima	2007	Moderate	Cross sectional	Spain	Retrospective	Consecutive	One site	2001-2006	Children, Adolescents, Adults, Elderly	NR	NR	NR	Catarrhal, Perforated, Suppurated, Gangrenous	53	2	26.3	9.7		NR	NR	NR	NR	300
Lin	2006	Moderate	Cross sectional	Taiwan	Retrospective	Consecutive	One site	2001-2003	Adults	57.6	37.5	NR	Perforated	NR	100	NR	NR	100	Laparoscopy or Open Surgery	1.4	Not described	NR	229
Litz	2016	Moderate	Cohort	USA	Retrospective	Consecutive	One site	2012-2015	Children, Adolescents	NR	11.4	17.7	Catarrhal, Perforated, Suppurated, Gangrenous, Interval, Normal	54	11.4	15.0	11.9		Laparoscopy	0.5	General	NR	413
Liu	2017	High	Cross sectional	China	Retrospective	Consecutive	Unclear	2015-2016	Children	53.6	6.6	NR	Catarrhal, Suppurated, Gangrenous	34.8	0	38.4	26.8		Laparoscopy or Open Surgery	1.0	General	NR	112
Mahmood	2016	Moderate	Clinical trial	Pakistan	Prospective	Random	One site	2012	Children, Adolescents, Adults	55.5	22.3	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	NR	General	Based on Wound Asepsis Score	200
Martinez	2012	Moderate	Cross sectional	Spain	Retrospective	Random	One site	2011	Adults	60	35.8	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	NR	75
Mbah	2006	Moderate	Cohort	Nigeria	Prospective	Consecutive	One site	2005	Children, Adolescents, Adults, Elderly	70	25	NR	Unclear	NR	NR	NR	NR		Open Surgery	NR	General	NR	136
Memon	2017	Moderate	Clinical trial	Pakistan	Prospective	Random	One site	2014-2016	Adults	53.3	26	NR	Catarrhal	100	0	0	0	100	Laparoscopy or Open Surgery	NR	NR	NR	227
Menezes	2008	Moderate	Cross sectional	Ireland	Retrospective	Consecutive	One site	2000-2006	Children, Adolescents	62.7	10.5	NR	Perforated, Gangrenous	0	81.4	0	17.8		Laparoscopy or Open Surgery	NR	NR	NR	118
Merenda	2013	Moderate	Cross sectional	Poland	Retrospective	Consecutive	One site	2006-2012	Children, Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	NR	317
Michailidou	2015	Low	Cross sectional	USA	Retrospective	Systematic	One site	2007-2013	Children, Adolescents	56.1	9.6	NR	Perforated, Negative appendectomy	NR	26.5	NR	NR		Laparoscopy or Open Surgery	1.3	NR	According to CDC-NNIS diagnostic criteria	264
Michailidou	2015	Moderate	Cross sectional	USA	Retrospective	Consecutive	Multisite	2012	Children, Adolescents	60.1	11.2	22.5	Catarrhal, Perforated, Suppurated, Gangrenous	NR	NR	NR	NR	100	Laparoscopy	0	General	NR	2812

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Mickovic	2015	Moderate	Cross sectional	Serbia	Retrospective	Not clear	One site	2010	Children	46.4	11.7	NR	Catarrhal, Perforated, Gangrenous	45.9	2.2	NR	19.5	100	Laparoscopy or Open Surgery	0.7	General	NR	218
Ming	2009	Moderate	Cross sectional	China	Retrospective	Consecutive	One site	2003-2005	Adults	57.2	48.8	NR	Perforated, Gangrenous, Appendicular abscess	NR	72.3	NR	38.2	100	Laparoscopy or Open Surgery	NR	General	NR	173
Mingmalairak	2009	Low	Clinical trial	Thailand	Prospective	Random	One site	2006-2007	Adults	61	29.5	0	Catarrhal, Perforated, Suppurated, Gangrenous	24	16	52	8.0	100	Open Surgery	43	General	NR	100
Miyano	2010	Low	Cohort	Japan	Prospective	Consecutive	One site	2004-2008	Children, Adolescents	56.5	7.7	NR	Peritonitis complicating appendicitis	0	100	0	0	100	Laparoscopy or Open Surgery	1.9	General	NR	23
Moazzez	2013	Low	Cohort	USA	Retrospective	Not clear	One site	2005-2009	Elderly	49.3	74	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	NR	2060
Monge Jodra	2003	Moderate	Cohort	Spain	Prospective	Consecutive	Multisite	1997-2000	Children, Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR		NR	NR	NR	According to CDC-NNIS diagnostic Criteria	5780
Mueck	2017	Moderate	Cohort	USA	Prospective	Consecutive	One site	2012-2015	Children, Adolescents	62.5	11.0	NR	Catarrhal, Suppurated	NR	NR	NR	NR	95	Laparoscopy with Open Surgery	NR	General	NR	697
Muensterer	2011	Low	Cohort	USA	Prospective	Consecutive	One site	2009-2010	Children, Adolescents	NR	11.2	NR	Catarrhal, Perforated	78.1	10.4	0	0	100	Laparoscopy	0.6	General	Infected umbilicus requiring antibiotics, or incision and drainage	183
Muensterer	2009	Moderate	Cross sectional	USA	Prospective	Consecutive	One site	2009	Children	61.3	11	NR	Perforated	NR	21.4	NR	NR		Laparoscopy	0.73	General	NR	75
Mustafa	2016	Low	Clinical trial	Pakistan	Prospective	Random	One site	2015-2016	Adults	52.9	26.6	NR	Perforated	0	100	0	0	100	Open Surgery	NR	NR	Redness around the wound, serosangious discharge, fever > 100°F	68
Nadler	2003	High	Cross sectional	USA	Retrospective	Systematic	One site	1998-2001	Children	62.2	9.35	NR	Perforated	NR	100	NR	NR	100	Open Surgery	NR	General	NR	94
Nataraja	2010	Moderate	Cohort	United Kingdom	Retrospective	Consecutive	One site	2008-2010	Children, Adolescents	59.1	11	NR	Catarrhal, Perforated, Suppurated	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	NR	191
Nataraja	2012	Moderate	Case control	United Kingdom	Retrospective	Consecutive	Multisite	2003-2010	Children, Adolescents	58.2	11.3	NR	Catarrhal, Perforated, Suppurated, Gangrenous	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	Post op intra abdominal abcess	1205
Obayashi	2015	Moderate	Cross sectional	Japan	Retrospective	Consecutive	One site	2006-2014	Children, Adolescents	60	11	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	NR	485
Obinwa	2015	Moderate	Cohort	Ireland	Retrospective	Consecutive	One site	1995-2008	Children	54.5	9.6	NR	Catarrhal, Perforated, Suppurated, Gangrenous	62.7	NR	NR	4.2	100	NR	NR	NR	NR	1037
Ohene	2006	Moderate	Cross sectional	Ghana	Prospective	Consecutive	One site	1998-2004	Adults	63.9	32.4	NR	Unclear	NR	NR	NR	NR	100	Open Surgery	NR	General	NR	638
Okkyung	2002	Moderate	Clinical trial	Korea	Prospective	Random	One site	2002	Children, Adolescents, Adults, Elderly	54.7	30.5	NR	Catarrhal, Suppurated, Gangrenous	NR	0	50	27.3	100	Open Surgery	NR	General	NR	84

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Onieva	2017	Moderate	Cross sectional	Spain	Retrospective	Consecutive	One site	2012-2014	Children, Adolescents, Adults, Elderly	53.7	32	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	NR	294
Page	2010	Moderate	Cross sectional	USA	Retrospective	Exhaustive	Multisite	2008	Adults	51.4	39.2	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	0.94	General	NR	17199
Palesty	2004	Moderate	Cross sectional	USA	Retrospective	Consecutive	One site	2000-2002	Adults	47	25.2	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy	1.2	General	NR	50
Pandit	2016	High	Cohort	Nepal	Retrospective	Consecutive	Multisite	2009-2014	Children, Adolescents, Adults	51	24.3	NR	Perforated, Suppurated	NR	2.6	97.4	0		Open Surgery	0.6	Spinal and General	NR	101
Parcells	2009	Low	Cohort	USA	Retrospective	Systematic	One site	1997-2007	Adults	NR	39.3	NR	Perforated, Not perforated	NR	33.1	NR	NR		Laparoscopy or Open Surgery	NR	NR	According to CDC-NNIS diagnostic criteria	1063
Park	2017	Low	Cohort	Korea	Prospective	Systematic	One site	2012-2014	Adults	53.3	37.45	NR	Perforated, Gangrenous	NR	38.7	NR	45.9		Laparoscopy	1.1	General	According to CDC-NNIS diagnostic Criteria	1343
Park	2018	Moderate	Cohort	Korea	Retrospective	Consecutive	One site	2009-2013	Adults	53.7	34.2	NR	Perforated	NR	13.2	NR	NR		Laparoscopy with Open Surgery	1.1	General	NR	986
Pascual	2017	Moderate	Cohort	Spain	Prospective	Consecutive	One site	2013-2017	Adults	49	41	NR	Unclear	NR	NR	NR	NR		Laparoscopy	0.1	General	NR	100
Patel	2003	High	Cohort	Kenya	Retrospective	Consecutive	One site	1996-2002	Children, Adolescents, Adults	30.2	30.6	NR	Catarrhal, Suppurated, Gangrenous, Carcinoid tumor	94.3	0	0.9	2.8	100	Laparoscopy with Open Surgery	1.5	General	NR	106
Pearcy	2017	Moderate	Case control	USA	Retrospective	Random	Multisite	2010-2014	Adults	54	36	NR	Unclear	NR	NR	NR	NR		NR	1.1	NR	NR	2903
Pishori	2003	Low	Cross sectional	Pakistan	Prospective	Systematic	One site	1997-1999	Children, Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR		NR	NR	NR	According to CDC-NNIS diagnostic criteria	3304
Putnam	2016	Moderate	Cross sectional	USA	Prospective	Consecutive	One site	2012-2015	Children, Adolescents	61	9.4	NR	Perforated, Suppurated, Gangrenous	0	100	0	0	100	Laparoscopy or Open Surgery	0.9	General	NR	410
Qahtani	2014	Moderate	Cohort	Saudi Arabia	Prospective	Random	One site	2012	Adolescents, Adults	68	23.6	NR	Catarrhal, Perforated, Gangrenous	9.6	19.9	NR	22.4	100	Open Surgery	1.5	General	NR	91
Quezada	2015	Moderate	Cohort	Chile	Retrospective	Consecutive	One site	2003-2013	Adults	43	39	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	2.2	NR	NR	227
Raakow	2014	High	Cohort	Germany	Prospective	Not clear	One site	2009-2013	Adolescents, Adults	28.8	27.2	NR	Catarrhal, Suppurated, Gangrenous	12.8	0	16	4		Laparoscopy	0.8	General	NR	156
Rafiq	2015	Low	Clinical trial	Pakistan	Prospective	Random	One site	2012-2014	Adolescents, Adults, Elderly	48.5	22.6	0	Unclear	NR	NR	NR	NR	100	Open Surgery	0.7	General	NR	390
Rajabi-Mashhadi	2012	Moderate	Clinical trial	Iran	Prospective	Random	One site	2006-2007	Adults	62.5	26.2	NR	Unclear, Non perforated	NR	NA	NR	NR	100	Open Surgery	NR	NR	NR	291

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Reinisch	2017	Moderate	Cross sectional	Germany	Retrospective	Consecutive	One site	2008-2015	Adults	56	32	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy with Open Surgery	NR	General	NR	680
Rios	2004	High	Cross sectional	Peru	Not reported/Unclear	Consecutive	One site	2001-2002	Children, Adolescents, Adults, Elderly	NR	30.6	NR	Catarrhal, Perforated, Suppurated, Gangrenous	15.38	16.35	44.23	24.04	100	NR	0.98	Unclear	NR	104
Romano	2014	Moderate	Cross sectional	USA	Retrospective	Systematic	One site	2010-2012	Adults	66	35.7	NR	Gangrenous	NR	NR	NR	9.7	86	Laparoscopy	NR	General	NR	372
Romel Hilaire	2014	Moderate	Cross sectional	Cuba	Retrospective	Consecutive	One site	2007-2009	Adults	100	NR	NR	Suppurated	0	0	100	0		Laparoscopy or Open Surgery	NR	NR	NR	720
Romeo	2009	Moderate	Cross sectional	Colombia	Retrospective	Consecutive	One site	1997	Children, Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR		Laparoscopy	NR	NR	NR	310
Romy	2008	Low	Cross sectional	Switzerland	Prospective	Systematic	Multisite	1998-2004	Children, Adolescents, Adults, Elderly	53.9	32.7	NR	Unclear	NR	NR	NR	NR	59.5	Laparoscopy or Open Surgery	NR	NR	According to CDC-NNIS diagnostic criteria	2468
Rooh-ul-Muqim	2010	Moderate	Cohort	Pakistan	Prospective	Consecutive	One site	2008-2009	Adolescents, Adults, Elderly	48.5	24	NR	Catarrhal, Perforated, Suppurated, Gangrenous	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	0.5	General	NR	165
Rossem	2015	Moderate	Cohort	Netherlands	Prospective	Consecutive	Multisite	2014	Adults	47.5	44	NR	Perforated, Gangrenous	NR	68	10.4	21.7	100	Laparoscopy with Open Surgery	0.9	General	NR	415
Rossem	2016	Low	Cohort	Netherlands	Prospective	Not clear	Multisite	2014	Children, Adolescents, Adults	46.2	28.0	NR	Unclear	NR	NR	NR	NR		Laparoscopy	0.8	General	Superficial surgical site infection: recorded when administration of antibiotics, opening of the incision or both was necessary. An intra-abdominal abscess was defined as a postoperative intra-abdominal fluid collection diagnosed by cross-sectional imaging for which administration of antibiotics or a radiological or surgical intervention was needed.	1995
Rotermann	2004	Moderate	Cohort	Canada	Retrospective	Consecutive	Multisite	1997-2000	Children, Adolescents, Adults, Elderly	55.2	NR	NR	Unclear	NR	NR	NR	NR		NR	NR	NR	According to CDC-NNIS diagnostic criteria	80867

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Saar	2016	Low	Cross sectional	Estonia	Prospective	Consecutive	One site	2013-2014	Adults	48.9	35.4	NR	Perforated, Gangrenous	NR	15.4	NR	59.4	95.1	Laparoscopy or Open Surgery	0.7	General	According to CDC-NNIS diagnostic Criteria	266
Saber	2010	Moderate	Clinical trial	USA	Prospective	Consecutive	One site	2008-2009	Adults	42.3	33	NR	Catarrhal	100	0	0	0		Laparoscopy	0.8	NR	NR	26
Sadraei-Mosavi	2017	Moderate	Clinical trial	Iran	Prospective	Random	One site	2013-2014	Adults	NR	28.4	NR	Catarrhal	100	0	0	0	100	Open Surgery	NR	NR	SSI=pus discharge from wound, redness, tenderness, edema	152
Saha	2010	Moderate	Cohort	Bangladesh	Prospective	Consecutive	One site	2007-2008	Children	NR	NR	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	NR	NR	NR	60
Sahm	2010	Moderate	Cross sectional	Germany	Prospective	Systematic	One site	1998-2006	Adults	54	39	NR	Catarrhal, Perforated, Gangrenous	50.7	17.0	NR	6.9	100	Laparoscopy or Open Surgery	1.0	General	NR	1710
Sahm	2015	Moderate	Cross sectional	Germany	Prospective	Exhaustive	Multisite	1988-2009	Children, Adolescents, Adults, Elderly	43	31	NR	Perforated, Non Perforated 91.5	NR	8.5	NR	NR		Laparoscopy or Open Surgery	NR	NR	NR	12570
Salö	2016	High	Cohort	Sweden	Retrospective	Consecutive	One site	2006-2014	Children	55.6	10.4	NR	Perforated, Gangrenous, Phlegmonous	NR	7.3	NR	11.6	100	Laparoscopy	0.94	NR	NR	259
Sanchez-Santana	2017	Low	Cohort	Spain	Prospective	Consecutive	One site	2007-2015	Adults	55.2	32.9	2.6	Unclear	NR	NR	NR	NR	71.3	Laparoscopy or Open Surgery	NR	NR	According to CDC-NNIS diagnostic criteria	930
Sauvain	2016	Moderate	Cohort	Switzerland	Retrospective	Consecutive	Multisite	2007-2011	Adults	53.2	34	NR	Catarrhal, Perforated, Suppurated, Gangrenous	NR	19	NR	NR		Laparoscopy or Open Surgery	NR	NR	NR	2559
Scarborough	2012	Low	Cross sectional	USA	Retrospective	Systematic	Multisite	2005-2009	Children, Adolescents, Adults, Elderly	52	38.9	NR	Perforated, Non rupture	NR	11.2	NR	NR		Laparoscopy or Open Surgery	0.9	NR	According to CDC-NNIS diagnostic criteria	39122
Scarless	2013	Moderate	Clinical trial	Scotland	Prospective	Random	One site	2011	Adults	53	32	NR	Unclear	NR	NR	NR	NR		Laparoscopy	1.4	General	NR	38
Seifarth	2016	Moderate	Cohort	USA	Retrospective	Consecutive	Multisite	2007-2012	Children, Adults	60	12	NR	Catarrhal	100	0	0	0		Laparoscopy	NR	General	NR	1283
Seifarth	2016	Low	Cohort	USA	Retrospective	Consecutive	Multisite	2007-2012	Children, Adolescents, Adults	60	12	NR	Perforated, Suppurated, Gangrenous	100	0	0	0		Laparoscopy	NR	NR	NR	1283
Senekjan	2013	Moderate	Cohort	USA	Retrospective	Consecutive	Multisite	2005-2009	Adolescents	56.5	40.3	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	0.9	NR	1) SSI (superficial and deep incisional)...infection within 30 days of operation and involved skin, subcutaneous tissue or deep soft tissue 2) Organ space infection (OSI)...infection within 30 days of operation when the infection appeared to be related to the operation and involved any part of the anatomy other than the incision	61830

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Seo	2002	Moderate	Cross sectional	Korea	Retrospective	Systematic	One site	2000	Adults	0	NR	NR	Catarrhal, Perforated, Suppurated, Gangrenous	14.7	15.6	49.5	20.2		NR	NR	NR	NR	129
Sesia	2011	Moderate	Cohort	Germany	Prospective	Consecutive	One site	2006-2008	Children, Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	1	NR	NR	265
Shaikg	2011	Moderate	Cross sectional	Pakistan	Prospective	Consecutive	One site	2007-2009	Adults	51.4	29	NR	Catarrhal, Perforated, Suppurated	82.86	8.67	1.51	0		Open Surgery	NR	General	NR	461
Shang	2017	Moderate	Cohort	China	Retrospective	Consecutive	One site	2013-2016	Adults	54.3	2.2	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	Erythema, swelling and purulent discharge	398
Shimizu	2014	Low	Cross sectional	Japan	Retrospective	Not clear	One site	2000-2012	Adults	44	35	NR	Catarrhal, Gangrenous	19	NR	NR	37		Open Surgery	NR	General	According to CDC-NNIS diagnostic Criteria	300
Shindholimath	2011	Moderate	Cross sectional	India	Retrospective	Consecutive	One site	2007-2009	Adults	68.4	NR	NR	Perforated, Suppurated, Gangrenous, Appendicular abscess	0	36.8	5.3	26.3	100	Laparoscopy	1.6	General	NR	19
Siam	2017	Moderate	Cohort	Israel	Retrospective	Consecutive	One site	2008-2015	Adults	62.8	34.1	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy with Open Surgery	0.7	General	NR	1649
Silva	2008	Moderate	Cohort	Chile	Prospective	Random	One site	2005-2006	Adults	58.9	NR	NR	Unclear	NR	NR	NR	NR		Open Surgery	NR	General	NR	433
Singh	2017	Moderate	Clinical trial	India	Prospective	Consecutive	One site	2014-2015	Adults	43.2	28.7	11.4	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	NR	44
Siribumrungwong	2013	Low	Cohort	Thailand	Retrospective	Systematic	One site	2006	Adults	65	37	NR	Perforated	NR	100	NR	NR	100	Open Surgery	1.2	NR	According to CDC-NNIS diagnostic criteria	128
Sivrikoz	2015	Moderate	Cohort	USA	Retrospective	Exhaustive	Multisite	2004-2010	Children, Adolescents, Adults, Elderly	52.1	48	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	0.9	NR	NR	4844
Soll	2016	Low	Cohort	Switzerland	Retrospective	Consecutive	One site	2009-2013	Children, Adolescents, Adults, Elderly	54.7	26.5	NR	Catarrhal, Perforated, Suppurated, Gangrenous	NR	46	NR	NR	100	Laparoscopy	1	NR	According to CDC-NNIS diagnostic Criteria	813
Sozutek	2013	Low	Clinical trial	Turkey	Retrospective	Consecutive	One site	2010-2011	Adults	44	30.9	NR	Catarrhal, Perforated	57	20	NR	NR		Laparoscopy or Open Surgery	0.5	General	NR	75
Srishewachart	2016	Moderate	Cross sectional	Thailand	Retrospective	Consecutive	One site	2012-2014	Children, Adolescents, Adults, Elderly	52	43.7	7.4	Unclear	NR	NR	NR	NR		Open Surgery	NR	General	NR	450
Staszewicz	2014	Moderate	Cohort	Switzerland	Prospective	Systematic	Multisite	1998-2011	Children, Adolescents, Adults, Elderly	54	34.2	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	1	NR	According to CDC-NNIS diagnostic Criteria	6383
Suttie	2004	High	Case control	Scotland	Retrospective	Not clear	One site	1997-2002	Children	50	10.8	NR	Perforated, Suppurated, Gangrenous	0	2	50	14		Laparoscopy	1	General	NR	60
Svensson	2016	Moderate	Cohort	Sweden	Prospective	Consecutive	One site	2006-2010	Children, Adolescents	60.2	11.3	NR	Catarrhal, Perforated, Suppurated, Gangrenous, not described	6.6	21.8	44.6	29.8	100	Laparoscopy or Open Surgery	0.7	General	NR	1745

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Taguchi	2015	Moderate	Clinical trial	Japan	Prospective	Random	One site	2009-2014	Adults	65.43	47.5	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	1.2	General	According to CDC-NNIS diagnostic Criteria	81
Tanaka	2007	Moderate	Cohort	Japan	Retrospective	Consecutive	One site	2002-2005	Children	54.3	2.2	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	NR	95
Tijerina	2010	Low	Clinical trial	Mexico	Prospective	Exhaustive	One site	2005-2007	Children, Adolescents, Adults, Elderly	46	NR	NR	Unclear	NR	NR	NR	NR	100	Open Surgery	NR	General	NR	529
Toro Pablo	2017	Moderate	Cohort	Spain	Retrospective	Consecutive	One site	2012-2016	Children, Adolescents, Adults	NR	26	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	NR	600
Towfigh	2011	Low	Clinical trial	USA	Prospective	Random	One site	2007-2009	Adults	77.3	33	NR	Perforated	0	100	0	0		Open Surgery	NR	NR	NR	75
Troillet	2017	Low	Cohort	Switzerland	Prospective	Consecutive	Multisite	2011-2015	Children, Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR	92.2	Laparoscopy or Open Surgery	NR	NR	According to CDC-NNIS diagnostic Criteria	15439
Tsioplis	2013	Moderate	Cross sectional	Germany	Retrospective	Consecutive	One site	1999-2008	Children, Adolescents, Adults, Elderly	51	23	9	Catarrhal, Perforated, Suppurated, Gangrenous	19	NR	50	25	75	Laparoscopy or Open Surgery	NR	Not reported	NR	1439
Vahdad	2016	Moderate	Cross sectional	Germany	Retrospective	Systematic	One site	2008-2012	Children, Adolescents	52.4	NR	NR	Catarrhal, Perforated, Phelgmonous in 43% of cases	48.2	8.7	NR	NR		Laparoscopy	1.1	NR	NR	309
Van Rossem	2016	High	Cohort	Netherlands	Prospective	Consecutive	Multisite	2014	Adults	49.7	39.0	NR	Catarrhal, Perforated, Gangrenous	73.7	11.0	NR	9.9	96.6	Laparoscopy or Open Surgery	0.72	NR	NR	1378
Van Rossem	2014	High	Cohort	Netherlands	Retrospective	Consecutive	Multisite	2004-2010	Adults	53.2	49	NR	Perforated	0	100	0	0	100	Laparoscopy or Open Surgery	0.85	NR	NR	267
Wang-Chan	2017	Low	Cross sectional	Switzerland	Retrospective	Consecutive	One site	2013-2014	Children, Adolescents, Adults, Elderly	55.3	47	13.8	Unclear	NR	NR	NR	NR		Laparoscopy with Open Surgery	NR	General	According to CDC-NNIS diagnostic Criteria	246
Watanabe	2011	Low	Cross sectional	Japan	Prospective	Consecutive	Multisite	2005-2006	Adults	59.4	63.8	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	According to CDC-NNIS diagnostic Criteria	903
Willis	2016	Moderate	Cohort	USA	Prospective	Consecutive	One site	2013-2014	Children, Adolescents	58.5	8.8	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	NR	General	NR	313
Wong	2015	High	Cohort	Peru	Prospective	Not clear	Multisite	2005-2010	Adults	NR	NR	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	NR	352
Wu	2006	Low	Cross sectional	Taiwan	Retrospective	Not clear	One site	2001-2005	Adults	75	42	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	0.95	General	NR	1795

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Wu	2011	Moderate	Cohort	Taiwan	Retrospective	Exhaustive	Multisite	2004-2009	Children, Adolescents, Adults, Elderly	58.1	36.4	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	NR	1366
Wu	2017	Moderate	Cross sectional	China	Retrospective	Consecutive	One site	2014-2016	Elderly	59	71	NR	Perforated, Suppurated, Gangrenous	0	61.7	10	28.7	100	Laparoscopy or Open Surgery	1	General	NR	115
Wu	2014	Moderate	Clinical trial	China	Prospective	Random	One site	2011-2013	Children, Adolescents	60	8.5	NR	Catarrhal	100	0	0	0		Laparoscopy	1	General	NR	60
Yaghoubian	2010	High	Cross sectional	USA	Retrospective	Exhaustive	Multisite	1998-2007	Children, Adolescents, Adults, Elderly	61.5	29.2	NR	Catarrhal, Perforated	73.4	26.6	0	0		Laparoscopy or Open Surgery	NR	NR	NR	4325
Yagnik	2010	Moderate	Cross sectional	India	Retrospective	Consecutive	One site	2007-2009	Children, Adolescents, Adults	32.5	23.41	NR	Catarrhal	100	0	0	0	100	Laparoscopy or Open Surgery	1	General	NR	151
Yousef	2017	Moderate	Cohort	Canada	Prospective	Consecutive	One site	2015-2016	Children, Adolescents	63.1	9.3	NR	Perforated	0	100	0	0	100	Laparoscopy	NR	General	NR	122
Zhang	2015	Moderate	Clinical trial	China	Prospective	Random	One site	2012-2013	Adults	47.2	30.8	NR	Unclear	10.2	7.4	54.6	9.3		Laparoscopy	0.9	General	NR	108

NR: not reported

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Global incidence of surgical-site infection after appendectomy: a systematic review and meta-analysis

Celestin Danwang[1,2], Jean Joel Bigna[3*], Joel Noutakdie Tochie[4], Aime Mbonda[5], Clarence Mvalo Mbanga[6], Rolf Nyah Tuku Nzalie[7], Marc Leroy Guifo[1], Arthur Essomba[1]

1. Department of Surgery and Specialties, Faculty of Medicine and Biomedical Sciences, University of Yaoundé I, Yaoundé, Cameroon.
2. School of Public Health, Université Libre de Bruxelles, Brussels, Belgium.
3. Department of Epidemiology and Public Health, Centre Pasteur of Cameroon, Yaoundé, Cameroon.
4. Department of Anesthesiology and Critical Care Medicine, Faculty of Medicine and Biomedical Sciences, University of Yaoundé I, Yaoundé, Cameroon.
5. Department of General Medicine, Djohong District Hospital, Djohong, Cameroon.
6. Department of General Medicine, Mankon Sub-Divisional Hospital, Bamenda, Cameroon.
7. Department of General Medicine, Ngong District Hospital, Ngong, Cameroon.

*Corresponding author: Dr. Jean Joel Bigna, MD, MPH

Department of Epidemiology and Public Health, Centre Pasteur of Cameroon, Yaoundé, Cameroon. E-Mail: bignarimjj@yahoo.fr

E-mail addresses:

CD: danram07@yahoo.fr; JJB: bignarimjj@yahoo.fr; JNT: joeltochie@gmail.com; AM: aimembonda@yahoo.fr; CMM: mbangaclarence@gmail.com; RNN: nzalierolf@yahoo.com; GML: marcleroyguifo@gmail.com; AE: artgessomba@gmail.com

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Abstract

Background: Although surgical-site infection (SSI) is one of the most studied healthcare-associated infections, the global burden of SSI after appendectomy remains unknown.

Objectives: We estimated the incidence of SSI after appendectomy at global and regional levels.

Design: Systematic review and meta-analysis.

Participants: Patients with appendectomy.

Data sources: EMBASE, PubMed, and Web of Science were searched to identify observational studies and clinical trials, published between January 1, 2000 and December 30, 2018 and reporting on the incidence of the SSI after an appendectomy; with no language restriction. A random-effect models meta-analysis served to obtain the pooled incidence of SSI after 100 surgical procedures in patients with appendectomy.

Results: In total, 226 studies (729,434 participants from 49 countries) were included in the meta-analysis. Concerning the methodological quality, 59 (26.1%) studies had a low risk, 147 (65.0%) a moderate risk, and 20 (8.8%) a high risk of bias. We found an overall incidence of SSIs of 7.0 per 100 surgical procedures (95% prediction interval: 1.0-17.6) for appendectomy varying from 0 to 37.4 per 100 surgical procedures. Subgroup analysis for identifying sources of heterogeneity showed that the incidence varied from 5.8 in Europe to 12.6 per 100 surgical procedures in Africa, $p < 0.0001$. The incidence of SSI after appendectomy increased when the level of income decreased; from 6.2 in high-income countries to 11.1 per 100 surgical procedures in low-income countries ($p = 0.015$). Open appendectomy (11.0 per 100 surgical procedures) was found to have a higher incidence of SSI compared to laparoscopy (4.6 per 100 surgical procedures), $p = 0.0002$.

Conclusion: This study suggests a high burden of SSIs after appendectomy in some regions (especially Africa) and in low-income countries. Strategies are needed to implement and vulgarize WHO guidelines to decrease the burden of SSI after appendectomy in these regions.

Registration: PROSPERO, CRD42017075257.

Keywords:

Surgical wound infection; Global Health; Hospital infections; Cross infection; Healthcare associated infection

Strengths and limitations of this study

- This meta-analysis is the first to summarize the global incidence of SSIs after appendectomy.
- We investigated WHO regions, level of income, and surgical procedure as sources of heterogeneity.
- We were not able to investigate all sources of heterogeneity because of missing information in the original studies.
- There were few studies from low income countries and from Africa.

Introduction

Defined as an acute inflammation of the vermiform appendix,[1] evidence abounds that acute appendicitis is the most common abdominal surgical emergency,[2] with an incidence of almost 100 per 100,000 person-years reported in Australia, Europe and North America.[3 4] Evidence suggests appendectomy, a surgical remove of the vermiform appendix as first-line treatment for acute appendicitis, although antibiotic therapy may be efficacious for a selected group of patients with uncomplicated acute appendicitis.[5-7] Appendectomy is a relatively safe surgical intervention with a case fatality rate of 2.1 - 2.4 per 1000 patients as reported in studies conducted in Europe.[8 9]

Innovations in appendectomy, especially with the advent of minimally invasive or laparoscopic surgery in 1983,[10] which has replaced the traditional open appendectomy in most of high-income countries, has led to a drastic reduction in the morbidity and mortality related to appendectomy.[11-13] Laparoscopic appendectomy is now recognized as the gold standard surgical approach for uncomplicated acute appendicitis owing to its merits over open surgery; due to less postoperative pain, reduced postoperative ileus, shorter hospital stay, rapid postoperative recovery, and better aesthetic scars.[14-19]

However, regardless of the surgical technique (laparoscopic or open surgery), appendectomy remains a sceptical surgical intervention associated with a substantial risk of surgical-site infections (SSIs). SSIs after appendectomy are postoperative nosocomial infections affecting the incision site, deep tissues, organs at the operative site within 30 days after the surgical procedure.[20-22] SSI following appendectomy is a serious post-operative medical concern that increases the financial burden for both healthcare systems and patient, and also have a negative impact on the patients' health related quality of life.[23-28]

SSI is both the most frequently studied and the leading healthcare-associated infections reported hospital-wide in low- and middle-income countries.[29] A recently published prospective international multicentre cohort study suggested a high burden of SSIs after any gastrointestinal surgery in low-income countries compared to high-income countries.[30] Actually, there is no global systematic review with meta-analysis reporting the burden of SSI after appendectomy or comparing the burden between regions and between country level of income. It would be interesting to have such accurately estimated data to construct efficient strategies to curb globally the burden of SSIs after appendectomy. To fill this gap, the current systematic review and meta-analysis aimed at summarizing contemporary data on the occurrence of SSIs after appendectomy.

Methods

Design

This systematic review and meta-analysis was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number CRD42017075257. The protocol has been published in a peer-review journal.[31] This review is reported according to MOOSE and PRISMA guidelines.[32 33]

Eligibility criteria

We considered observational studies (cross-sectional, case-control, and cohort) and clinical trials of patients with appendectomy. Outcome of interest was incidence of SSI of enough data (number of cases of SSI and sample size) to compute this estimate. We excluded letters, reviews, commentaries and editorials, and studies lacking key data and/or explicit method description as well as studies in which relevant data on SSIs after appendectomy was impossible to extract even after contacting the corresponding author.

Search strategy

We searched EMBASE, PubMed, and Web of Science (Web of Science Core Collection, Current Contents Connect, KCI-Korean Journal Database, SciELO Citation Index, Russian Science Citation Index) to identify observational studies, published between January 1, 2000 and December 30, 2018. No language restriction was applied. The initial search strategy was designed for EMBASE and was adapted for the use in other databases. The search strategy as illustrated in the Supplementary Table 1 and in the study protocol,[31] was based on the combination of relevant text words and medical subject headings related to SSIs. Moreover, the references of all relevant articles found were scrutinized for potential additional data sources. When a full text was not available, it was requested via the corresponding author by email. For duplicates or studies published in more than one report, the one reporting the largest sample size was considered.

Study selection

Two reviewers (CD and AM) independently screened the titles and abstract of articles for eligibility. Full texts of potentially eligible articles were retrieved and screened for final inclusion. Disagreements between the two reviewers were solved by discussion and when a consensus was not reached, a third reviewer (JNT) resolved discrepancies. Studies in other languages than French, English, and Spanish were translated using Google Translate.

Data extraction and management

A standardized and pretested data extraction form was used by five reviewers (CD, JNT, AM, RNZ, CMM) to independently extract data from individual studies. A sixth reviewer (JJB) independently extracted data for accuracy. The last name of the first author, year of publication, country, study design, age groups, sample size, mean or median age, proportion of males, specific conditions of the study population, the surgical method (open surgery or laparoscopy), and incidence of SSIs after appendectomy in the study population (or enough data to compute this estimate) were extracted.

To assess the methodological quality of each study, two reviewers (CD and CMM) used an adapted version of the tool of bias assessment for prevalence studies developed by Hoy and colleagues.[34]

Data synthesis and analysis

A meta-analysis was used to summarize data concerning incidence of SSIs, by pooling together data of studies reporting the incidence of SSIs. Study-specific estimates were then pooled through a Dersimonian and Laird random-effects meta-analysis model to obtain an overall summary estimate of the incidence across studies, after stabilizing the variance of individual studies using the Freeman-Tukey double arc-sine transformation.[35] Incidence was expressed by 100 surgical procedures with their 95% confidence interval and 95% prediction interval. Heterogeneity was evaluated by the χ^2 test on Q statistic which is quantified by I^2 values,[36] assuming that I^2 values of 25%, 50% and 75% represent low, medium and high heterogeneity respectively.[37] Where substantial heterogeneity ($I^2 > 50\%$) was detected, a subgroup analysis was performed to detect its possible sources using the following grouping variables: type of surgery (laparoscopy or open), World Health Organization regions, and country level of income. A p value <0.05 was indicative of significant difference. The meta-regression analysis was performed to estimate the explained heterogeneity of each covariate included in the subgroup analysis. Inter-rater agreement for study inclusion was assessed using Cohen's κ coefficient.[38] Funnel plots analysis and Egger's test ($p < 0.10$) were performed to detect the presence of publication bias.[39] Since we believe that the incidence estimates of interest would likely be published even if substantially different from previously reported estimates, we have not reported adjusted incidence estimate in the case of publication bias. Data were analysed using the '*meta*' package in R, version 3.6.1.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination of our research.

Results

Study selection and characteristics

Overall, 619 records were initially identified. After removal of duplicates, screening of study titles, abstracts, and full texts; 226 studies including 729,434 patients were finally retained for meta-analysis **(**Supplementary Figure 1**)**. The full list of included studies is in the Appendix. Concerning the methodological quality, 59 (26.1%) studies had a low risk, 147 (65.0%) a moderate risk and 20 (8.8%) a high risk of bias. Supplementary Table 2 presents characteristics of included studies. Among the included studies, 154 were done in high-income, 36 upper-middle, 27 lower-middle, and nine in low-income countries. Overall, most of studies were from Europe (n = 68) and Americas (n = 67). SSIs were defined according to Center of Disease Control and Prevention criteria in 50 studies while 25 studies used other criteria. The definition of SSIs was not clearly given in 151 studies. Individuals characteristics of included studies are in the Supplementary Table 3.

Overall prevalence

The overall incidence of SSI after appendectomy was 7.0 per 100 surgical procedures (95% prediction interval: 1.0-17.6) varying from 0% to 37.4% with substantial heterogeneity and publication bias (Supplementary Figure 2). The sensitive analysis including only studies with low risk of bias yielded a very close incidence to crude analysis (Table 1).

Sources of heterogeneity

According to country level of income (Figure 1), the incidence of SSI after appendectomy increased when the level of income decreased; from 6.2 in high income countries to 11.1 per 100 surgical procedures in low income countries ($p = 0.015$) (Table 1).

The incidence varied widely across WHO regions (Figure 2). The incidence varied from 5.8 in Europe to 12.6 per 100 surgical procedures in Africa, $p < 0.0001$ (Table 1). Two regions (Europe and Americas) had an incidence < 6 per 100 surgical procedures, three an incidence between 6-10 per 100 procedures (South-East Asia, Eastern Mediterranean, and Western Pacific), and one an incidence > 10 per 100 procedures (Africa) (Table 1). The incidence also varied widely in different regions. The incidence varied from 0.2 to 32.0 in Africa, from 1.9 to 37.4 in Western Pacific, from 1.3 to 33.8 in Eastern Mediterranean, from 1.2 to 25.8 in South-East Asia, from 0.1 to 37.4 in Americas, and from 0 to 20.0 per 100 surgical procedures in Europe (Figure 2).

Open appendectomy with an incidence of 11.0 (95% prediction interval: 0.0-39.3) per 100 surgical procedures was found to have a higher incidence of SSI compared to laparoscopic appendectomy with an incidence of 4.6 (95% prediction interval: 0.0-14.3) per 100 surgical procedures, $p = 0.0002$ (Figure 3).

Heterogeneity of the overall incidence of SSI after appendectomy was explained by WHO regions (17.1%), country level of income (11.1%), and type of surgical procedure (4.9%). We conducted a post hoc analysis; then in a meta-regression analysis of 119 studies reporting the information of the use of antibiotics, there was no association between the variation of SSI incidence and proportion of patients with the use of antibiotics (coefficient: 0.0010 [95%CI: -0.0004; 0.0023]; $p = 0.170$). however, most (79.5%) of these studies reported using antibiotics for all patients.

Discussion

This first systematic review and meta-analysis of data of 729,434 surgical procedures in 226 studies from 49 countries found an overall incidence of SSIs of 7.0 per 100 surgical procedures for appendectomy varying from 0 to 37.4 per 100 surgical procedures with substantial heterogeneity according to WHO regions, country level of income, and type of surgical procedure. The incidence increased with decreasing country level of income and was higher when using open surgery compared to laparoscopy. The incidence significantly varied by WHO regions with Africa having the highest burden followed by Western Pacific, Eastern-Mediterranean, and South-East Asia. We found no association between SSI incidence and proportion of using antibiotics.

Health care-associated infections are acquired by patients when receiving care and are the most frequent adverse event affecting patient safety worldwide. This includes SSIs after appendectomy.[40] As reported in a previous systematic review and meta-analysis, SSIs were the leading infection in hospitals in developed countries.[29] The high incidence we found in this study suggests that SSIs after appendectomy remains a global public concern. WHO reported that of every 100 hospitalized patients at any given time, seven in developed and 15 in developing countries will acquire at least one health care-associated infection.[40] SSIs are mainly caused by micro-organisms resistant to commonly-used antimicrobials, which can be multidrug-resistant. Indeed, more than 50% of SSIs can be antibiotic-resistant.[41] The leading micro-organisms identified in SSIs are *Staphylococcus aureus*, coagulase-negative staphylococci, and *Escherichia coli* as reported by National Healthcare Safety Network.[41] It is important to worry since *Staphylococcus aureus* and *Escherichia coli* are the micro-organisms with highest proportion of antibiotic resistance, respectively resistant to oxacillin/methicillin in 43% of cases and to fluoroquinolones in 25% of cases.[41] A recent international prospective cohort study shown that 21.6% of patients with SSI after any gastrointestinal surgery had an infection that was resistant to the prophylactic antibiotic used.[30] There are many factors that can favour SSI including patient-related and procedural-related variable.[42] These factors can be classified in two categories; non-modifiable like age and sex and modifiable including nutritional status, tobacco use, correct use of antibiotics, obesity, diabetes, prolonged surgery duration, pre-surgery hospital stay of at least two days, lower volume of hospital and surgeons, and the intraoperative techniques.[40] Strategies to curb the burden of SSIs should therefore focus on addressing these identified factors. However, we were not able to find an association between SSI with the use antibiotics, may be due to the low variability in the proportion of antibiotics in the original studies.

In our present study looking at specifically SSI after appendectomy, we also found that SSI was higher in low income countries. Interestingly, there was a trend with increasing incidence when the country income decreased. The WHO Africa region essentially constituted with sub-Saharan Africa was the region with highest incidence in this study. The WHO estimates that the endemic burden of health care-associated infections is two to three time significantly higher in low- and middle-income countries than in high-income nations.[40] The highest burden found in Africa may be associated with the fact most of countries in this continent are low income countries compared to other regions. Indeed, factors associated with increased risk of SSI after appendectomy may be higher in low-income settings. The burden of diabetes, obesity, and undernutrition are increasing in low-income countries.[43 44] There is also inadequate use of antimicrobial in low- and middle-income countries and micro-organisms are more resistant to prophylactic antibiotics used to prevent SSI in low-income countries compared to high-income countries.[30 45 46] Lower level income is also associated with lower volume of surgeon and hospital, factors recognised as associated increased risk of SSIs.[40] The higher incidence found in low income countries may also be explained by the fact open surgery is the most used surgical procedure in this setting. Indeed, we found as in other studies that open surgery is associated with higher incidence of SSIs compared to laparoscopy.[47 48] Laparoscopy is generally indicated for uncomplicated appendicitis where the dissemination of micro-organism is lower compared open surgery indicated for perforated appendicitis with peritonitis for example. Moreover, only few low-income countries have the necessary infrastructure to carry out laparoscopy procedures compared to high-income countries.[49-51]

Our findings have important implications for healthcare providers and health policy makers. SSIs are among the most preventable healthcare-associated infections.[52 53] They still represent a significant burden in terms of patient morbidity and mortality and additional costs for healthcare systems.[40] The prevention of SSI has received considerable attention from surgeons, infection control professionals, health policy makers, the media and the public since there is a perception among the public that SSIs may reflect a poor quality of care.[54] However, special attention is needed for low-income countries and Africa. Strategy to curb the burden of SSIs after appendectomy as for other surgery procedures should be focused on strategies than can help to address factors associated with increased risk of SSIs. Therefore, strategies should be a package including how to address the factors cited above. The 26 WHO recommendations to avoid SSIs should be vulgarized and implemented,[40] especially in low-income countries. Strengthening the healthcare systems of low-income countries and of countries in WHO Afro region is also a paramount by education of healthcare providers and skilling them on the use of very less invasive surgical procedures.

This study should however be interpreted in the context of some drawbacks. Firstly, the same definition of SSIs was not used by all the included studies. In addition, there were some heterogeneity according to the surgical procedure and the profile of patients. This may lead to an overestimation or underestimation of the SSIs incidence by individual studies (depending on the study characteristics). Secondly, few studies reported on the participants' characteristics and details on the surgical procedure since this can modify the risk for developing SSIs. We were not therefore able to measure the impact on our outcome of interest. Thirdly, only a quarter of studies had low risk of bias, however our analysis including only studies with low risk of bias yielded an estimate close to the crude incidence. Fourth, the various geographic regions and countries were variably represented, with some countries with only one study or even no study, which could affect the generalizability of our findings.

Despite these limitations, this is the first systematic review and meta-analysis providing a global estimate of the burden of SSIs after appendectomy. A protocol had been published before, and we used rigorous methodological and statistical procedures to obtain and pool data. Furthermore, subgroup analyses were conducted to investigate the various factors likely affecting our estimate.

Conclusion

This systematic review and meta-analysis compiled data from more than 700,000 people with appendicitis in 49 countries and pointed a high incidence of SSIs after appendectomy, at 7 per 100 surgical procedures. This estimate seemed higher in some WHO regions (especially Africa) and in low-income countries. These data suggest that less invasive procedure is associated with low incidence of SSIs after appendectomy. Strategies are needed to implement already known guidelines to decrease the burden of SSI after appendectomy. However, in low-income countries which have weak health systems, cost-effectiveness studies are needed to inform policies regarding the best strategies for decreasing the burden of SSI after appendectomy.

Contributors

CD and JJB conceived the idea of the study and developed the protocol. JJB, CD, and JNT did the literature search. CD, AM, and JNT selected the studies, CD, JNT, RNZ, AM, CMM, JJB extracted the relevant information. CD, JJB, and CMM synthesized the data. CD, JNT, CMM, and JJB wrote the first draft of the paper. CD, JJB, JNT, AB, RNZ, CMM, GML, and AE critically revised successive drafts of the paper and approved the final version. GML and AE supervised the overall work, CD and JJB are the guarantors of the review.

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Competing interests

We declare no competing interests.

Patient consent

Not applicable.

Data sharing statement

All data generated for this study are in the manuscript and its supporting files.

Figures Legend

Figure 1. Global incidence of SSI (surgical site infection) after appendectomy by level of country income

Figure 2. Global incidence of SSI (surgical site infection) after appendectomy by WHO regions

Figure 3. Global incidence of SSI (surgical site infection) after appendectomy by type of surgical procedures

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Table 1. Summary statistics of meta-analysis incidence of surgery site infections after appendectomy

	Incidence per 100 surgical procedures (95%CI)	95% Prediction interval	N studies	N participants	H (95%CI)	I² (95%CI)	P heterogeneity	P Egger test	P difference
Global	7.0 (6.4-7.7)	1.0-17.7	226	729,434	8.9 (8.7-9.1)	98.7 (98.7-98.8)	< 0.0001	< 0.0001	-
- Low risk of bias	6.9 (6.0-7.9)	1.6-15.2	59	204,450	6.7 (6.3-7.1)	97.7 (97.4-98.0)	< 0.0001	< 0.0001	-
By Level of income									
- Low	11.1 (5.5-18.2)	0.0-42.2	9	1,496	3.8 (3.0-4.8)	93.1 (89.0-95.6)	< 0.0001	0.735	0.015
- Lower-middle	9.2 (6.3-12.6)	0.0-31.6	27	10,379	5.1 (4.6-5.7)	96.2 (95.3-96.9)	< 0.0001	0.960	
- Upper-middle	8.5 (6.5-10.8)	0.3-25.3	36	26,557	5.4 (2.9-5.9)	96.6 (95.9-97.1)	< 0.0001	0.392	
- High	6.2 (5.6-6.9)	0.9-15.3	154	691,002	9.5 (9.2-9.8)	98.9 (98.8-99.0)	< 0.0001	< 0.0001	
By WHO regions									
- Africa	12.6 (3.3-26.4)	0.0-72.5	8	3,001	9.1 (7.9-10.5)	98.8 (98.4-99.1)	< 0.0001	0.628	< 0.0001
- Western Pacific	9.6 (8.1-11.2)	2.3-20.8	43	30,822	3.8 (3.5-4.2)	93.2 (91.7-94.4)	< 0.0001	0.150	
- Eastern Mediterranean	8.2 (6.4-10.2)	1.7-18.6	23	7,779	2.6 (2.2-3.1)	85.3 (79.1-89.6)	< 0.0001	0.515	
- South-East Asia	7.6 (4.7-11.1)	0.0-24.6	16	5,782	3.8 (3.2-4.5)	93.0 (90.1-95.0)	< 0.0001	0.0001	
- Americas	5.9 (5.2-6.6)	1.9-11.7	67	401,931	7.5 (7.1-7.9)	98.2 (98.0-98.4)	< 0.0001	0.0004	
- Europe	5.8 (4.6-7.0)	0.0-19.1	68	276,793	10.4 (10.0-10.8)	99.1 (99.0-99.1)	< 0.0001	< 0.0001	
By type of surgical procedure									
- Laparoscopy with open surgery	4.6 (2.5-7.2)	0.0-15.6	10	4,892	3.2 (2.6-4.2)	90.7 (85.0-94.2)	< 0.0001	0.942	0.0002
- Laparoscopy	4.6 (3.4-5.9)	0.0-14.3	40	33,873	4.4 (4.0-4.8)	94.7 (93.6-95.7)	< 0.0001	0.0002	
- Open surgery	11.0 (7.9-14.4)	0.0-39.3	44	13,120	5.7 (5.2-6.1)	96.9 (96.4-97.3)	< 0.0001	0.077	

WHO: World Health Organization; CI: confidence interval; H: H statistics

Author, Year	Sample	Incidence	[95% C.I.]
Level of income = 1. Low			
Adhikar, 2008	50	12.0	[4.5; 24.3]
Al-Saadi, 2006	160	5.0	[2.2; 9.6]
Asefa, 2002	200	32.0	[25.6; 38.9]
Asefa, 2014	322	18.9	[14.8; 23.7]
Batajoo, 2012	226	8.0	[4.8; 12.3]
Bharathi, 2011	26	3.8	[0.1; 19.6]
Giiti, 2010	199	2.0	[0.6; 5.1]
Kumar, 2016	212	9.0	[5.5; 13.6]
Pandit, 2016	101	18.8	[11.7; 27.8]
Subgroup Incidence	**1496**	**11.1**	**[5.5; 18.2]**
Heterogeneity: I^2 = 93.1% [89%; 95.6%], τ^2 = 0.0209, p = 0			
Level of income = 2. Lower-Middle			
Adejumo, 2015	141	5.0	[2.0; 10.0]
Ahmad, 2014	158	22.8	[16.5; 30.1]
Ahmed, 2015	79	16.5	[9.1; 26.5]
Ali, 2012	1257	28.3	[25.8; 30.9]
Ali, 2015	121	5.8	[2.4; 11.6]
Chaudhary, 2005	677	5.9	[4.3; 8.0]
Choudhary, 2014	92	7.6	[3.1; 15.1]
Hung, 2016	752	7.0	[5.3; 9.1]
Iqbal, 2015	166	15.1	[10.0; 21.4]
Khan, 2012	100	9.0	[4.2; 16.4]
Khan, 2014	270	6.7	[4.0; 10.3]
Khiria, 2011	497	3.6	[2.2; 5.7]
Kumar, 2008	100	10.0	[4.9; 17.6]
Mahmood, 2016	200	5.5	[2.8; 9.6]
Mbah, 2006	136	22.8	[16.0; 30.8]
Memon, 2017	227	7.0	[4.1; 11.2]
Mustafa, 2016	68	33.8	[22.8; 46.3]
Ohene, 2006	638	0.2	[0.0; 0.9]
Patel, 2003	106	8.5	[4.0; 15.5]
Pishori, 2003	3304	8.5	[7.6; 9.5]
Rafiq, 2015	390	8.5	[5.9; 11.7]
Rooh-ul-Muqim, 2010	165	7.9	[4.3; 13.1]
Saha, 2010	60	13.3	[5.9; 24.6]
Shaikg, 2011	461	2.2	[1.0; 4.0]
Shindholimath, 2011	19	10.5	[1.3; 33.1]
Singh, 2017	44	9.1	[2.5; 21.7]
Yagnik, 2010	151	4.6	[1.9; 9.3]
Subgroup Incidence	**10379**	**9.2**	**[6.3; 12.6]**
Heterogeneity: I^2 = 96.2% [95.3%; 96.9%], τ^2 = 0.0183, p < 0.0001			
Level of income = 3. Upper-Middle			
Akkoyun, 2012	234	5.1	[2.7; 8.8]
Álvarez-Moreno, 2014	947	3.9	[2.8; 5.3]
Bali, 2015	126	6.3	[2.8; 12.1]
Bıçakcı, 2011	279	14.3	[10.4; 19.0]
Bozkurt, 2014	1849	1.6	[1.1; 2.3]
Cao, 2015	12586	8.8	[8.3; 9.3]
Cervantes-sánchez, 2000	350	14.3	[10.8; 18.4]
Chamisa, 2009	324	25.3	[20.7; 30.4]
Chen, 2010	69	2.9	[0.4; 10.1]
Garcell, 2016	603	3.6	[2.3; 5.5]
Golub, 2016	332	14.5	[10.9; 18.7]
Hamzaoglu, 2004	100	8.0	[3.5; 15.2]
Javadi, 2017	69	4.3	[0.9; 12.2]
Kasatpibal, 2005	1487	1.9	[1.3; 2.7]
Kasatpibal, 2006	2139	1.2	[0.8; 1.8]
Kilic, 2016	110	12.7	[7.1; 20.4]
Li, 2005	160	6.9	[3.5; 12.0]
Li, 2017	398	11.6	[8.6; 15.1]
Liu, 2017	112	8.0	[3.7; 14.7]
Mickovic, 2015	218	4.1	[1.9; 7.7]
Ming, 2009	173	23.1	[17.1; 30.1]
Mingmalairak, 2009	100	9.0	[4.2; 16.4]
Rajabi-Mashhadi, 2012	291	6.5	[4.0; 10.0]
Rios, 2004	104	22.1	[14.6; 31.3]
Romel Hilaire, 2014	720	7.9	[6.1; 10.1]
Romeo, 2009	310	9.7	[6.6; 13.5]
Sadraei-Mosavi, 2017	152	1.3	[0.2; 4.7]
Shang, 2017	398	11.3	[8.4; 14.8]
Siribumrungwong, 2013	128	25.8	[18.5; 34.3]
Sozutek, 2013	75	6.7	[2.2; 14.9]
Srishewachart, 2016	450	5.8	[3.8; 8.4]
Tijerina, 2010	529	21.9	[18.5; 25.7]
Wong, 2015	352	2.8	[1.4; 5.2]
Wu, 2014	60	3.3	[0.4; 11.5]
Wu, 2017	115	37.4	[28.5; 46.9]
Zhang, 2015	108	1.9	[0.2; 6.5]
Subgroup Incidence	**26557**	**8.5**	**[6.5; 10.8]**
Heterogeneity: I^2 = 96.6% [95.9%; 97.1%], τ^2 = 0.0122, p < 0.0001			
Level of income = 4. High			
Aguillo, 2005	792	5.2	[3.7; 7.0]
Al-Temimi, 2017	92	8.7	[3.8; 16.4]
Almström, 2016	2756	6.2	[5.4; 7.2]
Anderson, 2014	169896	0.5	[0.4; 0.5]
Andert, 2017	2136	2.4	[1.8; 3.2]
Aranda-Narváez, 2010	30	20.0	[7.7; 38.6]
Aranda-Narvaez, 2014	868	13.4	[11.2; 15.8]
Arthur, 2017	1189	1.9	[1.2; 2.9]
Bae, 2016	25	4.0	[0.1; 20.4]
Bae, 2016	143	2.8	[0.8; 7.0]
Baek, 2011	77	13.0	[6.4; 22.6]
Banghu, 2013	3326	6.1	[5.3; 7.0]
Bansal, 2012	187	5.9	[3.0; 10.3]
Bickel, 2011	210	9.5	[5.9; 14.3]
Blackwood, 2017	115	29.6	[21.4; 38.8]
Blakely, 2011	131	37.4	[29.1; 46.3]
Bonadjo, 2017	203	7.9	[4.6; 12.5]
Boomer, 2014	1388	5.1	[4.0; 6.4]
Boomer, 2016	1338	2.5	[1.8; 3.5]
Brandt, 2008	10969	2.4	[2.1; 2.7]
Brummer, 2009	14209	2.0	[1.7; 2.2]
Cairo, 2017	20981	1.5	[1.4; 1.7]
Cameron, 2017	1389	1.8	[1.2; 2.6]
Chen, 2012	117	6.8	[3.0; 13.0]
Chen, 2015	236	19.9	[15.0; 25.6]
Chiang, 2006	390	7.9	[5.5; 11.1]
Chiang, 2012	70	21.4	[12.5; 32.9]
Cho, 2014	101	12.9	[7.0; 21.0]
Clyde, 2008	1198	7.9	[6.5; 9.6]
Coakley, 2011	728	8.4	[6.5; 10.6]
Crandall, 2009	176	5.1	[2.4; 9.5]
Dede, 2008	273	11.4	[7.8; 15.7]
Dhiman, 2013	1250	0.1	[0.0; 0.4]
Dimitriou, 2013	404	9.2	[6.5; 12.4]
Durkin, 2015	14763	1.0	[0.8; 1.2]
Ein, 2013	496	26.8	[23.0; 30.9]
Fukuda, 2016	2074	4.3	[3.5; 5.3]
Gandaglia, 2014	97780	2.0	[1.9; 2.1]
Ghnnam, 2011	63	9.5	[3.6; 19.6]
Giesen, 2017	637	6.6	[4.8; 8.8]
Gross, 2016	2585	7.2	[6.2; 8.3]
Gurien, 2016	484	2.7	[1.4; 4.5]
Harmon, 2016	411	5.6	[3.6; 8.3]
Helling, 2017	611	5.1	[3.5; 7.1]
Helmer, 2002	438	6.4	[4.3; 9.1]
Hesami, 2014	90	15.6	[8.8; 24.7]
Hissain, 2012	377	4.5	[2.6; 7.1]
Horvath, 2016	1516	2.6	[1.9; 3.6]
Hughes, 2013	266	9.4	[6.2; 13.6]
Inigo, 2006	721	6.4	[4.7; 8.4]
Jenkins, 2016	12410	3.4	[3.1; 3.7]
Kang, 2012	217	6.9	[3.9; 11.1]
Kapischke, 2013	159	2.5	[0.7; 6.3]
Karam, 2016	101	2.0	[0.2; 7.0]
Karam, 2016	625	5.1	[3.5; 7.2]
Kato, 2008	64	6.2	[1.7; 15.2]
Kell, 2003	149	16.1	[10.6; 23.0]
Khan, 2007	134	6.0	[2.6; 11.4]
Kim, 2011	3335	1.4	[1.1; 1.9]
Kim, 2015	2587	4.6	[3.8; 5.5]
Kim, 2016	207	15.9	[11.2; 21.7]
Kiriakopoulos, 2006	42	0.0	[0.0; 8.4]
Kirshtein, 2009	1435	1.5	[0.9; 2.2]
Kiudelis, 2013	152	5.9	[2.7; 10.9]
Kleif, 2017	1151	7.8	[6.3; 9.5]
Koizumi, 2014	185	8.6	[5.0; 13.7]
Kubota, 2014	10	10.0	[0.3; 44.5]
Kumamoto, 2014	124	4.0	[1.3; 9.2]
Lacher, 2012	415	6.0	[3.9; 8.8]
Le, 2009	507	11.0	[8.5; 14.1]
Lee, 2009	109	7.3	[3.2; 14.0]
Lee, 2010	75	4.0	[0.8; 11.2]
Lee, 2010	264	7.2	[4.4; 11.0]
Lee, 2010	2462	6.7	[5.8; 7.8]
Lee, 2011	7650	3.8	[3.3; 4.2]
Lemieux, 2008	45	2.2	[0.1; 11.8]
Levy, 2013	312	10.9	[7.7; 14.9]
Lim, 2011	60	8.3	[2.8; 18.4]
Lima, 2007	300	2.3	[0.9; 4.7]
Lin, 2006	229	27.1	[21.4; 33.3]
Litz, 2016	413	8.0	[5.6; 11.0]
Martinez, 2012	75	12.0	[5.6; 21.6]
Menezes, 2008	118	11.0	[6.0; 18.1]
Merenda, 2013	317	6.0	[3.6; 9.2]
Michailidou, 2015	2812	4.2	[3.5; 5.0]
Michailidou, 2015	264	3.8	[1.8; 6.9]
Miyano, 2010	23	17.4	[5.0; 38.8]
Moazzez, 2013	2060	2.6	[1.9; 3.4]
Monge Jodra, 2003	5780	7.9	[7.3; 8.7]
Mueck, 2017	697	1.4	[0.7; 2.6]
Muensterer, 2009	75	5.3	[1.5; 13.1]
Muensterer, 2011	183	3.8	[1.6; 7.7]
Nadler, 2003	94	14.9	[8.4; 23.7]
Nataraja, 2010	191	7.9	[4.5; 12.6]
Nataraja, 2012	1205	3.9	[2.9; 5.2]
Obayashi, 2015	485	6.0	[4.0; 8.5]
Obinwa, 2015	1037	3.7	[2.6; 5.0]
Okkyung, 2002	84	2.4	[0.3; 8.3]
Onieva, 2017	294	7.1	[4.5; 10.7]
Page, 2010	17199	3.7	[3.4; 4.0]
Palesty, 2004	50	4.0	[0.5; 13.7]
Parcells, 2009	1063	14.2	[12.2; 16.4]
Park, 2017	1343	13.6	[11.8; 15.6]
Park, 2018	986	4.4	[3.2; 5.8]
Pascual, 2017	100	1.0	[0.0; 5.4]
Pearcy, 2017	2903	0.4	[0.2; 0.7]
Putnam, 2016	410	20.5	[16.7; 24.7]
Qahtani, 2014	91	6.6	[2.5; 13.8]
Quezada, 2015	227	4.4	[2.1; 8.0]
Raakow, 2014	156	3.8	[1.4; 8.2]
Reinisch, 2017	680	8.4	[6.4; 10.7]
Romano, 2014	372	1.6	[0.6; 3.5]
Romy, 2008	2468	7.1	[6.1; 8.2]
Rossem, 2015	415	14.2	[11.0; 18.0]
Rossem, 2016	1995	1.9	[1.3; 2.5]
Rotermann, 2004	80867	3.8	[3.7; 4.0]
Saar, 2016	266	7.1	[4.4; 10.9]
Saber, 2010	26	3.8	[0.1; 19.6]
Sahm, 2010	1710	1.6	[1.1; 2.4]
Sahm, 2015	12570	7.0	[6.6; 7.5]
Salö, 2016	259	3.1	[1.3; 6.0]
Sanchez-Santana, 2017	930	4.6	[3.4; 6.2]
Sauvain, 2016	2559	2.3	[1.7; 2.9]
Scarborough, 2012	39122	4.2	[4.0; 4.4]
Scarless, 2013	38	5.3	[0.6; 17.7]
Seifarth, 2016	1283	2.7	[1.8; 3.7]
Seifarth, 2016	1283	2.7	[1.8; 3.7]
Senekjan, 2013	61830	3.6	[3.5; 3.8]
Seo, 2002	129	15.5	[9.7; 22.9]
Sesia, 2011	265	1.1	[0.2; 3.3]
Shimizu, 2014	300	16.3	[12.3; 21.0]
Siam, 2017	1649	4.7	[3.8; 5.9]
Silva, 2008	433	12.0	[9.1; 15.4]
Sivrikoz, 2015	4844	4.7	[4.2; 5.4]
Soll, 2016	813	3.1	[2.0; 4.5]
Staszewicz, 2014	6383	6.4	[5.8; 7.0]
Suttie, 2004	60	8.3	[2.8; 18.4]
Svensson, 2016	1745	6.0	[4.9; 7.2]
Taguchi, 2015	81	29.6	[20.0; 40.8]
Tanaka, 2007	95	13.7	[7.5; 22.3]
Toro Pablo, 2017	600	6.7	[4.8; 9.0]
Towfigh, 2011	75	24.0	[14.9; 35.3]
Troillet, 2017	15439	3.9	[3.6; 4.3]
Tsioplis, 2013	1439	8.5	[7.1; 10.0]
Vahdad, 2016	309	1.9	[0.7; 4.2]
Van Rossem, 2014	267	11.2	[7.7; 15.7]
Van Rossem, 2016	1378	8.1	[6.7; 9.6]
Wang-Chan, 2017	246	2.8	[1.2; 5.8]
Watanabe, 2011	903	11.2	[9.2; 13.4]
Willis, 2016	313	20.4	[16.1; 25.3]
Wu, 2006	1795	10.3	[8.9; 11.8]
Wu, 2011	1366	8.3	[6.9; 9.9]
Yaghoubian, 2010	4325	5.8	[5.1; 6.6]
Yousef, 2017	122	14.8	[9.0; 22.3]
Subgroup Incidence	**691002**	**6.2**	**[5.6; 6.9]**
Heterogeneity: I^2 = 98.9% [98.8%; 99%], τ^2 = 0.0055, p < 0.0001			
Overall Incidence	**729434**	**7.0**	**[6.4; 7.7]**
Prediction interval			**[1.0; 17.6]**

Heterogeneity: I^2 = 98.7% [98.7%; 98.8%], τ^2 = 0.0067, p = 0

Residual heterogeneity: I^2 = 98.6% [98.5%; 98.6%], p = 0

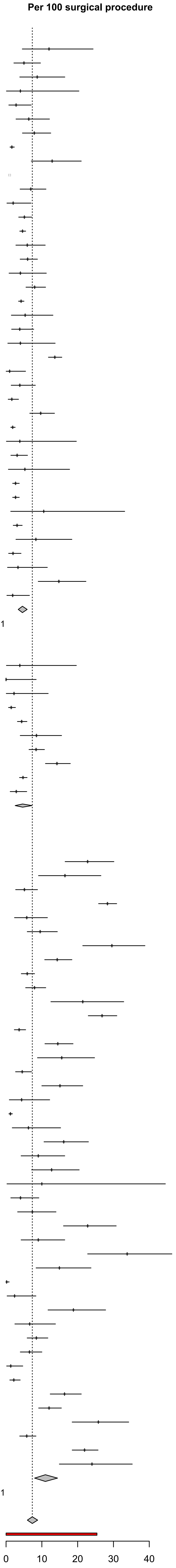
Test for subgroup differences: χ^2_3 = 10.50, df = 3 (p = 0.0148)

Author, Year	Sample	Incidence	[95% C.I.]
WHO Region = Africa			
Adejumo, 2015	141	5.0	[2.0; 10.0]
Ali, 2012	1257	28.3	[25.8; 30.9]
Asefa, 2002	200	32.0	[25.6; 38.9]
Chamisa, 2009	324	25.3	[20.7; 30.4]
Giiti, 2010	199	2.0	[0.6; 5.1]
Mbah, 2006	136	22.8	[16.0; 30.8]
Ohene, 2006	638	0.2	[0.0; 0.9]
Patel, 2003	106	8.5	[4.0; 15.5]
Subgroup Incidence	**3001**	**12.6**	**[3.3; 26.4]**
Heterogeneity: I^2 = 98.8% [98.4%; 99.1%], τ^2 = 0.0629, p = 0			
WHO Region = Americas			
Al-Temimi, 2017	92	8.7	[3.8; 16.4]
Álvarez-Moreno, 2014	947	3.9	[2.8; 5.3]
Bae, 2016	143	2.8	[0.8; 7.0]
Blackwood, 2017	115	29.6	[21.4; 38.8]
Blakely, 2011	131	37.4	[29.1; 46.3]
Bonadjo, 2017	203	7.9	[4.6; 12.5]
Boomer, 2014	1388	5.1	[4.0; 6.4]
Boomer, 2016	1338	2.5	[1.8; 3.5]
Cairo, 2017	20981	1.5	[1.4; 1.7]
Cameron, 2017	1389	1.8	[1.2; 2.6]
Cervantes-sánchez, 2000	350	14.3	[10.8; 18.4]
Clyde, 2008	1198	7.9	[6.5; 9.6]
Coakley, 2011	728	8.4	[6.5; 10.6]
Crandall, 2009	176	5.1	[2.4; 9.5]
Dhiman, 2013	1250	0.1	[0.0; 0.4]
Durkin, 2015	14763	1.0	[0.8; 1.2]
Ein, 2013	496	26.8	[23.0; 30.9]
Gandaglia, 2014	97780	2.0	[1.9; 2.1]
Garcell, 2016	603	3.6	[2.3; 5.5]
Gross, 2016	2585	7.2	[6.2; 8.3]
Gurien, 2016	484	2.7	[1.4; 4.5]
Harmon, 2016	411	5.6	[3.6; 8.3]
Helling, 2017	611	5.1	[3.5; 7.1]
Helmer, 2002	438	6.4	[4.3; 9.1]
Jenkins, 2016	12410	3.4	[3.1; 3.7]
Karam, 2016	101	2.0	[0.2; 7.0]
Karam, 2016	625	5.1	[3.5; 7.2]
Kim, 2011	3335	1.4	[1.1; 1.9]
Lacher, 2012	415	6.0	[3.9; 8.8]
Le, 2009	507	11.0	[8.5; 14.1]
Lee, 2009	109	7.3	[3.2; 14.0]
Lee, 2010	2462	6.7	[5.8; 7.8]
Lee, 2011	7650	3.8	[3.3; 4.2]
Lemieux, 2008	45	2.2	[0.1; 11.8]
Levy, 2013	312	10.9	[7.7; 14.9]
Litz, 2016	413	8.0	[5.6; 11.0]
Michailidou, 2015	2812	4.2	[3.5; 5.0]
Michailidou, 2015	264	3.8	[1.8; 6.9]
Moazzez, 2013	2060	2.6	[1.9; 3.4]
Mueck, 2017	697	1.4	[0.7; 2.6]
Muensterer, 2009	75	5.3	[1.5; 13.1]
Muensterer, 2011	183	3.8	[1.6; 7.7]
Nadler, 2003	94	14.9	[8.4; 23.7]
Page, 2010	17199	3.7	[3.4; 4.0]
Palesty, 2004	50	4.0	[0.5; 13.7]
Parcells, 2009	1063	14.2	[12.2; 16.4]
Pearcy, 2017	2903	0.4	[0.2; 0.7]
Putnam, 2016	410	20.5	[16.7; 24.7]
Quezada, 2015	227	4.4	[2.1; 8.0]
Rios, 2004	104	22.1	[14.6; 31.3]
Romano, 2014	372	1.6	[0.6; 3.5]
Romel Hilaire, 2014	720	7.9	[6.1; 10.1]
Romeo, 2009	310	9.7	[6.6; 13.5]
Rotermann, 2004	80867	3.8	[3.7; 4.0]
Saber, 2010	26	3.8	[0.1; 19.6]
Scarborough, 2012	39122	4.2	[4.0; 4.4]
Seifarth, 2016	1283	2.7	[1.8; 3.7]
Seifarth, 2016	1283	2.7	[1.8; 3.7]
Senekjan, 2013	61830	3.6	[3.5; 3.8]
Silva, 2008	433	12.0	[9.1; 15.4]
Sivrikoz, 2015	4844	4.7	[4.2; 5.4]
Tijerina, 2010	529	21.9	[18.5; 25.7]
Towfigh, 2011	75	24.0	[14.9; 35.3]
Willis, 2016	313	20.4	[16.1; 25.3]
Wong, 2015	352	2.8	[1.4; 5.2]
Yaghoubian, 2010	4325	5.8	[5.1; 6.6]
Yousef, 2017	122	14.8	[9.0; 22.3]
Subgroup Incidence	**401931**	**5.9**	**[5.2; 6.6]**
Heterogeneity: I^2 = 98.2% [98%; 98.4%], τ^2 = 0.0026, p = 0			
WHO Region = Eastern Mediterranean			
Ahmad, 2014	158	22.8	[16.5; 30.1]
Ahmed, 2015	79	16.5	[9.1; 26.5]
Al-Saadi, 2006	160	5.0	[2.2; 9.6]
Ali, 2015	121	5.8	[2.4; 11.6]
Chaudhary, 2005	677	5.9	[4.3; 8.0]
Ghnnam, 2011	63	9.5	[3.6; 19.6]
Hesami, 2014	90	15.6	[8.8; 24.7]
Hissain, 2012	377	4.5	[2.6; 7.1]
Iqbal, 2015	166	15.1	[10.0; 21.4]
Javadi, 2017	69	4.3	[0.9; 12.2]
Khan, 2012	100	9.0	[4.2; 16.4]
Khan, 2014	270	6.7	[4.0; 10.3]
Kumar, 2008	100	10.0	[4.9; 17.6]
Mahmood, 2016	200	5.5	[2.8; 9.6]
Memon, 2017	227	7.0	[4.1; 11.2]
Mustafa, 2016	68	33.8	[22.8; 46.3]
Pishori, 2003	3304	8.5	[7.6; 9.5]
Qahtani, 2014	91	6.6	[2.5; 13.8]
Rafiq, 2015	390	8.5	[5.9; 11.7]
Rajabi-Mashhadi, 2012	291	6.5	[4.0; 10.0]
Rooh-ul-Muqim, 2010	165	7.9	[4.3; 13.1]
Sadraei-Mosavi, 2017	152	1.3	[0.2; 4.7]
Shaikg, 2011	461	2.2	[1.0; 4.0]
Subgroup Incidence	**7779**	**8.2**	**[6.4; 10.2]**
Heterogeneity: I^2 = 85.3% [79.1%; 89.6%], τ^2 = 0.0051, p < 0.0001			
WHO Region = Europe			
Aguillo, 2005	792	5.2	[3.7; 7.0]
Akkoyun, 2012	234	5.1	[2.7; 8.8]
Almström, 2016	2756	6.2	[5.4; 7.2]
Anderson, 2014	169896	0.5	[0.4; 0.5]
Andert, 2017	2136	2.4	[1.8; 3.2]
Aranda-Narváez, 2010	30	20.0	[7.7; 38.6]
Aranda-Narvaez, 2014	868	13.4	[11.2; 15.8]
Asefa, 2014	322	18.9	[14.8; 23.7]
Bali, 2015	126	6.3	[2.8; 12.1]
Bansal, 2012	187	5.9	[3.0; 10.3]
Bıçakcı, 2011	279	14.3	[10.4; 19.0]
Bickel, 2011	210	9.5	[5.9; 14.3]
Bozkurt, 2014	1849	1.6	[1.1; 2.3]
Brandt, 2008	10969	2.4	[2.1; 2.7]
Brummer, 2009	14209	2.0	[1.7; 2.2]
Dede, 2008	273	11.4	[7.8; 15.7]
Dimitriou, 2013	404	9.2	[6.5; 12.4]
Giesen, 2017	637	6.6	[4.8; 8.8]
Golub, 2016	332	14.5	[10.9; 18.7]
Hamzaoglu, 2004	100	8.0	[3.5; 15.2]
Horvath, 2016	1516	2.6	[1.9; 3.6]
Hughes, 2013	266	9.4	[6.2; 13.6]
Inigo, 2006	721	6.4	[4.7; 8.4]
Kapischke, 2013	159	2.5	[0.7; 6.3]
Kell, 2003	149	16.1	[10.6; 23.0]
Khan, 2007	134	6.0	[2.6; 11.4]
Kilic, 2016	110	12.7	[7.1; 20.4]
Kiriakopoulos, 2006	42	0.0	[0.0; 8.4]
Kirshtein, 2009	1435	1.5	[0.9; 2.2]
Kiudelis, 2013	152	5.9	[2.7; 10.9]
Kleif, 2017	1151	7.8	[6.3; 9.5]
Lima, 2007	300	2.3	[0.9; 4.7]
Martinez, 2012	75	12.0	[5.6; 21.6]
Menezes, 2008	118	11.0	[6.0; 18.1]
Merenda, 2013	317	6.0	[3.6; 9.2]
Mickovic, 2015	218	4.1	[1.9; 7.7]
Monge Jodra, 2003	5780	7.9	[7.3; 8.7]
Nataraja, 2010	191	7.9	[4.5; 12.6]
Nataraja, 2012	1205	3.9	[2.9; 5.2]
Obinwa, 2015	1037	3.7	[2.6; 5.0]
Onieva, 2017	294	7.1	[4.5; 10.7]
Pascual, 2017	100	1.0	[0.0; 5.4]
Raakow, 2014	156	3.8	[1.4; 8.2]
Reinisch, 2017	680	8.4	[6.4; 10.7]
Romy, 2008	2468	7.1	[6.1; 8.2]
Rossem, 2015	415	14.2	[11.0; 18.0]
Rossem, 2016	1995	1.9	[1.3; 2.5]
Saar, 2016	266	7.1	[4.4; 10.9]
Sahm, 2010	1710	1.6	[1.1; 2.4]
Sahm, 2015	12570	7.0	[6.6; 7.5]
Salö, 2016	259	3.1	[1.3; 6.0]
Sanchez-Santana, 2017	930	4.6	[3.4; 6.2]
Sauvain, 2016	2559	2.3	[1.7; 2.9]
Scarless, 2013	38	5.3	[0.6; 17.7]
Sesia, 2011	265	1.1	[0.2; 3.3]
Siam, 2017	1649	4.7	[3.8; 5.9]
Soll, 2016	813	3.1	[2.0; 4.5]
Sozutek, 2013	75	6.7	[2.2; 14.9]
Staszewicz, 2014	6383	6.4	[5.8; 7.0]
Suttie, 2004	60	8.3	[2.8; 18.4]
Svensson, 2016	1745	6.0	[4.9; 7.2]
Toro Pablo, 2017	600	6.7	[4.8; 9.0]
Troillet, 2017	15439	3.9	[3.6; 4.3]
Tsioplis, 2013	1439	8.5	[7.1; 10.0]
Vahdad, 2016	309	1.9	[0.7; 4.2]
Van Rossem, 2014	267	11.2	[7.7; 15.7]
Van Rossem, 2016	1378	8.1	[6.7; 9.6]
Wang-Chan, 2017	246	2.8	[1.2; 5.8]
Subgroup Incidence	**276793**	**5.8**	**[4.6; 7.0]**
Heterogeneity: I^2 = 99.1% [99%; 99.1%], τ^2 = 0.0106, p < 0.0001			
WHO Region = Multiregional			
Banghu, 2013	3326	6.1	[5.3; 7.0]
Subgroup Incidence	**3326**	**6.1**	**[5.3; 6.9]**
Heterogeneity: not applicable			
WHO Region = South-East Asia			
Adhikar, 2008	50	12.0	[4.5; 24.3]
Batajoo, 2012	226	8.0	[4.8; 12.3]
Bharathi, 2011	26	3.8	[0.1; 19.6]
Choudhary, 2014	92	7.6	[3.1; 15.1]
Kasatpibal, 2005	1487	1.9	[1.3; 2.7]
Kasatpibal, 2006	2139	1.2	[0.8; 1.8]
Khiria, 2011	497	3.6	[2.2; 5.7]
Kumar, 2016	212	9.0	[5.5; 13.6]
Mingmalairak, 2009	100	9.0	[4.2; 16.4]
Pandit, 2016	101	18.8	[11.7; 27.8]
Saha, 2010	60	13.3	[5.9; 24.6]
Shindholimath, 2011	19	10.5	[1.3; 33.1]
Singh, 2017	44	9.1	[2.5; 21.7]
Siribumrungwong, 2013	128	25.8	[18.5; 34.3]
Srishewachart, 2016	450	5.8	[3.8; 8.4]
Yagnik, 2010	151	4.6	[1.9; 9.3]
Subgroup Incidence	**5782**	**7.6**	**[4.7; 11.1]**
Heterogeneity: I^2 = 93% [90.1%; 95%], τ^2 = 0.0110, p = NA			
WHO Region = Western Pacific			
Arthur, 2017	1189	1.9	[1.2; 2.9]
Bae, 2016	25	4.0	[0.1; 20.4]
Baek, 2011	77	13.0	[6.4; 22.6]
Cao, 2015	12586	8.8	[8.3; 9.3]
Chen, 2010	69	2.9	[0.4; 10.1]
Chen, 2012	117	6.8	[3.0; 13.0]
Chen, 2015	236	19.9	[15.0; 25.6]
Chiang, 2006	390	7.9	[5.5; 11.1]
Chiang, 2012	70	21.4	[12.5; 32.9]
Cho, 2014	101	12.9	[7.0; 21.0]
Fukuda, 2016	2074	4.3	[3.5; 5.3]
Hung, 2016	752	7.0	[5.3; 9.1]
Kang, 2012	217	6.9	[3.9; 11.1]
Kato, 2008	64	6.2	[1.7; 15.2]
Kim, 2015	2587	4.6	[3.8; 5.5]
Kim, 2016	207	15.9	[11.2; 21.7]
Koizumi, 2014	185	8.6	[5.0; 13.7]
Kubota, 2014	10	10.0	[0.3; 44.5]
Kumamoto, 2014	124	4.0	[1.3; 9.2]
Lee, 2010	75	4.0	[0.8; 11.2]
Lee, 2010	264	7.2	[4.4; 11.0]
Li, 2005	160	6.9	[3.5; 12.0]
Li, 2017	398	11.6	[8.6; 15.1]
Lim, 2011	60	8.3	[2.8; 18.4]
Lin, 2006	229	27.1	[21.4; 33.3]
Liu, 2017	112	8.0	[3.7; 14.7]
Ming, 2009	173	23.1	[17.1; 30.1]
Miyano, 2010	23	17.4	[5.0; 38.8]
Obayashi, 2015	485	6.0	[4.0; 8.5]
Okkyung, 2002	84	2.4	[0.3; 8.3]
Park, 2017	1343	13.6	[11.8; 15.6]
Park, 2018	986	4.4	[3.2; 5.8]
Seo, 2002	129	15.5	[9.7; 22.9]
Shang, 2017	398	11.3	[8.4; 14.8]
Shimizu, 2014	300	16.3	[12.3; 21.0]
Taguchi, 2015	81	29.6	[20.0; 40.8]
Tanaka, 2007	95	13.7	[7.5; 22.3]
Watanabe, 2011	903	11.2	[9.2; 13.4]
Wu, 2006	1795	10.3	[8.9; 11.8]
Wu, 2011	1366	8.3	[6.9; 9.9]
Wu, 2014	60	3.3	[0.4; 11.5]
Wu, 2017	115	37.4	[28.5; 46.9]
Zhang, 2015	108	1.9	[0.2; 6.5]
Subgroup Incidence	**30822**	**9.6**	**[8.1; 11.2]**
Heterogeneity: I^2 = 93.2% [91.7%; 94.4%], τ^2 = 0.0058, p < 0.0001			
Overall Incidence	**729434**	**7.0**	**[6.4; 7.7]**
Prediction interval			**[1.0; 17.6]**

Heterogeneity: I^2 = 98.7% [98.7%; 98.8%], τ^2 = 0.0067, p = 0
Residual heterogeneity: I^2 = 98.2% [98.1%; 98.3%], p = 0
Test for subgroup differences: χ^2_6 = 33.60, df = 6 (p < 0.0001)

Author, Year	Sample	Incidence	[95% C.I.]
Procedure = Laparoscopy			
Adhikar, 2008	50	12.0	[4.5; 24.3]
Al-Saadi, 2006	160	5.0	[2.2; 9.6]
Al-Temimi, 2017	92	8.7	[3.8; 16.4]
Bae, 2016	25	4.0	[0.1; 20.4]
Bae, 2016	143	2.8	[0.8; 7.0]
Bali, 2015	126	6.3	[2.8; 12.1]
Bonadjo, 2017	203	7.9	[4.6; 12.5]
Bozkurt, 2014	1849	1.6	[1.1; 2.3]
Cho, 2014	101	12.9	[7.0; 21.0]
Durkin, 2015	14763	1.0	[0.8; 1.2]
Kang, 2012	217	6.9	[3.9; 11.1]
Karam, 2016	101	2.0	[0.2; 7.0]
Karam, 2016	625	5.1	[3.5; 7.2]
Kim, 2015	2587	4.6	[3.8; 5.5]
Kiudelis, 2013	152	5.9	[2.7; 10.9]
Lacher, 2012	415	6.0	[3.9; 8.8]
Lee, 2010	75	4.0	[0.8; 11.2]
Litz, 2016	413	8.0	[5.6; 11.0]
Michailidou, 2015	2812	4.2	[3.5; 5.0]
Muensterer, 2009	75	5.3	[1.5; 13.1]
Muensterer, 2011	183	3.8	[1.6; 7.7]
Palesty, 2004	50	4.0	[0.5; 13.7]
Park, 2017	1343	13.6	[11.8; 15.6]
Pascual, 2017	100	1.0	[0.0; 5.4]
Raakow, 2014	156	3.8	[1.4; 8.2]
Romano, 2014	372	1.6	[0.6; 3.5]
Romeo, 2009	310	9.7	[6.6; 13.5]
Rossem, 2016	1995	1.9	[1.3; 2.5]
Saber, 2010	26	3.8	[0.1; 19.6]
Salö, 2016	259	3.1	[1.3; 6.0]
Scarless, 2013	38	5.3	[0.6; 17.7]
Seifarth, 2016	1283	2.7	[1.8; 3.7]
Seifarth, 2016	1283	2.7	[1.8; 3.7]
Shindholimath, 2011	19	10.5	[1.3; 33.1]
Soll, 2016	813	3.1	[2.0; 4.5]
Suttie, 2004	60	8.3	[2.8; 18.4]
Vahdad, 2016	309	1.9	[0.7; 4.2]
Wu, 2014	60	3.3	[0.4; 11.5]
Yousef, 2017	122	14.8	[9.0; 22.3]
Zhang, 2015	108	1.9	[0.2; 6.5]
Subgroup Incidence	**33873**	**4.6**	**[3.4; 5.9]**
Heterogeneity: I^2 = 94.7% [93.6%; 95.7%], τ^2 = 0.0066, p < 0.0001			
Procedure = Laparoscopy with Open Surgery			
Bharathi, 2011	26	3.8	[0.1; 19.6]
Kiriakopoulos, 2006	42	0.0	[0.0; 8.4]
Lemieux, 2008	45	2.2	[0.1; 11.8]
Mueck, 2017	697	1.4	[0.7; 2.6]
Park, 2018	986	4.4	[3.2; 5.8]
Patel, 2003	106	8.5	[4.0; 15.5]
Reinisch, 2017	680	8.4	[6.4; 10.7]
Rossem, 2015	415	14.2	[11.0; 18.0]
Siam, 2017	1649	4.7	[3.8; 5.9]
Wang-Chan, 2017	246	2.8	[1.2; 5.8]
Subgroup Incidence	**4892**	**4.6**	**[2.5; 7.2]**
Heterogeneity: I^2 = 90.7% [85%; 94.2%], τ^2 = 0.0056, p < 0.0001			
Procedure = Open Surgery			
Ahmad, 2014	158	22.8	[16.5; 30.1]
Ahmed, 2015	79	16.5	[9.1; 26.5]
Akkoyun, 2012	234	5.1	[2.7; 8.8]
Ali, 2012	1257	28.3	[25.8; 30.9]
Ali, 2015	121	5.8	[2.4; 11.6]
Bickel, 2011	210	9.5	[5.9; 14.3]
Blackwood, 2017	115	29.6	[21.4; 38.8]
Cervantes-sánchez, 2000	350	14.3	[10.8; 18.4]
Chaudhary, 2005	677	5.9	[4.3; 8.0]
Chiang, 2006	390	7.9	[5.5; 11.1]
Chiang, 2012	70	21.4	[12.5; 32.9]
Ein, 2013	496	26.8	[23.0; 30.9]
Garcell, 2016	603	3.6	[2.3; 5.5]
Golub, 2016	332	14.5	[10.9; 18.7]
Hesami, 2014	90	15.6	[8.8; 24.7]
Hissain, 2012	377	4.5	[2.6; 7.1]
Iqbal, 2015	166	15.1	[10.0; 21.4]
Javadi, 2017	69	4.3	[0.9; 12.2]
Kasatpibal, 2006	2139	1.2	[0.8; 1.8]
Kato, 2008	64	6.2	[1.7; 15.2]
Kell, 2003	149	16.1	[10.6; 23.0]
Khan, 2012	100	9.0	[4.2; 16.4]
Kilic, 2016	110	12.7	[7.1; 20.4]
Kubota, 2014	10	10.0	[0.3; 44.5]
Kumamoto, 2014	124	4.0	[1.3; 9.2]
Lee, 2009	109	7.3	[3.2; 14.0]
Mbah, 2006	136	22.8	[16.0; 30.8]
Mingmalairak, 2009	100	9.0	[4.2; 16.4]
Mustafa, 2016	68	33.8	[22.8; 46.3]
Nadler, 2003	94	14.9	[8.4; 23.7]
Ohene, 2006	638	0.2	[0.0; 0.9]
Okkyung, 2002	84	2.4	[0.3; 8.3]
Pandit, 2016	101	18.8	[11.7; 27.8]
Qahtani, 2014	91	6.6	[2.5; 13.8]
Rafiq, 2015	390	8.5	[5.9; 11.7]
Rajabi-Mashhadi, 2012	291	6.5	[4.0; 10.0]
Sadraei-Mosavi, 2017	152	1.3	[0.2; 4.7]
Shaikg, 2011	461	2.2	[1.0; 4.0]
Shimizu, 2014	300	16.3	[12.3; 21.0]
Silva, 2008	433	12.0	[9.1; 15.4]
Siribumrungwong, 2013	128	25.8	[18.5; 34.3]
Srishewachart, 2016	450	5.8	[3.8; 8.4]
Tijerina, 2010	529	21.9	[18.5; 25.7]
Towfigh, 2011	75	24.0	[14.9; 35.3]
Subgroup Incidence	**13120**	**11.0**	**[8.0; 14.4]**
Heterogeneity: I^2 = 96.9% [96.4%; 97.3%], τ^2 = 0.0270, p < 0.0001			
Overall Incidence	**51885**	**7.3**	**[5.9; 8.8]**
Prediction interval			**[0.0; 25.4]**

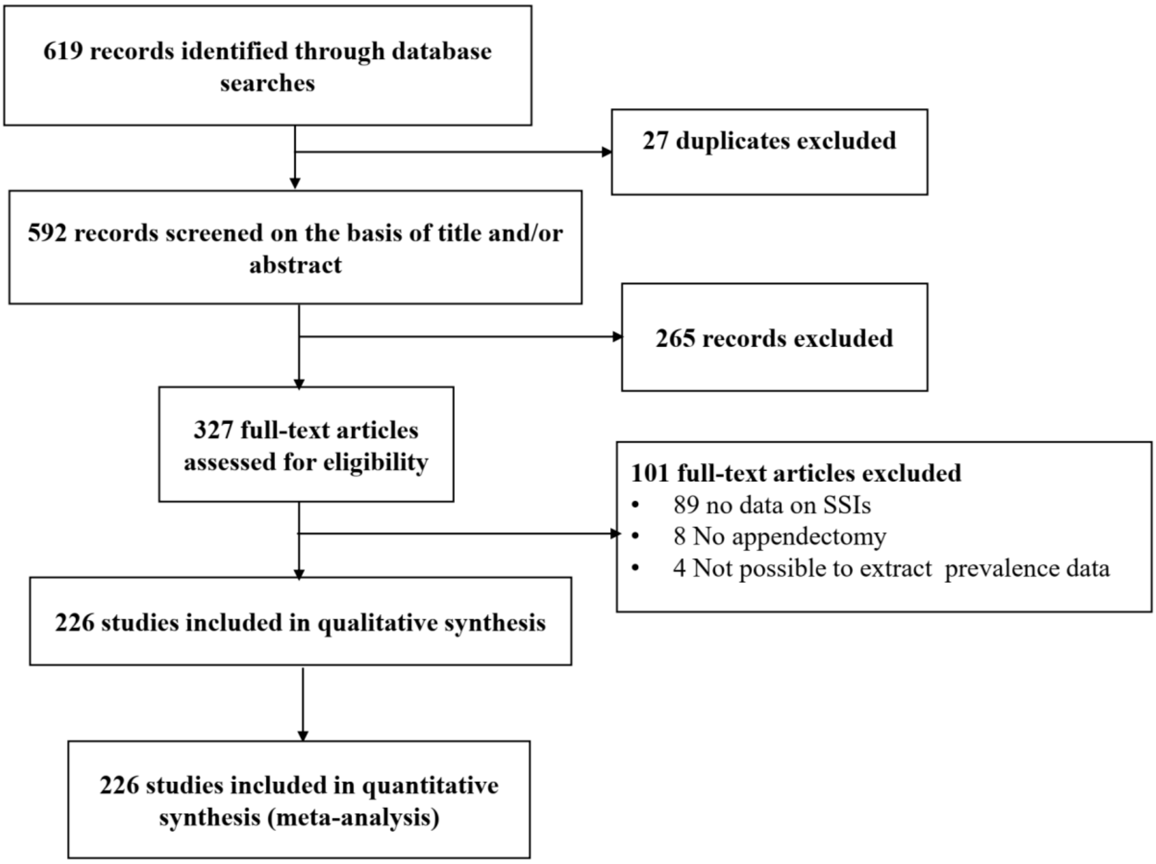
Heterogeneity: I^2 = 96.9% [96.6%; 97.2%], τ^2 = 0.0156, p = 0
Residual heterogeneity: I^2 = 95.9% [95.4%; 96.4%], p = 0
Test for subgroup differences: χ^2_2 = 16.75, df = 2 (p = 0.0002)



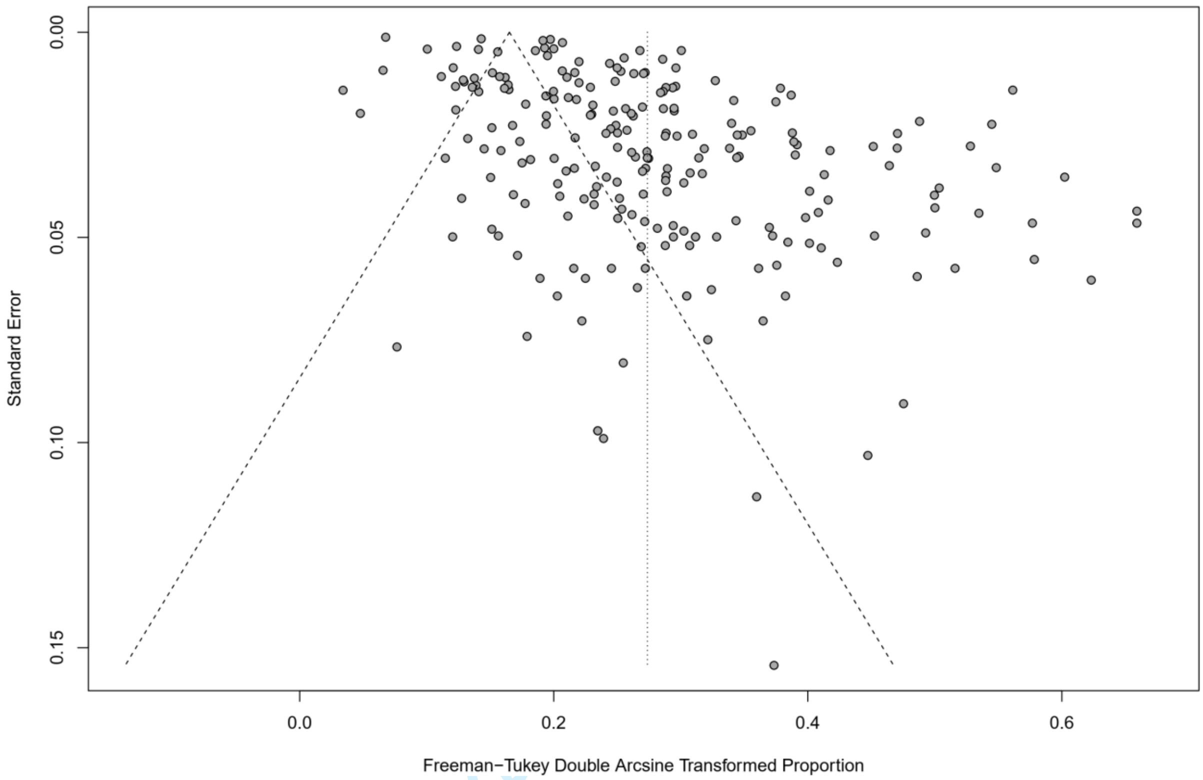
Global incidence of surgical-site infection after appendectomy: a systematic review and meta-analysis

APPENDIX

Celestin **Danwang**, Jean Joel **Bigna**, Joel Noutakdie **Tochie**, Aime **Mbonda**, Clarence Mvalo **Mbanga**, Rolf Nyah Tuku **Nzalie**, Marc Leroy **Guifo**, Arthur **Essomba**



Supplementary Figure 1. Study flow



Supplementary Figure 2. Funnel plot for publication bias

Supplementary Table 1. Search strategy in EMBASE

	Search terms
#1	'appendectomy'/exp OR appendectomy OR 'appendicectomy'/exp OR appendicectomy OR appendices OR 'appendix epiploica' OR 'omental appendix' OR 'appendicitis'/exp OR appendicitis
#2	'surgical site infection'/exp OR 'surgical site infection' OR 'surgical wound infection'/exp OR 'surgical wound infection' OR 'surgical wound infections'/exp OR 'surgical wound infections' OR 'surgical site infections' OR 'operative site infections' OR 'postoperative wound infections'/exp OR 'postoperative wound infections' OR 'postoperative wound infection'/exp OR 'postoperative wound infection'
#3	[2000-2018]/py
#4	#1 AND #2 AND #3

Supplementary Table 2 : Characteristics of included studies

Characteristics	**N = 226**
Year of publication, range	2000-2018
%Male, range	0-100 (n = 195)
Mean/median age, range	7-74 (n = 186)
%HIV	0-13.1 (n = 2)
%Diabetes	0-95.7 (n = 34)
%Obesity	0-7.4 (n = 18)
Design, n	
- Cross sectional	120
- Cohort study	99
- Case control	7
WHO regions, n	
- Africa	8
- Americas	67
- Eastern Mediterranean	23
- Europe	68
- Multiregional	1
- South-East Asia	16
- Western Pacific	43
Level of income, n	
- Low	9
- Lower-middle	27
- Upper-middle	36
- High	154
Timing of data collection	
- Retrospective	123
- Prospective	101
- Unclear	2
Sampling	

- Consecutive	131
- Systematic	37
- Random	32
- Exhaustive	11
- Unclear	15
Number of sites	
- Multisite	51
- One site	170
- Unclear	5
Pattern of appendicitis, range	
- %Catarrhal	0-100 (n = 84)
- %Perforated	0-100 (n = 110)
- %Suppurated	0-100 (n = 70)
- %Gangrenous	0-46.7 (n = 89)
%With administered antibiotics	24.1-100 (n = 109)
%With administered analgesics	64.5-100 (n = 20)
%With diet > 6 or 8 hours	50-100 (n = 3)
Type of surgery	
- %Open surgery	0-100 (n = 134)
- %Laparoscopy	0-100 (n = 187)
Mean/median time to complete the intervention (in hours), range	0.1-2.2 (n = 106)
Type of anesthesia, n	
- General	118
- Spinal and general	2
- Unclear	106
SSI definition, n	
- CDC-NNIS criteria	50
- Other criteria	25
- Not reported/Unclear	151

Supplementary Table 3. *Individual characteristics of included studies*

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Adejumo (1)	2015	Moderate	Cohort	Nigeria	Retrospective	Consecutive	One site	2007-2014	Adults	39	26	NR	Catarrhal, Perforated, Suppurated, Gangrenous	48.9	NR	NR	NR	100	NR	NR	NR	NR	141
Aguillo (2)	2005	Moderate	Cohort	Spain	Prospective	Consecutive	Unclear	NR	Children, Adolescents, Adults, Elderly	63.1	NR	NR	Unclear	NR	NR	NR	NR	100	NR	NR	NR	NR	792
Adhikar (3)	2008	Moderate	Cohort	Nepal	Prospective	Consecutive	One site	2005-2006	Children, Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy	0.5	General	NR	50
Ahmad(4)	2014	Moderate	Clinical trial	Pakistan	Prospective	Consecutive	One site	2012	Adults	35.4	27.4	NR	Perforated	0	100	0	0	100	Open Surgery	NR	General	NR	158
Ahmed (5)	2015	Moderate	Cross sectional	Pakistan	Retrospective	Consecutive	One site	2009-2010	Children, Adolescents	51.89	10.1	NR	Unclear	NR	NR	NR	NR	100	Open Surgery	NR	NR	NR	79
Akkoyun (6)	2012	Moderate	Case control	Turkey	Retrospective	Consecutive	One site	1998-2011	Children	64.5	8.9	NR	Perforated	0	100	0	0	100	Open Surgery	0.6	General	NR	234
Al-Saadi (7)	2006	Moderate	Cohort	Yemen	Retrospective	Consecutive	One site	2003-2005	Children, Adolescents, Adults	75	NR	NR	Catarrhal, Perforated, Suppurated, Gangrenous	NR	60	NR	13	100	Laparoscopy	NR	NR	NR	160
Al-Temimi (8)	2017	Low	Cohort	USA	Prospective	Systematic	One site	2016	Children, Adolescents, Adults, Elderly	40.2	36	NR	Catarrhal, Perforated, Suppurated, Gangrenous, Normal	73	17.4	3.3	3.3		Laparoscopy	0.6	NR	NR	92
Ali (9)	2012	Moderate	Cohort	Nigeria	Prospective	Consecutive	One site	2002-2009	Children, Adolescents, Adults, Elderly	33.9	32	NR	Catarrhal, Perforated, Suppurated, Gangrenous	NR	23.47	NR	NR		Open Surgery	NR	NR	NR	1257
Ali (10)	2015	Moderate	Cross sectional	Pakistan	Prospective	Consecutive	One site	2014	Adults	46.3	27.4	NR	Unclear	NR	NR	NR	NR	100	Open Surgery	NR	General	NR	121
Almström (11)	2016	Moderate	Cohort	Sweden	Retrospective	Systematic	One site	2006-2013	Children, Adolescents	59.5	NR	NR	Perforated, Non Perforated 76%	NR	24	NR	NR		Laparoscopy or Open Surgery	0.8	NR	NR	2756
Álvarez-Moreno (12)	2014	Low	Cohort	Colombia	Prospective	Systematic	Multisite	2008-2010	Children, Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR		NR	NR	NR	According to CDC-NNIS diagnostic criteria	947
Andert (13)	2017	Moderate	Cohort	Germany	Retrospective	Consecutive	One site	2003-2014	Adults	48.6	30.5	NR	Catarrhal, Perforated, Suppurated, Gangrenous	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	NR	NR	Local signs of inflammation	2136
Anderson (14)	2014	Moderate	Cohort	Sweden	Retrospective	Exhaustive	Multisite	1992-2008	Adults	54	NR	NR	Perforated, Not perforated	NR	19.4	0	0		Laparoscopy or Open Surgery	NR	NR	NR	169896
Aranda-Narváez (15)	2010	Low	Cohort	Spain	Retrospective	Random	One site	1997-2009	Children, Adolescents, Adults, Elderly	63.3	3[illegible]	NR	Suppurated, Gangrenous	0	0	53.3	46.7	100	Laparoscopy or Open Surgery	NR	General	According to CDC-NNIS diagnostic Criteria	30
Aranda-Narvaez (16)	2014	Moderate	Cohort	Spain	Not reported/Unclear	Not clear	One site	2007-2010	Adults	57	2[illegible]	NR	Catarrhal, Perforated, Suppurated, Gangrenous	65.8	NR	NR	NR	62.00	Laparoscopy or Open Surgery	0.92	NR	According to CDC-NNIS diagnostic Criteria	868

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Arthur (17)	2017	Low	Cross sectional	Australia	Prospective	Systematic	Multisite	2016	Children, Adolescents, Adults, Elderly	49.5	31.4	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	1	NR	NR	1189
Asefa (18)	2002	High	Cross sectional	Ethopia	Retrospective	Consecutive	One site	1997-1999	Adults	79.5	25.6	NR	Catarrhal, Perforated	45.4	44	0	0		NR	NR	NR	NR	200
Asefa (19)	2014	Moderate	Cross sectional	Ethopia	Retrospective	Consecutive	One site	2006-2010	Children	62.1	1[illegible]	NR	Catarrhal, Perforated, Suppurated, Gangrenous	32.3	59.6	6.2	1.9		NR	NR	NR	NR	322
Bae (20)	2016	Moderate	Cross sectional	USA	Retrospective	Systematic	One site	2010-2013	Children, Adolescents, Adults	NR	3[illegible]	NR	Unclear	NR	NR	NR	NR	36.4	Laparoscopy	NR	NR	According to CDC-NNIS diagnostic criteria	143
Bae (21)	2016	Low	Cross sectional	Korea	Prospective	Systematic	One site	2014-2016	Adults	52	6[illegible]	NR	Perforated, Suppurated, Gangrenous	NR	4	72	24	100	Laparoscopy	1.2	General	According to CDC-NNIS diagnostic criteria	25
Baek (22)	2011	Moderate	Cross sectional	Korea	Retrospective	Exhaustive	One site	2007-2009	Elderly	45.5	68.2	NR	Catarrhal, Perforated, Suppurated, Gangrenous	22.1	29.9	32.5	15.6	100	Laparoscopy or Open Surgery	1.05	General	NR	77
Bali (23)	2015	Moderate	Cohort	Turkey	Prospective	Consecutive	One site	2009-2013	Adults	35.7	32.33	NR	Unclear	NR	NR	NR	NR		Laparoscopy	1	NR	NR	126
Banghu (24)	2013	Low	Cohort	UK, Spain, Japan, Hong Kong, Australia, New Zealand	Prospective	Consecutive	Multisite	2012	Children, Adolescents, Adults, Elderly	51.1	NR	NR	Unclear	NR	NR	NR	NR	96.9	Laparoscopy or Open Surgery	NR	NR	According to CDC-NNIS diagnostic criteria	3326
Bansal (25)	2012	Low	Cohort	Switzerland	Prospective	Consecutive	One site	NR	Children	62	9.8	NR	Catarrhal, Perforated	74.3	25.7	NR	NR	49.2	Laparoscopy or Open Surgery	1.0	NR	According to CDC-NNIS diagnostic Criteria	187
Batajoo(26)	2012	Moderate	Cross sectional	Nepal	Retrospective	Consecutive	One site	2009-2012	Children, Adolescents, Adults, Elderly	45.6	29.6	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	0.8	NR	NR	226
Bharathi (27)	2011	Moderate	Cohort	Nepal	Prospective	Consecutive	One site	2008-2009	Children, Adolescents, Adults, Elderly	50	22.9	NR	Catarrhal, Perforated, Suppurated, Gangrenous	80	NR	NR	NR	100	Laparoscopy with Open Surgery	0.5	NR	NR	26
Bıçakcı (28)	2011	High	Cross sectional	Turkey	Retrospective	Systematic	Unclear	2006-2009	Children, Adolescents	64.5	1[illegible]	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	NR	279
Bickel (28)	2011	Moderate	Clinical trial	Israel	Prospective	Random	One site	2006-2009	Adults	73	28	NR	Catarrhal, Gangrenous, Phlegmonous 58.6 , Normal 4.3%	17	NR	NR	20.5	100	Open Surgery	0.5	General	NR	210
Blackwood (29)	2017	Moderate	Cross sectional	USA	Retrospective	Random	One site	2010-2015	Children	55.6	10.4	29.6	Unclear	NR	NR	NR	NR		Open Surgery	2	General	According to CDC-NNIS diagnostic Criteria	115
Blakely (31)	2011	Low	Clinical trial	USA	Prospective	Random	One site	2006-2009	Children, Adolescents	55.7	10.2	NR	Perforated	0	100	0	0	100	Laparoscopy or Open Surgery	1.9	NR	NR	131

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Bonadio (32)	2017	Moderate	Cross sectional	USA	Retrospective	Consecutive	One site	2008-2015	Children, Adolescents	56.2	8.4	NR	Perforated	0	100	0	0	100	Laparoscopy	NR	General	NR	203
Boomer (33)	2014	Low	Cohort	USA	Retrospective	Consecutive	One site	2010-2012	Children, Adolescents	61.1	10.9	NR	Catarrhal, Perforated, Gangrenous	66.2	NR	NR	NR	97.8	Laparoscopy or Open Surgery	NR	General	Wound infection or abdominal/pelvic abscess	1388
Boomer (34)	2016	Low	Cross sectional	USA	Retrospective	Systematic	Multisite	2010-2012	Children, Adolescents	60.3	11.0	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	According to CDC-NNIS diagnostic criteria	1338
Bozkurt (35)	2014	Moderate	Case control	Turkey	Retrospective	Consecutive	One site	2008-2012	Children, Adolescents, Adults, Elderly	54	30.4	NR	Catarrhal	100	0	0	0		Laparoscopy	0.8	General	NR	1849
Brandt (36)	2008	Moderate	Cross sectional	Germany	Retrospective	Systematic	Multisite	2000-2004	Children, Adolescents, Adults, Elderly	NR	NR	NR	NR	NR	NR	NR	NR		NR	NR	NR	According to CDC-NNIS diagnostic criteria	10969
Brümmer (37)	2009	Moderate	Cohort	Germany	Retrospective	Consecutive	Multisite	2004-2007	Children, Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	According to CDC-NNIS diagnostic Criteria	14209
Cairo (38)	2017	Moderate	Cohort	USA	Retrospective	Consecutive	Multisite	2012-2015	Children, Adolescents	61.3	11.0	29.9	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	NR	20981
Cameron (39)	2017	Low	Cohort	USA	Retrospective	Systematic	Multisite	2012-2015	Children, Adolescents	60.4	1[illegible]	11.7	Unclear	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	NR	NR	According to CDC-NNIS diagnostic criteria	1389
Cao (40)	2015	Moderate	Cohort	China	Retrospective	Consecutive	Multisite	2011-2013	Adults	54.2	37.3	12.4	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	0.8	General	NR	12586
Cervantes-sánchez (41)	2000	Low	Clinical trial	Mexico	Prospective	Random	One site	1994-1995	Children, Adults	53.4	28	NR	Unclear	NR	NR	NR	NR		Open Surgery	NR	General	Pus or a positive bacteriologic culture from a wound discharge	350
Chamisa (42)	2009	High	Cross sectional	South Africa	Retrospective	Exhaustive	One site	2002-2004	Children, Adolescents, Adults, Elderly	78.4	NR	NR	Catarrhal, Perforated, Gangrenous, Normal	53	30.5	NR	10.2		Laparoscopy or Open Surgery	NR	NR	NR	324
Chaudhary (43)	2005	Moderate	Clinical trial	Pakistan	Prospective	Random	One site	1999-2003	Children, Adolescents, Adults, Elderly	45.4	NR	NR	Catarrhal	NR	0	0	0		Open Surgery	NR	NR	NR	677
Chen (44)	2011	High	Cross sectional	China	Prospective	Systematic	One site	2008-2009	Adults	NR	NR	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	0.8	Spinal and General	NR	69
Chen (45)	2012	High	Cross sectional	Taiwan	Prospective	Consecutive	One site	2010	Adults	60	38	NR	Unclear	NR	NR	NR	NR	73	Laparoscopy or Open Surgery	NR	General	NR	117
Chen (46)	2015	Moderate	Cohort	Taiwan	Retrospective	Consecutive	One site	2010-2012	Adults	43.6	42.5	NR	Catarrhal, Perforated	87.3	12.7	0	0		Laparoscopy or Open Surgery	NR	NR	NR	236
Chiang (47)	2006	Moderate	Cross sectional	Taiwan	Retrospective	Exhaustive	One site	2002-2004	Adults	59.7	3[illegible]	NR	Catarrhal, Perforated	68	17	0	0	100	Open Surgery	1.1	General	NR	390

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Chiang (48)	2012	Moderate	Cohort	Taiwan	Prospective	Consecutive	One site	2008-2009	Adults	58.6	37.8	10	Unclear	NR	NR	NR	NR	100	Open Surgery	NR	General	Presence of gross or purulent discharge at the incision site with or without a positive bacterial culture	70
Cho (49)	2014	Low	Cross sectional	Korea	Prospective	Consecutive	One site	2011-2012	Adults	53	38.7	18.8	Unclear	NR	NR	NR	NR		Laparoscopy	NR	General	According to CDC-NNIS diagnostic Criteria	101
Choudhary (50)	2014	Moderate	Cross sectional	India	Prospective	Random	One site	2010-2013	Adults	67	NR	NR	Appendicular mass	0	0	0	0		NR	NR	NR	NR	92
Clyde (51)	2008	High	Cross sectional	USA	Retrospective	Systematic	One site	2002-2007	Children, Adolescents, Adults, Elderly	52	3[illegible]	NR	Catarrhal, Perforated, Unclear	77	14	0	0		Laparoscopy or Open Surgery	NR	NR	NR	1198
Coakley (52)	2011	Low	Cohort	USA	Retrospective	Exhaustive	One site	2005-2010	Adults	47.3	28.7	NR	Catarrhal, Perforated, Suppurated, Gangrenous	38.3	1.2	47.1	9.8	100	Laparoscopy or Open Surgery	1.0	NR	According to CDC-NNIS diagnostic Criteria	728
Crandall (53)	2009	High	Cross sectional	USA	Retrospective	Not clear	One site	2004-2005	Adults	54	32.5	NR	NR	NR	74	NR	NR		Laparoscopy or Open Surgery	0.9	General	NR	176
Dede (54)	2008	Moderate	Cohort	Hungary	Prospective	Consecutive	One site	2005-2007	Children, Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	NR	273
Dhiman (55)	2013	High	Cross sectional	USA	Retrospective	Not clear	Multisite	2003-2009	Adults	58	30.1	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	NR	1250
Dimitriou (56)	2013	Moderate	Cohort	Germany	Retrospective	Consecutive	One site	2007-2010	Children, Adolescents, Adults, Elderly	53.5	34.9	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	1	NR	NR	404
Durkin (57)	2015	Moderate	Cohort	USA	Retrospective	Consecutive	Multisite	2007-2012	Adults	NR	NR	NR	Unclear	NR	NR	NR	NR		Laparoscopy	NR	NR	NR	14763
Ein (58)	2013	Moderate	Cross sectional	Canada	Retrospective	Consecutive	One site	1969-2003	Children	70		NR	Perforated	0	100	0	0	78.8	Open Surgery	NR	General	1.Wound infection=pus draining from between the stitches or staples 2.Intra-abdominal abscess=presence of fever, abdominal pain and or gastrointestinal dysfunction and confirmed by radiologic evidence of intra-abdominal fluid collection	496

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Fukuda (59)	2016	Moderate	Cohort	Japan	Retrospective	Consecutive	Multisite	2007-2011	Children, Adolescents, Adults	54.4	64.5	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	1.3	General	NR	2074
Gandaglia (60)	2014	Low	Cohort	USA	Prospective	Consecutive	Multisite	2005-2011	Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	NR	General	According to CDC-NNIS diagnostic Criteria	97780
Garcell (61)	2016	Low	Cohort	Cuba	Prospective	Consecutive	One site	2013-2015	Children, Adolescents, Adults, Elderly	95.3	30.7	2.1	Unclear	NR	NR	NR	NR		Open Surgery	NR	NR	According to CDC-NNIS diagnostic Criteria	603
Ghnnam(62)	2011	Moderate	Cross sectional	Saudi Arabia	Retrospective	Not clear	One site	2007-2010	Adults	63.4	49.0	NR	Perforated, Unclear	NR	38.1	NR	NR		NR	NR	NR	NR	63
Giesen(63)	2017	Moderate	Cohort	Netherlands	Retrospective	Consecutive	Multisite	2014-2015	Children, Adults	54.3	3[illegible]	NR	Catarrhal, Perforated, Suppurated, Gangrenous	48.2	17.3	23.2	11.3	100	Laparoscopy or Open Surgery	0.52	NR	According to CDC-NNIS diagnostic criteria	637
Giiti (64)	2010	Moderate	Cross sectional	Tanzania	Prospective	Systematic	One site	2008-2009	Children, Adolescents, Adults, Elderly	44.7	2[illegible]	NR	Catarrhal, Perforated, Suppurated, Mass	87.4	7.0	1.5	0		NR	NR	NR	NR	199
Golub (65)	2016	Moderate	Cohort	Russia	Retrospective	Consecutive	Multisite	2012	Adolescents, Adults	NR	34.8	NR	Unclear	NR	NR	NR	NR	100	Open Surgery	NR	General	NR	332
Gross (66)	2016	Moderate	Cross sectional	USA	Retrospective	Consecutive	Multisite	2012-2013	Children, Adolescents	60.1	NR	17.8	Perforated	0	100	0	0		Laparoscopy or Open Surgery	NT	General	NR	2585
Gurien (67)	2016	Moderate	Cohort	USA	Retrospective	Consecutive	One site	2009-2012	Children, Adolescents	62	10.5	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	NR	General	Wound infections or intra abdominal abscesses	484
Hamzaoglu (68)	2004	Low	Cross sectional	Turkey	Prospective	Consecutive	One site	1999-2001	Adults	57	46.7	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	NR	100
Harmon (69)	2016	Low	Cohort	USA	Retrospective	Systematic	One site	2007-2012	Children, Adolescents, Adults, Elderly	47.4	39.7	NR	Non perforated	0	0	0	0		Laparoscopy or Open Surgery	NR	NR	According to CDC-NNIS diagnostic criteria	411
Helling (70)	2017	Low	Cross sectional	USA	Retrospective	Systematic	One site	2009-2014	Adults	64.3	34.4	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	NR	NR	According to CDC-NNIS diagnostic criteria	611
Helmer (71)	2002	Low	Cross sectional	USA	Retrospective	Systematic	One site	1998-1999	Children, Adolescents, Adults, Elderly	NR	NR	NR	Perforated, Non perforated	NR	19.4	NR	NR	100	NR	NR	NR	A surgical wound infection was defined as purulent drainage from the wound, cellulitis requiring antibiotics, or the opening of a closed wound. An intra-abdominal abscess was defined as an intraabdominal fluid collection that contained purulent material.	438
Hesami (72)	2014	Low	Clinical trial	Iran	Prospective	Random	Unclear	2010-2011	Children, Adolescents, Adults	58.9	2[illegible]	NR	Unclear	NR	NR	NR	NR	100	Open Surgery	NR	NR	1..wound unfection=Purulent discharge, redness, inflammation, and the need to reooen	90

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
																						the wound 2...intra-abdominal abscess=abdominal pain, fullness, fever and confirmed by ecography	
Hussain (73)	2012	Moderate	Clinical trial	Saudi Arabia	Prospective	Consecutive	One site	2010-2011	Adults	NR	32.2	NR	Catarrhal	100	0	0	0	100	Open Surgery	NR	NR	1..SSI=Pus discharge from wound needing its opening and drainage 2..Intra-abdominal collection=fluid collection inside the peritoneal cavity confirmed by ultrasound or CT scan that required drainage	377
Horvath (74)	2016	Moderate	Cross sectional	Germany	Retrospective	Consecutive	One site	2005-2013	Adults	47	28.6	NR	Perforated, phelgmonous	NR	52	NR	NR		Laparoscopy or Open Surgery	1.0	General	According to CDC-NNIS diagnostic Criteria	1516
Hughes (75)	2013	Moderate	Cross sectional	United Kingdom	Retrospective	Systematic	One site	2009-2010	Adults	55.6	30	NR	Unclear, simple and complicated	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	NR	General	NR	266
Hung (76)	2016	Moderate	Cross sectional	Vietnam	Prospective	Systematic	Multisite	2008-2010	Adults	45	41.6	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	1	General	NR	752
Iñigo (77)	2006	Low	Cohort	Spain	Prospective	Consecutive	One site	1998-2002	Adults	NR	NR	NR	Unclear	NR	NR	NR	NR		NR	0.7	NR	According to CDC-NNIS diagnostic Criteria	721
Iqbal (78)	2015	Low	Clinical trial	Pakistan	Prospective	Random	One site	2011	Adolescents, Adults, Elderly	66.3	26	NR	Catarrhal	100	0	0	0	100	Open Surgery	NR	General	According to Southampton criteria. Southampton grade 2 and above was considered as surgical site infection.	166
Javadi (79)	2017	Moderate	Clinical trial	Iran	Prospective	Random	One site	2016	Children, Adolescents, Adults	65	19.3	NR	Catarrhal, Suppurated, Gangrenous	NR	0	NR	NR		Open Surgery	0.5	General	NR	69
Jenkins (80)	2016	Low	Cohort	USA	Prospective	Systematic	Multisite	2006-2011	Children, Adolescents, Adults, Elderly	51.3	40.1	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	According to CDC-NNIS diagnostic criteria	12410
Kang (81)	2012	Moderate	Case control	Korea	Retrospective	Random	One site	2010-2012	Adults	54.4	31.7	NR	Catarrhal, Perforated, Suppurated, Gangrenous	NR	5.1	NR	NR	100	Laparoscopy	1.1	General	NR	217
Kapischke (82)	2013	Low	Case control	Germany	Retrospective	Consecutive	One site	1999-2001	Children, Adolescents	47.8	11.5	NR	Catarrhal, Perforated	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	0.6	General	According to CDC-NNIS diagnostic criteria	159
Karam (83)	2016	Moderate	Cross sectional	USA	Retrospective	Not clear	One site	2010-2015	Children	62	1[illegible]	NR	Perforated, Gangrenous	NR	20.6	NR	6.2		Laparoscopy	NR	General	NR	625
Karam (84)	2016	Moderate	Cross sectional	USA	Retrospective	Consecutive	One site	2010-2015	Children, Adolescents	63	NR	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy	1	General	NR	101
Kasatpibal (85)	2005	Low	Cross sectional	Thailand	Prospective	Systematic	Multisite	2003-2004	Children, Adolescents, Adults, Elderly	26.6	37.2	NR	Unclear	NR	NR	NR	NR	24.1	NR	0.8	NR	According to CDC-NNIS diagnostic criteria	1487
Kasatpibal (85)	2006	Moderate	Cohort	Thailand	Prospective	Not clear	Multisite	2003-2004	Children, Adolescents, Adults, Elderly	46.9	26	NR	Catarrhal	100	NR	NR	NR	92.2	Open Surgery	0.97	NR	According to CDC-NNIS diagnostic criteria	2139

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Kato (87)	2008	Low	Cohort	Japan	Prospective	Systematic	One site	2004-2006	Children	NR	9.4	NR	Perforated, Non perforated 75%	NR	25	NR	NR	100	Open Surgery	NR	NR	NR	64
Kell (88)	2003	Moderate	Cohort	Ireland	Prospective	Consecutive	Unclear	NR	Children, Adolescents, Adults, Elderly	75.2	20.7	NR	Unclear	NR	NR	NR	NR	100	Open Surgery	NR	General	Defined based on clinical and microbiological criteria	149
Khan (89)	2007	Low	Cohort	United Kingdom	Prospective	Consecutive	One site	2006	Children, Adolescents, Adults, Elderly	47.0	24	NR	Catarrhal, Perforated	63.4	20.1	0	0	100	Laparoscopy or Open Surgery	0.9	General	According to CDC-NNIS diagnostic Criteria	134
Khan (90)	2012	Moderate	Clinical trial	Pakistan	Prospective	Random	Multisite	2006-2009	Adults	69	33.3	NR	Unclear	NR	NR	NR	NR	100	Open Surgery	0.6	General	NR	100
Khan (91)	2014	Moderate	Clinical trial	Pakistan	Prospective	Random	Multisite	2013-2014	Children, Adolescents, Adults, Elderly	56.7	24	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	Observation of pain, redness, tenderness and purulent discharge	270
Khiria (92)	2011	Moderate	Cross sectional	India	Retrospective	Consecutive	One site	1999-2009	Adults	66	33.4	NR	Perforated, Gangrenous	NR	14.3	NR	5.2		Laparoscopy or Open Surgery	1.2	General	Any evidence of infection(erythema, purulent discharge, induration...) and requiring suture removal, antibiotic treatment, or evidence of dehiscence	497
Kilic (93)	2016	Moderate	Cross sectional	Turkey	Retrospective	Consecutive	One site	2004-2010	Children	62.1	9.5	NR	Perforated	0	100	0	0	100	Open Surgery	NR	NR	According to CDC-NNIS diagnostic Criteria	110
Kim (94)	2015	Low	Cross sectional	Korea	Retrospective	Systematic	One site	2008-2013	Children, Adolescents, Adults, Elderly	47.8	32.6	NR	Perforated, Suppurated, Gangrenous, Normal	6	13.8	64.5	7.1		Laparoscopy	0.7	NR	According to CDC-NNIS diagnostic criteria	2587
Kim (95)	2011	Moderate	Cross sectional	USA	Prospective	Consecutive	One site	2005-2008	Elderly	48.1	73.4	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	According to CDC-NNIS diagnostic Criteria	3335
Kim(96)	2016	Moderate	Cohort	Korea	Retrospective	Consecutive	One site	2005-2012	Adults	59	NR	NR	Perforated, Gangrenous	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	1.9	General	NR	207
Kiriakopoulos (97)	2006	Moderate	Cross sectional	Greece	Retrospective	Consecutive	One site	2000-2004	Adults	73.8	42.3	NR	Perforated, Suppurated, Generalized peritonitis	0	61.9	9.5	0	100	Laparoscopy with Open Surgery	1.1	General	NRR	42
Kirshtein (98)	2009	Moderate	Cross sectional	Israel	Retrospective	Consecutive	One site	2000-2007	Adults	31.9	70.1	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	0.7	General	NR	1435
Kiudelis (99)	2013	Moderate	Cross sectional	Lithuania	Prospective	Consecutive	One site	2004-2009	Adults	46.3	32.3	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy	1.1	General	NR	152
Kleif (100)	2017	Moderate	Cross sectional	Denmark	Retrospective	Not clear	Multisite	2012-2014	Adults	53	47	NR	Suppurated, Gangrenous	NR	NR	NR	NR	98	Laparoscopy or Open Surgery	NR	General	NR	1151
Koizumi (101)	2014	Moderate	Cross sectional	Japan	Prospective	Consecutive	One site	2010	Adults	57.9	39.8	NR	Catarrhal, Perforated, Gangrenous, phelmong	6.4	6.4	NR	25 4		Laparoscopy or Open Surgery	0.9	General	NR	185
Kubota (102)	2014	Low	Clinical trial	Japan	Prospective	Random	One site	2008-2012	Children	63.6	NR	NR	Unclear	NR	NR	NR	NR	100	Open Surgery	NR	General	According to CDC-NNIS diagnostic Criteria	10

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Kumamoto (103)	2014	Low	Cohort	Japan	Prospective	Consecutive	One site	1997-2011	Adults	0	2[illegible]	NR	Catarrhal, Gangrenous, Phlegmonous	21.8	NR	NR	33.4	100	Open Surgery	0.7	General	NR	124
Kumar (104)	2008	Moderate	Cohort	Pakistan	Prospective	Consecutive	One site	1997-2000	Children, Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR	50	Laparoscopy or Open Surgery	0.7	NR	NR	100
Kumar (105)	2016	Moderate	Cohort	Nepal	Prospective	Consecutive	One site	2015-2016	Adolescents, Adults	49	33.9	NR	Catarrhal, Perforated, Suppurated, Gangrenous, Normal	88.6	4.7	1.9	2.4		Laparoscopy or Open Surgery	0.7	General	According to CDC-NNIS diagnostic Criteria	212
Lacher (106)	2012	Moderate	Cohort	USA	Prospective	Consecutive	One site	2009-2011	Children, Adolescents	64.1	10.9	22.4	Catarrhal, Perforated	71.8	19	NR	NR	100	Laparoscopy	0.7	General	NR	415
Le (107)	2009	Moderate	Cross sectional	USA	Retrospective	Systematic	One site	1997-2007	Children, Adolescents, Adults, Elderly	52.1	31.8	NR	Catarrhal, Perforated, Gangrenous, Normal Appendix	92.9	2	0	2.2	86	Laparoscopy or Open Surgery	0.9	NR	According to CDC-NNIS diagnostic criteria	507
Lee (108)	2009	Low	Clinical trial	USA	Prospective	Random	One site	2006-2008	Children, Adolescents, Adults, Elderly	64.2	34.2	NR	Catarrhal, Perforated, Suppurated, Gangrenous	46.8	26.6	16.5	10.1	100	Open Surgery	NR	NR	Any significant subcutaneous SSI necessitating wound opening or treatment with antibiotics. This also included any subject who was prescribed a separate course of antibiotics after discharge from the hospital.	109
Lee (109)	2010	Moderate	Cross sectional	Taiwan	Prospective	Consecutive	One site	2006-2008	Children	58	11.1	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	2	General	NR	264
Lee (110)	2010	Moderate	Cross sectional	Korea	Retrospective	Consecutive	One site	2008-2009	Adults	49.3	26.7	NR	Perforated, Suppurated	0	26.7	73.3	0		Laparoscopy	1.0	General	NR	75
Lee (111)	2011	Moderate	Cohort	USA	Retrospective	Consecutive	Multisite	1998-2007	Children, Adolescents	61.5	11	NR	Perforated, Non perforated	NR	25.7	NR	NR		Laparoscopy or Open Surgery	NR	General	NR	2462
Lee (112)	2011	Moderate	Cohort	USA	Retrospective	Systematic	Multisite	1998-2007	Children, Adolescents	61	11.6	NR	Perforated, Non perforated 70.8%	NR	29.2	NR	NR		Laparoscopy or Open Surgery	NR	NR	NR	7650
Lemieux (113)	2008	Moderate	Cohort	Canada	Retrospective	Consecutive	One site	1997-2007	Adults	0	28.8	NR	Perforated	NR	NR	NR	NR		Laparoscopy with Open Surgery	0.8	NR	NR	45
Levy(114)	2013	Moderate	Cohort	USA	Retrospective	Consecutive	One site	2010-2011	Children	NR	NR	NR	Catarrhal, Perforated, Suppurated, Gangrenous	56.4	32.7	4.2	6.7		Laparoscopy or Open Surgery	NR	NR	NSQIP criteria	312

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Li (115)	2005	Moderate	Cohort	China	Prospective	Consecutive	One site	2002-2004	Children, Adolescents	71.3	7.9	NR	Catarrhal, Suppurated, Gangrenous	11.0	0	69.4	19.7	100	Laparoscopy or Open Surgery	0.65	General	NR	160
Li (115)	2017	Moderate	Cohort	China	Retrospective	Consecutive	One site	2005-2016	Children	58.8	5.2	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	1	NR	Erythema, swelling and pus at the site of operation	398
Lim (116)	2011	Low	Cohort	Korea	Retrospective	Consecutive	One site	2009-2011	Adults	47.8	50.8	NR	Perforated, Gangrenous	0	61.6	NR	18.3	100	Laparoscopy or Open Surgery	1.3	General	Any evidence of infection (e.g., erythema, purulent discharge, induration, etc) requiring suture removal, antibiotics or dehiscence.	60
Lima (117)	2007	Moderate	Cross sectional	Spain	Retrospective	Consecutive	One site	2001-2006	Children, Adolescents, Adults, Elderly	NR	NR	NR	Catarrhal, Perforated, Suppurated, Gangrenous	53	2	26.3	9.7		NR	NR	NR	NR	300
Lin (118)	2006	Moderate	Cross sectional	Taiwan	Retrospective	Consecutive	One site	2001-2003	Adults	57.6	37.5	NR	Perforated	NR	100	NR	NR	100	Laparoscopy or Open Surgery	1.4	Not described	NR	229
Litz (119)	2016	Moderate	Cohort	USA	Retrospective	Consecutive	One site	2012-2015	Children, Adolescents	NR	11.4	17.7	Catarrhal, Perforated, Suppurated, Gangrenous, Interval, Normal	54	11.4	15.0	11.9		Laparoscopy	0.5	General	NR	413
Liu (120)	2017	High	Cross sectional	China	Retrospective	Consecutive	Unclear	2015-2016	Children	53.6	6.6	NR	Catarrhal, Suppurated, Gangrenous	34.8	0	38.4	26.8		Laparoscopy or Open Surgery	1.0	General	NR	112
Mahmood (121)	2016	Moderate	Clinical trial	Pakistan	Prospective	Random	One site	2012	Children, Adolescents, Adults	55.5	22.3	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	NR	General	Based on Wound Asepsis Score	200
Martinez (122)	2012	Moderate	Cross sectional	Spain	Retrospective	Random	One site	2011	Adults	60	35.8	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	NR	75
Mbah (123)	2006	Moderate	Cohort	Nigeria	Prospective	Consecutive	One site	2005	Children, Adolescents, Adults, Elderly	70	2[illegible]	NR	Unclear	NR	NR	NR	NR		Open Surgery	NR	General	NR	136
Memon (124)	2017	Moderate	Clinical trial	Pakistan	Prospective	Random	One site	2014-2016	Adults	53.3	2[illegible]	NR	Catarrhal	100	0	0	0	100	Laparoscopy or Open Surgery	NR	NR	NR	227
Menezes (125)	2008	Moderate	Cross sectional	Ireland	Retrospective	Consecutive	One site	2000-2006	Children, Adolescents	62.7	10.5	NR	Perforated, Gangrenous	0	81.4	0	17.8		Laparoscopy or Open Surgery	NR	NR	NR	118
Merenda (126)	2013	Moderate	Cross sectional	Poland	Retrospective	Consecutive	One site	2006-2012	Children, Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	NR	317
Michailidou (127)	2015	Low	Cross sectional	USA	Retrospective	Systematic	One site	2007-2013	Children, Adolescents	56.1	9.6	NR	Perforated, Negative appendectomy	NR	26.5	NR	NR		Laparoscopy or Open Surgery	1.3	NR	According to CDC-NNIS diagnostic criteria	264
Michailidou (128)	2015	Moderate	Cross sectional	USA	Retrospective	Consecutive	Multisite	2012	Children, Adolescents	60.1	11.2	22.5	Catarrhal, Perforated, Suppurated, Gangrenous	NR	NR	NR	NR	100	Laparoscopy	0	General	NR	2812

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Mickovic (129)	2015	Moderate	Cross sectional	Serbia	Retrospective	Not clear	One site	2010	Children	46.4	11.7	NR	Catarrhal, Perforated, Gangrenous	45.9	2.2	NR	19.5	100	Laparoscopy or Open Surgery	0.7	General	NR	218
Ming (130)	2009	Moderate	Cross sectional	China	Retrospective	Consecutive	One site	2003-2005	Adults	57.2	48.8	NR	Perforated, Gangrenous, Appendicular abscess	NR	72.3	NR	38.2	100	Laparoscopy or Open Surgery	NR	General	NR	173
Mingmalairak(131)	2009	Low	Clinical trial	Thailand	Prospective	Random	One site	2006-2007	Adults	61	29.5	0	Catarrhal, Perforated, Suppurated, Gangrenous	24	16	52	8.0	100	Open Surgery	43	General	NR	100
Miyano (132)	2010	Low	Cohort	Japan	Prospective	Consecutive	One site	2004-2008	Children, Adolescents	56.5	7.7	NR	Peritonitis complicating appendicitis	0	100	0	0	100	Laparoscopy or Open Surgery	1.9	General	NR	23
Moazzez (133)	2013	Low	Cohort	USA	Retrospective	Not clear	One site	2005-2009	Elderly	49.3	74	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	NR	2060
Monge Jodra (134)	2003	Moderate	Cohort	Spain	Prospective	Consecutive	Multisite	1997-2000	Children, Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR		NR	NR	NR	According to CDC-NNIS diagnostic Criteria	5780
Mueck (135)	2017	Moderate	Cohort	USA	Prospective	Consecutive	One site	2012-2015	Children, Adolescents	62.5	11.0	NR	Catarrhal, Suppurated	NR	NR	NR	NR	95	Laparoscopy with Open Surgery	NR	General	NR	697
Muensterer (136)	2011	Low	Cohort	USA	Prospective	Consecutive	One site	2009-2010	Children, Adolescents	NR	11.2	NR	Catarrhal, Perforated	78.1	10.4	0	0	100	Laparoscopy	0.6	General	Infected umbilicus requiring antibiotics, or incision and drainage	183
Muensterer (137)	2009	Moderate	Cross sectional	USA	Prospective	Consecutive	One site	2009	Children	61.3	11	NR	Perforated	NR	21.4	NR	NR		Laparoscopy	0.73	General	NR	75
Mustafa (138)	2016	Low	Clinical trial	Pakistan	Prospective	Random	One site	2015-2016	Adults	52.9	26.6	NR	Perforated	0	100	0	0	100	Open Surgery	NR	NR	Redness around the wound, serosangious discharge, fever > 100°F	68
Nadler (139)	2003	High	Cross sectional	USA	Retrospective	Systematic	One site	1998-2001	Children	62.2	9.35	NR	Perforated	NR	100	NR	NR	100	Open Surgery	NR	General	NR	94
Nataraja (140)	2010	Moderate	Cohort	United Kingdom	Retrospective	Consecutive	One site	2008-2010	Children, Adolescents	59.1	11	NR	Catarrhal, Perforated, Suppurated	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	NR	191
Nataraja (141)	2012	Moderate	Case control	United Kingdom	Retrospective	Consecutive	Multisite	2003-2010	Children, Adolescents	58.2	11.3	NR	Catarrhal, Perforated, Suppurated, Gangrenous	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	Post op intra abdominal abcess	1205
Obayashi (142)	2015	Moderate	Cross sectional	Japan	Retrospective	Consecutive	One site	2006-2014	Children, Adolescents	60	11	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	NR	485
Obinwa (143)	2015	Moderate	Cohort	Ireland	Retrospective	Consecutive	One site	1995-2008	Children	54.5	9.6	NR	Catarrhal, Perforated, Suppurated, Gangrenous	62.7	NR	NR	4.2	100	NR	NR	NR	NR	1037
Ohene (144)	2006	Moderate	Cross sectional	Ghana	Prospective	Consecutive	One site	1998-2004	Adults	63.9	32.4	NR	Unclear	NR	NR	NR	NR	100	Open Surgery	NR	General	NR	638
Okkyung (145)	2002	Moderate	Clinical trial	Korea	Prospective	Random	One site	2002	Children, Adolescents, Adults, Elderly	54.7	30.5	NR	Catarrhal, Suppurated, Gangrenous	NR	0	50	27.3	100	Open Surgery	NR	General	NR	84

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Onieva (146)	2017	Moderate	Cross sectional	Spain	Retrospective	Consecutive	One site	2012-2014	Children, Adolescents, Adults, Elderly	53.7	3[illegible]	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	NR	294
Page (147)	2010	Moderate	Cross sectional	USA	Retrospective	Exhaustive	Multisite	2008	Adults	51.4	39.2	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	0.94	General	NR	17199
Palesty (148)	2004	Moderate	Cross sectional	USA	Retrospective	Consecutive	One site	2000-2002	Adults	47	25.2	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy	1.2	General	NR	50
Pandit (149)	2016	High	Cohort	Nepal	Retrospective	Consecutive	Multisite	2009-2014	Children, Adolescents, Adults	51	24.3	NR	Perforated, Suppurated	NR	2.6	97.4	0		Open Surgery	0.6	Spinal and General	NR	101
Parcells (150)	2009	Low	Cohort	USA	Retrospective	Systematic	One site	1997-2007	Adults	NR	39.3	NR	Perforated, Not perforated	NR	33.1	NR	NR		Laparoscopy or Open Surgery	NR	NR	According to CDC-NNIS diagnostic criteria	1063
Park (151)	2017	Low	Cohort	Korea	Prospective	Systematic	One site	2012-2014	Adults	53.3	37.45	NR	Perforated, Gangrenous	NR	38.7	NR	45.9		Laparoscopy	1.1	General	According to CDC-NNIS diagnostic Criteria	1343
Park (152)	2018	Moderate	Cohort	Korea	Retrospective	Consecutive	One site	2009-2013	Adults	53.7	34.2	NR	Perforated	NR	13.2	NR	NR		Laparoscopy with Open Surgery	1.1	General	NR	986
Pascual (153)	2017	Moderate	Cohort	Spain	Prospective	Consecutive	One site	2013-2017	Adults	49	4[illegible]	NR	Unclear	NR	NR	NR	NR		Laparoscopy	0.1	General	NR	100
Patel (154)	2003	High	Cohort	Kenya	Retrospective	Consecutive	One site	1996-2002	Children, Adolescents, Adults	30.2	30.6	NR	Catarrhal, Suppurated, Gangrenous, Carcinoid tumor	94.3	0	0.9	2.8	100	Laparoscopy with Open Surgery	1.5	General	NR	106
Pearcy (155)	2017	Moderate	Case control	USA	Retrospective	Random	Multisite	2010-2014	Adults	54	36	NR	Unclear	NR	NR	NR	NR		NR	1.1	NR	NR	2903
Pishori (156)	2003	Low	Cross sectional	Pakistan	Prospective	Systematic	One site	1997-1999	Children, Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR		NR	NR	NR	According to CDC-NNIS diagnostic criteria	3304
Putnam (157)	2016	Moderate	Cross sectional	USA	Prospective	Consecutive	One site	2012-2015	Children, Adolescents	61	9.4	NR	Perforated, Suppurated, Gangrenous	0	100	0	0	100	Laparoscopy or Open Surgery	0.9	General	NR	410
Qahtani (158)	2014	Moderate	Cohort	Saudi Arabia	Prospective	Random	One site	2012	Adolescents, Adults	68	23.6	NR	Catarrhal, Perforated, Gangrenous	9.6	19.9	NR	22.4	100	Open Surgery	1.5	General	NR	91
Quezada(159)	2015	Moderate	Cohort	Chile	Retrospective	Consecutive	One site	2003-2013	Adults	43	3[illegible]	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	2.2	NR	NR	227
Raakow (160)	2014	High	Cohort	Germany	Prospective	Not clear	One site	2009-2013	Adolescents, Adults	28.8	27.2	NR	Catarrhal, Suppurated, Gangrenous	12.8	0	16	4		Laparoscopy	0.8	General	NR	156
Rafiq (161)	2015	Low	Clinical trial	Pakistan	Prospective	Random	One site	2012-2014	Adolescents, Adults, Elderly	48.5	22.6	0	Unclear	NR	NR	NR	NR	100	Open Surgery	0.7	General	NR	390
Rajabi-Mashhadi (162)	2012	Moderate	Clinical trial	Iran	Prospective	Random	One site	2006-2007	Adults	62.5	26.2	NR	Unclear, Non perforated	NR	NA	NR	NR	100	Open Surgery	NR	NR	NR	291

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Reinisch (163)	2017	Moderate	Cross sectional	Germany	Retrospective	Consecutive	One site	2008-2015	Adults	56	3[illegible]	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy with Open Surgery	NR	General	NR	680
Rios (164)	2004	High	Cross sectional	Peru	Not reported/Unclear	Consecutive	One site	2001-2002	Children, Adolescents, Adults, Elderly	NR	30.6	NR	Catarrhal, Perforated, Suppurated, Gangrenous	15.38	16.35	44.23	24.04	100	NR	0.98	Unclear	NR	104
Romano (165)	2014	Moderate	Cross sectional	USA	Retrospective	Systematic	One site	2010-2012	Adults	66	35.7	NR	Gangrenous	NR	NR	NR	9.7	86	Laparoscopy	NR	General	NR	372
Romel Hilaire (166)	2014	Moderate	Cross sectional	Cuba	Retrospective	Consecutive	One site	2007-2009	Adults	100	NR	NR	Suppurated	0	0	100	0		Laparoscopy or Open Surgery	NR	NR	NR	720
Romero (167)	2009	Moderate	Cross sectional	Colombia	Retrospective	Consecutive	One site	1997	Children, Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR		Laparoscopy	NR	NR	NR	310
Romy (168)	2008	Low	Cross sectional	Switzerland	Prospective	Systematic	Multisite	1998-2004	Children, Adolescents, Adults, Elderly	53.9	32.7	NR	Unclear	NR	NR	NR	NR	59.5	Laparoscopy or Open Surgery	NR	NR	According to CDC-NNIS diagnostic criteria	2468
Rooh-ul-Muqim (169)	2010	Moderate	Cohort	Pakistan	Prospective	Consecutive	One site	2008-2009	Adolescents, Adults, Elderly	48.5	24	NR	Catarrhal, Perforated, Suppurated, Gangrenous	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	0.5	General	NR	165
Rossem (170)	2015	Moderate	Cohort	Netherlands	Prospective	Consecutive	Multisite	2014	Adults	47.5	44	NR	Perforated, Gangrenous	NR	68	10.4	21.7	100	Laparoscopy with Open Surgery	0.9	General	NR	415
Rossem (171)	2016	Low	Cohort	Netherlands	Prospective	Not clear	Multisite	2014	Children, Adolescents, Adults	46.2	28.0	NR	Unclear	NR	NR	NR	NR		Laparoscopy	0.8	General	Superficial surgical site infection: recorded when administration of antibiotics, opening of the incision or both was necessary. An intra-abdominal abscess was defined as a postoperative intra-abdominal fluid collection diagnosed by cross-sectional imaging for which administration of antibiotics or a radiological or surgical intervention was needed.	1995
Rotermann (172)	2004	Moderate	Cohort	Canada	Retrospective	Consecutive	Multisite	1997-2000	Children, Adolescents, Adults, Elderly	55.2	NR	NR	Unclear	NR	NR	NR	NR		NR	NR	NR	According to CDC-NNIS diagnostic criteria	80867

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Saar (173)	2016	Low	Cross sectional	Estonia	Prospective	Consecutive	One site	2013-2014	Adults	48.9	35.4	NR	Perforated, Gangrenous	NR	15.4	NR	59.4	95.1	Laparoscopy or Open Surgery	0.7	General	According to CDC-NNIS diagnostic Criteria	266
Saber (174)	2010	Moderate	Clinical trial	USA	Prospective	Consecutive	One site	2008-2009	Adults	42.3	3[illegible]	NR	Catarrhal	100	0	0	0		Laparoscopy	0.8	NR	NR	26
Sadraei-Mosavi (175)	2017	Moderate	Clinical trial	Iran	Prospective	Random	One site	2013-2014	Adults	NR	28.4	NR	Catarrhal	100	0	0	0	100	Open Surgery	NR	NR	SSI=pus discharge from wound, redness, tenderness, edema	152
Saha (176)	2010	Moderate	Cohort	Bangladesh	Prospective	Consecutive	One site	2007-2008	Children	NR	NR	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	NR	NR	NR	60
Sahm (177)	2010	Moderate	Cross sectional	Germany	Prospective	Systematic	One site	1998-2006	Adults	54	3[illegible]	NR	Catarrhal, Perforated, Gangrenous	50.7	17.0	NR	6.9	100	Laparoscopy or Open Surgery	1.0	General	NR	1710
Sahm (178)	2015	Moderate	Cross sectional	Germany	Prospective	Exhaustive	Multisite	1988-2009	Children, Adolescents, Adults, Elderly	43	3[illegible]	NR	Perforated, Non Perforated 91.5	NR	8.5	NR	NR		Laparoscopy or Open Surgery	NR	NR	NR	12570
Salö (179)	2016	High	Cohort	Sweden	Retrospective	Consecutive	One site	2006-2014	Children	55.6	10.4	NR	Perforated, Gangrenous, Phlegmonous	NR	7.3	NR	11.6	100	Laparoscopy	0.94	NR	NR	259
Sanchez-Santana (180)	2017	Low	Cohort	Spain	Prospective	Consecutive	One site	2007-2015	Adults	55.2	32.9	2.6	Unclear	NR	NR	NR	NR	71.3	Laparoscopy or Open Surgery	NR	NR	According to CDC-NNIS diagnostic criteria	930
Sauvain (181)	2016	Moderate	Cohort	Switzerland	Retrospective	Consecutive	Multisite	2007-2011	Adults	53.2	34	NR	Catarrhal, Perforated, Suppurated, Gangrenous	NR	19	NR	NR		Laparoscopy or Open Surgery	NR	NR	NR	2559
Scarborough (182)	2012	Low	Cross sectional	USA	Retrospective	Systematic	Multisite	2005-2009	Children, Adolescents, Adults, Elderly	52	38.[illegible]	NR	Perforated, Non rupture	NR	11.2	NR	NR		Laparoscopy or Open Surgery	0.9	NR	According to CDC-NNIS diagnostic criteria	39122
Scarless (182)	2013	Moderate	Clinical trial	Scotland	Prospective	Random	One site	2011	Adults	53	32	NR	Unclear	NR	NR	NR	NR		Laparoscopy	1.4	General	NR	38
Seifarth (183)	2016	Moderate	Cohort	USA	Retrospective	Consecutive	Multisite	2007-2012	Children, Adults	60	1[illegible]	NR	Catarrhal	100	0	0	0		Laparoscopy	NR	General	NR	1283
Seifarth (184)	2016	Low	Cohort	USA	Retrospective	Consecutive	Multisite	2007-2012	Children, Adolescents, Adults	60	1[illegible]	NR	Perforated, Suppurated, Gangrenous	100	0	0	0		Laparoscopy	NR	NR	NR	1283
Senekjan (185)	2013	Moderate	Cohort	USA	Retrospective	Consecutive	Multisite	2005-2009	Adolescents	56.5	40.3	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	0.9	NR	1) SSI (superficial and deep incisional)...infection within 30 days of operation and involved skin, subcutaneous tissue or deep soft tissue 2) Organ space infection (OSI)...infection within 30 days of operation when the infection appeared to be related to the operation and involved any part of the anatomy other than the incision	61830

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Seo (186)	2002	Moderate	Cross sectional	Korea	Retrospective	Systematic	One site	2000	Adults	0	NR	NR	Catarrhal, Perforated, Suppurated, Gangrenous	14.7	15.6	49.5	20.2		NR	NR	NR	NR	129
Sesia (187)	2011	Moderate	Cohort	Germany	Prospective	Consecutive	One site	2006-2008	Children, Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	1	NR	NR	265
Shaikh (188)	2011	Moderate	Cross sectional	Pakistan	Prospective	Consecutive	One site	2007-2009	Adults	51.4	29	NR	Catarrhal, Perforated, Suppurated	82.86	8.67	1.51	0		Open Surgery	NR	General	NR	461
Shang (189)	2017	Moderate	Cohort	China	Retrospective	Consecutive	One site	2013-2016	Adults	54.3	2.2	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	Erythema, swelling and purulent discharge	398
Shimizu (102)	2014	Low	Cross sectional	Japan	Retrospective	Not clear	One site	2000-2012	Adults	44	3[illegible]	NR	Catarrhal, Gangrenous	19	NR	NR	37		Open Surgery	NR	General	According to CDC-NNIS diagnostic Criteria	300
Shindholimath (190)	2011	Moderate	Cross sectional	India	Retrospective	Consecutive	One site	2007-2009	Adults	68.4	NR	NR	Perforated, Suppurated, Gangrenous, Appendicular abscess	0	36.8	5.3	26.3	100	Laparoscopy	1.6	General	NR	19
Siam (191)	2017	Moderate	Cohort	Israel	Retrospective	Consecutive	One site	2008-2015	Adults	62.8	34.1	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy with Open Surgery	0.7	General	NR	1649
Silva (192)	2008	Moderate	Cohort	Chile	Prospective	Random	One site	2005-2006	Adults	58.9	NR	NR	Unclear	NR	NR	NR	NR		Open Surgery	NR	General	NR	433
Singh (193)	2017	Moderate	Clinical trial	India	Prospective	Consecutive	One site	2014-2015	Adults	43.2	28.7	11.4	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	NR	44
Siribumrungwong (194)	2013	Low	Cohort	Thailand	Retrospective	Systematic	One site	2006	Adults	65	37	NR	Perforated	NR	100	NR	NR	100	Open Surgery	1.2	NR	According to CDC-NNIS diagnostic criteria	128
Sivrikoz (195)	2015	Moderate	Cohort	USA	Retrospective	Exhaustive	Multisite	2004-2010	Children, Adolescents, Adults, Elderly	52.1	4[illegible]	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	0.9	NR	NR	4844
Soll (196)	2016	Low	Cohort	Switzerland	Retrospective	Consecutive	One site	2009-2013	Children, Adolescents, Adults, Elderly	54.7	26.5	NR	Catarrhal, Perforated, Suppurated, Gangrenous	NR	46	NR	NR	100	Laparoscopy	1	NR	According to CDC-NNIS diagnostic Criteria	813
Sozutek (197)	2013	Low	Clinical trial	Turkey	Retrospective	Consecutive	One site	2010-2011	Adults	44	30.9	NR	Catarrhal, Perforated	57	20	NR	NR		Laparoscopy or Open Surgery	0.5	General	NR	75
Srishewachart (198)	2016	Moderate	Cross sectional	Thailand	Retrospective	Consecutive	One site	2012-2014	Children, Adolescents, Adults, Elderly	52	43.7	7.4	Unclear	NR	NR	NR	NR		Open Surgery	NR	General	NR	450
Staszewicz (199)	2014	Moderate	Cohort	Switzerland	Prospective	Systematic	Multisite	1998-2011	Children, Adolescents, Adults, Elderly	54	34.2	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	1	NR	According to CDC-NNIS diagnostic Criteria	6383
Suttie (200)	2004	High	Case control	Scotland	Retrospective	Not clear	One site	1997-2002	Children	50	10.8	NR	Perforated, Suppurated, Gangrenous	0	2	50	14		Laparoscopy	1	General	NR	60
Svensson (201)	2016	Moderate	Cohort	Sweden	Prospective	Consecutive	One site	2006-2010	Children, Adolescents	60.2	11.3	NR	Catarrhal, Perforated, Suppurated, Gangrenous, not described	6.6	21.8	44.6	29.8	100	Laparoscopy or Open Surgery	0.7	General	NR	1745

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Taguchi (202)	2015	Moderate	Clinical trial	Japan	Prospective	Random	One site	2009-2014	Adults	65.43	47.5	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	1.2	General	According to CDC-NNIS diagnostic Criteria	81
Tanaka (203)	2007	Moderate	Cohort	Japan	Retrospective	Consecutive	One site	2002-2005	Children	54.3	2.2	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	NR	95
Tijerina (204)	2010	Low	Clinical trial	Mexico	Prospective	Exhaustive	One site	2005-2007	Children, Adolescents, Adults, Elderly	46	NR	NR	Unclear	NR	NR	NR	NR	100	Open Surgery	NR	General	NR	529
Toro Pablo (205)	2017	Moderate	Cohort	Spain	Retrospective	Consecutive	One site	2012-2016	Children, Adolescents, Adults	NR	2[illegible]	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	NR	NR	600
Towfigh (206)	2011	Low	Clinical trial	USA	Prospective	Random	One site	2007-2009	Adults	77.3	3[illegible]	NR	Perforated	0	100	0	0		Open Surgery	NR	NR	NR	75
Troillet (207)	2017	Low	Cohort	Switzerland	Prospective	Consecutive	Multisite	2011-2015	Children, Adolescents, Adults, Elderly	NR	NR	NR	Unclear	NR	NR	NR	NR	92.2	Laparoscopy or Open Surgery	NR	NR	According to CDC-NNIS diagnostic Criteria	15439
Tsioplis (208)	2013	Moderate	Cross sectional	Germany	Retrospective	Consecutive	One site	1999-2008	Children, Adolescents, Adults, Elderly	51	2[illegible]	9	Catarrhal, Perforated, Suppurated, Gangrenous	19	NR	50	25	75	Laparoscopy or Open Surgery	NR	Not reported	NR	1439
Vahdad (209)	2016	Moderate	Cross sectional	Germany	Retrospective	Systematic	One site	2008-2012	Children, Adolescents	52.4	NR	NR	Catarrhal, Perforated, Phelgmonous in 43% of cases	48.2	8.7	NR	NR		Laparoscopy	1.1	NR	NR	309
Van Rossem (210)	2016	High	Cohort	Netherlands	Prospective	Consecutive	Multisite	2014	Adults	49.7	39.0	NR	Catarrhal, Perforated, Gangrenous	73.7	11.0	NR	9.9	96.6	Laparoscopy or Open Surgery	0.72	NR	NR	1378
Van Rossem (170)	2014	High	Cohort	Netherlands	Retrospective	Consecutive	Multisite	2004-2010	Adults	53.2	4[illegible]	NR	Perforated	0	100	0	0	100	Laparoscopy or Open Surgery	0.85	NR	NR	267
Wang-Chan (211)	2017	Low	Cross sectional	Switzerland	Retrospective	Consecutive	One site	2013-2014	Children, Adolescents, Adults, Elderly	55.3	4[illegible]	13.8	Unclear	NR	NR	NR	NR		Laparoscopy with Open Surgery	NR	General	According to CDC-NNIS diagnostic Criteria	246
Watanabe (212)	2011	Low	Cross sectional	Japan	Prospective	Consecutive	Multisite	2005-2006	Adults	59.4	63.8	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	According to CDC-NNIS diagnostic Criteria	903
Willis (213)	2016	Moderate	Cohort	USA	Prospective	Consecutive	One site	2013-2014	Children, Adolescents	58.5	8.8	NR	Unclear	NR	NR	NR	NR	100	Laparoscopy or Open Surgery	NR	General	NR	313
Wong (214)	2015	High	Cohort	Peru	Prospective	Not clear	Multisite	2005-2010	Adults	NR	NR	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	NR	352
Wu (215)	2006	Low	Cross sectional	Taiwan	Retrospective	Not clear	One site	2001-2005	Adults	75	4[illegible]	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	0.95	General	NR	1795

Author	Year	Risk of bias	Design	Country	Timing	Sampling method	Sites	Period	Population	%Male	Mean or median age	%Obesity	Pattern of appendicitis	%Catarrhal	%Perforated	%Suppurated	%Gangrenous	% with antibiotic therapy	Type of surgery	Time to complete the surgery intervention (in hours)	Type of anesthesia	SSI Definition	Sample
Wu (216)	2011	Moderate	Cohort	Taiwan	Retrospective	Exhaustive	Multisite	2004-2009	Children, Adolescents, Adults, Elderly	58.1	36.4	NR	Unclear	NR	NR	NR	NR		Laparoscopy or Open Surgery	NR	General	NR	1366
Wu (217)	2014	Moderate	Clinical trial	China	Prospective	Random	One site	2011-2013	Children, Adolescents	60	8.5	NR	Catarrhal	100	0	0	0		Laparoscopy	1	General	NR	60
Wu (218)	2017	Moderate	Cross sectional	China	Retrospective	Consecutive	One site	2014-2016	Elderly	59	7[illegible]	NR	Perforated, Suppurated, Gangrenous	0	61.7	10	28.7	100	Laparoscopy or Open Surgery	1	General	NR	115
Yaghoubian (219)	2010	High	Cross sectional	USA	Retrospective	Exhaustive	Multisite	1998-2007	Children, Adolescents, Adults, Elderly	61.5	29.2	NR	Catarrhal, Perforated	73.4	26.6	0	0		Laparoscopy or Open Surgery	NR	NR	NR	4325
Yagnik (220)	2010	Moderate	Cross sectional	India	Retrospective	Consecutive	One site	2007-2009	Children, Adolescents, Adults	32.5	23.41	NR	Catarrhal	100	0	0	0	100	Laparoscopy or Open Surgery	1	General	NR	151
Yousef (221)	2017	Moderate	Cohort	Canada	Prospective	Consecutive	One site	2015-2016	Children, Adolescents	63.1	9.3	NR	Perforated	0	100	0	0	100	Laparoscopy	NR	General	NR	122
Zhang (222)	2015	Moderate	Clinical trial	China	Prospective	Random	One site	2012-2013	Adults	47.2	30.8	NR	Unclear	10.2	7.4	54.6	9.3		Laparoscopy	0.9	General	NR	108

NR: not reported

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MOOSE Checklist for Meta-analyses of Observational Studies

Item No	Recommendation	Reported on Page No
Reporting of background should include		
1	Problem definition	5
2	Hypothesis statement	6
3	Description of study outcome(s)	5
4	Type of exposure or intervention used	NA
5	Type of study designs used	5-6
6	Study population	5-6
Reporting of search strategy should include		
7	Qualifications of searchers (eg, librarians and investigators)	13
8	Search strategy, including time period included in the synthesis and key words	6; Suppl. Table 1
9	Effort to include all available studies, including contact with authors	6
10	Databases and registries searched	6
11	Search software used, name and version, including special features used (eg, explosion)	6
12	Use of hand searching (eg, reference lists of obtained articles)	6
13	List of citations located and those excluded, including justification	8, Suppl. Fig 1, Suppl. References
14	Method of addressing articles published in languages other than English	7
15	Method of handling abstracts and unpublished studies	7
16	Description of any contact with authors	6
Reporting of methods should include		
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	6
18	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	6-7
19	Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	6-7
20	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	8
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	8
22	Assessment of heterogeneity	7
23	Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	7-8
24	Provision of appropriate tables and graphics	Table 1; Fig 1-3
Reporting of results should include		
25	Graphic summarizing individual study estimates and overall estimate	Fig 1-3
26	Table giving descriptive information for each study included	Suppl. Table 1
27	Results of sensitivity testing (eg, subgroup analysis)	9; Table 1

28	Indication of statistical uncertainty of findings	9; Table 1; Fig 1-3

Item No	Recommendation	Reported on Page No
Reporting of discussion should include		
29	Quantitative assessment of bias (eg, publication bias)	12-13
30	Justification for exclusion (eg, exclusion of non-English language citations)	12-13
31	Assessment of quality of included studies	12-13
Reporting of conclusions should include		
32	Consideration of alternative explanations for observed results	13
33	Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	13
34	Guidelines for future research	13
35	Disclosure of funding source	14

From: Stroup DF, Berlin JA, Morton SC, et al, for the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) Group. Meta-analysis of Observational Studies in Epidemiology. A Proposal for Reporting. *JAMA*. 2000;283(15):2008-2012. doi: 10.1001/jama.283.15.2008.

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5-6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	8
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7-8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7-8

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7-8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	8
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	8-9
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	8-9
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	8-9
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	9
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	12
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	14

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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