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OPEN

The Global Incidence of Appendicitis

A Systematic Review of Population-based Studies

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Objective: We compared the incidence of appendicitis or appendectomy across the world and evaluated temporal trends.

Summary Background Data: Population-based studies reported the incidence of appendicitis.

Methods: We searched MEDLINE and EMBASE databases for population-based studies reporting the incidence of appendicitis or appendectomy. Time trends were explored using Poisson regression and reported as annual percent change (APC) with 95% confidence intervals (CI). APC were stratified by time periods and pooled using random effects models. Incidence since 2000 was pooled for regions in the Western world.

Results: The search retrieved 10,247 citations with 120 studies reporting on the incidence of appendicitis or appendectomy. During the 21st century the pooled incidence of appendicitis or appendectomy (in per 100,000 person-years) was 100 (95% CI: 91, 110) in Northern America, and the estimated number of cases in 2015 was 378,614. The pooled incidence ranged from 105 in Eastern Europe to 151 in Western Europe. In Western countries, the incidence of appendectomy steadily decreased since 1990 (APC after 1989=−1.54; 95% CI: −2.22, −0.86), whereas the incidence of appendicitis stabilized (APC=−0.36; 95% CI: −0.97, 0.26) for both perforated (APC=0.95; 95% CI: −0.25, 2.17) and nonperforated appendicitis (APC=0.44; 95% CI: −0.84, 1.73). In the 21st century, the incidence of appendicitis or appendectomy is high in newly industrialized countries in Asia (South Korea pooled: 206), the Middle East (Turkey pooled: 160), and Southern America (Chile: 202).

Conclusions: Appendicitis is a global disease. The incidence of appendicitis is stable in most Western countries. Data from newly industrialized countries is sparse, but suggests that appendicitis is rising rapidly.

Keywords: appendicitis, incidence, mortality, population-based, risk factors, systematic review, time trends

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The incidence of appendicitis escalated in Western countries during the 1900s[1] until without explanation the incidence decreased in the mid-part of the 20th century.[2] In contrast, appendicitis was relatively uncommon outside Western countries during the 20th century. However, at the turn of the 21st century newly industrialized countries are reporting a rising incidence of appendicitis.[3,4]

Understanding the global evolution of appendicitis in highly industrialized countries and in newly industrialized countries is necessary for planning healthcare resource utilization. In Western countries appendicitis is associated with morbidity, mortality and significant costs to the healthcare system.[5] The life-time risk of appendicitis is 1 in 15 in the United States.[5] One third of appendicitis cases present to hospital with a perforated appendix.[6] Appendicitis-related hospitalizations cost $3 billion in 1 year within the United States alone.[7] However, the impact of appendicitis on healthcare systems may need to be reevaluated in the context of changing epidemiological patterns throughout the world.

Moreover, the rising incidence of appendicitis in newly industrialized countries may indicate an outbreak of appendicitis outside Western countries. The clinical infrastructure in newly industrialized countries may need to be restructured to mitigate morbidity and mortality of appendicitis. Furthermore, contrasting the incidence of appendicitis between Western countries and newly industrialized countries may offer clues to the underlying environmental underpinning of appendicitis. By identifying environmental triggers of appendicitis, public policy initiatives can be instituted to modify environmental exposures that prevent appendicitis.

Thus, we conducted a systematic review of population-based studies reporting the incidence of appendicitis across the world, performed temporal trend analyses of incidence rates over the past century, and pooled incidence of appendicitis since the beginning of the 21st century.

METHODS

Search Strategy

We conducted a systematic review following the meta-analysis of observational studies (MOOSE) guidelines.[8] A systematic literature search of MEDLINE (1950 to June 3, 2015) and EMBASE (Excerpta Medica Database; 1980 to June 3, 2015) databases was conducted for population-based studies reporting the

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incidence of appendicitis. The search strategy is described in Appendix 1, http://links.lww.com/SLA/B195. The search was not limited by language. The reference lists of relevant studies were also reviewed. When possible, authors were contacted to answer questions.

Study Selection, Data Extraction, and Quality Assessment

Three reviewers (MF, SQ, and BK) independently identified articles eligible for further review by performing an initial screen of identified abstracts. Population-based articles were considered for inclusion if they reported incidence of appendicitis or appendectomy, or adequate information to calculate the incidence. Papers reporting incidence in extreme age groups (early childhood or elderly) were excluded.[9–11] Disagreement between reviewers was resolved in consultation with an expert (GGK). Reviewers independently extracted the data. Data extracted included geographic location including region and country; overall and yearly incidence per 100,000; study period; appendicitis versus appendectomy; source of data, either administrative database or medical record (eg, histological reports, operative reports and findings, and/or chart reviews); and age of study population. The incidence per 100,000 for each time period and time trends were recorded. We included population-based studies of appendicitis or appendectomy; however, if the incidences of appendicitis and appendectomy were both reported, the incidence of appendicitis was used. Age of study population was assumed to include all ages unless the paper specifically reported a pediatric-only or adult-only study population. Quality of the studies was assessed with the Cochrane Collaboration-endorsed Newcastle-Ottawa Quality Assessment Scale (NOS), which was modified to assess aspects of quality relevant to population-based studies of incidence.[12] To avoid duplicate reporting, studies were combined together when the same cohort was reported over the exact same time period.

Summarization of Data

Western countries are defined as highly industrialized countries with cultural heritage predominantly arising from Europe: Europe, the United States, Canada, Australia, and New Zealand. In contrast, newly industrialized countries refer to countries in Africa, Asia, the Middle East, and South America that are developing societal characteristics similar to the Western countries (eg, industrialization, diet, healthcare, urbanization).[13,14]

The incidence of appendicitis or appendectomy was summarized as annual cases per 100,000. If incidence was reported separately for males and females, the mean was calculated. The incidence data were grouped by geographic region. Division of color shades was stratified using quartiles of incidence. Incidences of local jurisdictions were extrapolated to the country except for China where data was limited and only Hong Kong and the province of Zhejiang were shaded. When incidence was reported for a multiyear period that extended over more than one time period, the study was included in the time period that captured the longest observation period. If multiple studies reported incidence for the same country and time period, the mean was taken and the most general landmass was displayed on the maps. The static maps were created using ArcMap 10.2.[15] The interactive map was created using QGIS 2.16.3[16] with the HTML Image Map Plugin.[17] The geographic data were created by the Natural Earth Community.[18]

We subanalyzed population-based studies that reported on the incidence of appendicitis in the 21st century, as defined by incidence in 2000 or later. We estimated the incidence of appendicitis since 2000 in Northern America, Northern Europe, Southern Europe, Western Europe, Eastern Europe, Africa, Asia, Southern and Central America, the Middle East, and Oceania. Countries included in these regions were based on definitions provided by the United Nations Statistics Division.[19] We identified all population-based studies that reported incidence from 2000 onward to define the geographic-specific incidence of appendicitis at the beginning of the 21st century. The number of cases of appendicitis or appendectomy and the at-risk population during the study period was recorded. When the at-risk population was not provided in the manuscript, we estimated this value from global population statistics.[20,21] Countries with multiple studies were pooled using a random effects model to create a single incidence per country. Next, we used a random effects model to pool the average annual incidence for the following regions: Northern America, Northern Europe, Southern Europe, Western Europe, Eastern Europe, and Oceania. Due to insufficient data from countries necessary to extrapolate to the entire region, we did not provide a pooled incidence for the following regions: Africa, Asia, Southern America, and the Middle East. For each country that provided incidence data in the 21st century we used data from the World DataBank and the Republic of China National Statistics to estimate the population size in 2015.[20,21] These data in conjunction with the country-specific incidence of appendicitis were used to calculate the number of individuals diagnosed with appendicitis in 2015. Heterogeneity was assessed using the using the I^2 and the Cochran Q-statistic, which were reported with the Forrest Plots.

Population-based studies that reported annual incidence of appendicitis or appendectomy for at least 5 years and included 3 or more time points were evaluated in temporal trend analyses. The median year was used if the time points reported were longer than 1 year. For each of these studies we calculated temporal trends in incidence using a generalized linear model that assumed a Poisson distribution with robust standard error adjustment. The parameter estimate used to characterize the temporal trends was the annual percent change (APC) with 95% confidence intervals (CI). APCs were stratified for the three time periods: <1970; 1970–1989; and 1990–2014. For studies arising from Northern America, Europe, and Oceania, we used a random effects model with restricted maximum likelihood estimation to combine the APCs for the time period 1990 to 2014. Beta coefficients of the regression segments were pooled using this model and then transformed into an APC. We stratified the temporal analyses conducted after 1990 by appendicitis versus appendectomy and by nonperforated versus perforated appendicitis. For the rest of the world and time periods, temporal trends were reported qualitatively due to the paucity of eligible studies.

RESULTS

The search strategy resulted in 5462 citations from MEDLINE and 8128 citations from EMBASE. After the removal of duplicated citations, 9455 were excluded after the initial screening of abstracts. Afterward, 792 full-text manuscripts were reviewed and another 687 were excluded (Appendix 2, http://links.lww.com/SLA/B195). The remaining 105 publications, along with 15 additional studies found through the references, were included in the systematic review (n=120) (Appendix 2, http://links.lww.com/SLA/B195). Quality assessment for each manuscript is presented in Appendix 3, http://links.lww.com/SLA/B195.

The incidences of appendicitis or appendectomy, and study characteristics are summarized in Appendix 4, http://links.lww.com/SLA/B195. The ranges in incidence stratified in quartiles were ≤81, 82–111, 112–149, and ≥150 per 100,000 person-years. Figure 1A–C demonstrates the incidence of appendicitis stratified by geographic region for the 3 time periods: <1970; 1970–1989; and 1990–2014. Peak incidence (in per 100,000 person-years) was observed in Northern America in the 1940s (New York State:

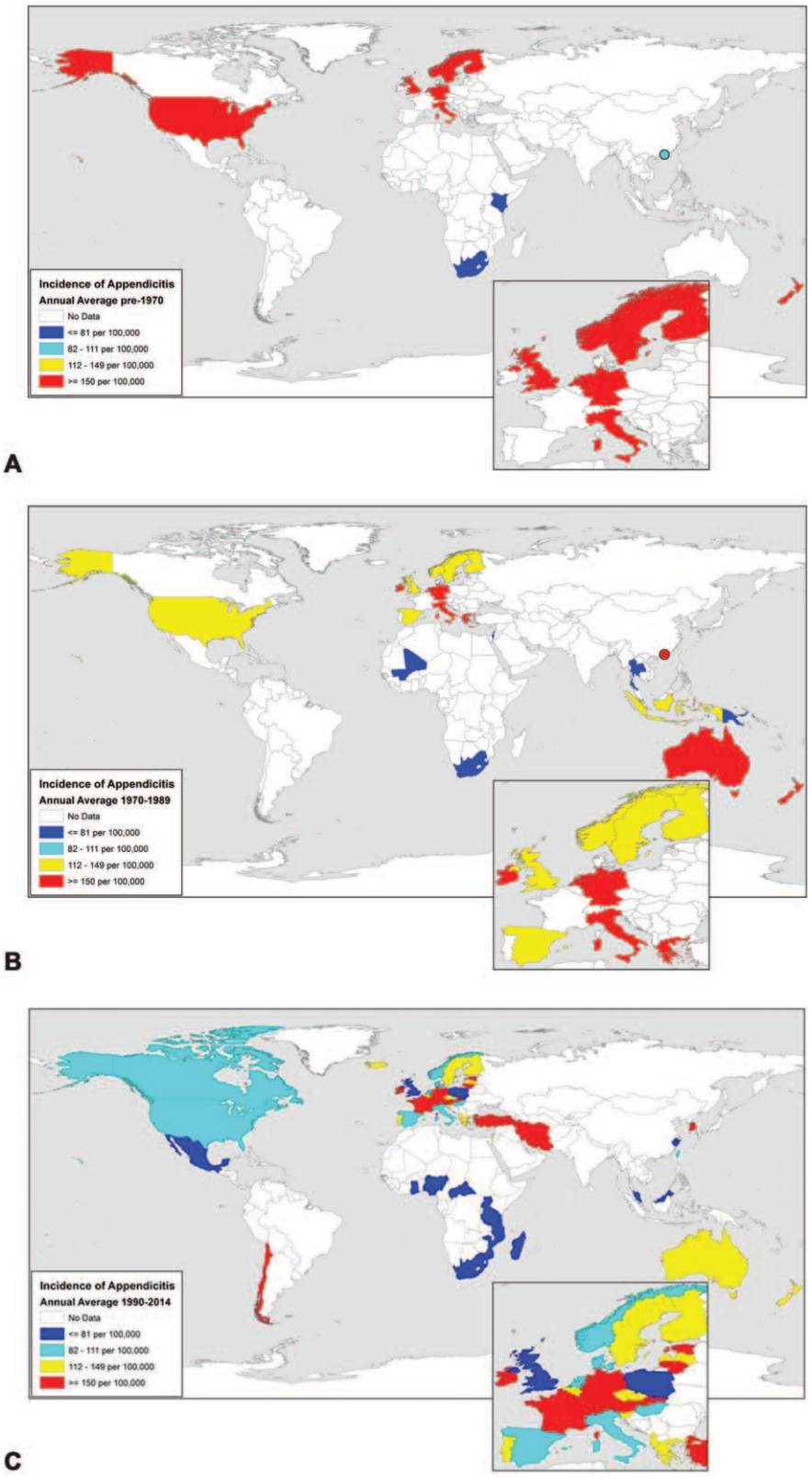

FIGURE 1. Worldwide appendicitis or appendectomy incidence rate quartiles for countries reporting incidence in 3 time periods: (A) before 1970; (B) 1970 to 1989; and (C) 1990 to 2014. The interactive global map of the incidence appendicitis can be found at the following address: https://people.ucalgary.ca/~ggkaplan/Append2016.html.

383), in Europe in the 1960s (Germany: 601), in Oceania in the 1940s (New Zealand: 331), in Asia in the 2000s (South Korea pooled: 206), in the Middle East in the 2000s (Turkey pooled: 160), in Southern America in the 2000s (Chile: 202), and in Africa in the 1990s (Madagascar: 77) (Appendixes 4 and 5, http://links.lww.com/SLA/B195).

During the 21st century, the pooled incidence was (in per 100,000 person-years): 100 (95% CI: 91, 110) for Northern America; 113 (95% CI: 90, 142) for Northern Europe; 112 (95% CI: 102, 123) for Southern Europe; 105 (95% CI: 84, 130) for Eastern Europe; 151 (95% CI: 127, 180) for Western Europe; and 140 (95% CI: 125, 158) for Oceania (Appendixes 5 and 6, http://links.lww.com/SLA/B195). In Northern America, we estimated that 378,614 cases of appendicitis were diagnosed in 2015. The estimated cases in 2015 per country are reported in Appendix 5, http://links.lww.com/SLA/B195.

Eighty-five time trends were obtained from 45 studies reported incidence over a period of 5 or more years (Appendix 7, http://links.lww.com/SLA/B195). In Northern America, Europe, and Oceania the incidence of appendectomy has been decreasing since 1990 (APC=−1.54; 95% CI: −2.22, −0.86). In contrast, since 1990 the incidence of appendicitis (APC=−0.36; 95% CI: −0.97, 0.26) has been stable for both perforated (APC=0.95; 95% CI: −0.25, 2.17) and nonperforated (APC=0.44; 95% CI: −0.84, 1.73) appendicitis (Table 1). Throughout the 21st century, the incidence has increased in Nigeria (APC=14.50%; 95% CI: 10.80, 18.33) and Chile (APC=3.87%; 95% CI: 0.66, 7.19). In contrast, the incidence in Taiwan (APC=−1.12%; 95% CI: −1.54, −0.70) has been decreasing according to the latest study (Appendix 7, http://links.lww.com/SLA/B195).

We created an interactive global map that illustrates and describes the incidence of appendicitis. The map can be found at the following address: https://people.ucalgary.ca/~ggkaplan/Append2016.html.

DISCUSSION

This paper comprehensively overviews the evolution of the global incidence of appendicitis over the past century. In Western countries, appendicitis has mostly stabilized during the latter portion of the 20th century. In Northern America the incidence is 100 per 100,000 person-years with nearly 400,000 diagnoses in 2015. In contrast, incidence is increasing in newly industrialized countries of Asia, the Middle East, Southern America, and Africa. Since 2000, the incidences of appendicitis in countries in Asia, Southern America, and the Middle East are higher than in many Western countries. A paucity of population-based studies on incidence of appendicitis from developing countries highlights a major gap in the literature. Nonetheless, appendicitis is a common and global concern.

In Western countries the incidence of appendicitis hits the highest point in the mid-portion of the 20th century; for example, in the United States the incidence (in 100,000 person-years) peaked at 383 in 1948 in New York,[22] then 152 in a nationwide study from 1970 to 1978,[23] then 110 in a nationwide study from 1979 to 1984,[2] and 94 in a nationwide study in 1997.[7] Throughout the 21st century, the incidence in Northern America has stabilized at an estimated value of 100. The incidence in Europe is variable with the highest values in Western Europe at 151 and the lowest in Eastern Europe at 105. In the 21st century, the incidence in Australia and New Zealand is comparable to Western Europe at 140.

In Western countries the incidence of appendicitis has currently stabilized for both perforated and nonperforated appendicitis, while the incidence of appendectomy has steadily decreased. Advances in diagnostic modalities, medical management, and surgical practices have led to fewer appendectomies.[24] For example, some cases of appendicitis may be managed with antibiotics without surgery.[25,26] Additionally, greater utilization of CT imaging has led to less false-negative appendectomies.[27] The routine practice of an appendectomy of a normal appendix to prevent future appendicitis has also fallen out of practice.[28] Differences in diagnostic, medical, and surgical practices may also explain some of the heterogeneity observed between Western countries.

Our systematic review suggests that newly industrialized countries, societies that have undergone rapid economic advancement, are experiencing an upswing in the incidence of appendicitis. In the 21st century the incidence is higher in some newly industrialized countries in Asia, Southern America, and the Middle East as compared with Western countries. An important question that remains is whether the incidence of appendicitis in newly industrialized countries will eventually spike to rates observed in the United States in the 1940s (eg, >300 per 100,000). Thus, surveillance cohorts that track hospitalization for appendicitis are essential for newly industrialized countries.

The Global Burden of Disease Study demonstrated that the age-standardized death rate for appendicitis decreased by 46% from 1990 to 2013.[29] Mitigating mortality for appendicitis is dependent on robust healthcare systems that are designed to quickly diagnose and treat acute presentations. Newly industrialized countries with high—and rising—incidence of appendicitis need to prepare their clinical infrastructure to rapidly diagnose and manage appendicitis or otherwise risk unnecessary morbidity and mortality. Furthermore, population-based incidence studies are necessary for many developing regions, as the impact of appendicitis is unknown in these areas. As the healthcare infrastructure improves to better track appendicitis, data on the incidence of appendicitis will be reported from these developing and newly industrialized countries. This will allow for more accurate predictions of temporal trends on the global burden of appendicitis.

Incidence trends observed in different geographic zones and across time suggest that the pathogenesis of appendicitis is dependent on environmental exposures associated with industrialization of society. Reduced fiber intake has been theorized as a cause of appendicitis[30]; however, the etiology of appendicitis is likely multifactorial. Our systematic review demonstrated that adolescents and males were more likely to be diagnosed with appendicitis. Prior studies have also shown that the winter season had the lowest incidence of disease.[2,31] Also, air pollution may increase the risk of perforated appendicitis.[32,33] Smoking has also been associated with an increased risk of appendicitis.[34] In Western countries the prevalence of smoking has steadily decreased over the past generation, whereas The Global Adult Tobacco Survey of newly industrialized countries showed that in countries like China nearly 50% of men were smokers in 2010,[35] which may in part explain the rising incidence of appendicitis outside Western countries. Consequently, ongoing research is needed to better explain the pathogenesis, the environmental risk factors, and the epidemiological patterns of appendicitis.

TABLE 1. The Pooled APC With 95% CI for the Incidence of Appendicitis in Northern America, Europe, and Oceania After 1990

	Year ≥1990 APC (95% CI)
Appendicitis or appendectomy	−1.06 (−1.56, −0.56)
Appendicitis	−0.36 (−0.97, 0.26)
Appendectomy	−1.54 (−2.22, −0.86)
Perforated appendicitis	0.95 (−0.25, 2.17)
Nonperforated appendicitis	0.44 (−0.84, 1.73)

Stratified by incidence of appendicitis, appendectomy, perforated, and nonperforated appendicitis. APC that do not cross 0 are significant.

Heterogeneity between studies may be explained by methodological limitations. First, several studies used administrative databases to capture appendicitis cases. A prior validation study demonstrated that the positive predictive value of the diagnostic codes for appendicitis was ~85%[36] and, therefore, a subset of patients were misclassified. Additionally, some population-based studies evaluated appendectomy that may include incidental appendectomy or appendectomy for uncommon diagnoses (eg, cancer of the appendix). Differences in definition of appendicitis versus appendectomy may explain some heterogeneity observed between population-based studies. Furthermore, differences in data quality, reporting, and completeness between different databases may have contributed to differences observed between countries. Patients with appendicitis of low socioeconomic status may have barriers to accessing healthcare that could lead to an underestimation in the incidence of appendicitis in developing or newly industrialized countries. Finally, studies reporting on small or rural catchment sites may transfer appendicitis cases to larger centers for further investigation and management. This may affect how appendicitis cases are being identified, documented, and reported.

Since Dr Fitz described appendicitis in 1886 the incidence has climbed, declined, and then plateaued in Western countries, whereas newly industrialized countries appear to be in the first stage of this sequence. In 2015, the peak in the incidence of appendicitis has likely not transpired in newly industrialized countries. Though, more comprehensive population-based incidence studies in developing and newly industrialized countries are necessary to accurately capture the global burden of appendicitis. The epidemiologic patterns of appendicitis support the notion that appendicitis is driven by multifactorial environmental triggers associated with the industrialization of society. Thus, future research should focus on identifying environmental risk factors observed during the early stages of industrialization of society to highlight avenues to prevent the development of appendicitis.

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