Development and validation of an administrative data algorithm to identify adults who have endoscopic sinus surgery for chronic rhinosinusitis

Kristian Macdonald MD FRCSC

Thesis submitted to the Faculty of Graduate and Postdoctoral Studies in partial fulfillment of the requirements for the Master of Science in Epidemiology

School of Epidemiology, Public Health and Preventive Medicine
Faculty of Science
University of Ottawa

TABLE OF CONTENTS

0.0 LIST OF TABLES IV

1.0 LIST OF FIGURES V

2.0 LIST OF APPENDICES VI

3.0 LIST OF ABBREVIATIONS VII

4.0 ABSTRACT VIII

5.0 ACKNOWLEDGMENTS IX

6.0 INTRODUCTION 1

7.0 THESIS OBJECTIVES 2

8.0 STATEMENT OF RESEARCH QUESTION 2

9.0 BACKGROUND – CHRONIC RHINOSINUSITIS 2

10.0 THE HIGHLY QUESTIONABLE EPIDEMIOLOGY OF CHRONIC RHINOSINUSITIS 6

11.0 SYSTEMATIC REVIEW, MANUSCRIPT: CHRONIC RHINOSINUSITIS IDENTIFICATION IN ADMINISTRATIVE DATABASES AND HEALTH SURVEYS: A SYSTEMATIC REVIEW 10

ABSTRACT 11
INTRODUCTION 12
METHODS 13
RESULTS 16
DISCUSSION 22
CONCLUSION 25

12.0 INTERVENING BRIDGE BETWEEN TWO MANUSCRIPTS 26

13.0 ALGORITHM DERIVATION AND VALIDATION, MANUSCRIPT: ADMINISTRATIVE DATA ACCURATELY PREDICTS PATIENTS WHO HAVE ENDOSCOPIC SINUS SURGERY FOR CHRONIC RHINOSINUSITIS 27

ABSTRACT 27
INTRODUCTION 29
METHODS 32
RESULTS 38
DISCUSSION 40
CONCLUSION 47

14.0 ACKNOWLEDGMENTS, FUNDING & FURTHER INFORMATION 48

15.0 FINAL DISCUSSION AND FUTURE DIRECTION 49

16.0 FINAL SUMMARY 51

17.0 REFERENCES 53

18.0 TABLES 58

19.0 FIGURES 68

20.0 APPENDICES 72

0.0 List of Tables

Table 1: Characteristics of studies measuring the accuracy of Chronic Rhinosinusitis (CRS) identification_____ 58

Table 2: Accuracy of Chronic Rhinosinusitis (CRS) identification_____ 59

Table 3: Accuracy of coding algorithm from Hsu et al. to identify patients with chronic rhinosinuitis (CRS) using health administrative data_____ 60

Table 4: Positive predictive value varies by disease prevalence_____ 61

Table 5: Lange's accuracy assessment of self-reported chronic rhinosinusitis (CRS) from health survey compared to Otolaryngologist-based clinical diagnosis with history and nasal endoscopy_____ 62

Table 6: Association of questionnaire-based symptomatic CRS with nasal endoscopy in Tomassen_____ 63

Table 7: Administrative database codes used in predictive mode_____ 64

Table 8: Comparison of validation statistics of three algorithms to predict CRS-ESS encounters_____ 65

Table 9: Predictive algorithm vs reference standard for ESS-CRS status_____ 66

Table 10: Internal validation of predictive algorithm of ESS-CRS status_____ 67

1.0 List of Figures

Figure 1: Summary of study identification_____ 68

Figure 2: QUADAS-2 assessment overview for the included studies_____ 69

Figure 3: Flow chart of chronic rhinosinusitis - endoscopic sinus surgery chart review_____ 70

Figure 4: Overview of final algorithm to identify CRS-ESS case encounters within a surgical cohort_____ 71

2.0 List of Appendices

Appendix A – MEDLINE Search Strategy 72

Appendix B: Final algorithm modified from Hsu et al. using administrative data to identify patients with chronic rhinosinuitis (CRS) 75

Appendix C – Diagnostic criteria of Chronic Rhinosinusitis 76

Appendix D – The Ottawa Hospital Data Warehouse Map 77

Appendix E: Overview of the major steps for this thesis project 78

Appendix F: Standards for Reporting Diagnostic Accuracy Studies Checklist (2015 version) 79

Appendix G: Variables assigned to the initial hospital cohort for use within the larger population administrative database (ICES) 80

Appendix H: Permission from publisher to use systematic review manuscript in this thesis 81

3.0 List of Abbreviations

CCI = Canadian Classification of Health Interventions

CPT = Current Procedural Terminology.

CRS = chronic rhinosinusitis

CRSwP = chronic rhinosinusitis with polyps

CRSsP = chronic rhinosinusitis without polyps

CT = computed tomography

Dx = diagnosis

ESS = endoscopic sinus surgery

ESS-CRS = Endoscopic sinus surgery for chronic rhinosinusitis

GA^{2}LEN = Global Allergy and Asthma European Network of Excellence (GA^{2}LEN) cohort

ICD = International Classification of Diseases

ICES = Institute for Clinical Evaluative Sciences

IGS = image-guidance

LR+ = positive likelihood ratio

LR- = negative likelihood ratio

NPV = negative predictive value

OHDW = Ottawa Hospital Data Warehouse

PPV = Positive predictive value

TOH = The Ottawa Hospital

4.0 Abstract

Objective: 1) Systematic review on the accuracy of Chronic Rhinosinusitis (CRS) identification in administrative databases; 2) Develop an administrative data algorithm to identify CRS patients who have endoscopic sinus surgery (ESS).

Methods: A chart review was performed for all ESS surgical encounters at The Ottawa Hospital from 2011-12. Cases were defined as encounters in which ESS for performed for Otolaryngologist-diagnosed CRS. An algorithm to identify patients who underwent ESS for CRS was developed using diagnostic and procedural codes within health administrative data. This algorithm was internally validated.

Results: Only three studies meeting inclusion criteria were identified in the systematic review and showed inaccurate CRS identification. The final algorithm using administrative and chart review data found that encounters having at least one CRS diagnostic code and one ESS procedural code had excellent accuracy for identifying ESS: sensitivity 96.0% sensitivity, specificity 100%, and positive predictive value 95.4%. Internal validation showed similar accuracy.

Conclusion: Most published AD studies examining CRS do not consider the accuracy of case identification. We identified a simple algorithm based on administrative database codes accurately identified ESS-CRS encounters.

5.0 Acknowledgments

I would like to thank my thesis supervisor, Dr. Carl van Walraven, (CvW) for his mentorship, availability, feedback, direction, and support throughout the work leading up to this final thesis, and Dr. Shaun Kilty, (SK) for his clinical expertise and guidance. Above all, I would like to thank my wife Ashley, and children, Austin and Valerie, for their love and support. The Ottawa Hospital Academic Medical Organization provided funding in support of this project.

The Ottawa Health Science Network Research Ethics Board approved this project (OHSN-REB 20140164). There are two manuscripts in this thesis. The first, a systematic review, was recently published (**Section 11.0**), and the second one is being prepared for submission (**Section 13.0**). I was the lead author for both studies, and was responsible for the thesis design, OHSN-REB application, Institute for Clinical Evaluative Sciences (ICES) application, systematic review, chart review, algorithm development and internal validation, statistical analysis, and preparation of the thesis.

CvW was the last author for both manuscripts, and provided intellectual expertise, guidance, and thoroughly reviewed and revised all content. SK was the second reviewer in the systematic review, and reviewed and provided feedback for both manuscripts.

Appendix H displays the first page of the publisher's permission to use the published systematic review in this thesis manuscript. The full contract can be obtained by emailing me at krmacdonald@toh.on.ca.

6.0 Introduction

This manuscript-based thesis deals with a common and debilitating medical condition called chronic rhinosinusitis (CRS). I first demonstrate with a systematic review that we know very little about the epidemiology of this disease. This is because of inadequate methods that have been used in epidemiological studies to identify these patients in population-based cohorts. I then describe how I developed an accurate algorithm using administrative data to identify a population-based cohort of CRS patients who receive endoscopic surgery. This algorithm, and the resulting cohort, will permit population-based studies in the future to deliver much needed accurate epidemiological data on the health outcomes and resource utilization of patients with CRS.

This thesis will state my research question (**Section 8.0**) and provide a background to CRS and endoscopic sinus surgery (ESS) (**Section 9.0**). **Section 10.0** discusses the highly questionable epidemiology of CRS. **Section 11.0** includes a recently published systematic review, showing that previous methods used to identify CRS in administrative databases are inaccurate. The algorithm derivation and validation is detailed in **Section 13.0**, followed by future direction that this work may lead to (**Section 15.0**).

7.0 Thesis Objectives

My thesis has the following objectives:

7.1 Perform a systematic review to identify all studies that measured the accuracy of CRS diagnoses in large administrative databases or within health surveys. The Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool will be used to assess study quality.

7.2 Using data from the Ottawa Hospital Data Warehouse (OHDW) and primary chart review, identify all patients who undergo ESS for CRS at The Ottawa Hospital (TOH) over a 2-year period.

7.3 Link the cohort from 7.2 to population-based administrative data at the Institute for Clinical Evaluative Sciences (ICES) to derive and internally validate a method to identify patients having ESS for CRS using routinely collected health administrative data.

8.0 Statement of Research Question

Derive and validate an algorithm using Ontario health administrative data to accurately identify adults who have endoscopic sinus surgery for chronic rhinosinusitis.

9.0 Background – Chronic Rhinosinusitis

Chronic Rhinosinusitis (CRS) is a common and debilitating inflammatory disease of the sinonasal cavities that is associated with significant resource utilization and billions of dollars of health care expenditures.[2] The prevalence of CRS has been quoted as between 5 and 15% of the population.[2,3] Canadians with CRS self-report their overall health status at a level similar to those with other chronic

diseases including current or previous cancer, asthma, migraine, arthritis and epilepsy.[4]

The underlying pathophysiology of CRS has not been clearly defined; potential etiologic factors are numerous and include allergy, immunodeficiency, genetic or congenital malformations of the sinonasal cavities, mucociliary dysfunction, endocrine abnormalities, anatomic abnormalities of the sinonasal cavities, neoplasms, trauma, previous sinus surgery, and infectious agents such as bacteria, viruses and fungi.[5] Regardless of the cause, CRS manifests as a clinical syndrome of mucosal inflammation affecting the sinonasal cavities, in many ways analogous to the chronic inflammation of the lower respiratory system seen in asthma. There is disruption of normal mucociliary clearance with resulting mucous stagnation as a prominent feature. This results in a favourable environment for pathogens, which in turn precipitates further inflammation, creating a chronic cycle.[5]

The following three criteria must all be satisfied to establish the diagnosis of CRS:

- Two or more symptoms of nasal congestion, nasal obstruction, nasal discharge, a decreased sense of smell, and facial pain or pressure;
- Objective findings of either: inflammation or pus on nasal endoscopy; or sinus opacification on CT scan;
- Symptoms for greater than 12 weeks duration.

More detail regarding the clinical diagnosis of CRS is listed in Appendix C.[6]

Canadian guidelines for CRS,[6] recently developed by a panel of experts, recommend that patients should initially be treated medically with topical and / or

systemic medications including saline irrigation, antibiotics, steroids, anti-leukotriene agents, and antihistamines. Treatment should also be targeted to optimize any comorbid illnesses associated with CRS including allergy, asthma, cystic fibrosis, and immunodeficiency.

While approximately 75-80% of patients with CRS will respond to medical therapy alone, those who do not may be considered candidates for endoscopic sinus surgery (ESS).[7] Although it is recommended that Otolaryngologists consider surgery management only after patients fail "maximal medical therapy", there is no consensus on what this entails, with one survey showing significant practice variation.[8] With the development of endoscopes and powered instruments in the last 30 years, ESS has evolved as the gold standard for surgical management of CRS.

The primary goals of ESS include the removal of diseased mucosal tissue and the re-establishment of sinus opening patency and mucociliary clearance.[9] Intraoperatively, an endoscope is used to visualize and provide a magnified view of the sinonasal cavities. A variety of instruments are then used to perform a careful and meticulous dissection of the sinuses and their openings into the nasal cavities. During the procedure the sinus outflow tracts are widened, polyps are removed, and nasal passages are cleared. By restoring normal mucociliary clearance, CRS patients benefit from improved symptomatology and quality of life.[6] Opening the sinuses also allows improved access for the delivery of topical medications, such as intranasal steroids and saline rinses.[6] With our increasing understanding of the inflammatory (as opposed to infectious) nature of CRS, this improved delivery of topical therapies has emerged as a major objective of ESS in treating this chronic

condition. Indeed, meta-analyses examining the effects of topical nasal steroid therapy show improved symptom scores, a greater reduction in polyp size and decreased rate of polyp recurrence in patients who had endoscopic sinus surgery versus those who did not.[7]

As part of their preoperative workup, patients routinely have a CT scan of the sinuses. Surgeons use this imaging study to determine the pattern and the extent of sinonasal disease, and as a roadmap for ESS surgery. Major points noted on a CT sinus scan preoperatively include: the extent of sinus opacification; opacification of sinus drainage pathways; anatomical variants such as a dehiscent orbital wall or skull base; critical variants such as an encephalocele or aberrant carotid artery; and the overall condition of surrounding soft tissues of the neck, brain and orbits.[10]

ESS is safe and effective for the management of CRS.[11-13] Studies have consistently shown a benefit in quality of life outcomes, many with at least one year of follow-up.[12,14-16] Dalziel and colleagues performed a systematic review of the clinical effectiveness of ESS for CRS with nasal polyps.[17] CRS is commonly sub grouped into those with and without nasal polyps.[6] Studies included in this review were specific to ESS for CRS with nasal polyps and were English-language primary research comparative studies that reported relevant outcomes of complications and symptom improvement. Case series were included if they met the above criteria and enrolled more than 50 patients. Within the 33 studies included, 75 to 95% of patients judged their symptoms to be 'improved' or 'greatly improved'. Minor complication rates in the individual studies ranged from 1.1 to 20.8% and major complications from 0 to 1.5%.

In addition to the sinonasal passages, CRS has an impact on associated diseases that affect the airway, such as asthma and cystic fibrosis. An increasing number of studies are showing significant and sustained benefit in these diseases after ESS.[18-20] For example, a case series of 43 patients with asthma and CRS demonstrated improved pulmonary function testing after ESS surgery.[21] There is conflicting evidence that ESS in patients with cystic fibrosis decreases the number of days spent in hospital and need for intravenous antibiotics, with only some studies showing benefit.[20]

10.0 The Highly Questionable Epidemiology of Chronic Rhinosinusitis

The prevalence of CRS in adults has been estimated to be 5% in Canadians[3] and 14% in Americans.[22] As mentioned above, CRS is associated with extensive health resource utilization and low self-perceived health status, comparable to other chronic conditions such as cancer, asthma, migraine, arthritis and epilepsy.[4] Ray *et. al.* reported in 1996 that more than 26 million U.S. physician visits, hospital admissions, and emergency department visits were related to sinusitis.[2] Using population health data, the overall U.S. health-care expenditure attributable to sinusitis was estimated to be $5.8 billion.[2] Goetzel and colleagues used data based on absenteeism and short-term disability to determine the major physical and mental health conditions affecting six large U.S. employers in 1999. Sinusitis was in the top 10 and accounted for 73 million restricted-activity days.[23]

These and other similar data are frequently cited when describing the epidemiology of CRS. However, there are several reasons to question the validity of these data:

- The diagnostic criteria of CRS are not universally defined, with clinical diagnostic guidelines that vary from country to country. As such, the ability to compare summary statistics about CRS between countries is questionable. While a 2011 review of American, British and European guidelines for the diagnosis of CRS showed a high degree of similarity, older guidelines may show higher incongruence.[24]
- The symptoms of CRS are non-specific and overlap with other conditions, including upper respiratory tract infections, conjunctivitis, asthma and allergies.[6] As a result, the diagnosis of CRS is frequently incorrectly assigned to these other diseases. Conversely, true CRS may be misdiagnosed as one of these other diseases.
- Many of the epidemiologic studies rely on self-reported CRS diagnosis, which has been shown to be inaccurate. For example,
    - Two studies found that the self-reporting of CRS symptoms were inaccurate.[25,26] After further testing of a cohort of patients with self-reported symptoms consistent with CRS, the majority of patients (65 - 73%) **had no significant sinus disease** on either nasal endoscopy or CT scan, and therefore did not meet standard diagnostic criteria for CRS.
- Shashy et al. challenged estimates from the National Health Interview Survey (NIHS) that, using data on self-reported disease, ranked CRS as one of the most

prevalent chronic diseases in the United States.[22] The authors identified a community subset of NIHS participants who had been assigned a physician-diagnosed code for CRS. They found a prevalence of less than 2%, and concluded that NIHS estimates on the prevalence of CRS may be over-exaggerated.

- The diagnosis of CRS in these studies was often made by a non-Otolaryngologist (eg. Respirologist, Family Physician) who may not be aware of updated guidelines. Otolaryngologists themselves may not employ strict criteria when diagnosing CRS. As such, the application of accepted standard criteria for the diagnosis of CRS is likely variable.

The overarching limitation of these studies is their inability to validate CRS diagnoses using accepted diagnostic criteria in a population-based cohort. My goal with this thesis was to create a valid administrative database cohort of a subset of patients with CRS, those who are treated surgically. Analysis of such a cohort will produce epidemiological data on surgically managed CRS that is more accurate than that which is currently available and should trump previously inaccurate estimates on the prevalence, resource-utilization, and outcomes of this disease. Using this validated cohort, numerous research questions can then be addressed. I anticipate these data will be of great interest to Otolaryngologists and primary care physicians who treat patients with CRS.

The next chapter presents the first of two manuscripts in this thesis, a systematic review of studies that use administrative databases and health surveys to study CRS. It was accepted for publication in The Laryngoscope.[51] The manuscript is presented in this thesis as it was submitted for publication; as such

there is some redundancy in the introduction and discussion sections with the thesis manuscript.

11.0 Systematic Review, Manuscript: Chronic rhinosinusitis identification in administrative databases and health surveys: a systematic review

Kristian Macdonald, MD, Shaun J Kilty, MD, Carl van Walraven, MD
Keywords: Chronic Rhinosinusitis, Administrative Database Research, Self-reported, Health surveys.

Abstract

***Introduction*:** Much of the epidemiological data on chronic rhinosinusitis (CRS) are based on large administrative databases and health surveys. The accuracy of CRS identification with these methods is unknown.

Methods: A systematic review was performed to identify studies that measured the accuracy of CRS diagnoses in large administrative databases or within health surveys. The Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool was used to assess study quality.

Results: Of 512 abstracts initially identified, 122 were selected for full-text review; only three studies (2.5%) measured the accuracy of CRS patient identification. In a single, large administrative database study with a CRS prevalence of 54.8%, a single ICD-9 diagnostic code for CRS had a positive predictive value (PPV) of only 34%. A diagnostic code algorithm identified CRS patients with a PPV of 91.3% (95% CI 85.3-95.1); in a population with a CRS prevalence of 5%, this algorithm had a PPV of 31%. In health survey studies having an estimated CRS prevalence of 25-46%, self-reported symptom-based CRS diagnosis had a PPV of 62% (95% CI 50.2-72.1) when nasal endoscopy was the gold standard for CRS diagnosis, and 70% (95% CI 57.4-

80.8) when Otolaryngologist-based CRS diagnosis (after interview and nasal endoscopy) was the gold standard.

Conclusion: Most health administrative data and health surveys examining CRS did not consider the accuracy of case identification. For unselected populations, administrative data and health surveys using self-reported diagnoses inaccurately identify patients with CRS. Epidemiological results based on such data should be interpreted with these results in mind.

Introduction

Chronic rhinosinusitis (CRS) is a common and debilitating inflammatory condition involving the nasal mucosa and paranasal sinuses.[5,6] CRS patients rate their health at a level similar to those with asthma, arthritis, inflammatory bowel disease, and cancer.[4,6] Sinusitis is one of the top 10 health conditions impacting US employers[23] and costs billions of US dollars per year in health care resources.[2]

The prevalence of CRS is notoriously variable between studies.[27] For example, self-reported CRS prevalence estimates from national surveys vary widely between 5 and 14%.[5,28] These estimates are much higher than those based on physician-assigned diagnostic codes (which one US study estimated at 2%).[22] These differences in prevalence estimates could be due to error associated with classifying patients with or without CRS. Several studies have pointed out that self-reported CRS could be inaccurate due to its nonspecific symptoms being caused by other upper respiratory conditions.[6,24,29] CRS epidemiological data could also be inaccurate due to errors associated with assigning diagnostic codes in health administrative data.[22]

These widely divergent results could be due to inaccuracies of CRS identification in epidemiological studies. If CRS is inaccurately identified in a study, its results will be unreliable. We should ascribe more weight to data that are based on valid methods of case identification. The purpose of this systematic review was to assess the validity of methods used to identify CRS patients in epidemiological studies. The overall goal of our analysis was to determine if validated and accurate methods exist to identify CRS patients in general, non-selected populations.

Methods

Literature Search

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[30] With the help of an experienced librarian, we performed a comprehensive search of the MEDLINE, EMBASE, and Cochrane databases from each search engine's inception to 25 January 2015. The search strategies are listed in Appendix A and their objective was to identify all administrative database and health survey studies of chronic rhinosinusitis so that we could determine how cases were identified and the accuracy thereof (if measured). No protocol for this systematic review was previously published.

Inclusion Criteria

We reviewed the abstracts identified by our search strategy to identify all peer-reviewed, English-language articles that identified adult patients (≥18 years old) with chronic rhinosinusitis (CRS) in administrative databases or national surveys. We also included studies that identified patients who had undergone endoscopic sinus surgery (ESS) because ESS is usually performed for CRS; therefore, articles identified by this method could capture studies that included CRS patients that might not have been otherwise identified.

KM and SK independently reviewed all abstracts that were identified in the search and excluded studies: that did not include CRS or ESS as major study components; that involved pediatric patients <18 years old; or that did not

differentiate between acute and chronic rhinosinusitis. Any discrepancies were discussed until consensus was reached. If necessary, a third reviewer (CvW) was consulted to resolve disagreements.

The full-text of all abstracts meeting these inclusion criteria was retrieved and reviewed by KM and SK to determine if the accuracy of the method used to identify CRS or ESS patients was measured. If the paper referenced another study in which the accuracy was measured, we obtained and reviewed the referenced study. Finally, we reviewed the bibliographies of all articles meeting inclusion criteria to identify other potentially relevant studies.

Data Extraction

Study characteristics were abstracted including the year of publication, the year data were obtained, and the country of origin. In each study, we focused on three study characteristics: the population used for the validation (to determine its similarity to other populations); how CRS cases were identified; and the methods used to determine the validity of case ascertainment using a "gold standard" reference diagnosis. The gold (or reference) standard is an acceptable method of truly diagnosing or excluding a condition so that all true cases can be identified to which the other samples can be compared to calculate validation statistics. In validation studies, the gold standard is commonly obtained through a retrospective chart review or prospective clinical examination.[31]

To assess the adequacy of the gold standard used in the studies, we reviewed national CRS guidelines from the US,[5] Canada,[6] and Europe.[7] There is a high degree of similarity, and each establish a CRS diagnosis based on: symptoms including facial

pain/pressure, congestion, obstruction, hyposmia, or discharge for at least 12 weeks duration; and objective evidence of disease by either anterior rhinoscopy, nasal endoscopy (eg. polyps, edema, mucopurulence) or CT scan (eg. sinonasal opacification).

Quality Assessment

The Quality Assessment of Diagnostic Accuracy Studies, version 2, (QUADAS-2, *quadas.org*) tool was used to evaluate the quality of the included studies.[32] The original QUADAS tool was developed to assess the quality of diagnostic accuracy studies included in systematic reviews, and has been previously used to assess the validity of diagnostic codes in heart failure,[31] diabetes mellitus,[33] and myocardial infarction.[34] The second version was developed and published in 2011. For each study, "potential bias" was assessed for four domains: patient selection, index test, reference standard, and flow and timing. The "concern regarding applicability" was also assessed for the first three of these domains. The two reviewers independently evaluated each study with the QUADAS-2 tool. Any discrepancies were addressed, and the third reviewer was consulted if needed.

Statistical Analysis

Summary validation statistics - including sensitivity, specificity, and positive and negative predictive values - were abstracted from each study if reported. If unreported, we calculated them from available data provided. To calculate positive predictive values in populations with a given disease prevalence, we used the test's

sensitivity and specificity to calculate a positive likelihood ratio and then used standard techniques to calculate the post-test probability of disease.[35]

Results

Literature Search

After removing duplicate abstracts, our search strategy identified 451 abstracts in the Medline, EMBASE, and Cochrane databases (Figure 1). 329 abstracts were excluded because they did not identify CRS or ESS through administrative databases or national surveys, leaving 122 manuscripts for full-review. Of these, 119 were excluded primarily because no validation was performed. This resulted in 3 studies being included in the final analysis.

Study Characteristics

Table 1 summarizes the included study characteristics, and Table 2 lists the method of identifying CRS, the CRS prevalence of the validation populations, and summary statistics for each study. One study used health administrative data to study CRS while the other two used health surveys that solicited responses directly from participants. Each study was published in 2010 or after, with data collection performed from 2008 to 2013. The studies included between 250 and 366 patients. The studies were conducted in the United States, Denmark, and Netherlands/Belgium.

- HSU et. al., 2015[36]

In this study, American investigators developed an algorithm based on ICD-9 and Current Procedural Terminology (CPT) codes to identify CRS patients in a large administrative database. The source population included patients with two or more office visits to one of several major hospitals and ambulatory clinics affiliated with Northwestern University in Chicago, Illinois, US, between Jan. 20th, 1989, and Feb. 6th, 2013. The source population was screened to identify CRS cases using the presence of ICD-9 diagnostic codes for CRS or CPT procedural codes for ESS. (Appendix B) Controls were patients that: (1) did not have any CRS or ESS code; (2) did not have a CT scan of the sinuses (because this could represent a patient with a potential CRS diagnosis); and (3) did not have an ICD-9 code for chronic lower or upper airway disease (because symptoms from these conditions could overlap with CRS and a patient with one of these codes could have "undiagnosed" CRS). Patients that did not meet the criteria for either cases or controls were excluded from potential selection for the validation population. It was not stated what proportion of people in the source population were classified as case, control, or were excluded in the validation population.

From patients meeting criteria for case or control, 996 were randomly selected and their charts were reviewed. The results are presented in a 2x2 table (Table 3) for 250 patients, however it is unclear how this number was selected from the 996 charts. CRS prevalence in this sample of 250 was 54.8%. Two independent clinicians conducted the chart review to determine true CRS status based on accepted European[7] and US diagnostic criteria,[37] forming the gold standard to which

the algorithm was compared. Interobserver concordance between the two clinicians was found to be 92%.

Compared to the gold standard chart review, the presence of an ICD-9 CRS diagnostic code (473.x) in the initial algorithm output had a positive predictive value (PPV) of only 34%.

The authors therefore adjusted the algorithm based on analysis of data in their validation sample to improve CRS identification accuracy. Specifically, the authors compared the billing codes that were applied to patients with definite CRS to those *without* CRS to optimize the algorithm in a trial and error approach. For example, the authors found that most patients with true CRS had been assessed by an Otolaryngologist or Allergist-Immunologist; whether or not patients had been seen by one of these specialists was added to the algorithm.

The final algorithm (Appendix B) classified patients with CRS if they met all of these criteria: had at least 2 office visits; did *not* have a diagnostic code for cystic fibrosis; had a code for CRS, nasal polyps, or ESS; and had at least one code for specialty evaluation by Otolaryngology or Allergy-Immunology. Patients not meeting these criteria were classified as without CRS. The exclusion group consisted of 25% of the entire population.

In the validation sample, the algorithm very accurately identified CRS (Table 2). Of the 250 patients, 137 were classified with CRS using gold-standard criteria, for a disease prevalence of 54.8%. 150 out of the 250 people (60%) met criteria for the coding algorithm. In this sample, the algorithm had a sensitivity of 100% (95%CI 96.6-100), a specificity of 88.5% (95% CI 80.8-93.5), a PPV of 91.3% (95%

CI 85.3-95.1) and a NPV of 100% (95% CI 95.4-100). The positive likelihood ratio was 8.7 (95% CI 5.2-14.5).

The positive predictive value from this sample cannot be applied to populations having a different CRS prevalence because positive predictive value (PPV) is highly dependent on disease prevalence (i.e. PPV values will decrease when disease prevalence decreases even when the test's sensitivity and specificity remain the same).[35] To estimate the algorithm's ability to identify patients with CRS, we can use Bayesian methods and the positive likelihood ratio to calculate the probability that a person with meeting the algorithm criteria truly has CRS. In a population having a CRS prevalence of 5%, a person meeting algorithm criteria has only a 31% of truly having CRS (Table 4). This probability is much lower at 8% if the true CRS prevalence is 1%.

- Lange et al., 2013[38]

This was a sub-study of the Global Allergy and Asthma European Network of Excellence (GA²LEN) cohort. GA²LEN was a large, multi-centre epidemiological study of allergy, asthma, CRS, and other upper airway diseases that started with a postal survey (phase 1, the GA²LEN Survey) followed in some centres with nasal endoscopy and other clinical measurements (phase 2, the GA²LEN Survey Follow-up). In phase 2, each centre used questionnaire results from the phase 1 postal survey to invite 120 randomly selected subjects with self-reported asthma, 120 with self-reported CRS, 40 with both self-reported asthma and CRS, and 120 people with neither self-reported asthma or CRS. Compliant invitees then underwent further

examination with a clinician, which included nasal endoscopy by an Otolaryngologist, to obtain objective evidence of CRS.

Lange et al. reported on 362 participants of phase 2 of the GA²LEN Survey, 64 of whom had self-reported CRS from the phase 1 postal questionnaire. An Otolaryngologist blinded to the survey results performed nasal endoscopy to determine objective evidence of CRS. True CRS prevalence in this population was 25.1%. The authors found that the accuracy of self -reported CRS was poor (Tables 2 and 5) with a sensitivity of 49.5 (95% CI 38.9-60.0), a specificity of 93.0 (89.1-95.6), a PPV of 70.3% (95% CI 57.4-80.8), and a NPV of 84.9% (95% CI 79.8-88.4).

Similar to the calculations used in the previous section, a person from a population having a CRS prevalence of 5% that has self-reported CRS has only a 27% probability of truly having the disease (Table 4). In a population with a CRS prevalence of 1%, this probability decreases to 6.6%.

- Tomassen et al., 2010[39]

At another participating centre of the phase 2 of the GA²LEN Survey Follow-up study, Tomassen et al. reported on 342 randomly-selected participants who underwent nasal endoscopy at their centre. This was performed by Otolaryngologists who were blinded to the symptom-based CRS status from phase 1 of the GA²LEN survey. Table 6 summarizes the study's results. CRS prevalence in this population was 43.6%. Comparing a symptom-based CRS diagnosis to nasal endoscopy as the gold standard, the authors reported a sensitivity of 33.6 (95% CI

26.2-41.8), specificity of 83.9 (95% CI 77.8-88.7), and a PPV of 61.7% (95% CI 50.2-72.1).

Calculating PPV in a population having a CRS prevalence of 5%, a person with self-reported CRS would have only a 10% probability of truly having CRS (Table 4). If population CRS prevalence was 1%, a person with self-reported CRS would only have a 2.1% probability of truly having the disease.

Study Quality and Risk of Bias

Figure 2 displays an overview of the risk of bias and concern regarding applicability of the three included studies, stratified by QUADAS-2 tool domain. The study by Hsu et al. had a high risk of bias and concern regarding applicability for the index test domain, because the algorithm was revised and fitted to the chart review. In other words, the index test was interpreted with the knowledge of the results of the reference standard.[32] In addition, because 25% of patients were excluded, and results were displayed for 250 of 996 charts selected for review for unclear reasons, we perceived a high risk of bias in the timing and flow domain.

As for the studies by Lange et al., and Tomassen et al., there was a high risk of bias and concern regarding applicability for the patient selection domain. This was because 1) patients were invited to participate in phase 2 of the GA^{2}LEN study, leading to self-selection bias, and 2) authors aimed to recruit 120 cases and 120 controls, resulting in the abnormally high proportion of CRS patients in the final validation populations in these two studies.

Discussion

The majority of large epidemiological studies on CRS use data from health administrative data or large health surveys. In this study, we determined how often these studies determined the accuracy of case identification along with those accuracy statistics. While acknowledging the previous important work that has led to our review, we found that studies using these data infrequently validated the accuracy of case identification, with three research teams doing this important work. A non-validated CRS-identification algorithm for administrative data, while highly accurate in the study population, would erroneously identify a majority of people with the disease when applied to a general population (Table 4). Self-reported CRS in people from health surveys is highly inaccurate. These results should be considered when interpreting epidemiological analyses of CRS that are based on such data.

These results highlight: the importance of such validation work; that results of CRS epidemiological studies based on health administrative data or health surveys should be interpreted with caution; and that further research is required to develop methods that accurately identify patients with true CRS in large populations.

Although the authors of the included studies are to be commended for their work in determining the accuracy of CRS case identification, these studies have several limitations. Hsu and colleagues could not apply their final administrative data algorithm to approximately 25% of the source population, limiting the ability to make firm conclusions on how well it would identify CRS patients in general

populations. The excluded patients were those who likely had a probability of truly having CRS that was somewhere between the controls and those with possible CRS (Appendix B). This preliminary exclusion of almost a quarter of patients limits the algorithm's applicability to a general population. In addition, we highlight in Table 4 how the probability that a person identified by the algorithm truly has CRS is highly dependent on the disease's prevalence; the extremely high prevalence of CRS in this study means its PPV is much higher than that in a general population. This final algorithm was not externally validated and is subject to overfitting.[40]

Two studies examined the accuracy of self-reported CRS in a large population-based health survey. These studies found that self-reported diagnosis was inaccurate even in a population with very high disease prevalence. These findings are consistent with several cohort studies that demonstrated a lack of concordance between symptom-based CRS diagnosis and objective findings.[41,42-44] When applied to a lower estimated CRS prevalence in the general population, we found that less than 10% of patients with self-reported disease would truly have CRS.

Our study found that the majority of studies using health administrative data or results of large health surveys to examine CRS did not determine the accuracy of CRS case identification in their respective data media. This is an important consideration because the crux of all cohort and cross-sectional studies is the accuracy of case ascertainment.[45] Inaccurate case ascertainment will result in biased prevalence estimates and will also influence measures of association in often extreme and unexpected ways.[46] Lack of validation of case-selection methods is

common in studies using health administrative data.[47] Although such validation studies can be laborious, they are essential and required first steps before more clinically applicable research can be reliably done using such data.

As for the rest of frequently cited CRS epidemiological data including prevalence rates, resource utilization, missed days of work, and self-reported health status, the method of case identification employed in the majority of these studies is therefore of unknown accuracy. Prevalence estimates, for example, are frequently determined in health surveys by trained interviewers asking patients if they have been previously diagnosed with chronic sinusitis.[5,28] This method of identifying health conditions is prone to recall bias and misclassification. Other data, such as the claim that sinusitis is one of the top 10 conditions affecting health and productivity of major US employers, are based on ICD-9 diagnostic codes in large administrative databases.[23,28,48] We know from at least one of the studies included in this review that this method of case identification is poor. Aside from the three studies included in our review we could not identify other studies that determined the accuracy of these methods of identifying CRS. It follows then that we should interpret all results based on these data with scepticism.

There are some limitations to our systematic review. The inclusion criteria may have missed relevant non-English articles. We did not review articles published after Jan. 25th, 2015, and there may have been relevant articles since then. It is possible then that there was incomplete retrieval of relevant studies due to human error.

We could not adhere to some of the PRISMA guidelines, as by nature administrative database studies do not involve interventions or comparisons, limiting a PICOS statement to the population, outcomes and study design.

We suggest that further work be done to derive and validate accurate methods that use population-based health administrative data to identify patients with CRS. This has been used to identify other diseases, for example rheumatoid arthritis, in large administrative databases with good accuracy.[49] Improvements in natural language processing (NLP) technology could help identify key terms in CT reports, OR dictation summaries, and patient charts to improve efficiency and accuracy in developing CRS algorithms.[36]

Conclusion

In summary, the vast majority of studies using health administrative or survey data do not measure their accuracy of CRS identification. In the rare situation where they are assessed, current methods used in health administrative data or health surveys to identify patients with CRS are inaccurate.

These results should be considered when CRS epidemiological data based on administrative data or health surveys are reviewed.

Funding

The Ottawa Hospital Academic Medical Organization supported this project.

12.0 Intervening bridge between two manuscripts

In Section 5.0, I showed that the current epidemiological knowledge base for CRS, which forms much of our understanding of this disease, is unlikely to be accurate. This is very concerning because these data are frequently used and cited in most articles that study CRS. If we are going to use administrative data to study CRS, it behooves us to ensure that we are able to accurately identify the condition we are trying to study.

In the following section, I describe a method of using administrative data at The Ottawa Hospital to identify a subset of patients with CRS, those who had ESS. Some of the sections and discussion points are expanded in this thesis version, and will be made more concise for manuscript submission.

13.0 Algorithm derivation and validation, Manuscript: Administrative data accurately predicts patients who have endoscopic sinus surgery for chronic rhinosinusitis

Kristian Macdonald, MD, Shaun J Kilty, MD, Carl van Walraven, MD
Keywords: Chronic Rhinosinusitis, Endoscopic Sinus Surgery, Administrative Database Research, Diagnostic Accuracy Studies, Predictive Algorithm.

Abstract

Introduction: Current methods to identify chronic rhinosinusitis (CRS) within administrative databases (AD) are inaccurate. Our objective was to develop a algorithm that accurately identified CRS patients who had endoscopic sinus surgery (ESS) at a tertiary level hospital.

Methods: This was a diagnostic accuracy study. Beginning January 1st, 2011 to December 31st, 2012, a chart review was performed for all surgical encounters in which ESS was performed. True cases were defined as those in which ESS was performed for Otolaryngologist-diagnosed CRS; all other surgical patients during the 2-year period were controls. We derived a predictive algorithm based on International Classification of Diseases, version 10 (ICD-10) diagnostic codes and Canadian Classification of Health Interventions (CCI) procedural codes. Internal validation of our algorithm was performed with a chart review for all algorithm-identified cases and 200 randomly selected controls during the following year, January 1st to December 31st, 2013.

Results: During the study period, 347 cases and 185,007 controls were identified. The predictive algorithm assigned identified as cases all encounters that contained at least one CRS ICD-10 diagnostic code **and** one or more ESS CCI procedural code. This algorithm was very accurate: sensitivity 96.0% (95%CI 93.2-97.7), specificity

100% (95% CI 99.9-100), and positive predictive value 95.4% (95%CI 92.5-97.3). Internal validation using chart review revealed similar accuracy: sensitivity 98.9% (95%CI 95.8-99.8), specificity 97.1% (95%CI 93.4-98.8), and positive predictive value 96.9% (95%CI 93.0-99.8).

Conclusion: A simple algorithm based on administrative database codes accurately identified surgical encounters in which endoscopic sinus surgery was performed for chronic rhinosinusitis. If externally validated, this algorithm can be used in population-based cohorts to study longitudinal outcomes for this population.

Introduction

Chronic Rhinosinusitis (CRS) is a common and debilitating inflammatory disease of the sinonasal cavities. CRS is associated with significant resource utilization and burden on health care expenditures.[2] The prevalence of CRS has been quoted as between 5 and 15% of the population,[2,3] and appears to be rising.[50] Patients with CRS self-report their overall health status at a level similar to those with other chronic diseases including current or previous cancer, asthma, migraine, arthritis and epilepsy.[4]

Much of the epidemiological data that forms our understanding of CRS is based on studies that identify CRS within large administrative databases and health surveys. We recently published a systematic review of studies that determined the accuracy of these methods for identifying CRS.[51] We found only 3 studies that compared CRS identification (ascertained from diagnostic codes and self-reporting) to a reference standard (including clinician-performed chart review, nasal endoscopy, and Otolaryngologist-based CRS clinical diagnosis). Compared to a reference standard, our review found that none of the CRS identification methods were accurate. This finding makes one question any statement (such as those included in the first paragraph of this introduction) based on these inaccurate epidemiological studies.

Despite the inability thus far to demonstrate accurate CRS case ascertainment, health administrative (HA) data may provide the best research modality to develop reliable population-based statistics for CRS patients. HA data are routinely collected during the provision of health services for large populations.

They have great potential to answer important research questions because of their low cost (since the data are already collected), wide external validity (since the data can cover all people within a particular health care system), and large numbers of patients to provide statistical power.[52] Within Canada, our publically funded health care system potentially allows for the complete capture of patient cohorts with specific conditions through linkable databases. These factors help to minimize selection and recall bias.[34]

Within HA data, diseases and procedures are represented with codes. The validity of using HA data to answer research questions is dependent on the accuracy of these codes for the entity they are supposed to represent. Inaccuracies via coding errors that occur in defining the initial cohort, the exposure, or the outcome in an administrative data project can result in biased conclusions. Despite the importance of establishing the accuracy of administrative database codes, such validation is performed in less than 20% of administrative database studies.[47]

Our initial objective was to identify a algorithm that that would accurately identify CRS patients within HA data. The single physician diagnostic CRS code "473.x" (Version 9 of the International Classification of Disease (ICD-9)) is one such algorithm for identifying CRS cases. However, our aforementioned systematic review identified one study in which this code had just a 34% positive predictive value (PPV). It is therefore highly unlikely that retrieving a patient cohort assigned a 473.x code would represent patients with true CRS. This misclassification is likely in part because of the overlapping symptoms of CRS and other conditions (eg. nonallergic rhinitis, anosmia, septal perforation), leading the physician to assign

other conditions this diagnostic code when there is not another more appropriate one available.[6] In addition, performing a retrospective chart review for the validation of patients with the CRS diagnostic code would not be practical, as it would require the review of medical records in physician private medical offices, with likely incomplete data collection.

A more feasible solution to meet our objective of capturing a CRS cohort within HA data was to examine CRS patients who had ESS. CRS patients who fail medical therapy are potential surgical candidates, and this subgroup therefore represents patients with more advanced CRS.[6] A validated cohort of patients who had ESS for CRS would allow us to study this surgery as an intervention for CRS patients. ESS surgery is publicly funded under the Ontario Health Insurance Plan (OHIP), and so hospital and provincial health records should capture all ESS surgeries performed. This method would be advantageous as it should be relatively straightforward to determine whether a patient had ESS surgery unless there are major systemic errors in data recording. The challenge will then be to accurately refine the cohort, through a detailed chart review, into those who had ESS for CRS, and eliminate those who had other conditions, such as recurrent sinusitis, tumours, traumatic injuries, cerebrospinal fluid leaks, and intracranial/intraorbital pathologies.[53-55]

After creating a chart review-based reference standard cohort of patients who had ESS for CRS, we will then derive a algorithm based on health administrative data to identify ESS-CRS cases within a surgical cohort. The final objective will be a

algorithm that, when applied to all surgical patients, accurately identifies ESS-CRS patients.

Methods

This was a validation study of diagnostic test accuracy using several measures of accuracy including sensitivity, specificity and predictive values. To achieve current standards in performing studies of diagnostic accuracy, we adhered to the Standards for Reporting of Diagnostic Accuracy Studies (STARD, 2015 version,[56] Appendix F). The Ottawa Health Science Network Research Ethics Board approved this study protocol (OHSN-REB 20140164).

Databases used

The **Ottawa Hospital Data Warehouse (OHDW)** contains data from several source systems of patient data dating back to as far as 1996 for patients treated at The Ottawa Hospital (TOH), a 1000-bed tertiary care hospital serving over 1.2 million patients and affiliated with the University of Ottawa. Appendix D displays an overview of the tables within the OHDW. Several groups of variables are recorded for each patient encounter including patient demographics, encounter type, diagnoses, and services rendered (including surgeries).

Several tables within the OHDW were used, including the: 1) ***Encounter table,*** in which each row represents one patient encounter; its important variables include patient demographics (at the time of the encounter), unique identifiers (that allow for linkage to databases outside TOH), inpatient details, and discharge disposition; 2) ***Procedures table,*** in which each row represents one procedure

performed during the in-patient encounter; its important variables include the date, the time, and the duration of surgery, its surgeon and anesthetist, the Canadian Classification of Interventions (CCI) code for the procedure, and the International Classification of Diseases (ICD) code for the most responsible diagnosis associated with the procedure; ***Surgical Information Management System (SIMs),*** which is an online computerized charting and scheduling system for all operations that occur at TOH back to April 2008 having several checklists in place to ensure the correct surgery for the correct indication is recorded (such as the surgeon completing and submitting the paperwork for the surgery, the actual procedure(s) that was (were) performed during the operation), all of which is confirmed by the surgeon at the end of the case with each surgeon identified using a unique identifier.

While the above tables contain data for TOH patients, the ***Institute for Clinical Evaluative Sciences (ICES)*** maintains administrative data for over 13 million people covered by the Ontario Health Insurance Plan (OHIP). Patients treated at TOH can be identified and linked through both databases with unique identifiers. Some of the datasets maintained by ICES that were used in this project included: 1) ***Discharge Abstract Database,*** *(DAD)* which captures all hospitalizations and same-day surgeries in Ontario with each row representing one encounter with the patient, hospital, admit and discharge date, diagnoses, and procedures all recorded; patients who had same-day surgeries, such as ESS, can be identified in specific hospitals, such as TOH; 2) ***Same-day Surgery,*** which captures all same-day surgeries in Ontario with each row representing one encounter for a same-day surgery and records the patient, date, and procedure.

Identifying Patients Undergoing ESS for CRS at TOH

A graphical overview of the major steps of this project is shown in Appendix E. From the SIMS database, we obtained a cohort of all TOH surgical encounters that were recorded as Otolaryngologist-performed ESS procedures between January 1st, 2011 and December 31st, 2012. This study period was chosen to ensure adequate and complete coverage of administrative data for this project. The anticipated volume of case reviews (about 200 per year) during this 2-year period was also feasible to complete for this project.

The encounters selected for the chart review were identified as follows: Given that ESS is only performed by Otolaryngologists, we first identified all surgical encounters performed by this type of surgeon. We then selected all encounters that listed ESS as at least a minor component of the surgery performed during that encounter. This included surgeries in which some or all of the sinuses were addressed, and those that were performed in combination of other surgeries, such as septoplasty or open approaches to the sinuses. Encounters were excluded if they definitely did not consist of ESS being performed (eg. thyroidectomy, neck dissection, tympanomastoidectomy).

The extracted cohort therefore included all ESS surgeries performed by TOH Otolaryngologists, meaning that all other surgeries conducted at TOH during this time period (all by non Otolaryngologists) were effectively ***not*** ESS.

Chart review: Determine whether ESS was conducted for CRS

A chart review was performed of all Otolaryngologist-performed ESS cases to identify those in which ESS was the predominant surgery performed (as opposed to other Otolaryngologist procedures such as open surgical approaches to the sinuses), and in which ESS was performed for Otolaryngologist-diagnosed CRS (as opposed to other non-CRS indications such as benign tumours, cerebrospinal fluid leaks, encephaloceles, trauma, foreign bodies, and invasive fungal sinusitis).[53-55] The chart review involved an analysis of primary care physician referrals, clinic notes, operative notes, and sinus CT imaging. We decided to use Otolaryngologist-diagnosed CRS as opposed to a retrospective chart review to identify symptoms and objective findings meeting CRS diagnostic criteria,[6] because the latter approach would more likely result in incomplete data collection and misclassification. A reference standard based on Otolaryngologist-diagnosed CRS was recently used in a similar diagnostic accuracy study.[38] If the listed diagnosis was recurrent sinusitis, a more detailed chart review was performed to determine if the patient had coexisting CRS using physicians' clinical notes and CT scans. If the patient had associated CRS, the encounter was labeled as a case, otherwise a control. We did this because significant overlap exists between CRS and recurrent sinusitis, and ESS treats both conditions.

Patient encounters in which the chart review confirmed ESS for CRS were categorized as cases. All other encounters were categorized as controls.

Linkage to Population-Based Datasets at ICES

This dataset (containing case status for all TOH patients between 1 January 2011 and 31 December 2012) was linked to DAD via unique identifiers that were encrypted to maintain patient confidentiality. This linked dataset with assigned ESS-CRS cases and controls then provided the reference standard from which the predictive algorithm was created.

Derivation and internal validation of algorithm to identify ESS for CRS encounters

The same clinician (KM) who performed the chart review created the algorithm. Algorithm development was based on an *a priori* identification of codes that could differentiate cases and controls. Table 7 lists the ICD-10 (International classification of diseases, version 10[57]) diagnostic codes for CRS and CCI (Canadian Classification of Health Interventions, version 2015[58]) codes for ESS that were identified from this process.

For each encounter, binomial variables were created to identify the presence or absence for all diagnostic and procedural codes listed in Table 7. For example, the variable "_J321" was created, with a 1 indicating that the encounter was coded with a diagnosis of frontal sinusitis (ICD-10 code of J32.1) in any of the diagnostic fields and 0 indicating no such diagnosis. Similarly, the variable "_1EX" code was created, with a 1 indicating that the encounter was coded with surgery of the frontal sinus (CCI code of 1.EX.^^). This process was completed for all diagnostic and procedural codes listed in Table 7 for all patient encounters.

Algorithm variations were developed in a trial and error approach. We considered several variable types for algorithm inclusion, including hospital length

of stay (as most ESS is day surgery), age and major comorbidities (because ESS for CRS is usually an elective surgery that may be performed in younger and healthier people compared to other major surgeries), and the CCI and ICD-10 codes listed in Table 7. Our aim was to develop a simple algorithm that used as few codes and variable types as possible, but that made clinical sense. We theorized that each ESS-CRS surgical encounter should contain some variation of ICD-10 CRS and CCI ESS codes, and so we determined to use at least these two variable types in our algorithm. The algorithm was built and adjusted based on comparing the accuracy of algorithm case ascertainment to the reference standard.

The final algorithm accuracy was displayed in a 2x2 table comparing the case status of the algorithm output to the reference standard. Validation statistics with 95% confidence intervals (95% CI) were calculated, using SAS version 9.3 for UNIX (SAS Institute, Inc., USA).

Internal validation was then performed to determine algorithm accuracy within another TOH cohort from a different time-period. Using algorithm criteria, all TOH patient encounters identified by the algorithm as cases and 200 randomly selected controls between Jan. 1st, 2013 and Dec. 31st, 2013 were retrieved. A chart review was performed of the approximately 400 patients to determine reference standard case status, by the same clinician, (KM) **blinded to the algorithm-predicted case status**. Once the chart review was competed, algorithm case status was revealed, and another 2x2 table and set of validation statistics were created to determine internal validation of the algorithm.

Results

Chart Review

From Jan. 1st 2011, to Dec. 31st, 2012, 411 TOH surgical encounters were identified as having ESS (Figure 3). Of these, 17 were excluded after the chart review revealed that the major surgery was one other than ESS, leaving 394 encounters that included at least endoscopic antrostomy and ethmoidectomy. Another 37 encounters were excluded because the procedures had been done for diagnoses other than chronic sinusitis, including 18 sinonasal tumours and 8 with recurrent sinusitis with no evidence of associated CRS. This resulted in 357 cases of ESS for CRS during the study period.

Linkage of chart review data to ICES dataset

Patient encounters within the TOH chart review cohort and DAD dataset were linked via encrypted unique identifiers. Thirteen patients (ten cases and three controls) were lost in the linkage due to missing unique identifiers. The linked dataset contained 185,354 hospital encounters representing all surgeries performed at TOH from Jan. 1st, 2011, to Dec. 31st, 2012. This linked dataset, with 347 cases and 185,007 controls, was used to develop the predictive algorithm.

Algorithm development

The algorithm was created through a trial and error approach, using variables within the linked dataset. It was evident from analyzing the variable types and values for each case encounter that they were commonly assigned CRS diagnostic and ESS procedural codes. The first algorithm was based on diagnostic codes only. That is, algorithm #1 assigned cases if an encounter listed any of the ICD-10 CRS diagnostic codes listed in Table 7. Compared to the reference standard case ascertainment, this algorithm had excellent validation statistics: sensitivity 96.5% (95% CI 93.9-98.1) and positive predictive value (PPV) 93.3% (95% CI 90.1-95.6).

The second algorithm was based on procedural ESS codes only. Cases were assigned if an encounter listed any one of the CCI ESS procedural codes listed in Table 7. Compared to the reference standard case ascertainment, this algorithm had similarly high validation statistics: sensitivity 96.8% (95%CI 94.2-98.3) and PPV 93.3% (95%CI 90.1-95.6).

The third and final algorithm combined features from the first two algorithms, resulting in a slightly improved PPV. Encounters were classified by the final algorithm as ESS for CRS if they had been coded with ***any*** of the ICD-10 CRS diagnostic codes listed in Table 7 **along with** any of the CCI ESS surgical codes listed in Table 7. All encounters **not** meeting these criteria were classified as controls (i.e. not ESS for CRS). Table 8 compares validation statistics of the three algorithm variations. Specificity for all three algorithms was 100%.

Table 9 displays a 2x2 table comparing the final algorithm output to the reference standard, with validation statistics including sensitivity 96.0% (95%CI 93.2-97.7), specificity 100% (95%CI 99.9-100), positive predictive value 95.4% (95%CI 92.5-97.3), positive likelihood ratio 11,096 (95%CI 6,794-18,120), and negative likelihood ratio 0.04 (95%CI 0.02-0.07). Figure 4 displays a graphical overview of the final algorithm.

Further examination of the 16 false positives (encounters identified as cases by the algorithm but were controls by the reference standard), revealed that eight were patients with recurrent sinusitis according to the reference standard.

Internal validation of algorithm

Using criteria from the final algorithm, we retrieved an OHDW cohort of all cases and 200 randomly selected controls from year following the derivation cohort (i.e. Jan. 1st, 2013 to Dec. 31st, 2013). A chart review, blinded to algorithm output case status, was then performed to determine reference standard case status. After the algorithm output case status was revealed, a 2x2 table was again created with excellent accuracy: sensitivity 98.9% (95%CI 95.8-99.8) and specificity 97.1% (95%CI 93.4-98.8). (Table 10)

Discussion

We developed an internally validated algorithm that accurately identified patient encounters in which endoscopic sinus surgery was performed for chronic rhinosinusitis at The Ottawa Hospital over a 3-year period. This algorithm is simple

and includes readily available administrative data to accurately differentiate between ESS-CRS cases and controls within a surgical cohort. The criteria for a case (at least one ICD-10 CRS diagnostic code and at least one CCI ESS procedural code) were not created a priori, but instead through a trial and error process with the observations and variables contained within the dataset, with knowledge of the chart review data. However, we argue that this algorithm has excellent face validity for Otolaryngologic epidemiology research.

This algorithm's accuracy is impressive for two major reasons. First, despite the abundance of readily available and commonly-cited CRS epidemiological data (as demonstrated in our recently published systematic review), only three studies previously examined the accuracy of methods of identifying CRS patients with all finding that these methods were inaccurate.[51] Our algorithm appears to be the first validated algorithm to be published that accurately identifies CRS patients within health administrative data (albeit for a subset of those who had ESS). Second, also as discussed in our systematic review, the positive predictive value is highly influenced by disease prevalence. For a disease with a low prevalence such as CRS, a algorithm would have to achieve a very high sensitivity and specificity to produce a similarly high positive predictive value. The prevalence of cases in our derivation population was just 0.19% (Table 9 - 347 encounters in which ESS was performed for CRS, out of all surgeries performed over the 2 year period at TOH). Achieving this high PPV with a low case prevalence reflects this algorithm's accuracy. This algorithm's 95.4% PPV means that a patient encounter identified as a case is

incorrect less than one time out of 20. This result needs to be confirmed in other centres before our algorithm can confidently be applied for health services research.

Conducting such health administrative database research in Ontario is aided by the fact that ESS is a publically funded procedure. As a result, all ESS performed in Ontario (representing approximately 40% of Canada's population) should be captured within these databases. This provincial population-based database has been previously used to study chronic disease,[59,60] and other algorithms based on HA database codes have been used to identify diseases, with varying accuracies.[61-63] Some advantages of this population-based method to identify patients undergoing ESS for CRS includes: 1) minimal cost, as most work for this research is at the computer and through a chart review; 2) large numbers of patients from a population-based database allows complete analyses without sampling; and 3) if externally validated, our algorithm can be used to study longitudinal outcomes for ESS as an intervention in CRS patients.

Others have identified ESS procedures (for all indications, not just CRS) in HA databases using similar procedural codes for ESS (similar CCI codes in Alberta,[64] and Common Procedural Terminology codes in the US[65]). In these studies, the authors did not attempt to determine code accuracy to determine if patients identified by these methods actually had ESS. The major difference in our study is that we determined the accuracy of these codes compared to a reference standard, followed by internal validation. Our chart review revealed that 17/411 (4%) patients who were identified as having ESS actually had a more invasive open procedure, and 37/394 (9.4%) patients who had at least endoscopic antrostomy/ethmoidectomy

did not have CRS. Combined, 54/411 (13.1%) patients who were coded at TOH as having ESS did not truly have ESS or CRS. However, despite these potential inadequacies in code accuracy, a algorithm based only on ESS codes from the DAD database achieved almost the same accuracy in identifying ESS-CRS cases as our final algorithm (sensitivity 96.8% (95%CI 94.2-98.3), specificity 100% (95%CI 99.9-100), PPV 93.3% (95%CI 90.1-95.6)), giving credence to previous authors' work. In an analysis similar to ours (although again without an attempt at code validation), Benninnger et al. identified ESS-CRS patients within a cohort of 35.5 million patients enrolled in the Market Scan Commercial Claims and Encounter database in 2010.[66] They used analogous codes: sinus surgery codes (CPT-4 31254-31288 [Common Procedure Terminology, 4th Ed]), and ICD-9 CRS diagnostic codes (473.X), and identified 2,833 ESS-CRS patients. Our results give evidence that these methods of identifying ESS procedures can be accurate – this statement would be further supported if our results were externally validated or if other authors carried out similar validation projects.

Although it would perhaps be preferable to capture a more general cohort of CRS patients (including nonsurgical patients), this may not be possible. This is because of the heterogeneity of a CRS diagnosis (that was discussed in this manuscript's introduction) and was illustrated in a similar attempt to create a algorithm to identify patients with obstructive sleep apnea (OSA), a diagnosis with several criteria similar to CRS.[52] The authors identified 2,427 patients with OSA based on a chart review reference standard, and linked data to health administrative databases. The authors could not develop a algorithm based on codes that

accurately identified OSA patients, concluding that readers should be skeptical of other studies that review OSA from administrative database studies.

Our algorithm is rather unique within health administrative data algorithms in that it captures a specific procedure for a specific disease. We argue that CRS codes within a surgical cohort are likely more accurate than in a more general cohort, such as those for office-visits that would be captured by physician-billing billings or claims. As mentioned previously, CRS symptoms are nonspecific and overlap several other conditions, and there is likely misclassification in ICD-10 CRS diagnoses. As such, disorders for which there is no ICD-10 diagnosis (eg. anosmia, nonallergic rhinitis, septal perforation), may be misclassified as CRS. The ICD-10 acknowledges that "not every problem or reason for coming into contact with health services can be categorized" as a specific diagnosis, [57] and the diagnostic accuracy of ICD codes has not been assessed.[52] Within administrative databases, diagnostic codes have shown inconsistent accuracy in identifying true disease. For example, Quan et al. performed a chart review on patients who had a specific diagnosis of many conditions (not including CRS) and found a varying degree of validation statistics, such as PPV varying from as low as 32% (blood loss anemia) to 100% (AIDS/HIV).[67]

However procedural codes should, in theory, be more accurate. It is obviously important for a surgeon to perform a procedure for an appropriate condition, and document as such. Rhinologic procedures including ESS are among the more commonly successfully litigated Otolaryngologic procedures, one of the many imperatives for a surgeon to correctly diagnose CRS when performing ESS.[68]

However, it may not be as imperative to the physician to accurately document an in-office patient diagnosis for the purpose of physician billing. In this way, capturing CRS patients who had ESS increases the accuracy of the CRS diagnostic codes to a level that may not be achievable through another method. This of course limits the generalizability of our findings – we can use this cohort to study longitudinal outcomes on CRS patients who have ESS, but not for non-surgical CRS patients.

Finally, we found that eight of the false positives identified by the final algorithm were encounters in which ESS was performed for recurrent sinusitis with no coexisting CRS. This misclassification of recurrent sinusitis as CRS reflects a potential inability of administrative database codes to differentiate between these two conditions. Although this did not greatly affect our validation statistics, it could affect external validity, for example in centres where a greater proportion of ESS is performed for recurrent sinusitis.

Several assumptions must be made that could be interpreted as study weaknesses. First, development of the reference standard, predictive algorithm, and internal validation were all performed by the same clinician (KM). During algorithm development, this researcher had knowledge of the reference standard case assignment. Similarly, during the internal validation chart review, although he was blinded to the case/control status, he had knowledge of the reference standard case ascertainment and the final algorithm criteria. This bias could have influenced case ascertainment in the reference standard and internal validation, as well as variable selection for the final algorithm, falsely elevating the algorithm accuracy. To help address this, a second blinded clinician could have performed the chart reviews for

both the reference standard and internal validation. This bias is mitigated by the fact that these three major steps were developed with transparent and reproducible criteria, leaving little interpretation, as follows: 1) Reference standard and 2) Internal validation chart reviews: the vast majority of cases were assigned based on information from the easy-to-read and readily available OR report, which listed the indication for surgery and the surgery performed; 3) Algorithm development: as described above, the algorithm criteria, consisting of all ICD-10 CRS diagnostic and all CCI ESS procedural codes, are simple and have face value.

Second, we used Otolaryngologist-diagnosed CRS for reference standard case ascertainment. This infers that the Otolaryngologist correctly diagnosed CRS. It is possible that strict diagnostic criteria were not applied. To help address this, we could have performed a more detailed chart review to determine if patients satisfied the symptomatic and objective criteria (such as a minimum Lund-McKay score on preoperative CT) of CRS. However, this method would likely suffer from incomplete data capture inherent to retrospective chart reviews, and as a result, misclassification in the reference standard.[69] It is possible that surgeons performed ESS for incorrectly diagnosed CRS. Reports of abuse have been noted for a select few surgeons in which ESS was performed for no accepted indications.[70] If indeed ESS procedures were performed for patients who did not truly have CRS, but who were labeled as such in the reference standard, this would result in overestimation of the algorithm's true accuracy.

Third, we must also assume that patient encounters are correctly recorded in the OHDW database, and specifically that ESS encounters were correctly identified

for the chart review. Procedure documentation begins with the surgeon entering the procedure on an OR booking form, and ends with the nurse documenting the procedure, with surgeon confirmation, directly into the SIMS database immediately after the procedure is performed. To retrieve ESS cases for the chart review, we searched first for all Otolaryngologist-performed procedures, and then for those coded as being ESS either preoperatively or postoperatively. This method should minimize the possibility of false negatives (procedures incorrectly identified as not having ESS), as only Otolaryngologists perform ESS, and any procedures that were incorrectly coded preoperatively would hopefully have been captured as cases postoperatively. It is possible that some ESS procedures were not identified by the SIMS dataset because they were recorded as a different procedure. To help minimize the chance of false negatives in the reference standard, we could have performed a more detailed chart review of all Otolaryngologist-performed surgeries to determine if ESS was correctly coded in this group.

Our future direction includes external validation at other tertiary care centres, similar to the methods used in internal validation. An externally validated algorithm can then be used to study longitudinal outcomes and health services research of this population. Other centres may be encouraged to perform their own external validation based on our algorithm criteria, with the overarching objective of producing much needed accurate CRS epidemiological data.

Conclusion

A simple algorithm based on administrative database codes accurately identified surgical encounters in which endoscopic sinus surgery was performed for chronic rhinosinusitis (CRS) at a tertiary care centre. Compared to a reference standard including a chart review and Otolaryngologist-diagnosed CRS, this algorithm achieved excellent validation statistics: sensitivity 96.0% (95%CI 93.2-97.7), specificity 100%, and positive predictive value 95.4% (95%CI 92.5-97.3). Internal validation was achieved with similarly high validation statistics.

If externally validated, this algorithm can then be used in large population-based cohorts to study longitudinal outcomes of patients who have endoscopic sinus surgery for chronic rhinosinusitis.

14.0 Acknowledgments, Funding & Further Information

The lead author would like to thank his thesis supervisor, Dr. Carl van Walraven, for his mentorship and support throughout the work leading up to this final thesis. The Ottawa Hospital Academic Medical Organization supported this project. The full study protocol can be obtained by contacting the lead author at krmacdonald@toh.on.ca.

15.0 Final Discussion and Future Direction

Although there is a need to develop methods to accurately identify CRS patients within HA databases, it is unlikely that other researchers will undertake a similar project. Such a validation process can be time-consuming and expensive, and robust databases such as the OHDW and ICES are not common worldwide. In addition, a code-validation study may not be attractive for grant approval. Finally, as a new staff Otolaryngologist with a special interest in sinus disease, I am in an exciting and unique position to carry out this type of research.

Future plans

The next two major follow-up projects after this thesis is defended will include:

1. Further algorithm refinement, using a Bootstrap technique, to eliminate variables that are not strongly associated with the algorithm's accuracy.[71] Further algorithm simplification may help entice other researchers to perform similar validation projects of ESS-CRS patients.
2. External validation of the final algorithm. Through a similar process as the internal validation performed in this project, I will perform a chart review on algorithm-identified cases and controls at other tertiary care centres in Ontario. Achieving accurate external validation will justify the use of this algorithm to study longitudinal outcomes in ESS-CRS patients in Ontario.

With a validated cohort of patients in Ontario who have ESS for CRS, there are multiple other research questions that can be addressed. The following is a few examples:

- There is significant evidence linking outcomes in lower airway disease, such as asthma, to CRS.[21] Data is conflicting whether pulmonary function tests (PFTs) improve after endoscopic sinus surgery. A research project could explore a cohort of asthmatic CRS patients and determine if PFTs change after ESS.
- Many patients with CRS require revision surgery.[6] There is significant phenotypic variability in how frequent and how many revision surgeries a patient will need. Some predictors have been identified, such as polyp disease. With a validated cohort, I could develop a predictive algorithm for revision surgery and lead the way to developing clinical practice guidelines to support these patients and their families.
- Although not discussed in the manuscript, several additional variables were created from the chart review. These variables were selected to characterize CRS disease severity and the extent of surgery. For example, the variable LM_CODE was created to separate patients with Lund-McKay scores of <= 14 ("1") and > 14 ("2").[72] Patients without a preoperative CT were assigned "0". A score of "2" thus represents more advanced preoperative sinus disease. Four variables were created to characterize details of the surgical procedure, including whether one or both frontal sinuses or sphenoid sinuses were addressed (FR_CODE or SPHENOIDOTOMY, respectively), whether a

septoplasty to correct a septal deviation was performed (SEPTOPLASTY), and whether pneumatized middle turbinates were excised (CONCHABULL). Finally, the variable IMAGE_GUIDANCE was created to display whether an image-guidance system, another indicator of the complexity of surgery, was used intraoperatively (See Appendix G for full list of variables created from the chart review).

Several further studies could be done with these additional variables. Frontal and sphenoid sinus is challenging, due to the complex anatomy and proximity to vital structures such as the skull base, optic nerve and carotid artery. Others in the US have noted that an increase in frontal and sphenoid sinus surgery is associated with an increase in the use of image-guidance surgery.[73] Physician-billing codes for ESS surgeries include codes for what sinuses were opened, including the frontal and sphenoid sinuses, whether IGS was used, and if a septoplasty was performed. I could compare physician-billing codes within ICES to these collected chart review variables, and perform a similar validation to see if physician-billing codes accurately capture the specifics of ESS procedures. These could then be used as predictors for ESS revision rates, as discussed above.

16.0 Final Summary

Our systematic review of studies that examined the accuracy of methods to identify CRS in large population-based studies identified only three studies that met inclusion criteria. These found that current methods to identify CRS are inaccurate.

We developed a algorithm based on readily available administrative database codes that identified surgical encounters in which ESS was performed for CRS. The final algorithm found that encounters having at least one CRS diagnostic code and one ESS procedural code had excellent accuracy for identifying ESS-CRS encounters: sensitivity 96.0% (95%CI 93.2-97.7), specificity 100% (95%CI 99.9-100), positive predictive value 95.4% (95%CI 92.5-97.3). Internal validation showed similar accuracy. This validation project will allow for future longitudinal outcome studies for this population.

17.0 References

1. Shea BJ, Grimshaw JM, Wells GA et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. *BMC Med Res Methodol* 7**,** 10 (2007).
2. Ray NF, Baraniuk JN, Thamer M, et al. Healthcare expenditures for sinusitis in 1996: Contributions of asthma, rhinitis, and other airway disorders. *J Allergy Clin Immunol* 1999;103(3):408–414.
3. Chen Y, Dales R, Lin M. The epidemiology of chronic rhinosinusitis in Canadians. *Laryngoscope* 2003;113(7):1199–1205.
4. Macdonald KI, McNally JD, Massoud E. The health and resource utilization of Canadians with chronic rhinosinusitis. *Laryngoscope* 2009;119(1):184–189.
5. Benninger M, Ferguson B, Hadley J, et al. Adult chronic rhinosinusitis: Definitions, diagnosis, epidemiology, and pathophysiology. *Otolaryng Head Neck Surg*. 2003;129(3):S1–S32.
6. Desrosiers M, Evans GA, Keith PK, et al. Canadian clinical practice guidelines for acute and chronic rhinosinusitis. *J Otolaryngol Head Neck Surg* 2011;40 Suppl 2:S99–193.
7. Fokkens WJ, Lund VJ, Mullol J, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2012. *Rhinol Suppl*. 2012;(23):1–298.
8. Dubin MG, Liu C, Lin, et al. American Rhinologic Society member survey on 'maximal medical therapy' for chronic rhinosinusitis. *Amer J Rhinol 2007;* 21**,** 483–488.
9. Lee JM, Chiu AG. Role of maximal endoscopic sinus surgery techniques in chronic rhinosinusitis. *Otolaryngologic Clinics of NA* 2010; 43, 579–589.
10. Cashman EC, MacMahon PJ, Smyth D. Computed tomography scans of paranasal sinuses before functional endoscopic sinus surgery. *World J Radiol* 2011; 3, 199.
11. Smith TL, Litvack JR, Hwang PH et al. Determinants of outcomes of sinus surgery: A multi-institutional prospective cohort study. *Otolaryngol - Head Neck Surg* 2010; 142, 55–63.
12. Bhattacharyya N. Clinical outcomes after endoscopic sinus surgery. *Curr Opin Aller Clin Immunol* 2006; 6, 167–171.
13. Welch KC, Stankiewicz JA. A contemporary review of endoscopic sinus surgery: Techniques, tools, and outcomes. *Laryngoscope* 2009; 119, 2258–2268.
14. Rudmik L, Smith TL. Quality of Life in Patients with Chronic Rhinosinusitis. *Curr Allergy Asthma Rep* 2011; 11, 247–252.
15. Macdonald KI, McNally JD, Massoud, E. Quality of life and impact of surgery on patients with chronic rhinosinusitis. *J Otolaryngol Head Neck Surg* 2009; 38, 286–293.
16. Olsson P, Ehnhage A, Nordin S, et al. Quality of life is improved by endoscopic surgery and fluticasone in nasal polyposis with asthma. *Rhinology* 2010; 48, 325–330.

17. Dalziel K., Stein K, Round A, et al. Systematic review of endoscopic sinus surgery for nasal polyps. *Health Technol Assess* 2003 7, iii–1–159.
18. Batra PS, Kern RC, Tripathi A et al. Outcome analysis of endoscopic sinus surgery in patients with nasal polyps and asthma. *Laryngoscope* 2010; 113, 1703–1706.
19. Ikeda K, Tanno N, Tamura G et al. Endoscopic sinus surgery improves pulmonary function in patients with asthma associated with chronic sinusitis. *Ann Otol Rhinol Laryngol* 1999; 108, 355–359.
20. Macdonald KI, Gipsman A, Magit A et al. Endoscopic sinus surgery in patients with cystic fibrosis: a systematic review and meta-analysis of pulmonary function. *Rhinology* 2010; 50, 360–369.
21. Ragab A, Clement P, Vincken W. Objective Assessment of Lower Airway Involvement in Chronic Rhinosinusitis. Am J Rhinol 2004; 18(1); 15-21.
22. Shashy RG, Moore EJ, Weaver A. Prevalence of the chronic sinusitis diagnosis in Olmsted County, Minnesota. *Arch Otolaryngol Head Neck Surg*. 2004;130(3):320–323
23. Goetzel RZ, Hawkins K, Ozminkowski RJ, Wang S. The Health and Productivity Cost Burden of the "Top 10" Physical and Mental Health Conditions Affecting Six Large U.S. Employers in 1999. *J Occup Environ Med*. 2003;45(1):5.
24. Meltzer EO, Hamilos DL. Rhinosinusitis diagnosis and management for the clinician: a synopsis of recent consensus guidelines. *Mayo Clin Proc*. 2011;86(5):427–443.
25. Tahamiler R, Canakcioglu S, Ogreden S et al. The accuracy of symptom-based definition of chronic rhinosinusitis. *Allergy* 2007; 62, 1029–1032.
26. Bhattacharyya, N. Clinical and Symptom Criteria for the Accurate Diagnosis of Chronic Rhinosinusitis. *Laryngoscope* 2006; **116,** 1–22.
27. Van Cauwenberge P. Epidemiology of chronic rhinosinusitis. *Thorax* 2000; **55,** 20S–21 2000.
28. Chen Y, Dales R, Lin M. The epidemiology of chronic rhinosinusitis in Canadians. *Laryngoscope* 2003; **113,** 1199–1205.
29. Bhattacharyya N. Contemporary assessment of the disease burden of sinusitis. *Aller Rhinol* 2010; 1, 1–8.
30. Liberati A, Altman DG, Tezlaff J et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Ann Intern Med* 2009; 151:W-65-94.
31. McCormick N, Lacaille D, Bhole V, Avina-Zubieta JA. Validity of heart failure diagnoses in administrative databases: a systematic review and meta-analysis. *PLoS ONE*. 2014;9(8):e104519.
32. Whiting PF. QUADAS-2: A Revised Tool for the Quality Assessment of Diagnostic Accuracy Studies. *Ann Intern Med*. 2011;155(8):529.
33. Leong A, Dasgupta K, Bernatsky S, Lacaille D, Avina-Zubieta A, Rahme E. Systematic review and meta-analysis of validation studies on a diabetes case definition from health administrative records. *PLoS ONE*. 2013;8(10):e75256.
34. McCormick N, Lacaille D, Bhole V, Avina-Zubieta JA. PLOS ONE: Validity of Myocardial Infarction Diagnoses in Administrative Databases: A Systematic

Review. *PLOS ONE*. 2014;9(3):e92286.
35. Sacket DL (2012). Testing Quality Improvement Interventions. In: Haynes HR (Ed.), *Clinical Epidemiology*. How to do clinical practice research. Chapter 7; pages 173-243. Lippincott Williams & Wilkins.
36. Hsu J, Pacheco JA, Stevens WW, Smith ME, Avila PC. Accuracy of phenotyping chronic rhinosinusitis in the electronic health record. *Am J Rhinol Allergy*. 2014;28(2):140–144.
37. Meltzer EO, Hamilos DL, Hadley JA, et al. Rhinosinusitis: Developing guidance for clinical trials. *Otolaryngol Head Neck Surg*. 2006;135(5 Suppl):S31–80.
38. Lange B, Thilsing T, Baelum J, Holst R, Kjeldsen A. Diagnosing chronic rhinosinusitis: comparing questionnaire-based and clinical-based diagnosis. *Rhinology*. 2013;51(2):128–136.
39. Tomassen P, Newson RB, Hoffmans R, et al. Reliability of EP3OS symptom criteria and nasal endoscopy in the assessment of chronic rhinosinusitis - a GA2LEN study. *Allergy*. 2010;66(4):556–561.
40. Siontis GCM, Tzoulaki I, Castaldi PJ, Ioannidis JPA. External validation of new risk prediction algorithms is infrequent and reveals worse prognostic discrimination. *J Clin Epidemiol* 2015;68(1):25–34.
41. Bhattacharyya N, Lee LN. Evaluating the diagnosis of chronic rhinosinusitis based on clinical guidelines and endoscopy. *Otolaryngol - Head Neck Surg*. 2010;143(1):147–151.
42. Bhattacharyya T, Piccirillo J, Wippold FJ. Relationship between patient-based descriptions of sinusitis and paranasal sinus Computed Tomographic findings. *Arch Otolaryngol Head Neck Surg*. 1997;123(11):1189–1192.
43. Kenny TJ, Duncavage J, Bracikowski J, Yildirim A, Murray JJ, Tanner SB. Prospective analysis of sinus symptoms and correlation with paranasal computed tomography scan. *Otolaryngol Head Neck Surg*. 2001;125(1):40–43.
44. Bhattacharyya N. A comparison of symptom scores and radiographic staging systems in chronic rhinosinusitis. *Am J Rhinol*. 2005;19(2):175–179.
45. Gurwitz JH. Reader's guide to critical appraisal of cohort studies: 1. Role and design. *BMJ*. 2005;330(7496):895–897.
46. Copeland KT, Checkoway H, McMichael AJ, Holbrook RH. Bias due to misclassification in the estimation of relative risk. *Am J Epidemiol*. 1977;105(5):488–495.30.
47. van Walraven C, Bennett C, Forster AJ. Administrative database research infrequently used validated diagnostic or procedural codes. *J Clin Epidemiol* 2011;64(10):1054–1059.
48. Benson V, MA M. Current Estimates From the National Health Interview Survey, 1995. Hyattsville, Md: National Center for Health Statistics; 1995. Data from Vital and Health Statistics, series 10: data from the National Health Survey, No. 199:1-428.
49. Cho S-K, Sung Y-K, Choi C-B, Kwon J-M, Lee E-K, Bae S-C. Development of an algorithm for identifying rheumatoid arthritis in the Korean National Health Insurance claims database. *Rheumatol Int* 2013;33(12):2985–2992.
50. Kilty, S. Canadian guidelines for rhinosinusitis: practical tools for the busy clinician. *BMC Ear Nose Throat Disord* 2012; 12, 1.

51. Macdonald KI, Kilty SJ, van Walraven C. Chronic rhinosinusitis identification in administrative databases and health surveys: A systematic review. *Laryngoscope* 2015; Dec 9; epub ahead of print doi:10.1002/lary.25804
52. McIsaac DI, Gershon A, Wijeysundera D, et al. Identifying Obstructive Sleep Apnea in Administrative Data: A Study of Diagnostic Accuracy. *Anesthesiology* 2015; 123, 253–263.
53. Harvey RJ, Parmar P, Sacks R et al. Endoscopic skull base reconstruction of large dural defects: A Systematic Review of Published Evidence. *Laryngoscope* 2010; 122, 452–459.
54. Gotlib T, Krzeski A, Held-Ziółkowska M et al. Endoscopic transnasal management of inverted papilloma involving frontal sinuses. *Videosurg Miniinv* 2010; 4, 299–303.
55. Woodworth BA, Bhargave GA, Palmer JN et al. Clinical outcomes of endoscopic and endoscopic-assisted resection of inverted papillomas: A 15-year experience. *Am j Rhinol* 2007; 21, 591–600.
56. Bossuyt PM, Reitsma JB, Bruns DE et al. STARD 2015: An Updated List of Essential Items for Reporting Diagnostic Accuracy Studies. *Radiology* 2015; 277, 826–832.
57. World Health Organization. (1992) *The ICD-10 classification of mental and behavioural disorders : clinical descriptions and diagnostic guidelines*. Geneva: World Health Organization.
58. Canadian Institute for Health Information. *Canadian Classification of Health Interventions, Version 2015*. Ottawa, ON: CIHI; 2015.
59. Gershon AS, Wang C, Guan J et al. Identifying patients with physician-diagnosed asthma in health administrative databases. *Can Respir J* 2009; 16, 183–188.
60. Tu K, Mitiku T, Guo H et al. Myocardial infarction and the validation of physician billing and hospitalization data using electronic medical records. *Chronic Dis Can* 2010 Sep;30(4):141-6.
61. Hux JE, Ivis F, Flintoft V, et al. Diabetes in Ontario: determination of prevalence and incidence using a validated administrative data algorithm. *Diabetes Care* 2002; 25, 512–516.
62. Tu K, Campbell NR, Chen XL, et al. Accuracy of administrative databases in identifying patients with hypertension. *Open Medicine* 2007; 1, 18–26.
63. Schultz SE, Rothwell DM, Chen Z et al. Identifying cases of congestive heart failure from administrative data: a validation study using primary care patient records. *Chronic Dis Inj Can* 2013; 33, 160–166.
64. Rudmik L, Holy CE, Smith TL. Geographic variation of endoscopic sinus surgery in the United States. *Laryngoscope* 2015; 125, 1772–1778.
65. Psaltis AJ, Soler ZM, Nguyen SA et al. Changing trends in sinus and septal surgery, 2007 to 2009. *Int Forum Allergy Rhinol* 2012; 2, 357–36.
66. Benninger MS, Sindwani R, Holy CE et al. Early versus Delayed Endoscopic Sinus Surgery in Patients with Chronic Rhinosinusitis: Impact on Health Care Utilization. *Otolaryngol - Head Neck Surg* 2015; 152, 546–552.
67. Quan H, Li B, Saunders LD et al. Assessing Validity of ICD-9-CM and ICD-10 Administrative Data in Recording Clinical Conditions in a Unique Dually

Coded Database. *Health Services Research* 2008; 43, 1424–1441.
68. Becker SS, Duncavage JA. Malpractice Claims in Nasal and Sinus Surgery: A Review of 15 Cases. *Otolaryngol Clin NA* 2010; 43, 929–932.
69. Gearing RE, Mian IA, Barber J et al. A methodology for conducting retrospective chart review research in child and adolescent psychiatry. *J Can Acad Child Adolesc Psychiatry* 2006; 15, 126–134.
70. Salman SD (2011). The story of chronic sinusitis and functional endoscopic sinus surgery In Salman SD, In *Scrubbed Out* (109-122). Bloomington IN, AuthorHouse.
71. Chen CH, George SL. The bootstrap and identification of prognostic factors via cox's proportional hazards regression algorithm. *Statist Med* 1985; 4, 39–46.
72. Hopkins C, Browne JP, Slack R, et al. The Lund-Mackay staging system for chronic rhinosinusitis: how is it used and what does it predict? *Otolaryngol - Head Neck Surg* 2007; 137, 555–561.
73. Psaltis AJ, Soler ZM, Nguyen SA. Changing trends in sinus and septal surgery, 2007 to 2009. *Internat Forum Allerg Rhinol* 2012; 2(5), 357-361.

18.0 Tables

Table 1: Characteristics of studies measuring the accuracy of Chronic Rhinosinusitis (CRS) identification

Authors	Year(s) of Data Collection, Country	Source Population	Validation Population	Method Used to Identify Patients with CRS or ESS (Index Test)	Gold Standard (Reference Standard)
Hsu[36] (2014)	2012-2013, USA	Patients with ≥2 medical visits captured in NMEDW between 1 March 2012 and 6 Feb 2013; cases and controls identified based on presence or absence (respectively) of CRS and ESS codes.	250 randomly selected charts from source population	Algorithm based on ICD-9 (471.x and 473.x) and CPT codes (31295, 21296, 21297, 31000, 31030, 31050, 31051, 31205 and 31090).	Independent, blinded chart review by two clinicians; true diagnosis of CRS based on subjective and objective criteria from CRS guidelines.
Lange[38] (2013)	2008-2009, Denmark	3,397 Danish participants who completed 1st phase GA²LEN project	362 participants, 64 with symptom-based CRS, from 2nd phase GA²LEN project	Questionnaire based on CRS symptoms (EP³OS criteria)	Clinical diagnosis by Otolaryngologist (blinded to 1st phase CRS status) based on symptoms and nasal endoscopy, using EP³OS criteria
Tomassen[39] (2010)	2009, Netherlands and Belgium	1700 European participants who completed both phases GA²LEN project	342 participants, 81 with symptom-based CRS, from 2nd phase GA²LEN project	Questionnaire based on CRS symptoms (EP³OS criteria)	Nasal endoscopy by Otolaryngologist (blinded to 1st phase CRS status) documented in medical record

NMEDW=Northwestern Medicine Enterprise Data Warehouse; CRS=Chronic Rhinosinusitis; ESS=Endoscopic Sinus Surgery; GA2LEN=Global Allergy and Asthma European Network; ICD-9=International Classification of Diseases, version 9; CPT=common procedural terminology; EP³OS=European Position Paper on Rhinosinusitis and Nasal Polyps[7]

Table 2: Accuracy of Chronic Rhinosinusitis (CRS) identification

First Author, Year	Index Test	Reference Standard	CRS Prevalenc in Validation Population (%	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	LR+ (95% CI)	LR- (95% CI)
Hsu[36] (2014)	ICD-9, CPT codes	Blinded clinician chart review	54.8	100 (96.6-100)	88.50 (80.79-93.49)	91.33 (85.34-95.11)	100 (95.39-100)	8.69 (5.21 14.50)	N/A
Lange[38] (201	Symptom-based diagnosis, from GA²LEN survey	Clinical diagnosis by Otolaryngologist based on symptoms and nasal endoscopy	25.1	49.45 (38.89-60.00)	93.00 (89.09-95.61)	70.31 (57.41-80.75)	84.85 (79.84-88.37)	7.05 (4.36 11.41)	0.54 (0.44-0.67)
Tomassen[39] (2010)	Symptom-based diagnosis, from GA²LEN survey	Nasal endoscopy	43.6	33.56 (26.16-41.81)	83.94 (77.81-88.67)	61.73 (50.22-72.11)	62.07 (55.85-67.92)	0.99 (0.67 1.46)	1.00 (0.93-1.09)

ICD-9 = International Classification of Diseases, version 9; CPT = common procedural terminology; PPV = positive predictive value; NPV = negative predictive value; LR+ = positive likelihood ratio; LR- = negative likelihood ratio; CRS = chronic rhinosinusitis; ESS = endoscopic sinus surgery; GA²LEN = Global Allergy and Asthma European Network of Excellence (GA²LEN) cohort.[7]

Table 3: Accuracy of coding algorithm from Hsu et al.[36] to identify patients with chronic rhinosinuitis (CRS) using health administrative data

Algorithm criteria for CRS present	CRS truly present		Total
	Yes	No	
Yes	137	13	150
No	0	100	100
Total	137	113	250

See Appendix B for the criteria required to be classified with or without CRS by the algorithm. To determine the final algorithm accuracy, 250 randomly selected charts were reviewed to determine true CRS status, based on accepted guidelines.[7,37] *Note that the prevalence of CRS prevalence in this sample is 54.8%. Summary statistics for algorithm accuracy to detect CRS: sensitivity 100% (95%CI 96.6-100); specificity 88.5% (95% CI 80.8-93.5), positive predictive value 91.3% (95% CI 85.3-95.1); negative predictive value 100% (95% CI 95.4-100), positive likelihood ratio 8.7 (95% CI 5.2-14.5). This table is based on data presented in Hsu et al.*[36] *CRS = chronic rhinosinusitis.*

Table 4: Positive predictive value varies by disease prevalence[47]

		Positive Predictive Value as a function of CRS Prevalence		
	Prevalence of CRS in Study	***CRS Prevalence in Study***	***CRS Prevalence of 5%***	***CRS Prevalence of 1%***
Hsu[36]	55	91	31	8
Lange[38]	25	70	27	6.6
Tomassen[39]	44	62	10	2.1

The validation populations in the included studies had exaggerated Chronic Rhinosinusitis (CRS) prevalence rates, leading to artificially elevated positive predictive values (PPV). The second column lists the PPV based on the CRS prevalence in that study, and the following columns list what the PPV would be with more realistic CRS prevalences, while keeping other study statistics such as sensitivity and specificity constant. Positive predictive value (PPV) = [Sensitivity x prevalence] / [Sensitivity x prevalence + (1-specificity) x (1-prevalence)].

Table 5: Lange's[38] accuracy assessment of self-reported chronic rhinosinusitis (CRS) from health survey compared to Otolaryngologist-based clinical diagnosis with history and nasal endoscopy

Self-reported CRS on questionnaire	CRS truly present		Total
	Yes	No	
Yes	45	19	64
No	46	252	298
Total	91	271	362

Questionnaire results were obtained from the phase 1 postal survey of the Global Allergy and Asthma European Network of Excellence (GA²LEN) cohort.[38] *A random selection of people from this survey was invited for this assessment in which further clinical examination and nasal endoscopy was conducted to confirm true CRS status. CRS prevalence in this was 25.1%. Summary statistics for accuracy of self reported CRS for true CRS: Sensitivity 49.5 (95% CI 38.9-60.0), specificity 93.0 (89.1-95.6), positive predictive value 70.3% (95% CI 57.4-80.8), negative predictive value 84.9% (95% CI 79.8-88.4). CRS, chronic rhinosinusitis. This table is based on data presented in Lange et. al.*[38]

Table 6: Association of questionnaire-based symptomatic CRS with nasal endoscopy in Tomassen[39]

CRS on questionnaire	Nasal endoscopy		Total
	Positive	Negative	
Yes	31	50	81
No	162	99	261
Total	193	149	342

Questionnaire results were obtained from the phase 1 postal survey of the Global Allergy and Asthma European Network of Excellence (GA²LEN) cohort.[38] *A random cohort was invited for phase 2 which consisted of nasal endoscopy to determine objective evidence of CRS. CRS prevalence 43.6%. Summary statistics for accuracy of self reported CRS for true CRS: sensitivity 33.6 (95% CI 26.2-41.8), specificity 83.9 (95% CI 77.8-88.7), PPV 61.7% (95% CI 50.2-72.1).*

Table 7: Administrative database codes used in predictive algorithm

Chronic Rhinosinusitis			Endoscopic sinus surgery	
Diagnosis	**ICD-10 code***	**ICD-09 code***	**Procedure**	**CCI code***
Chronic sinusitis	J32	473	Therapeutic Interventions on the Ethmoidal Sinus	1.EU.^^.^^
Chronic maxillary sinusitis	J32.0	473.0	Drainage, ethmoidal sinus	1.EU.52.^^
Chronic frontal sinusitis	J32.1	473.1	Excision partial, ethmoidal sinus	1.EU.87.^^
Chronic ethmoidal sinusitis	J32.2	473.2	Therapeutic Interventions on the Sphenoidal Sinus	1.EV.^^.^^
Chronic sphenoidal sinusitis	J32.3	473.3	Drainage, sphenoidal sinus	1.EV.52.^^
Chronic pansinusitis	J32.4	N/A	Excision partial, sphenoidal sinus	1.EV.87.^^
Other chronic sinusitis	J32.8	473.8	Therapeutic Interventions on the Maxillary Sinus	1.EW.^^.^^
Chronic sinusitis, unspecified	J32.9	473.9	Excision partial, sphenoidal sinus	1.EV.87.^^
Nasal polyp	J33	471	Therapeutic Interventions on the Maxillary Sinus	1.EW.^^.^^
Polyp of nasal cavity	J33.0	471.0	Drainage, maxillary sinus	1.EW.52.^^
Polypoid sinus degeneration	J33.1	471.1	Therapeutic Interventions on the Frontal Sinus	1.EX.^^
Other polyp of sinus	J33.8	471.8	Drainage, frontal sinus	1.EX.52.^^
Nasal polyp, unspecified	J33.9	471.9	Destruction, frontal sinus	1.EX.59.^^
			Repair, frontal sinus	1.EX.80.^^
			Excision partial, frontal sinus	1.EX.87.^^
			Therapeutic Interventions on the Paranasal Sinuses	1.EY.^^.^^
			Excision partial, paranasal sinuses	1.EY.87.^^
			Excision radical, paranasal sinuses	1.EY.91.^^

The codes listed in this table were used in a predictive algorithm to identify patients who had endoscopic sinus surgery for chronic rhinosinusitis, with a chart review as a reference standard.
The ICD-10, International Classification of Diseases, version 10, is the current version and international standard for classifying diseases.[57] *It replaced the 9th version (ICD-09) at the Ottawa Hospital in 2002. Although the ICD-09 codes were not used in the algorithm, they are listed to provide context to referenced studies within the manuscript that used these codes. The CCI, Canadian Classification of Health Interventions, 2012, Vol. III, is the current version for classifying health care procedures, and accompanies the International Classification of Diseases, version 10 (ICD-10).*
The CCI "^" designation refers to a subset of interventions within that category. For example, Therapeutic interventions of the frontal sinus, 1.EX.52.^^, includes two subset procedures, 1.EX.52.BA-TS (leaving drainage tube in situ, endoscopic per orifice approach), and 1.EX.52.BA (no drainage tube left in situ, endoscopic per orifice approach). The detailed subsets for all CCI codes are publicly accessible online at https://www.cihi.ca/en/cci_volume_three_2012_en.pdf.

Table 8: Comparison of validation statistics of three algorithms to predict CRS-ESS encounters

Algorithm version	Sensitivity % (95%CI)	Specificity % (95%CI)	PPV % (95%CI)
#1: Any CRS diagnostic ICD-10 code	96.5 (93.9-98.1)	100 (99.9-100)	93.3 (90.1-95.6)
#2: Any ESS procedural CCI code	96.8 (94.2-98.3)	100 (99.9-100)	93.3 (90.1-95.6)
#3: #1 AND #2	96.0 (93.2-97.7)	100 (99.9-100)	95.4 (92.5-97.2)

This table compares the accuracy of three different algorithm versions to predict CRS-ESS status, with the reference standard as the comparison. A case assignment for algorithm #3 required any CRS diagnostic code AND any ESS procedural code. See Table 7 for the full list of codes.
CI=confidence interval; CRS = Chronic rhinosinusitis; ESS = Endoscopic sinus surgery; PPV = positive predictive value.

Table 9: Predictive algorithm vs reference standard for ESS-CRS status

Algorithm output	Reference standard		Total
	Case	Control	
Case	333	16	349
Control	14	184,991	185,005
Total	347	185,007	185,354

A predictive algorithm (#3 from Table 8), based on administrative database codes, was used to determine case/control status. If a patient encounter had at least one of the ICD-10 CRS diagnostic codes, AND at least one of the CCI ESS surgical codes as in Table 7, the encounter was assigned a case; otherwise, a control. A chart review of the 411 ESS surgeries performed at TOH during the 2-year period was the basis of the reference standard. Summary statistics for algorithm accuracy: sensitivity 96.0% (95%CI 93.2-97.7), specificity 100% (95%CI 99.9-100) positive predictive value 95.4% (95%CI 92.5-97.3), positive likelihood ratio 11,096 (95%CI 6,794-18,120), and negative likelihood ratio of 0.04 (95%CI 0.02-0.07).
CCI = Canadian Classification of Health Interventions; CRS = Chronic rhinosinusitis; ESS = Endoscopic sinus surgery; ICD-10 = International Classification of Disease, version 10.

Table 10: Internal validation of predictive algorithm of ESS-CRS status

Algorithm output	Reference standard		Total
	Case	Control	
Case	186	6	192
Control	2	198	200
Total	188	204	392

The ESS-CRS predictive algorithm was applied to all TOH surgical patients in 2013. All cases and 200 randomly-selected controls were grouped together for a blinded chart review. Case control status was compared between the two methods to achieve internal validation of the algorithm. Summary statistics: sensitivity 98.9% (95%CI 95.8-99.8) specificity 97.1% (95%CI 93.4-98.8).
CRS = Chronic rhinosinusitis; ESS = Endoscopic sinus surgery; TOH = The Ottawa Hospital.

19.0 Figures

Figure 1: Summary of study identification

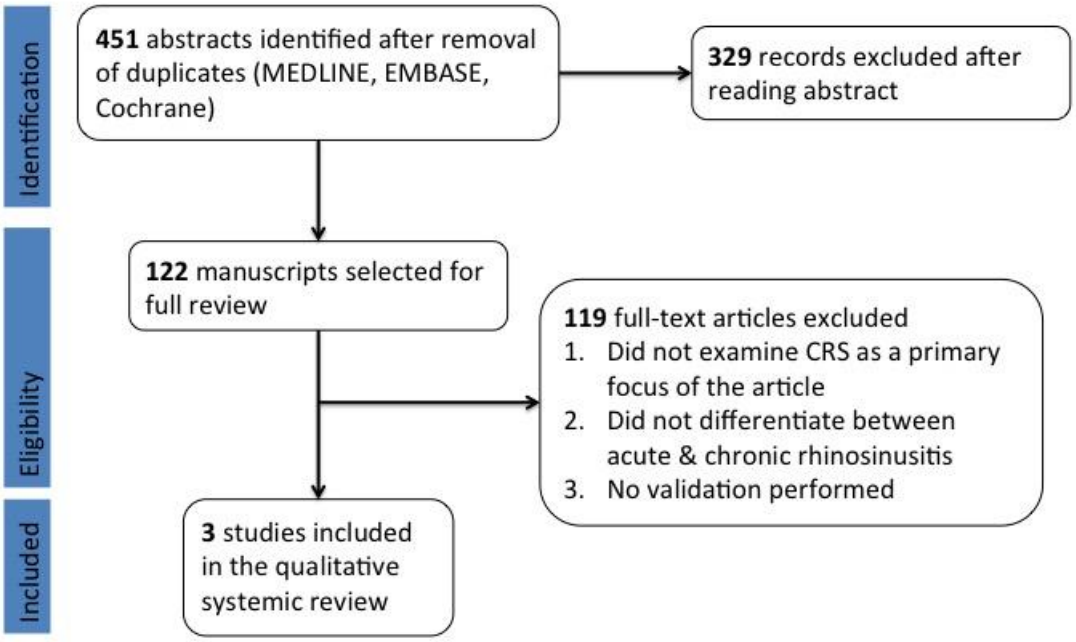
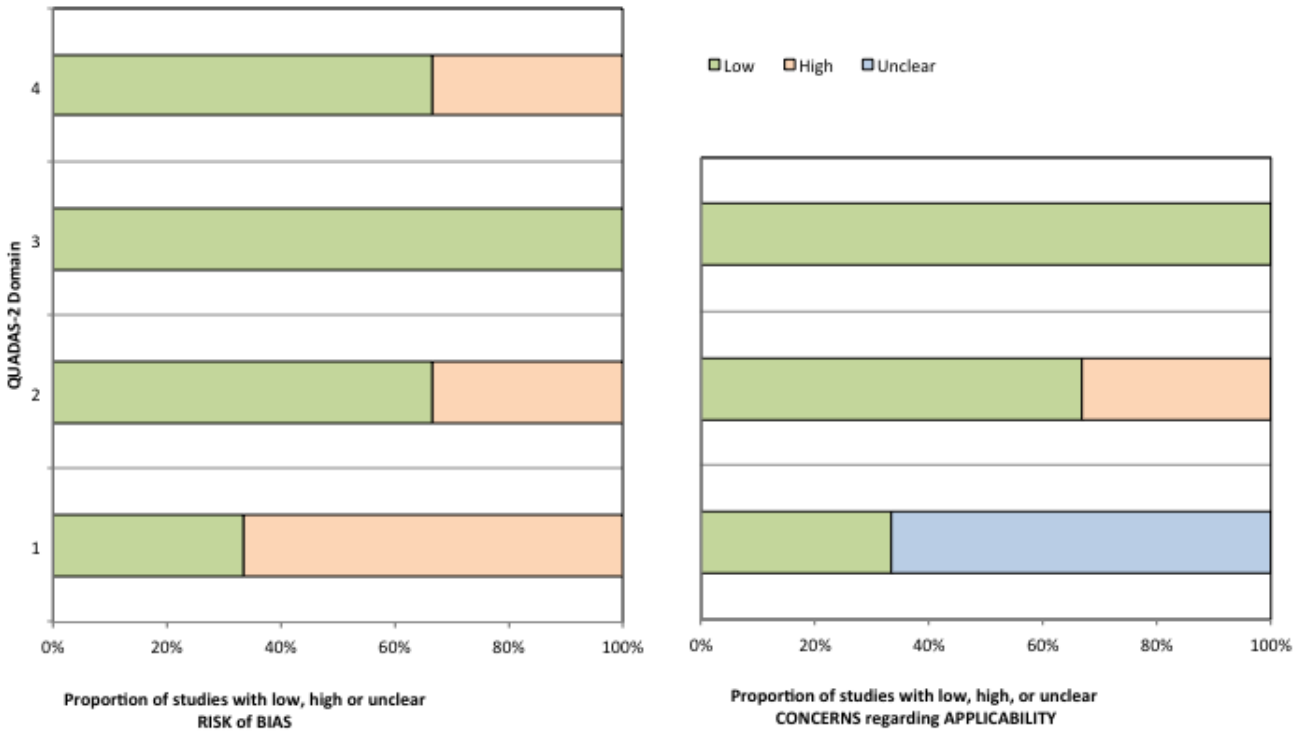
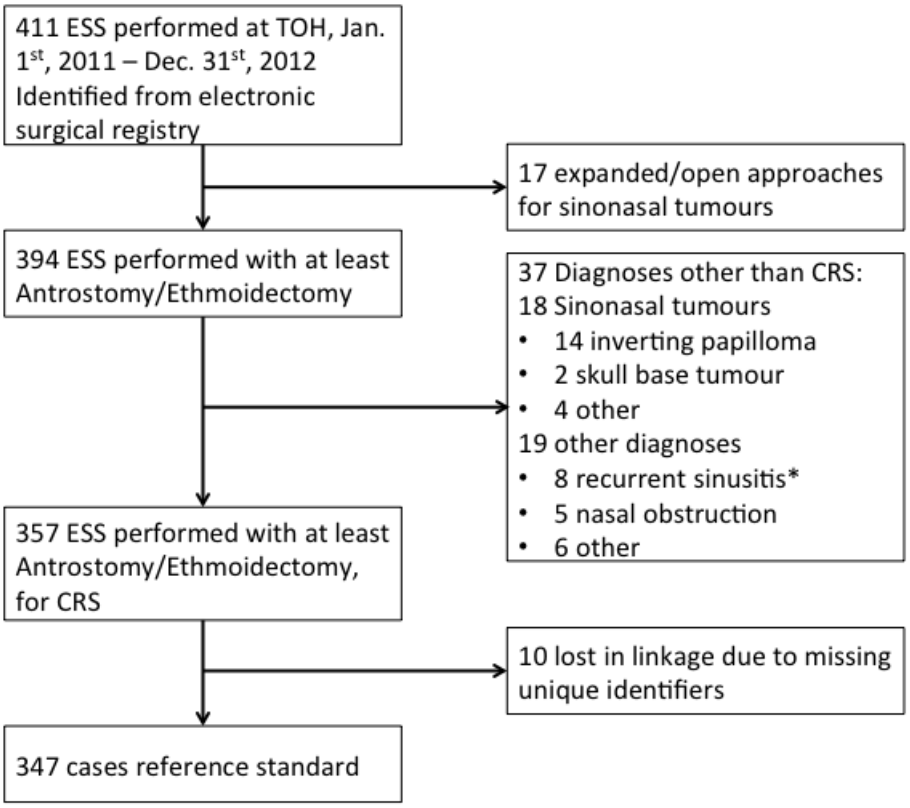


Figure 2: QUADAS-2 assessment overview for the included studies



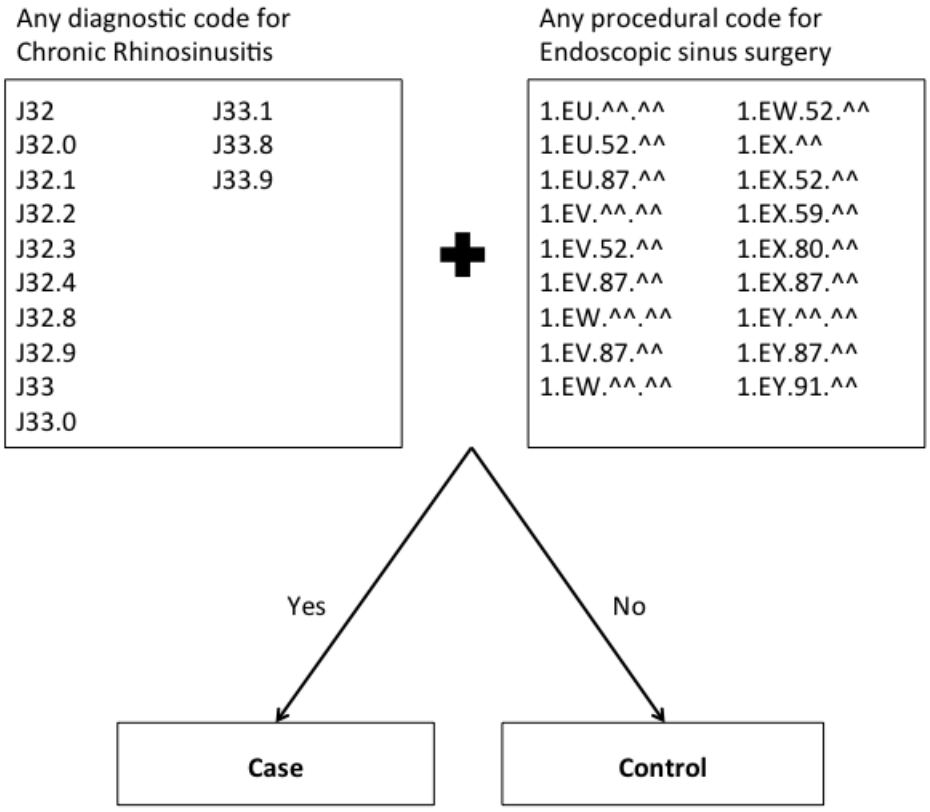
Each horizontal bar is a summary of the three included studies. Eg. Two of the studies ranked low risk of bias for the "flow and timing" domain, and one ranked high. Only the "reference standard" domain ranked consistently low in risk of bias and concern regarding applicability. See manuscript for individual study assessment. QUADAS-2 = Quality Assessment Tool for Diagnostic Accuracy Studies, version 2.

Figure 3: Flow chart of chronic rhinosinusitis - endoscopic sinus surgery chart review



The chart review was performed for TOH surgical encounters in which ESS was performed during the defined time period, identified by the Surgical Information Management System (SIMS). SIMS identified these 411 encounters by first selecting Otolaryngologist-performed surgeries, then those in which ESS was listed as at least some portion of the surgery performed during that encounter. Encounters were assigned as controls if they had a major surgery other than ESS, did not have ESS, or had a diagnosis other than CRS. CRS was determined to be the major indication for surgery if the chart listed that ESS was for Otolaryngologist-diagnosed CRS (obtained from the OR report in essentially all cases). The eight encounters with recurrent sinusitis did not have evidence of associated CRS, and so were assigned as controls. ESS = endoscopic sinus surgery; CRS = chronic rhinosinusitis; TOH = The Ottawa Hospital.

Figure 4: Overview of final algorithm to identify CRS-ESS case encounters within a surgical cohort



This algorithm was developed from an administrative database cohort of all surgical patient encounters at the Ottawa Hospital from Jan. 1st, 2011 to Dec. 31st, 2012. A case was assigned if an encounter contained any one of the ICD-10 diagnostic CRS codes, AND any one of the CCI procedural ESS codes. Otherwise, the encounter was assigned as a control.
Compared to the reference standard that included a chart review, this algorithm accurately identified encounters in which endoscopic sinus surgery was performed for chronic rhinosinusitis, with a 95.4% positive predictive value. CRS = Chronic Rhinosinusitis; ESS = Endoscopic sinus surgery; ICD-10 = International Classification of Diseases, version 10; CCI = Canadian Classification of Health Interventions.

20.0 Appendices

Appendix A – MEDLINE Search Strategy

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present> Search Strategy:

---

1 Sinusitis/ (13754)
2 (sinusitis or rhinosinusitis).tw. (16375)
3 Paranasal Sinuses/su or Rhinitis/su (2373)'
4 sinus surgery.tw. (4631)
5 or/1-4 (24123)
6 Chronic Disease/ (220619)
7 chronic.tw. (825212)
8 6 or 7 (887497)
9 5 and 8 (9250)
10 health surveys/ or health care surveys/ or registries/ or vital statistics/ (130728)
11 Population Surveillance/ (46130)
12 Databases, Factual/ (45082)
13 database$.tw. (207469)
14 (claims data or demographic data or administrative data).tw. (24188)
15 (survey adj5 data).tw. (24744)
16 national health interview survey.tw. (2528)
17 (health adj4 survey$).tw. (42972)
18 ((panel or care) adj survey$).tw. (3678)
19 "International Classification of Diseases"/ or International Classification of Diseases.tw. (10646)
20 icd.tw. (20780)
21 or/10-20 (480310)
22 9 and 21 (313)

EMBASE Search Strategy

Database: Embase Classic+Embase <1947 to 2015 January 21> Search Strategy:

---

1 chronic sinusitis/ (3618)
2 *sinusitis/ (9142)
3 (sinusitis or rhinosinusitis).tw. (22863)
4 2 or 3 (26057)
5 endoscopic sinus surgery/ (1795)
6 paranasal sinusitis/su [Surgery] (355)
7 rhinosinusitis/su [Surgery] (791)
8 sinus surgery.mp. (6591)
9 4 or 5 or 6 or 7 or 8 (29898)
10 chronic disease/ or chronic.tw. (1211060)
11 9 and 10 (11648)
12 1 or 11 (12662)
13 health survey/ (155642)
14 (claims data or demographic data or administrative data).tw. (38390)
15 (survey adj5 data).tw. (30169)
16 national health interview survey.tw. (2793)
17 (health adj4 survey$).tw. (50882)
18 ((panel or care) adj survey$).tw. (4672)
19 data base/ or database$.tw. (324111)
20 "International Classification of Diseases"/ (8400)
21 international classification of diseases.tw. (7208)
22 icd.tw. (39261)
23 or/13-22 (593090)
24 12 and 23 (449)

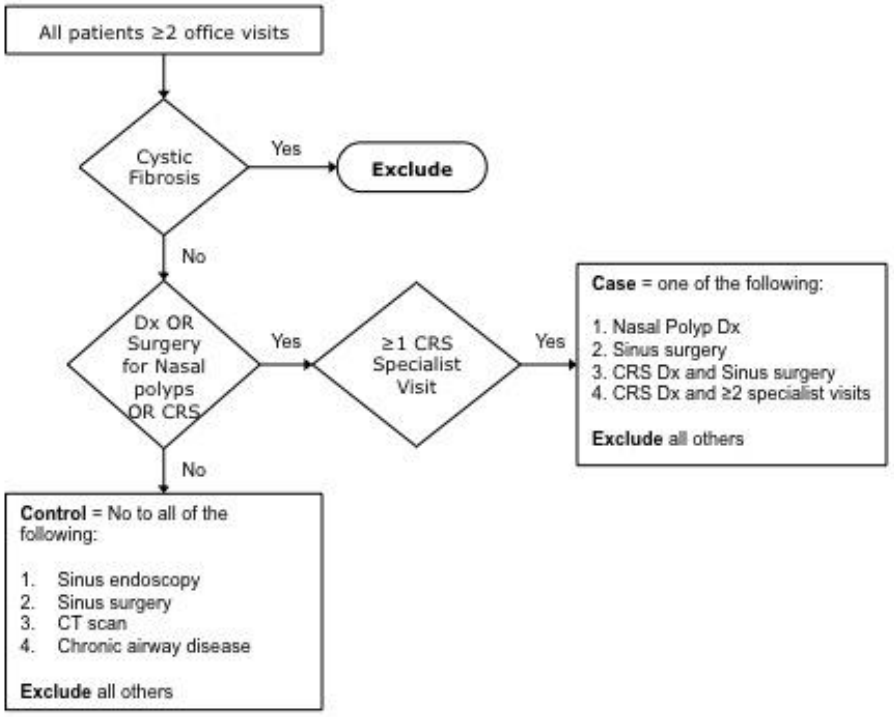
Cochrane Library Search Strategy

Cochrane

ID Search Hits
#1 MeSH descriptor: [Sinusitis] explode all trees 727
#2 (sinusitis or rhinosinusitis):ti,ab,kw (Word variations have been searched) 1812
#3 MeSH descriptor: [Paranasal Sinuses] explode all trees and with qualifier(s): [Surgery - SU] 264
#4 MeSH descriptor: [Rhinitis] explode all trees and with qualifier(s): [Surgery - SU] 100
#5 sinus surgery:ti,ab,kw (Word variations have been searched) 1286
#6 #1 or #2 or #3 or #4 or #5 2871
#7 MeSH descriptor: [Chronic Disease] explode all trees 11125
#8 chronic:ti,ab,kw (Word variations have been searched) 65431
#9 #7 or #8 65431
#10 #6 and #9 856
#11 MeSH descriptor: [Health Surveys] this term only 746
#12 MeSH descriptor: [Health Care Surveys] this term only 320
#13 MeSH descriptor: [Registries] this term only 701
#14 MeSH descriptor: [Vital Statistics] this term only 3
#15 MeSH descriptor: [Population Surveillance] explode all trees 579
#16 MeSH descriptor: [Databases, Factual] explode all trees 634
#17 (claims data or demographic data or administrative data):ti,ab,kw (Word variations have been searched) 5185
#18 survey near/5 data:ti,ab,kw (Word variations have been searched) 632
#19 national health interview survey:ti,ab,kw (Word variations have been searched) 140
#20 (health near/4 survey*):ti,ab,kw (Word variations have been searched) 3449
#21 panel survey*:ti,ab,kw (Word variations have been searched) 124
#22 database*:ti,ab,kw 8440
#23 care survey*:ti,ab,kw (Word variations have been searched) 3946
#24 MeSH descriptor: [International Classification of Diseases] explode all trees 61
#25 international classification of diseases:ti,ab,kw 572
#26 icd:ti,ab,kw 1227
#27 #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 21938
#28 #27 and #10 25

Database of Abstracts of Reviews of Effect : Issue 4 of 4, October 2014 – 1 result
Cochrane Central Register of Controlled Trials : Issue 12 of 12, December 2014 - 22 results
Cochrane Methodology Register : Issue 3 of 4, July 2012 – 2 results

Appendix B: Final algorithm modified from Hsu et al.[36] using administrative data to identify patients with chronic rhinosinuitis (CRS)



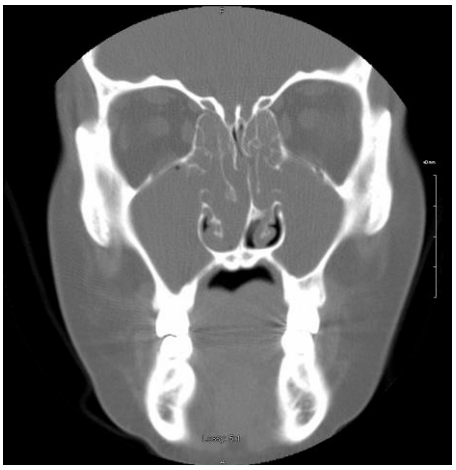
ICD-9 and CPT codes were used to diagnose patients with CRS, Nasal polyps, and to establish if patients had sinus surgery, sinus endoscopy or CT scan. Dx = diagnosis; CRS = chronic rhinosinusitis; CT = computed tomography; ICD-9 = International Classification of Diseases, version 9; CPT = Current Procedural Terminology.

Appendix C – Diagnostic criteria of Chronic Rhinosinusitis

Table 7. CRS Diagnosis Requires the Presence of at Least 2 Major Symptoms*

	Major Symptom
C	Facial **C**ongestion/fullness
P	Facial **P**ain/pressure/fullness
O	Nasal **O**bstruction/blockage
D	Purulent anterior/posterior nasal **D**rainage (discharge may be nonpurulent, nondiscolored)
S	Hyposmia/anosmia (**S**mell) [9, 21, 136].
*A diagnosis requires at least 2 CPODS, present for 8 to 12 weeks, plus evidence of inflammation of the paranasal sinusus or nasal mucosa.	
CRS is diagnosed on clinical grounds but must be confirmed with at least 1 objective finding on endoscopy or CT scan.	

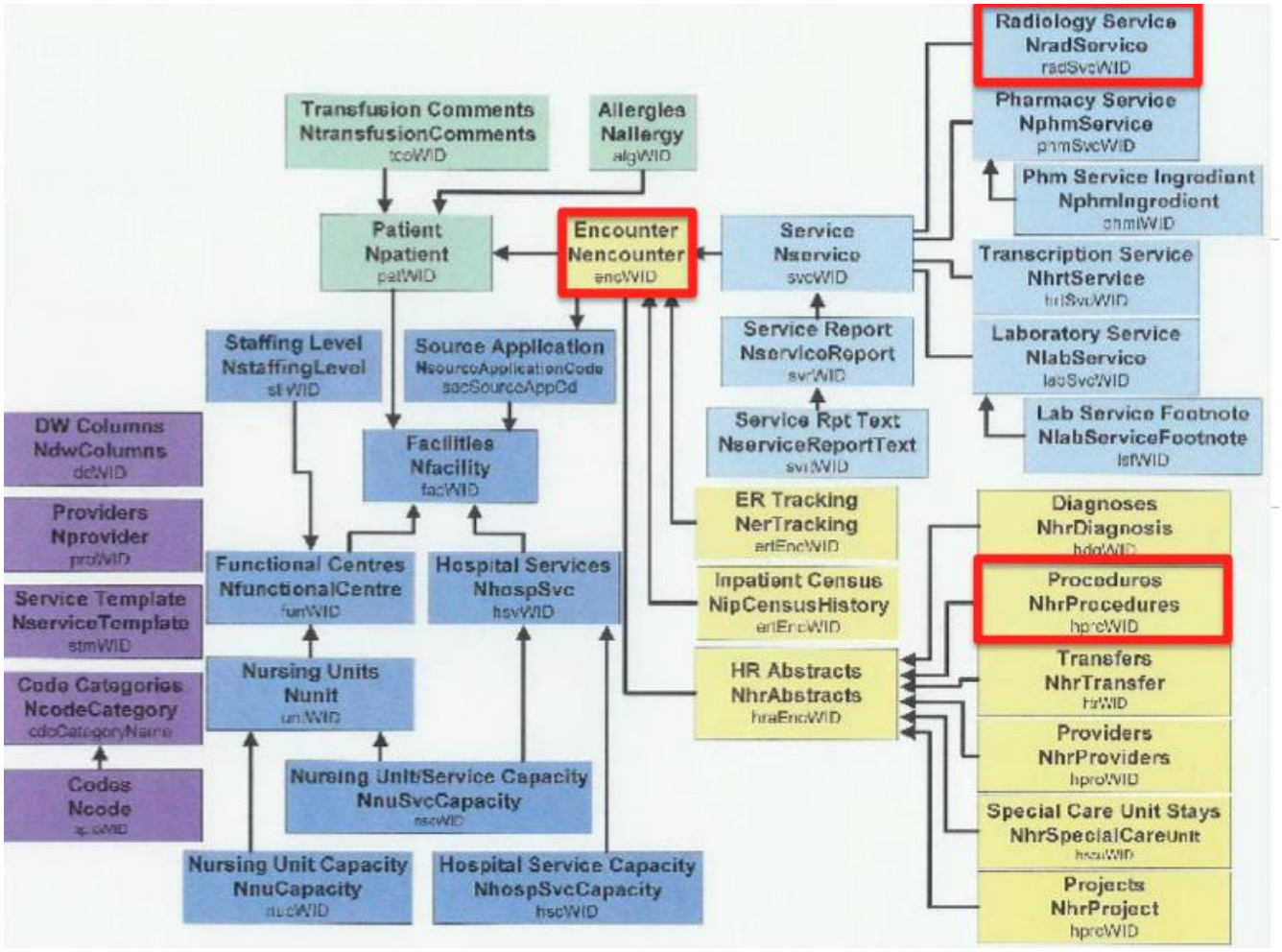
Diagnostic criteria for chronic rhinosinusitis. Adapted from the 2011 Canadian Guidelines for Acute and Chronic Rhinosinusitis.[6]



Coronal CT scan of a patient with pansinusitis, showing complete opacification of the ethmoid and maxillary sinuses. The Lund-McKay score here would be 24/24.

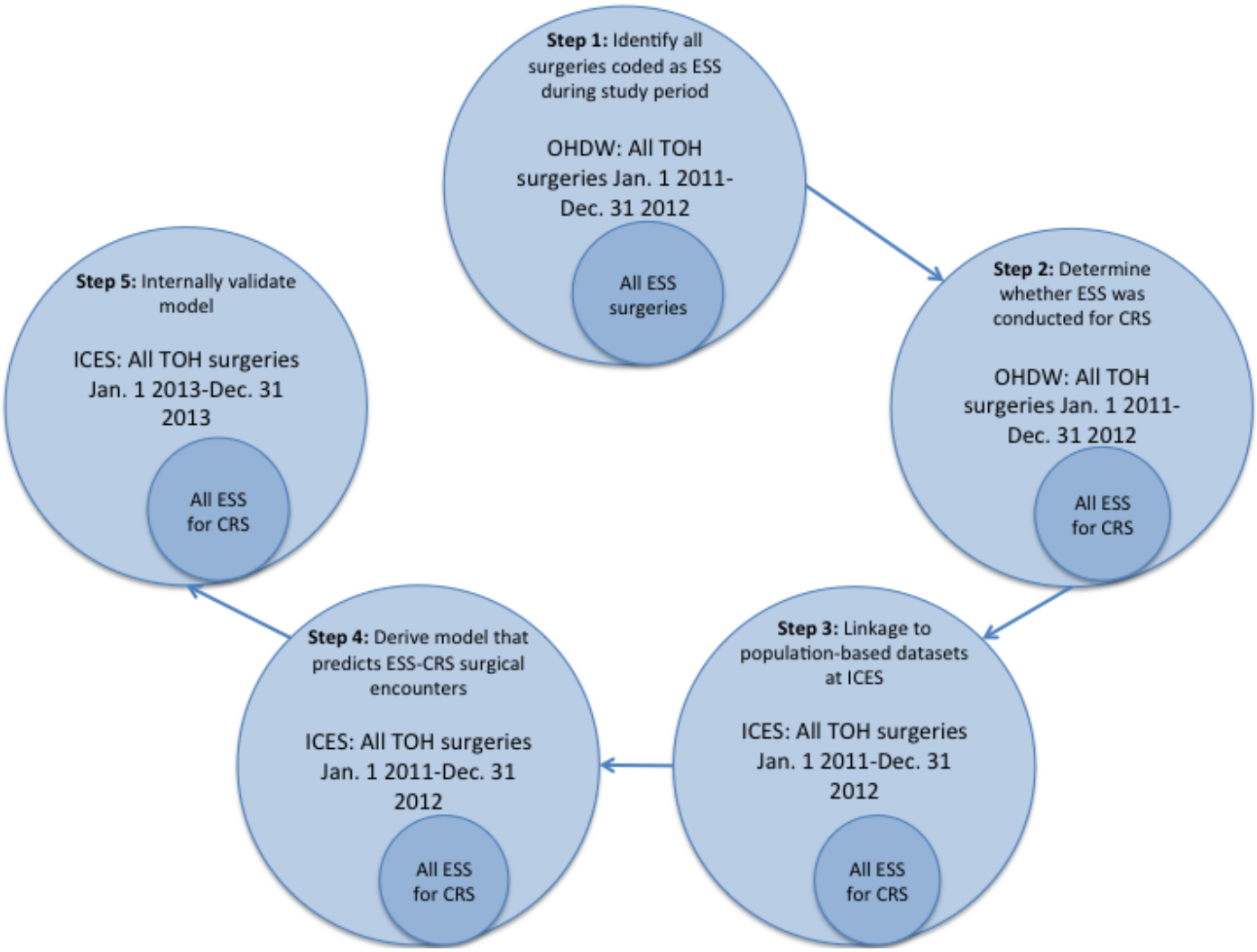
Lund-McKay Scale for evaluating objective CRS disease on CT scan[5]
The Lund-Mackay system scores each sinus (anterior ethmoid, posterior ethmoid, maxillary, frontal and sphenoid sinuses) according to the following scale: 0 (no opacification), 1 (partial opacification), or 2 (complete opacification). The osteomeatal complex is scored as 0 (not occluded) or 2 (occluded). Left and right sides are staged separately and the scores are summed so that the total Lund score may range from 0 to 24 for each patient.

Appendix D – The Ottawa Hospital Data Warehouse Map



This map displays an overview of the tables within the Ottawa Hospital Data Warehouse (OHDW). The OHDW contains data from several source systems containing patient data for those treated at the TOH since 1996. Several variables types are recorded for each patient encounter including demographics, type of encounter, diagnoses, and services (such as surgeries). The tables to be used in my thesis project are highlighted with a thick border, and described in **Section 7.0**.

Appendix E: Overview of the major steps for this thesis project



This graphical overview of the 4 major steps is described in further detail in section 8.0. Briefly, from step 1 to step 2, the TOH study cohort is identified and refined, as described by the text within the circles, for the two-year time period. In step 3, the TOH cohort is linked to ICES. In step 4, a logistic regression algorithm will be derived to measure the probability a person had ESS for CRS, using the TOH cohort as the gold standard. The derived algorithm can then be used to study all Ontario patients who had ESS for CRS, for a given time period.
OHDW = Ottawa Hospital Data Warehouse; TOH = The Ottawa Hospital; ICES = Institute for Clinical Evaluative Sciences; ESS-CRS = Endoscopic sinus surgery for chronic rhinosinusitis; CRS = Chronic rhinosinusitis; ESS = Endoscopic sinus surgery.

Appendix F: Standards for Reporting Diagnostic Accuracy Studies Checklist[56] (2015 version)

Section & Topic	No	Item	On page & line
Title or Abstract	1	Identification as a study of diagnostic accuracy using at least one measure of accuracy (such as sensitivity, specificity, predictive values, or AUC)	P27 L13
Abstract	2	Structured summary of study design, methods, results, and conclusions	P27
Introduction	3	Scientific and clinical background, including the intended use and clinical role of the index test	P39
	4	Study objectives and hypotheses	P30 L15
Methods			
Study design	5	Whether data collection was planned before the index test and reference standard were performed (prospective study) or after (retrospective study)	P35 L1
Participants	6	Eligibility criteria	P35 L1
	7	On what basis potentially eligible participants were identified (such as symptoms, results from previous tests, inclusion in registry)	P35 L1
	8	Where and when potentially eligible participants were identified (setting, location and dates)	P35 L1
	9	Whether participants formed a consecutive, random or convenience series	P35 L1
Test methods	10a	Index test, in sufficient detail to allow replication	P35 L7
	10b	Reference standard, in sufficient detail to allow replication	P35 L1
	11	Rationale for choosing the reference standard (if alternatives exist)	P35 L8
	12a	Definition of and rationale for test positivity cut-offs or result categories of the index test, distinguishing pre-specified from exploratory	P36 L22
	12b	Definition of and rationale for test positivity cut-offs or result categories of the reference standard, distinguishing pre-specified from exploratory	P35 L1
	13a	Whether clinical information and reference standard results were available to the performers/readers of the index test	P35 L1
	13b	Whether clinical information and index test results were available to the assessors of the reference standard	P35 L1
Analysis	14	Methods for estimating or comparing measures of diagnostic accuracy	P37 L10
	15	How indeterminate index test or reference standard results were handled	N/A
	16	How missing data on the index test and reference standard were handled	N/A
	17	Any analyses of variability in diagnostic accuracy, distinguishing pre-specified from exploratory	N/A
	18	Intended sample size and how it was determined	P34 L5
Results			
Participants	19	Flow of participants, using a diagram	Figure 3
	20	Baseline demographic and clinical characteristics of participants	N/A
	21a	Distribution of severity of disease in those with the target condition	N/A
	21b	Distribution of alternative diagnoses in those without the target condition	P40 L5
	22	Time interval and any clinical interventions between index test and reference standard	N/A
Test results	23	Cross tabulation of the index test results (or their distribution) by the results of the reference standard	Tables 9 & 10
	24	Estimates of diagnostic accuracy and their precision (such as 95% confidence intervals)	Tables 9 & 10
	25	Any adverse events from performing the index test or the reference standard	
Discussion			
	26	Study limitations, including sources of potential bias, statistical uncertainty, and generalisability	P45-47
	27	Implications for practice, including the intended use and clinical role of the index test	P47 L14
Other Information	28	Registration number and name of registry	N/A
	29	Where the full study protocol can be accessed	P48 L15
	30	Sources of funding and other support; role of funders	P48 L13

Appendix G: Variables assigned to the initial hospital cohort for use within the larger population administrative database (ICES)

Variable	0	1	2
CRS_ICES	No CRS or ESS	CRSsP	CRSwP
LM_CODE	No CT available	LM <= 14	LM >14
FR_CODE	No frontal sinusotomy	Unilateral frontal sinusotomy	Bilateral frontal sinusotomy
SPHENOIDOTOMY	No sphenoidotomy	Unilateral sphenoidotomy	Bilateral sphenoidotomy
SEPTOPLASTY	No septoplasty	Standard septoplasty	Endoscopic septoplasty
CONCHABULL	No excision of concha bullosa	Unilateral excision of concha bullosa	Bilateral excision of concha bullosa
IMAGE_GUIDANCE	No use of IGS	IGS used	N/A

ICES = institute for clinical evaluative sciences; ESS = endoscopic sinus surgery; CRS = chronic rhinosinusitis; CRSwP = chronic rhinosinusitis with polyps; CRSsP = chronic rhinosinusitis without polyps. IGS = image-guidance.

Appendix H: Permission to use article from publisher

JOHN WILEY AND SONS LICENSE TERMS AND CONDITIONS

Mar 03, 2016

This Agreement between Kristian I Macdonald ("You") and John Wiley and Sons ("John Wiley and Sons") consists of your license details and the terms and conditions provided by John Wiley and Sons and Copyright Clearance Center.

License Number	3821380900357
License date	Mar 03, 2016
Licensed Content Publisher	John Wiley and Sons
Licensed Content Publication	The Laryngoscope
Licensed Content Title	Chronic rhinosinusitis identification in administrative databases and health surveys: A systematic review
Licensed Content Author	Kristian I. Macdonald,Shaun J. Kilty,Carl van Walraven
Licensed Content Date	Dec 9, 2015
Pages	1
Type of use	Dissertation/Thesis
Requestor type	Author of this Wiley article
Format	Print
Portion	Full article
Will you be translating?	No
Title of your thesis / dissertation	Development and validation of an algorithm to identify adults who have endoscopic sinus surgery for chronic rhinosinusitis
Expected completion date	Jul 2016