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Use of an Electronic Date Warehouse to Enhance Cardiac Surgical Site Infection Surveillance at a Large Canadian Center

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USE OF AN ELECTRONIC DATA WAREHOUSE TO ENHANCE CARDIAC SURGICAL SITE INFECTION SURVEILLANCE AT A LARGE CANADIAN CENTRE

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Abstract

Surgical site infection surveillance (enumeration, and reporting of cases) reduces infection incidence. Data-driven "trigger" mechanisms focus surveillance on high-probability cases, yet often lack specificity. We aimed to develop trigger mechanisms with greater specificity for surveillance of cardiac surgical site infection.

We developed these mechanisms in a two part study: systematic review to identify potential trigger factors; and nested case-control study to derive trigger mechanisms from a novel information structure called a data warehouse.

Among 158 studies, we identified 570 trigger factors, which we grouped into themes, using the top 33 in the case-control study Using 203 cases and 516 controls, we derived two models for surveillance trigger mechanisms. These models provided true positive rates of 0.941 and 0.931 respectively (non-inferior to the current trigger mechanism), with false positive rates of 0.1085 each (superior to the current trigger mechanism.)

These trigger mechanisms may standardize and automate surgical site infection surveillance triggering.

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1 Introduction

1.1 Aim

The aim of this study is to evaluate whether the use of a complex electronic trigger mechanism can improve the accuracy and efficiency of surveillance for surgical site infection, compared to manual or simple electronic mechanisms.

1.2 Background

1.2.1 Clinical features and epidemiology of SSI

Adverse events may attend upon any surgical procedure. The various surgical specialties are attuned to the varied, and often unique, complications that may result from operative intervention – bleeding, anaesthetic reactions, loss of function to name but a few. Among these complications, the possibility of developing a surgical site infection (SSI) is common to all procedures, in all specialties. An SSI is a postoperative infection occurring anywhere along the excised tissues of the body wall, or at the site (e.g. organ or body space) of surgical manipulation.[1]

Surgical site infections occur when the incision, or organ/space, is contaminated by pathogenic microbes. This may occur intraoperatively (for example, by break in sterile technique,) or post-operatively by contamination of the incision.[2] Rarely, SSI may result from blood-borne dissemination of an infection distant from the actual surgical site. This is a particular concern when non-human derived material is implanted intraoperatively (e.g. prostheses or xenografts.)

The most common etiologic pathogens for SSI are the normal flora of the incised tissues, and thus are often procedure-specific. Bacterial normal flora cause the bulk of SSI, with gram positive skin flora (e.g. *Staphylococcus* species,) being the most common, and gram negative enteric flora (e.g. *Escherichia coli*) playing a large role in intraabdominal and genitourinary procedures.[3]

Similarly, risk factors for SSI acquisition include those common to all specialties, and those that are specialty-specific. Common risk factors include the patient's age and state of health, the attention paid to peri-operative sterile technique or adequate hemostasis, and the application of appropriate preoperative antimicrobial prophylaxis.[2] Procedure-specific risk factors include the use

of a posterior approach in spinal surgery,[4, 5] or the interaction of obesity with female gender in cardiac surgery.[6, 7]

Surgical site infection incidence varies with the operative procedure performed. It was once common to report an overall hospital-wide SSI incidence,[8] however the differing risk between surgical specialties renders this statistic meaningless. In patients considered "low risk" for infection, SSI incidence may range from 0.00% for coronary artery bypass graft to 4.97% for operative manipulation of the small bowel.[9] Amongst high-risk patients undergoing solid organ transplantation, the SSI incidence exceeds 25%.

At the population level, SSI's are common adverse events and incur excess mortality and cost. There were over 240,000 SSI's in United States' hospitals in 2002, complicating 2% of all surgical procedures, and associated with over 8,000 deaths.[10] Surgical site infections are the second most common healthcare-associated infection, and the most common among surgical inpatients.[2, 10] Furthermore, SSI's prolong inpatient admission 6.5 to 10 days, increase frequency of admission to intensive care units, and increase costs more than US$3,000 per infected patient.[8, 11]

We lack Canadian data on SSI incidence, mortality and cost. In the United States, the Centers for Disease Control and Prevention (CDC) have collected and reported standardized "benchmark" incidence of SSI for a voluntary network of healthcare facilities for nearly 40 years via the National Health Safety Network (NHSN) and its predecessor, the National Nosocomial Infection Surveillance system (NNIS).[12] Ironically, some Canadian SSI surveillance programs predate this monumental push by the CDC,[8] yet nonetheless there is no national Canadian surveillance network reporting on SSI. A commonly-used assumption estimates the number of healthcare-associated infections in Canada to be 10% that in the U.S.[13] By this rule, in Canada we likely have 24,000 SSI's annually with 800 associated deaths, incurring annual excess costs of US$72,000,000.

1.2.2 Surveillance as a tool to decrease SSI incidence

A significant portion of SSI is preventable, and may be countered by the introduction of effective infection prevention and control programs (IPCP's).[14, 15] The most effective SSI prevention program is surveillance of SSI incidence, with feedback reporting to surgeons and surgical

departments.[2, 8, 14] The theorized mechanism for incidence reduction is a negative feedback loop of information. An elevated or rising SSI incidence stimulates surgeons to enact a host of measures to reduce SSI, such as increased attention to sterile technique, intraoperative hemostasis, hand hygiene, and other basics.

An effective surveillance and feedback program may reduce SSI incidence substantially. This was first demonstrated in a 10-year cohort study performed at two hospitals in Calgary.[8] The investigators prospectively reviewed all surgical wounds at least once during the postoperative admission, with telephone followup 28 days postoperatively. They calculated SSI incidence, generating monthly and annual reports for program-wide and surgeon-specific incidence. Within six months of initiating this program, the investigators noted clean-procedure SSI incidence reduced from 3.6-5.8 cases per 100 operations to 1.8-2.5. This reduced incidence remained stable over 10 years of ongoing surveillance.

These findings were confirmed in the landmark SENIC study undertaken by the CDC.[14] This was a controlled before-and-after study performed retrospectively on 339,044 patients admitted to 338 US hospitals in 1970 (before the common implementation of surveillance programs) and 1975-1976 (after surveillance implemented.) After controlling for secular trends, the SENIC study demonstrated that an SSI surveillance program, in the setting of an effective IPCP, reduced incidence of SSI 23.6 to 48.0%.

In addition to helping prevent SSI, SSI surveillance programs are increasingly becoming mandatory. The last decade has seen the proliferation of jurisdictions mandating that hospitals report incidence of healthcare-associated infections, including SSI.[16-20] There are several proposed rationales: to provide inter-institutional comparisons for quality assurance; to provide performance measures to governments and health management organizations, and thus to improve performance; and to inform individual choices in healthcare providers. In this environment, it is vital to ensure accurate, consistent enumeration of SSI, without overtaxing under-resourced IPCP's. Unfortunately, most SSI surveillance programs remain labour-intensive, and there is no consensus on their ideal methods and structure.[2]

1.2.3 Structure of SSI surveillance programs

There are common features to successful SSI surveillance programs. Such programs require trained infection control professionals (ICP's) performing surveillance under the oversight of a physician trained in healthcare epidemiology.[14] They share two common goals: to accurately calculate SSI incidence for feedback reporting; and to identify individual cases of SSI patients for analysis of risk factors.[2] This second goal is separate from the clinician's goal of identifying patients to initiate therapy.

Additionally, most programs use the SSI definition criteria of the United States' CDC (Table 1.1).[1, 2, 21, 22] These criteria specify three classes of SSI: superficial incisional (infection of the skin or subcutaneous tissue), deep incisional (infection of deeper soft tissue or fascia), and organ/space (infection of any deeper structure). Organ or deep space infections draining through the incision (e.g. sternal osteomyelitis) are considered deep incisional SSI. The surveillance time frame depends on the depth of infection, and the nature of the procedure: 30 days for all superficial incisional SSI, and for most deep incisional or organ/space infections as well. However, for procedures involving implantation of non-human-derived prosthetic material (e.g. mechanical or porcine cardiac valves), the surveillance period is 365 days for deep incisional or organ/space SSI. [1, 2] The CDC SSI case definition criteria have been extensively validated. [1, 22-25]

1.3 Selective SSI surveillance

Even using common definition criteria for SSI, there are many ways in which surveillance may be applied. Surveillance may be done prospectively (where ICP's directly observe the patient) versus retrospectively (where ICP's review the patient records); universally (where ICP's review all post-operative patients or records) versus selectively (where only high-probability patients or records are reviewed).[2] Even in the CDC's NHSN, which mandates the use of prospective surveillance using CDC definition criteria, reporting centres may individualize what surgical specialties they will survey, how intensively/frequently they engage in surveillance, how they identify high-probability patients and whether they follow patients post-discharge.[26] Prospective and universal surveillance strategies are more cost-, and labour-intensive than retrospective and selective strategies, therefore financial and human resources dictate the structure of surveillance activities.[2]

Table 1.1: United States' Centers for Disease Control surgical site infection definition criteria[2, 10]

SUPERFICIAL INCISIONAL SSI*	
Infection occurs within 30 days after the operative episode *and*	
Infection involves only skin or subcutaneous tissue of the incision *and*	
At least one of the following:	
	Purulent drainage, with or without laboratory confirmation, from the superficial incision
	Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision
	At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat and superficial incision is deliberately opened by surgeon, *unless* incision is culture-negative
	Diagnosis of superficial incisional SSI* by the surgeon or attending physician
Definition specifically excludes the following:	
	Stitch abscess (minimal inflammation and discharge confined to the points of suture penetration)
	Infection of an episiotomy or newborn circumcision site
	Infected burn wound
	Incisional SSI* that extends into the fascial and muscle layers
DEEP INCISIONAL SSI*	
Infection occurs within 30 days after the operative episode if no non-human-derived implant is in place, or 1 year if non-human-derived implant is in place and the infection appears related to the operation *and*	
Infection involves deep soft tissues (e.g. fascial and muscle layers) of the incision *and*	
At least one of the following:	
	Purulent drainage from the deep incision but not from the organ/space component of the surgical site
	Deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever >38°C, localized pain, or tenderness, unless site is culture-negative
	Abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination
	Diagnosis of deep incisional SSI* by a surgeon or attending physician
Notes	
	Infection that involves both deep and superficial incision is classed as deep incisional SSI*
	Organ/space infection that drains through the incision is classed as deep incisional SSI*
ORGAN/SPACE SSI*	
Infection occurs within 30 days after the operative episode if no non-human-derived implant is in place, or 1 year if non-human-derived implant is in place and the infection appears related to the operation *and*	
Infection involves any part of the anatomy (e.g. organs or body spaces), other than the incision, which was opened or manipulated during an operation *and*	
At least one of the following:	
	Purulent drainage from a drain that is placed through a stab wound into the organ/space
	Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space
	Abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination
	Diagnosis of an organ/space SSI* by a surgeon or attending physician

Many infection control programs perform retrospective and selective surveillance of SSI, in order to minimize costs, and maximize efficiency. This is particularly true in Canada, where only a minority of hospitals are able to perform any effective SSI surveillance.[13] Most infection control programs focus activities on high-yield surgical specialties.[9] In this context, the highest-yield specialties are those with a high incidence of SSI despite a preponderance of "clean" procedures (i.e. surgical sites are unlikely to be contaminated peri-operatively, see Table 1.2), or those with particularly high morbidity and mortality due to SSI.[1, 2, 27] Cardiac surgery is one of the most commonly surveyed specialties [9], as virtually all cardiac procedures are defined as clean, yet there is nevertheless a persistently high SSI incidence (up to 10 per 100 operations in high-risk patients), with a particularly high SSI case-fatality ratio (7.2%)[9, 28-30]

Table 1.2: Wound classification scheme, based on degree of contamination of surgical site during index operative episode.[2, 10, 14]

Class	Description
I (Clean)	Uninfected operative wound with no inflammation. Not respiratory, alimentary, genital, or urinary tract
II (Clean-Contaminated)	Wound entering respiratory, alimentary, genital, or urinary tract, without unusual contamination
III (Contaminated)	Acute traumatic wound; operative wound with major break in sterile technique; gross spillage from alimentary tract; incision through inflamed, non-purulent tissue
IV (Dirty-Infected)	Old traumatic wound with devitalized tissue, clinical infection or perforated viscera

1.4 Trigger factors in SSI surveillance

After selecting a surgical specialty of interest, the next step in selection of surveillance activities is to concentrate labour-intensive case review among patients with high probability of SSI.[2, 26] High-probability SSI patients are identified by the presence of risk factors for the development of SSI (e.g. older age, or prolonged operative time)[31] or identification factors noted after the development of SSI (e.g. a positive microbiologic culture, or readmission to hospital for therapy of SSI). [26, 32, 33] When infection control programs use risk factors, or identification factors, to trigger surveillance activities, they are referred to as **'trigger factors'**.[34, 35] Similarly, we define a **'trigger mechanism'** as an algorithm using one or more trigger factor.

Although many SSI surveillance programs use trigger mechanisms, there is no consensus as to what form such mechanisms should take.[2, 26] Data sources for trigger mechanisms may include clinical, laboratory, administrative, or pharmacy records, or direct reporting from clinical staff.[2, 26, 34] Furthermore, information for trigger mechanisms may be harvested by manual review of records (e.g. ICP's review line listings for all hospital admissions, looking for an admitting diagnosis of SSI) or they may be automatically generated from electronic data (e.g. a computerized alert notifies the surveillance ICP when a microbiologic culture is obtained).[31, 33, 34, 36-38]

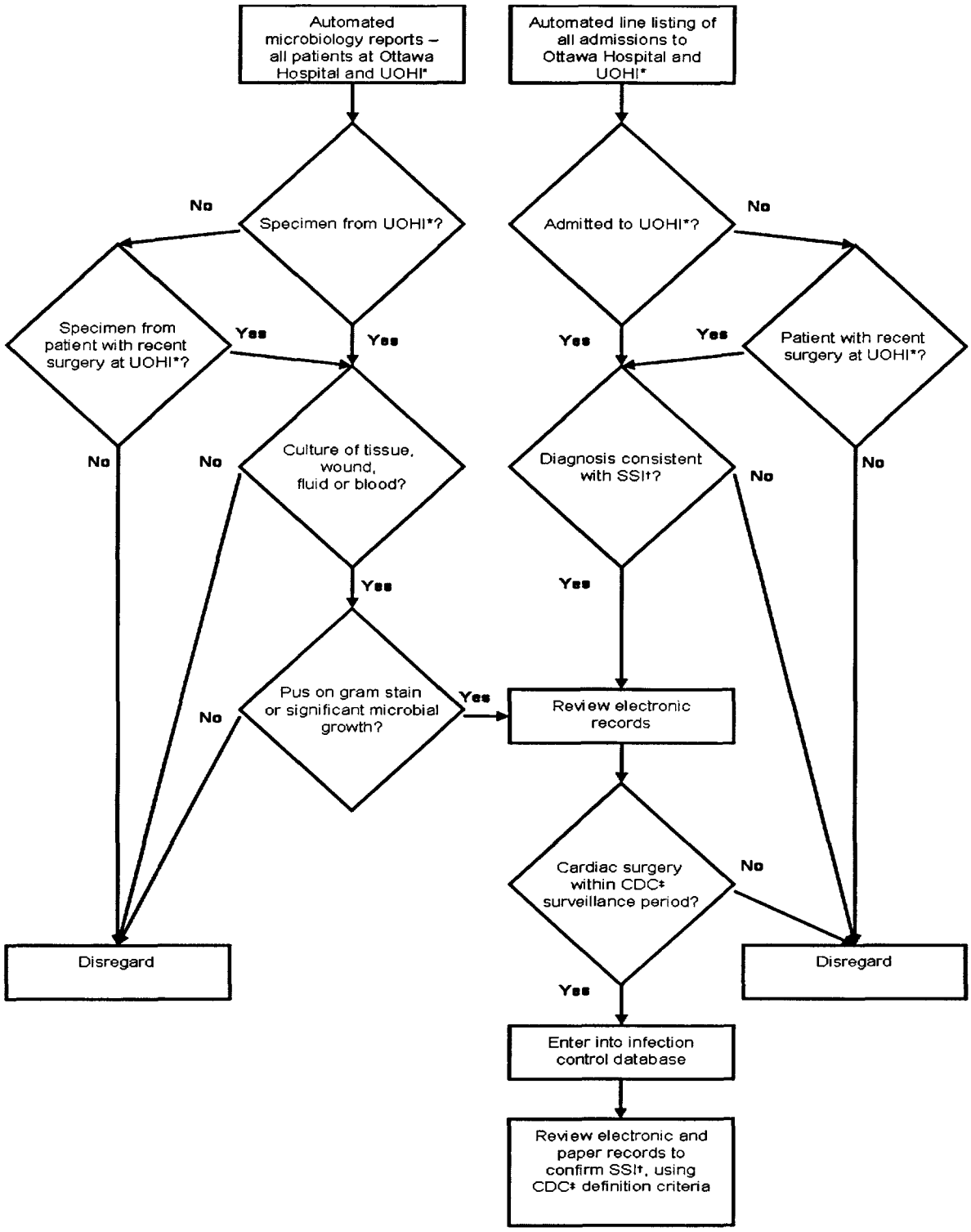
1.4.1 SSI surveillance at the University of Ottawa Heart Institute

A relevant case-study of a triggered SSI surveillance program is that undertaken at the University of Ottawa Heart Institute (UOHI). The Ottawa Hospital Infection Prevention and Control Program (TOH-IPCP) provides SSI surveillance and other infection control activities at UOHI. The TOH-IPCP methodology for cardiac SSI surveillance relies largely on active retrospective surveillance, and very rarely on passive reporting from clinical staff at UOHI. The bulk of surveillance is triggered by a mechanism involving either of two trigger factors: microbiology results, and readmission diagnoses (Figure 1.1).

The current TOH-IPCP trigger mechanism is considered positive only after manual review to confirm relevance. The ICP's receive an automatically-generated daily report on all microbiology results and admitting diagnoses at UOHI and The Ottawa Hospital. These are then reviewed in a multi-step iterative process to identify results suggestive of SSI within a standard surveillance period following clean cardiac surgery at UOHI (Figure 1.1). The ICP then reviews the medical records for all trigger positive cases, applying the CDC SSI definition criteria to confirm the presence or absence of SSI.

This process is quite labour intensive. It takes approximately 30 to 60 minutes daily to review microbiology results and readmission line listings. Ordering patient charts, and tracking down errant charts, takes a further 30 to 180 minutes.

Figure 1.1: Work flow for surveillance of cardiac surgical site infections using the current trigger mechanism at the University of Ottawa Heart Institute



*UOHI = University of Ottawa Heart Institute; †SSI = Surgical site infection; ‡CDC = United States' Centers for Disease Control and Surveillance

Depending on SSI status, chart review occupies approximately 15 to 30 minutes per patient, with non-cases taking less time. The TOH-IPCP reviews approximately 64 cases and 296 to 356 non-cases annually.[39] Annually this process consumes approximately 720 person-hours to trigger surveillance, and a further 105 to 120 person-hours to review charts.

1.5 Limitations of currently-used trigger mechanisms

As demonstrated in section 1.4.1, currently used trigger mechanisms are suboptimal. They are rarely validated, and remain labour-intensive.[26, 38] For manually-reviewed trigger factors, data gathering is itself labour-intensive, and may lack sensitivity.[34, 37] For electronically-reviewed trigger factors, sensitivity is generally acceptable, but positive predictive value (PPV) is poor.[34, 37] This results in excess chart review to confirm case status. A major stated goal of infection control research is to develop electronic trigger mechanisms with improved PPV.[36]

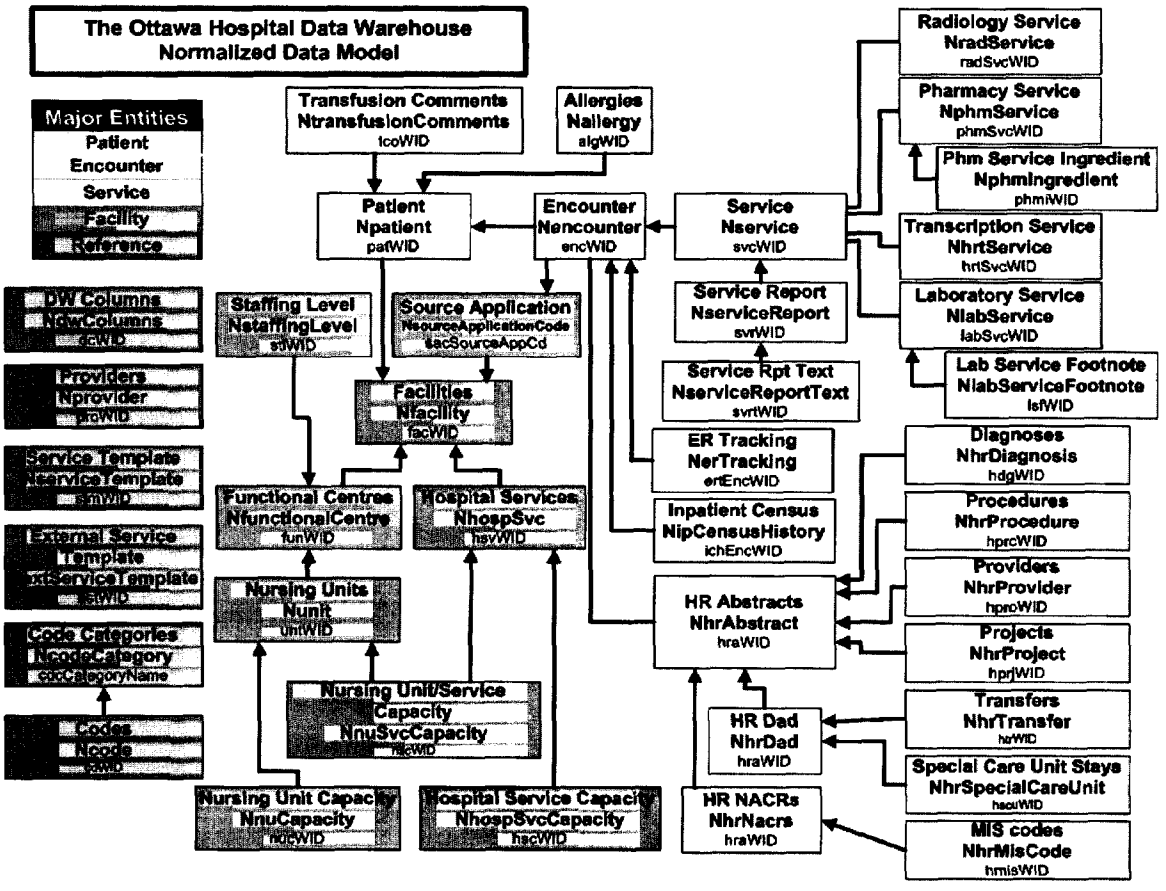
Currently used electronic trigger mechanisms are limited by available data sourcing. Previously described mechanisms are simple, relying on at most a few data sources including microbiology data,[33] pharmacy data,[34] discharge data,[38] or hospital registration data.[31] These simple trigger mechanisms tend to optimize either sensitivity, or PPV. For example, a simple electronic trigger mechanism using pharmacy data to trigger cardiac SSI surveillance afforded reasonable sensitivity (0.87 – 0.95) but poor PPV (0.28 – 0.31.)[40] Similarly, a recursive partitioning-derived trigger mechanism using administrative data for post-discharge SSI in various surgical specialties could provide high sensitivity with poor PPV (0.92, 0.21 respectively) or diminished sensitivity with moderate PPR (0.74, 0.48) depending on the cost applied to false positive.[41]

A more complex model may optimize both sensitivity and PPV. To a limited degree this has been demonstrated in the analogous field of endometritis following caesarean section.[34] In surveillance of post-caesarian endometritis, reliance on administrative-data derived diagnosis coding yielded sensitivity of 0.89 and PPV of 0.32, but introduction of a second data source, pharmacy records, preserved sensitivity, and increased PPV to 0.53.[34] Unfortunately complex models in SSI surveillance are considered too difficult to coordinate, as data must be acquired from disparate sources.[38]

1.6 The data warehouse as a source of electronic data

A healthcare data warehouse may be a solution to the problem of complex data sourcing. A data warehouse links various electronic health information databases, using common identification keys such as patient or visit identification codes.[42] Sources of data may include laboratory, pharmacy, radiology, and electronic health records, in addition to discharge and administrative data. Data are stored in a manner to facilitate complex queries and analyses. Data are updated according to a regular schedule, and periodically reviewed to ensure accuracy of recording from original data sources. Using this existing architecture, an SSI surveillance program could create a complex trigger mechanism without complicated and time-consuming data acquisition.

Figure 1.2: Map of data sources available in the Ottawa Hospital Data Warehouse

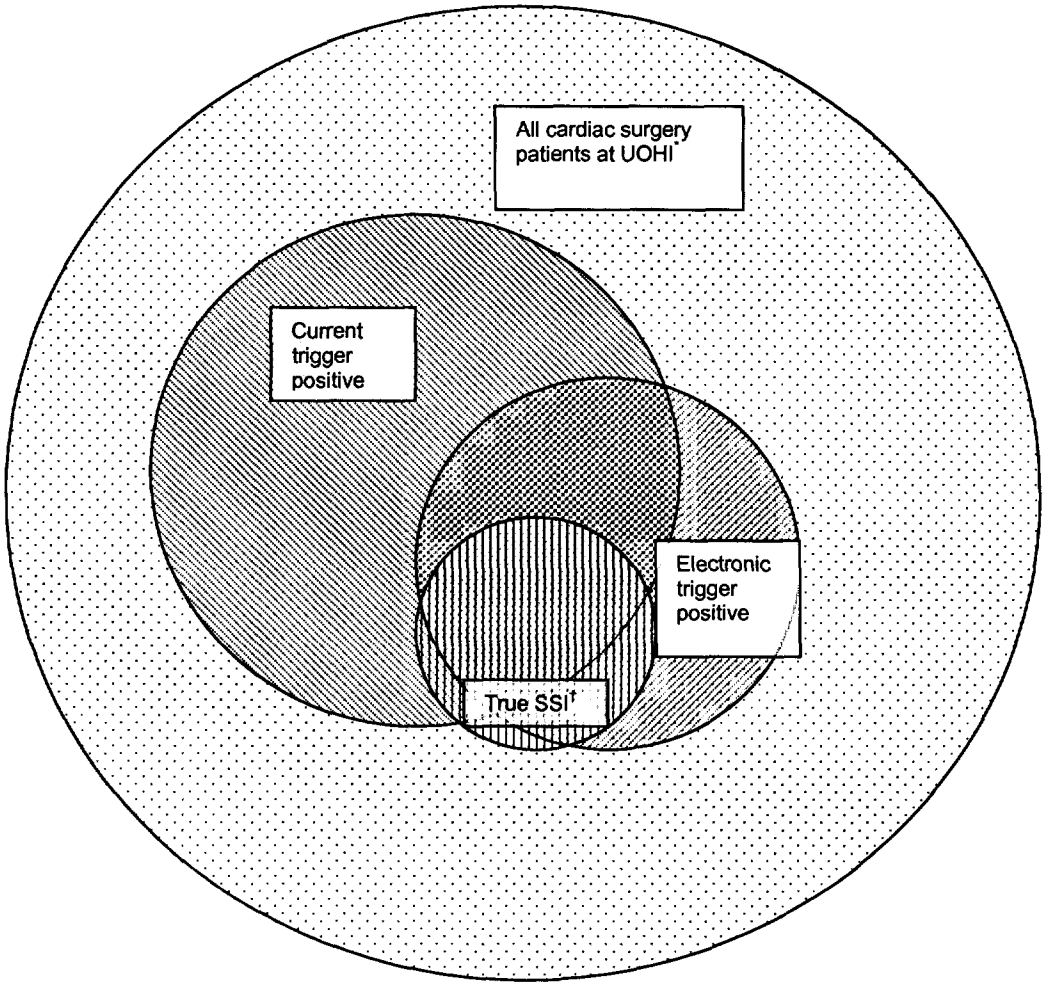


Each box represents a separate data table – bolded terms are the plain language description of the table and the table name, unbolded terms are the name of the common identification key linking to other data tables.

1.6.1 The Ottawa Hospital Data Warehouse

The Ottawa Hospital Data Warehouse (OHDW) is one such relational database, linking clinical, laboratory, and administrative data using common identification keys (Figure 1.2). It contains data for patients of UOHI and The Ottawa Hospital dating from 1996 to the present. Analysts and researchers involved in the OHDW have developed surveillance tools for a number of adverse events, including healthcare-associated infections (e.g. *Clostridium difficile*-associated diarrhea). It has not yet been applied to the somewhat more complex requirements of SSI surveillance.

Figure 1.3: Theoretical relationship between the accuracy of the current surgical site infection surveillance trigger mechanism used at the University of Ottawa Heart Institute, with a proposed electronic trigger mechanism, and the population with true surgical site infection



* UOHI = University of Ottawa Heart Institute; † SSI = Surgical site infection

We believe that the OHDW may prove a valuable tool to develop a more efficient cardiac surgery SSI surveillance program than that described in Section 1.4.1. As demonstrated in Figure 1.3, we believe that the current surveillance trigger mechanism captures a portion of the true SSI cases, as well as a large number of falsely trigger-positive cases. We believe that the higher accuracy likely afforded by a complex electronic trigger mechanism, based on the OHDW, will allow us to capture a similar portion of the true SSI cases, while reducing the number of falsely trigger-positive ones.

1.7 Summary

In summary:

1) SSIs are an important cause of avoidable patient injury and cost.

2) SSI surveillance is an effective infection prevention and control method (and increasingly a requirement for public reporting as an indicator of patient safety), but surveillance programs are not standardized centre-to-centre

3) As a labour saving measure, many surveillance programs use trigger mechanisms to identify probable cases of SSI, prior to undertaking costly and labour-intensive case review to confirm SSI status

4) Currently used trigger mechanisms, whether manually or electronically derived, are suboptimal. In particular, current electronic trigger mechanisms have low positive predictive value, perhaps as a consequence of the simplicity of available data sources

5) The ability to construct a complex electronic trigger mechanism has been limited by the difficulty in aggregating disparate data sources.

6) A data warehouse is an integrated data repository that aggregates multiple data sources linked by common identification keys, which could be used as a source of trigger factors to identify SSI.

2 Methods

2.1 Hypotheses to be tested

1) A complex electronic trigger mechanism for surveillance of cardiac surgical site infections incorporating integrated hospital data will be more specific than current trigger methods.
2) The sensitivity of the complex electronic trigger mechanism will not be inferior to current trigger methods for surgical site infection surveillance

2.2 Overview of study structure

This was a two phase study. The first phase of the study was a systematic review of the literature to identify potential trigger factors for inclusion in an electronic trigger mechanism. Potential trigger factors were risk or identification factors for SSI following cardiac surgery in adults. The second phase was a retrospective, nested case-control study to derive the electronic trigger mechanism by multiple logistic regression modelling. These were cases of SSI, and non-infected controls, drawn from a cohort of all specific clean cardiac surgical procedures at the UOHI from July 1, 2004 to June 30, 2007. For the electronic trigger mechanism, I included trigger factors derived from the systematic review, as well as a number I identified as likely of interest *a priori*.

2.3 Systematic review

I conducted this review to identify studies evaluating potential trigger factors for SSI surveillance in adult patients undergoing cardiac surgery. I performed this as a precursor to trigger mechanism model building in the second phase of the study (see 2.4.6). My joint goals were to ensure that no clinically relevant trigger factor was overlooked, and to reduce potential overfitting by eliminating less-relevant trigger factors *prior* to model building.

2.3.1 Search strategy

I used multiple identification strategies in the systematic review. In May of 2008, I carried out a search of Ovid MEDLINE(R)(1950 to May Week 1 2008),, EMBASE (1980 to 2008 Week 20), and EBM Reviews - Cochrane Central Register of Controlled Trials (2nd Quarter 2008), limiting results to adults and language of publication to English or French. I used combinations of terms to denote cardiac surgery, terms to denote surgical site infection, and terms to denote the trigger factor. I have listed specific search strings in Table 2.1. I also hand searched bibliographies of selected studies and topic reviews, and reviewed other articles published in topic-specific supplements.

I then preliminarily screened search results for suitability. I entered search results into Endnote X1.0.1 (Build 2682,Thomson Reuters, Carlsbad, CA, USA, 2007) and removed duplicate records. Within this resultant group, I screened titles for evidence of original analytic observational or experimental studies analyzing the risk factors for, preventive measures for, or incidence and surveillance of, SSI among adult humans undergoing cardiac surgery (specifically including at least one of coronary artery bypass grafting [CABG], cardiac valve repair or replacement, and heart transplantation). I specifically excluded studies that lacked indicators of the above, studies that analyzed the complications or therapy of established post-cardiac surgery SSI, as well as review articles, commentary or editorial articles, and publications in languages other than English or French.

After excluding studies based on information in the title, I then reviewed abstracts of remaining studies. I searched for evidence of analysis of risk or identification factors for SSI following cardiac surgery, excluding studies in which such analysis was not performed, studies in which SSI could not be separated from other outcomes, studies in which data for cardiac surgery could not be separated from data for other surgical disciplines, and commentary or review articles.

Where the abstract was deemed of interest, or was not available, I reviewed the complete manuscript. I recorded the study methodology, methodology of statistical analysis, study population, surgical interventions performed, definition of SSI, location of SSI (chest, harvest site, or both), depth of SSI (superficial incisional, deep incisional, organ space, or a combination), and post-operative time to identification of SSI. I then excluded studies lacking confounder-controlled analysis of risk or identification factors, and studies in which the incidence of SSI was not evaluated within the standard

NNIS surveillance period (30 days for most interventions, 365 days for interventions involving implantation of non-human derived material).[2]

Table 2.1: Data sources and search strings to identify studies reporting potential trigger factors for inclusion in electronic trigger mechanism for surgical site infection surveillance

Source	Ovid MEDLINE(R)	EMBASE	EBM Reviews - Cochrane Central Register of Controlled Trials
Date	1950 to May Week 1 2008	1980 to 2008 Week 20	2nd quarter 2008
Search string	1 exp Cardiac Surgical Procedures 2 exp Heart Diseases/su [Surgery] 3 ((heart or cardiac or coronary or cardiovascular or valve) adj2 (surg$ or operation$ or transplant$ or replacement$ or graft$ or repair$)).tw. 4 (coronary artery bypass or cabg).tw. 5 or/1-4 6 Surgical Wound Infection 7 (surgical adj2 infection$).tw. 8 (surgical adj2 wound$).tw. 9 (swi or ssi).tw. 10 ((postoperative or post operative) adj2 (infection$ or wound$)).tw. 11 Mediastinitis/ or mediastinitis.tw. 12 ((sternum or sternal) adj1 infection$).tw. 13 sternal osteomyelitis.tw. 14 Osteomyelitis 15 exp Sternum 16 14 and 15 17 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 16 18 risk factors/ or Risk Assessment/ 19 ((risk or trigger or identification) adj1 factor$).tw. 20 Mass screening/ 21 Sentinel Surveillance/ or surveillance.tw. 22 incidence/ 23 or/18-22 24 5 and 17 and 23 25 limit 24 to (english or french) 26 (child not adult).sh. 27 25 not 26	1 exp Heart Surgery/ 2 exp Heart Disease/su [Surgery] 3 ((heart or cardiac or coronary or cardiovascular or valve) adj2 (surg$ or operation$ or transplant$ or replacement$ or graft$ or repair$)).tw. 4 (coronary artery bypass or cabg).tw. 5 or/1-4 6 graft infection/ or postoperative infection/ or surgical infection/ 7 (surgical adj2 infection$).tw. 8 (surgical adj2 wound$).tw. 9 (swi or ssi).tw. 10 ((postoperative or post operative) adj2 (infection$ or wound$)).tw. 11 Mediastinitis/ 12 mediastinitis.tw. 13 ((sternal or sternum) adj1 infection$).tw. 14 Osteomyelitis/ 15 STERNUM/ 16 14 and 15 17 stern$ osteomyelitis.tw. 18 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 16 or 17 19 5 and 18 20 infection risk/ or population risk/ or risk assessment/ or risk factor/ 21 trigger factor 22 ((risk or trigger or identification) adj1 factor$).tw. 23 SCREENING/ 24 disease surveillance/ or surveillance.tw. 25 INCIDENCE/ 26 20 or 21 or 22 or 23 or 24 or 25 27 19 and 26 28 (child not adult).sh. 29 27 not 28 30 limit 29 to (english or french)	1 exp Cardiac Surgical Procedures/ 2 exp Heart Diseases/su [Surgery] 3 ((heart or cardiac or coronary or cardiovascular or valve) adj2 (surg$ or operation$ or transplant$ or replacement$ or graft$ or repair$)).tw. 4 (coronary artery bypass or cabg).tw. 5 or/1-4 6 Surgical Wound Infection/ 7 (surgical adj2 infection$).tw. 8 (surgical adj2 wound$).tw. 9 (swi or ssi).tw. 10 ((postoperative or post operative) adj2 (infection$ or wound$)).tw. 11 Mediastinitis/ or mediastinitis.tw. 12 ((sternum or sternal) adj1 infection$).tw. 13 sternal osteomyelitis.tw. 14 Osteomyelitis/ 15 exp Sternum/ 16 14 and 15 17 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 16 18 risk factors/ or Risk Assessment/ 19 ((risk or trigger or identification) adj1 factor$).tw. 20 Mass screening/ 21 Sentinel Surveillance/ or surveillance.tw. 22 incidence/ 23 or/18-22 24 5 and 17 and 23

2.3.2 Identification of potential trigger factors

From the included studies I extracted all potential risk or identification factors evaluated in confounder-controlled analyses. I recorded the definition of each trigger factor, the variable type (continuous, dichotomous, categorical), the nature and magnitude of measures of association and significance (relative risk or odds ratio with 95% confidence limits, or incidences with p-values), whether the analysis was the primary study endpoint (vs. secondary analysis), and whether the analysis was for a specific surgical procedure, SSI location, or SSI depth.

I then grouped trigger factors into larger trigger themes. For each specifically defined trigger factor I defined a main trigger theme, as well as a more specific trigger sub-theme. For example, if study A defines obesity as a body mass index (BMI) of 30 kg/m^2, the main trigger theme is obesity, and the sub-theme is obesity as defined by BMI. Similarly if study B defines obesity as a weight greater than 150% of ideal, then the main trigger theme is obesity, and the sub-theme is obesity as defined by weight.

Subsequently, I summarized the frequency with which each theme or sub-theme had been analyzed in the primary analysis model of all the included studies. Specifically, I noted the number of studies reporting positive, inverse, or no association with incidence of SSI. I repeated this summary for both primary and secondary analyses performed on five analysis subgroups: analyses reporting only SSI in the chest, SSI in harvest sites, SSI in all sites, deep incisional or operative site SSI in the chest only, and SSI following CABG (primary analyses only). Therefore, including the primary analysis model, I defined six classes of analysis.

Using these summaries, I then identified those themes and sub-themes most consistently associated with SSI. I evaluated this association qualitatively, rather than by meta-analysis. I wished to ensure that I only included trigger themes that had repeatedly, and consistently, been shown to be associated with SSI. Therefore, I retained only those which had been examined in 5 or more studies, and found to be associated (positively or inversely) with SSI in at least 20% of studies reported. I calculated an approximate ranking of the association by dividing the number of studies demonstrating a significant association by the total number of studies. Some trigger themes were positively associated with SSI in some studies, and inversely associated in others. These I ranked according to the frequency of the more common association.

Next, I selected potential trigger factors to make up the initial regression model. I selected the top 20 main themes and alternative themes from all subgroups of analyses, according to the frequency of a significant association. I generated potential trigger definitions from the specific definitions found in my systematic review. I then reviewed these themes and alternative themes with my thesis supervisory committee (AF, VR, KS) to confirm relevance, and ability to obtain these data from the OHDW. *A priori,* I had posited several trigger factors of interest, based on clinical grounds, or previously reviewed literature. When these *a priori* triggers were novel, or not evaluated in the systematic review, I included them in the initial model upon obtaining a consensus from my supervisory committee.

2.4 Nested case-control study

2.4.1 Setting

I carried out the nested case-control study using data from patients of the University of Ottawa Heart Institute (UOHI). The UOHI is a 138-bed academic cardiac care specialty centre, serving a catchment area of 1.5 million patients in the area of Eastern Ontario and Western Quebec. It is co-located with the Civic Campus of The Ottawa Hospital, in Ottawa, Ontario, Canada. Although a separate institution, it shares resources with The Ottawa Hospital, including consulting medical services, medical records, and coverage from The Ottawa Hospital Infection Prevention and Control Program (TOH-IPCP). Because of these shared resources, the Ottawa Hospital Data Warehouse (OHDW) contains data for UOHI patients as well.

The UOHI cardiac surgery program is considered high-volume. It performs approximately 1,300 operations annually, including coronary artery bypass grafts (CABG's), cardiac valve repair and replacement, and heart transplants. Patients may be admitted through The Ottawa Hospital emergency room, in transfer from other facilities, or through UOHI's **'Reference Centre'** (a high-acuity outpatient urgent care assessment unit). Since 2000, TOH-IPCP has provided dedicated coverage of healthcare-associated infections at UOHI, including surveillance for SSI following all cardiac surgical procedures. Using retrospective application of CDC SSI definition criteria, TOH-IPCP creates quarterly reports of program-wide SSI incidence.

2.4.2 Study population

The study population comprised cases of SSI, and randomly-selected controls without SSI, drawn from a cohort of episodes of selected cardiac surgical procedures at UOHI from July 1 2004 to June 30 2007. The selected procedures are: CABG (with saphenous vein, brachial artery, and/or internal mammary artery grafts), repair or replacement of cardiac valves (aortic, mitral, tricuspid, or pulmonic), and cardiac transplant. I also included mixed operations if they included one or more of the above procedures.

2.4.3 Data sources

I derived data from three sources for this study. The goal was to derive an electronic trigger mechanism for SSI surveillance, and compare accuracy of SSI identification to that of the current TOH-IPCP trigger mechanism, using retrospective application of CDC SSI definition criteria as the reference standard. Therefore, I used data from the following sources: 1) data from the OHDW (to define the cohort, and derive the electronic trigger mechanism); 2) records of TOH-IPCP (to preliminarily identify SSI cases, and to describe the accuracy of the current trigger mechanism); and 3) data from chart review (to confirm the presence of SSI). I shall describe these sources in order.

2.4.3.1 The Ottawa Hospital Data Warehouse

As described in section 1.6.1 and Figure 1.2, the OHDW is a relational database, maintained on a specialized data warehouse server (Sybase IQ v12.6, Sybase Inc., Dublin, CA, USA). The data warehouse contains data derived from operational information systems used at the Ottawa Hospital to conduct its clinical business. On a weekly basis, an 'extract, transform, and load' process occurs, which copies specific data from source systems into the data warehouse with or without a transformation process. Data warehouse administrators perform automated and regular manual assessments to ensure the data in the data warehouse reflect the data in source information systems.

The central data tables are classed as major **'entities'**, which relate using identification keys referring to the patient, or to the patient '**encounter**' (i.e. admission, emergency room or outpatient

clinic visit). Further, there are related sub-entities containing extra information regarding specific aspects of the major entity. These may relate to the major entity using encounter-level identification keys, or more specific sub-entity identification keys.

I used three major entities, and ten sub-entities to derive the electronic trigger mechanism. The "Patient" major entity contains data from the hospital's patient registration database (Invision 26, Siemens Medical Systems USA Inc, Malvern, PA, USA). It contains basic demographic data. From this table, I accessed the patients' chart number, patient-level common identification key, gender, native language, and whether the patient was isolated for a potential healthcare-acquired infection.

The "Services" major entity is a table of coded diagnostic and therapeutic services drawn from the TOH clinical data repository (vOacis v. r7.2.0_20080402, DINMAR Consulting Inc, Ottawa, ON, Canada, 2007). It contains the information present in the TOH electronic health record, and is maintained during the patient admission. From this table, I accessed the sub-entities "Lab Service", "Pharmacy Service", "Pharmacy Service Ingredient", "Radiology Service", and "Service Reports" to gain specifics on dates, tests ordered, results, medications provided, and doses.

The "Encounter" major entity is a summary of data pertaining to specific inpatient admissions, outpatient or emergency visits, or use of outpatient laboratory or radiologic services. It is created from data entered by unit or ward clerical staff, during the patient encounter and is also contained within the patient registration database. From this table, I accessed data regarding encounter date, time, location and duration. I also accessed data regarding the urgency of the encounter, the presenting/admitting diagnosis (non-coded, but free text), and the attending service.

The "Health Records Abstract" table is a sub-entity of the "Encounter" table, and itself has several sub-sub-entities. The Abstract (and its sub-sub-entities) is a retrospective summation of data regarding usage of resources. Health records technologists review the patient chart after the termination of an encounter (i.e. post-discharge) to summarize care providers and special care unit usage, codify procedures performed (using the Canadian Classification of Health Interventions [CCI][43]); and record and codify assigned diagnoses (since 2003 using the International Statistical Classification of Diseases and Related Health Problems, 10th Revision Canada [ICD-10-CA][44]). I accessed four sub-sub-entities: "Providers", "Procedures", "Diagnoses", and "Special Care Units".

The OHDW uploads data from its various component databases once weekly. For data tables that are maintained in "real time" (e.g. "Patient", "Services", and "Encounter") this means that data are available within 7 days of being recorded. However, "Health Records Abstract" data is compiled retrospectively, often many weeks or months post-discharge.

2.4.3.2 The Ottawa Hospital Infection Prevention and Control Program records

The TOH-IPCP records contain patient-level data on the status of health-care associated infections. These records are a manually-maintained electronic database (Pathnet® Laboratory Information System Classic 306, Cerner Corporation, Kansas City, MO, USA) of patients who have undergone surveillance for possible healthcare-associated infections. For SSI surveillance, the unit of observation is the '**operative episode**'. The ICP will create a database entry for any patient judged to be trigger-positive (see Section 1.4.1 and Figure 1.1), recording basic demographics, date of entry into surveillance records, date of hospitalization, and the nature of the trigger mechanism used to identify the patient. Upon reviewing the medical records, the ICP then records a judgement on the status of the potential healthcare-associated infection, the date of onset, any pertinent risk factors, and the date of the **'index operative episode'** (i.e. the individual trip to the operating room directly preceding the SSI).

2.4.3.3 Chart review

I used two sources of data used in the chart review: electronic health records, and paper charts. Electronic health records at UOHI include laboratory and radiology results, pharmacy records, and dictated operative reports, discharge summaries, and dictated outpatient clinic reports. I searched the paper charts for daily progress notes, nurses' flow sheets, and consultation reports. I also read handwritten outpatient notes from consulting services. Handwritten outpatient follow-up notes from the cardiac surgery service were usually not available. These notes are maintained in the private offices of individual cardiac surgeons, and are not kept under the mandate of The Ottawa Hospital health records, unless a dictated report is present in the electronic health record.

2.4.4 Selection of study population

I first created a cohort using data from the OHDW. I constructed the cohort by identifying in the OHDW all episodes of specific clean cardiac surgical procedures (CABG, cardiac valve repair, cardiac valve replacement, or cardiac transplant) at UOHI from July 1 2004 to June 30 2007. I chose this time period as I required a three-year cohort according to my sample size calculations (see Section 2.4.6.8 below).

My unit of observation was also the operative episode. During one operative episode, a patient may undergo one or more cardiac surgical procedures. I identified procedures of interest by appropriate CCI code (Table 2.2). Some patients underwent more than one operative episode with a procedure of interest; therefore there were multiple observations for some patients. I excluded operative episodes occurring in contaminated or infected operative sites (e.g. cardiac valve replacement for endocarditis).

Table 2.2: Canadian Classification of Health Intervention codes for procedures of interest, used to define cohort of study observations

Procedure	Canadian Classification of Health Intervention code
Coronary artery bypass graft	1.IJ.76.LA-XX-^^
Cardiac valve repair	1.HS.80.^^; 1.HT.80.^^; 1.HU.80.^^; 1.HV.80.^^
Cardiac valve replacement	1.HS.90.^^; 1.HT.90.^^; 1.HU.90.^^; 1.HV.90.^^
Cardiac transplant	1.HZ.85.^^

Next, I preliminarily identified SSI cases. I reviewed the TOH-IPCP database to identify all episodes of cardiac SSI attributed to an operative episode occurring within the timeframe of interest. Current TOH-IPCP practice surveys all clean (i.e. uninfected and uncontaminated) procedures performed through a midline chest and sternal incision as well as percutaneous device implantations, , therefore I had to exclude SSI cases following operative episodes which did not include CABG, valve repair, valve replacement, or cardiac transplant. The remaining TOH-IPCP-defined SSI cases became my preliminary case group.

I then selected the preliminary control group from the remaining cohort. The TOH-IPCP database records the date of operative episodes believed to have led to SSI. I censored observations for preliminary case observations from the OHDW-derived cohort where the operative

episode occurred on or after the date of the TOH-IPCP-recorded causative episode. From the remaining cohort I randomly selected three preliminary control observations for each preliminary case. I did this by using the "ranuni" function in SAS to assign a random number each uncensored observation, then selected the $3 \times n$ observations with the lowest randomly-assigned number, where n is the number of preliminarily identified cases. In order to calculate accuracy of the current surveillance trigger mechanism (see Section 2.4.6.7 below), I reviewed the TOH-IPCP records, noting whether the controls had been triggered for surveillance.

2.4.5 Confirmation of case and control status, and calculation of incidence

I undertook retrospective chart review of all observations to exclude inappropriate observations, and confirm the presence or absence of SSI. I excluded observations where chart review could not confirm the occurrence of a procedure of interest (CABG, valve repair or replacement, or cardiac transplant). I also excluded observations if the operative site was believed to be infected or contaminated by pathogenic micro-organisms prior to the index operative episode of interest (e.g. cardiac valve replacement performed to treat endocarditis). These excluded observations are classed as dirty/infected according to a commonly used wound classification scheme (Table 1.2).[1, 2, 27] I confirmed the presence or absence of SSI using the definition criteria used by the United States' Centers for Disease Control (Table 1.1).[1, 2]

Once I had confirmed the presence or absence of SSI, I reassigned observations to case or control status as appropriate. Where my judgement on SSI status disagreed with that in the TOH-IPCP database, or where an observation was not present in the TOH-IPCP database, another investigator with infection control experience (KS or VR) reviewed each chart to confirm. Thus all cases of SSI, and all disagreements with TOH-IPCP designation, were confirmed by two independent reviewers.

Finally, I calculated the predicted incidence in the total cohort using a stratified approach. I defined three strata: the preliminary case group as defined by TOH-IPCP (from which stratum all observations were included); observations found trigger positive by the current TOH-IPCP trigger mechanism, but judged to be not SSI (from which stratum I reviewed a random sample); and those observations not trigger positive by the current trigger mechanism (from which stratum I reviewed a

random sample). I estimated the population for each stratum by extrapolating from the OHDW-defined cohort the number of observations with corresponding records in the TOH-IPCP database, and the number of observations likely to be excluded as inappropriate observations. I then calculated incidence, with 95% confidence limits (95% CL), using a stratified approach (see Equation 2.1 and Equation 2.2).

Equation 2.1: Calculation of estimated cohort-wide incidence of surgical site infection from three strata within the nested group of cases and controls

$$\hat{i}_{str} = \sum_{h=1}^{3} \frac{N_h}{N} \hat{i}_h$$

$\hat{i}_{str}$ = Estimated incidence in the cohort
N_h = Size of stratum *h* in the cohort
N = Size of cohort
$\hat{i}_h$ = Observed incidence in sample of stratum *h*

Equation 2.2: Calculation of confidence limits of estimated cohort-wide incidence of surgical site infection from three strata within a nested group of cases and controls

$$\hat{i}_{str_{(L,U)}} : \hat{i}_{str} \pm Z_{(1-\alpha/2)} \sqrt{\sum_{h=1}^{3} \left(1 - \frac{n_h}{N_h}\right)\left(\frac{N_h}{N}\right)^2 \frac{\hat{i}_h\left(1-\hat{i}_h\right)}{n_h - 1}}$$

$\hat{i}_{str_{(L,U)}}$ = Lower and Upper confidence limits for estimated incidence in the cohort
$\hat{i}_{str}$ = Estimated incidence in the cohort
$Z_{(1-\alpha/2)}$ = Normal value for probability 1 – α/2 (0.975)
n_h = Sample size from within stratum *h*
N_h = Size of stratum *h* in the cohort
N = Size of cohort
$\hat{i}_h$ = Observed incidence in sample of stratum *h*

2.4.6 Derivation of electronic trigger mechanism

2.4.6.1 Accessing data

As described in Section 2.4.3.1 above, I accessed data from several data tables in the OHDW. I included data for all case and control observations for encounters of interest occurring within the surveillance timeframe. Encounters of interest include the **'index encounter'** (during which the index operative episode occurs), and all encounters beginning any time until 14 days following the end of a standard CDC surveillance period. I prolonged the electronic trigger surveillance timeframe in order to account for potential lag time from the onset of SSI to investigations and therapy.

I obtained static data tables from queries of the OHDW, rather than directly obtaining data from the constantly-updated OHDW. I requested specific variables from each of 3 major entities and 10 sub-entities of the OHDW (Figure 1.2), for encounters of interest amongst cases and control. A single data analyst (PS) queried the OHDW database server (Sybase IQ) using standard Structured Query Language (SQL), and exported requested data into SAS data tables (SAS 9.1.3 Service Pack 4, the SAS Institute, Cary North Carolina USA, release date 2003). Where possible, I compared data with expected values in order to assess completeness, and refined the SQL search mechanism to minimize missingness.

I then constructed potential trigger factors, according to the results of the systematic review (see Sections 2.3.2 and 3.1.4), using SAS 9.1.3 Service Pack 4 (the SAS Institute, Cary, NC, USA, release date 2003). I defined trigger factors according to the results of the systematic review, and according to the feasibility of "live application". I recorded demographic data unaltered from the "Patient" major entity, and data regarding urgency and nature of readmission episodes from the "Encounters" major entity.

I dichotomized the bulk of trigger factors as the presence or absence of data of interest. I recorded diagnoses of co-morbidities and complications by reviewing the "Health Records Abstracts" sub-entity "Diagnoses" for appropriate ICD-10-CA codes (see Appendix A:). I recorded diagnostic and therapeutic procedures from the "Health Records Abstracts" sub-entity "Procedures" using appropriate CCI codes (see Appendix A:). For healthcare providers and special care units, I assessed usage using the appropriate sub-entities of the "Health Records Abstracts". I classified

qualitative laboratory results, such as microbiology results, (from the "Service" sub-entity "Laboratory Services") and radiology reports (from the "Service" sub-entity "Service Reports Text") using natural language searches of text reports (see Appendix A:).

For continuous laboratory data, I collected values denoting the highest or lowest value at a given point before, during, or after the index operative episode (as appropriate). Wherever possible, I retained continuous variables as is, to maximize information. However, for model purposes I did not tolerate any missingness in continuous variables. That is, data had to be present in all observations, else I substituted dichotomized trigger factors, wherein a negative trigger factor may be defined as the absence of a recorded abnormal value. This is in keeping with a coherent philosophy regarding prospective use of large datasets: if data are missing in model derivation, they will similarly be missing when the model is applied prospectively in "real time". I also counted the number of times certain diagnostic tests were performed.

Finally, I recorded the use and duration of selected antimicrobial agents, and immunosuppressant medications, using a multi-step search of the "Pharmacy Service Ingredient" sub-entity. This search involved use of text descriptions of medication ingredients, Drug Identification Numbers (DIN), Anatomic Therapeutic Chemical Classification (ATC) codes, and American Hospital Formulary Service (AHFS) pharmacologic-therapeutic classifications (see Appendix A:).

2.4.6.2 Selection of candidate trigger factors

After creatingpotential trigger factors, I then assessed them for viability in both model construction, and in application for surveillance triggering.. To avoid problems with logistic regression model convergence, I eliminated dichotomous trigger factors where positive (or negative) responses comprised less than 10% of observations. Furthermore, I eliminated all trigger factors demonstrating any missingness. It is not possible to calculate the logit probability for a patient with any amount of missingness, unless one uses some method of imputation. Imputation is not a practical alternative for a prospectively applied surveillance mechanism, therefore missingness prohibit successful application of the resulting trigger mechanism to all patients.

Finally, where two or more potential trigger factors shared the same data elements, I selected the trigger factor that *a priori* seemed most clinically relevant. To make this judgement, I

prioritized the structure of current SSI surveillance at UOHI, trigger factors as described in the literature, and investigators' clinical experience. For example, using the trigger theme of 'comorbid respiratory disease', I elaborated three potential trigger factors based on ICD-10-CA coding: presence of chronic obstructive pulmonary disease (COPD); presence of COPD, asthma, or bronchitis; and presence of any chronic respiratory disease (including COPD). These definitions use many of the same ICD-10-CA codes. The systematic review demonstrated that COPD alone was the definition of respiratory disease used in the majority of studies, and was more frequently associated with SSI than other comorbid respiratory diseases. Therefore, after confirming that COPD occurred in more than 10% of all cases and controls, I selected this as the potential trigger factor best defining the trigger theme, for inclusion in the initial logistic regression model (see also Section 3.2.2.1).

In addition to the primary set of potential trigger factors, I selected a subset of these to create a second model excluding data from the Health Records Abstract and its sub-entities. As noted in section 2.4.3.1 above, the Abstract is compiled upon patient discharge, occasionally several weeks to months afterwards. As such, models relying on data in the Abstract (such as ICD-10-CA codes) may not provide surveillance triggering in a sufficiently timely fashion. Therefore I wished to create a model using only data from the "Patient", "Encounter" and "Services" tables that are updated in a more timely fashion.

2.4.6.3 Assessment and management of collinearity

I used two procedures to determine the presence of collinearity: assessment of multicollinearity, and assessment of collinear pairs of variables. First I used the REG procedure in SAS to assess the tolerances of all initially selected potential trigger factors. I considered a tolerance of less than 0.4 to be suspicious for multicollinearity.[45] Then I created a correlation matrix using the CORR procedure. I considered two trigger factors to be likely collinear if the correlation coefficient was greater than 0.6.

I used several approaches to avoid or correct collinearity. I first transformed some continuous variables, making values proportionate to the length of post-operative admission. In cases of severe multicollinearity (tolerance less than 0.2, and correlation coefficient greater than 0.8) I eliminated variables that were considered less clinically relevant, retaining the more relevant variables if

tolerance improved. Finally, where multicollinearity was mild (tolerance between 0.35 and 0.4) and all trigger factors were deemed clinically relevant, I retained all these potential trigger factors, and assessed their impact on final logistic regression models.

2.4.6.4 Model building

I employed a multi-step semi-Bayesian approach to construct a range of "candidate" models from which to select the final trigger mechanism model.[46-49] In this approach, I first used stepwise entry model building with broad p-values (p = 0.99 for entry, p = 0.995 for retention), in order to create a range of models ranging from no variables to the maximum possible. Within this range of models, I calculated two different information criteria (IC) from the $-2\log L$ statistic: the Akaike Information Criterion (AIC) [$AIC = -2\log L(M) + 2 \cdot K$,] and the related criterion IC(1) [$IC(1) = -2\log L(M) + 1 \cdot K$]. I identified the range of model sizes (i.e. number of variables) containing the model which minimized AIC (the AIC-optimized model), and the largest model yielding a minimal IC(1) (termed the "Right Border" from its appearance when IC(1) is plotted against the number of variables in the model).

I then used the score selection method to construct the best models within this range of sizes. I then inspected the resulting range of models, selecting the one which optimized AIC, and eliminating trigger factors for which parameter estimates strongly contradicted *a priori* expectations. I repeated all the above steps for the second, smaller, model (excluding data from the Health Records Abstracts).

2.4.6.5 Assessment of goodness-of-fit

I used two methods to assess the goodness-of-fit of each of my two final models (with and without Abstract data). First I visually inspected receiver-operator-characteristic curves (ROC), and evaluated the c-statistic (approximation of the area under the curve [AUC]). An ROC approaching the upper left corner, and a c-statistic of greater than 0.8 were considered to demonstrate good model fit.

Secondly, I assessed the relationship of observed to expected probability of SSI. I did this by calculating the Hosmer-Lemeshow χ^2 statistic. A non-significant p-value indicates a lack of significant difference between observed and expected probabilities, therefore a good fit. I summarized this relationship graphically by constructing calibration curves. In these curves, I divided the horizontal axis into deciles of the expected probabilities (i.e. the probability calculated by exponentializing the logit, see Equation 2.3). Amongst these deciles, I calculated the proportion of observed SSI cases, and the exact upper and lower confidence limits of this observed proportion. [50] I plotted the results, overlain on a line with a slope of one. A good fit is indicated by confidence limits crossing the diagonal line at most points.

Equation 2.3: Estimated probability of occurrence of surgical site infection as calculated from a logistic regression model including *y* trigger factors

$$\hat{p} = \frac{e^{\beta_0+\beta_1 X_1+\beta_2 X_2+\ldots+\beta_y X_y}}{1+e^{\beta_0+\beta_1 X_1+\beta_2 X_2+\ldots+\beta_y X_y}}$$

2.4.6.6 Selection of cutpoint and dichotomization

The goal of this study was to create an electronic mechanism to trigger SSI surveillance. Because results are to be calculated electronically, I used probability calculated from the logit (Equation 2.3) rather than create a simplified model using parameter estimates – thus preserving as much predictive power as possible. This needs to be dichotomized to be practically applied. Sensitivity of surveillance is of utmost importance, so I selected probability cut-points accordingly.[51] I first calculated the sensitivity of the current trigger mechanism using SSI confirmation by CDC criteria as the gold standard. I used the ROC data tables exported from the LOGISTIC procedure, selecting probability cut-points associated with sensitivity greater than, or equal to, that of the current trigger mechanism. Among the resultant range of cut-points, I selected the one with the greatest specificity. I defined electronic trigger positivity as having a calculated probability above that defined cutpoint, and applied this rule to each observation. I repeated these steps for the second model (excluding Health Records Abstracts data).

2.4.6.7 Comparison of electronic trigger mechanism to current trigger mechanism

I performed two related comparisons of trigger accuracy: a superiority analysis for specificity and a non-inferiority analysis of sensitivity, for the electronic trigger mechanism compared to the current trigger mechanism. To calculate these comparisons, and associated confidence limits, I used the methodology described by Alonzo and colleagues.[52] First I constructed paired two-by-two tables comparing the electronic trigger mechanism, and the current trigger mechanism in those

Table 2.3: Paired tables comparing results of electronic trigger mechanism versus current trigger mechanism in observations with and without confirmed surgical site infection

Confirmed SSI*					**No SSI***			
	CTM† +	CTM† -				CTM† +	CTM† -	
ETM‡ +	A	b			**ETM‡ +**	e	f	
ETM‡ -	C	d			**ETM‡ -**	g	h	
			n_{SSI}					n_{noSSI}

Total study population: $n = n_{SSI} + n_{noSSI}$

True positive ratio for ETM‡: $TPR_E = \frac{a+b}{a+b+c+d}$

True positive ratio for CTM†: $TPR_C = \frac{a+c}{a+b+c+d}$

False positive ratio for ETM‡: $FPR_E = 1 - \frac{g+h}{e+f+g+h}$

False positive ratio for CTM†: $FPR_C = 1 - \frac{f+h}{e+f+g+h}$

Relative true positive ratio $rTPR_{E:C} = \frac{a+b}{a+c}$

Relative false positive ratio $rFPR_{E:C} = \frac{e+f}{e+g}$

Variance of log of $rTPR_{E:C}$ $V(\log rTPR_{E:C}) = \frac{b+c}{(a+c)(a+b)}$

Variance of log of $rFPR_{E:C}$ $V(\log rFPR_{E:C}) = \frac{f+g}{(e+g)(e+f)}$

Confidence limits of $rTPR_{E:C}$ $e^{\log rTPR_{E:C} \pm Z(1-\alpha^*)\sqrt{V(\log rTPR_{E:C})}}$

Confidence limits of $rFPR_{E:C}$ $e^{\log rFPR_{E:C} \pm Z(1-\alpha^*)\sqrt{V(\log rFPR_{E:C})}}$

* SSI: surgical site infection; †CTM: current trigger mechanism; ‡ETM: Electronic trigger mechanism

observations with and without retrospective-chart-review-confirmed SSI (Table 2.3). I calculated the true positive ratio (TPR, also termed sensitivity) and false positive ratio (FPR, 1 minus specificity) for each trigger mechanism. I calculated an estimate of the positive predictive value (PPV) using the estimated SSI incidence amongst the cohort in which cases and controls were nested (see Equation 2.4). I also calculated 95% confidence limits for the PPV using the standard logit method described by Mercaldo and colleagues (see Equation 2.5).[53] I then calculated the relative true and false positive ratios ($rTPR_{E:C}$ and $rFPR_{E:C}$) by dividing the value for the electronic trigger mechanism by that of the current trigger mechanism.

Equation 2.4: Estimate of positive predicted value, using the true positive rate and false positive rate observed in a nested group of cases and controls, and the estimated disease incidence in the wider cohort

$$\overline{PPV} = \frac{TPR \cdot \hat{i}_{str}}{\left(TPR \cdot \hat{i}_{str}\right) + \left(1 - \hat{i}_{str}\right) \cdot FPR}$$

$\overline{PPV}$ = Estimate of positive predictive value
TPR = True positive rate (i.e. sensitivity)
$\hat{i}_{str}$ = Estimated incidence in the cohort
FPR = False positive rate (i.e. 1 – specificity)

I then constructed confidence limits for $rTPR_{E:C}$ and $rFPR_{E:C}$. I had to consider three issues: the paired comparison (i.e. the application of each trigger mechanism in the same observation group), the pre-existing relationship between TPR and FPR for each trigger mechanism, and the effect of multiple comparisons (i.e. $rTPR_{E:C}$ and $rFPR_{E:C}$) I addressed these issues using the "joint" confidence limit calculation in Alonzo et al[52] (with calculation of the variance of the $logrFPR_{E:C}$ from Cheng and Macalusio[54]). Deriving the variance of $logrTPR_{E:C}$ and $logrFPR_{E:C}$ from the paired two-by-two tables (Table 2.3) accounts for the pairwise comparisons. Constructing joint confidence limits (essentially a two-dimensional confidence space) accounts for the relationship between $rTPR_{E:C}$ and $rFPR_{E:C}$. Finally, using an adjusted alpha [$\alpha^* = 1 - \sqrt{(1-\alpha)}$] accounts for multiple comparisons.

Equation 2.5: Calculation of confidence limits for estimate of positive predicted value, using the true positive rate and false positive rate observed in a nested group of cases and controls, and the estimated disease incidence in the wider cohort

$$\overline{PPV_{(L,U)}} : \left(\frac{e^{\text{logit}\left(\overline{PPV}\right) - Z_{(1-\alpha/2)}\sqrt{\text{Var}\left(\text{logit}\left(\overline{\text{PPV}}\right)\right)}}}{1+e^{\text{logit}\left(\overline{PPV}\right) - Z_{(1-\alpha/2)}\sqrt{\text{Var}\left(\text{logit}\left(\overline{\text{PPV}}\right)\right)}}}, \frac{e^{\text{logit}\left(\overline{PPV}\right) + Z_{(1-\alpha/2)}\sqrt{\text{Var}\left(\text{logit}\left(\overline{\text{PPV}}\right)\right)}}}{1+e^{\text{logit}\left(\overline{PPV}\right) + Z_{(1-\alpha/2)}\sqrt{\text{Var}\left(\text{logit}\left(\overline{\text{PPV}}\right)\right)}}} \right)$$

where

$$\text{logit}\left(\overline{PPV}\right) = \log\left[\frac{TPR \cdot \hat{i}_{str}}{FPR \cdot \left(1-\hat{i}_{str}\right)}\right] \text{ and } \text{Var}\left(\text{logit}\left(\overline{\text{PPV}}\right)\right) = \left[\frac{1-TPR}{TPR}\right] \cdot \frac{1}{n_{case}} + \left[\frac{1-FPR}{FPR}\right] \cdot \frac{1}{n_{control}}$$

$\overline{PPV_{(L,U)}}$ = Confidence limits for estimate of positive predictive value

$\overline{PPV}$ = Estimate of positive predictive value

$Z_{(1-\alpha/2)}$ = Normal value for probability 1 – α/2 (0.975)

TPR = True positive rate (i.e. sensitivity)

$\hat{i}_{str}$ = Estimated incidence in the cohort

FPR = False positive rate (i.e. 1 – specificity)

n_{case} = Number of observed cases

$n_{control}$ = Number of observed controls

I calculated $rTPR_{E:C}$ and $rFPR_{E:C}$ and joint confidence limits for both the electronic trigger mechanisms (with and without data from Health Records Abstracts). To conclude superiority of specificity, the confidence limits of $rFPR_{E:C}$ should be entirely less than 1.0. This value is referred to as δ_{FPR}, the threshold at or above which superiority of FPR_E is not demonstrated. To conclude non-inferiority of sensitivity, the confidence limits of $rTPR_{E:C}$ should be entirely greater than the threshold value δ_{TPR}. I have previously defined δ_{TPR} as 0.7.[55]

2.4.6.8 Sample size justification

I chose the sample size to reflect the analysis plan outlined in Section 2.4.6.7 above.[55] I defined the minimally important difference (MID) for superiority of FPR_E to be an absolute decrease of 0.1 compared to FPR_C. In order to have 90% power to demonstrate this endpoint, I required at least 455 control observations, using the method described in Alonzo et al.[52, 55] The MID for non-inferiority of TPR_E was an absolute decrease of 0.25, compared to TPR_C. In order to demonstrate this with 90% power I required 97 cases of SSI. I had anticipated 64 SSI cases and 1236 uninfected

controls per year, and I had chosen a 1:3 case to control ratio, therefore I required a three year cohort to ensure sufficient cases and controls.

2.5 Ethical considerations

I conducted this study with the approval of the Ottawa Hospital Research Ethics Board (OHREB). In keeping with OHREB guidelines for retrospective research, I did not contact patients to obtain consent for use of information, but did take care to protect personal health information. Upon selecting observations to be cases and controls, I assigned a unique study number and stripped the chart review records of other identifiers. I then stored data harvested from the OHDW on a password-protected computer (backed up on a password-protected storage drive maintained by the OHDW), using only the study identifier. I also created a database linking the study number to unique identifiers, and stored this database on a separate, password-protected storage drive maintained by the Ottawa Hospital. I am the sole investigator with direct access to these databases, and I will retain these electronic records, and any paper records, for 15 years, as required.

3 Results

3.1 Systematic review

3.1.1 Identification of publications

I identified 1031 publications for potential inclusion in my systematic review, but eliminated the majority upon review of title, abstract, or manuscript (Figure 3.1). I rejected 616 (59.7%) upon review of titles and abstracts – 59 were in a language other than French or English, and the remaining 554 did not address research questions relevant to my review. I was unable to obtain the manuscript for one potential publication of interest. I reviewed the manuscript of 414 publications. Of these, 20 were not original research. A further 73 mixed SSI with other outcomes, or cardiac surgery patients with other populations. In 163 studies, I could find not evidence of confounding control.

Figure 3.1: Flowchart describing selection of 158 publications describing confounding-controlled analysis of potential trigger factors, among 1031 identified by systematic review of the literature

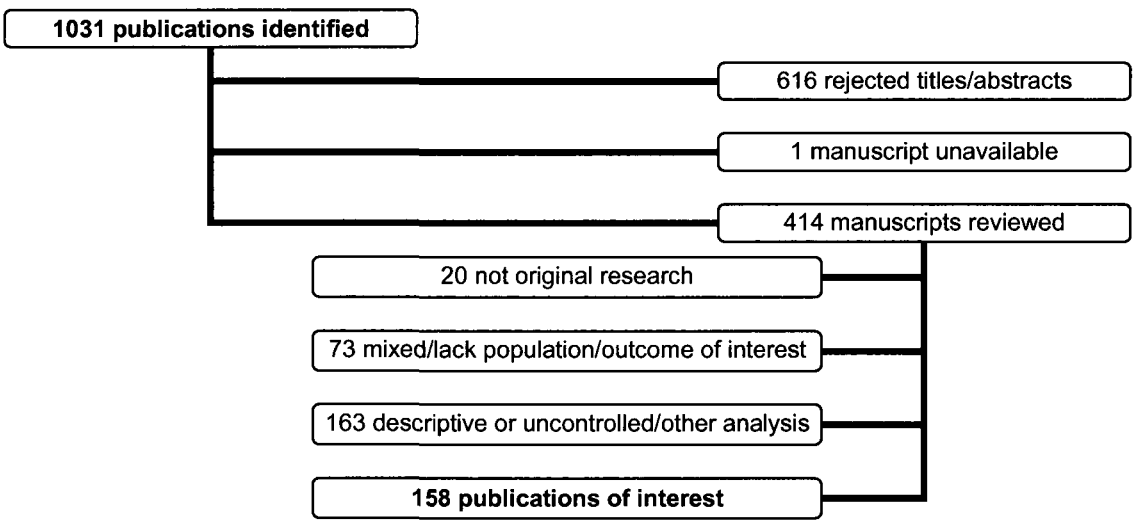


Table 3.1: Methodology of 158 studies of potential trigger factors to identify post-cardiac surgical site infection surveillance

		Trigger Factor Goal		Total (158 studies)
		Identification (2 studies)	Risk (156 studies)	
Number of Study Centres	1	2 100.0%	139 90.3%	141 90.4%
	2 to 20	0 0%	11 7.1%	11 7.1%
	Over 400	0 0%	4 2.6%	4 2.6%
Study type	Case-control	0 0%	15 9.7%	15 9.6%
	Interrupted time series analysis	0 0%	1 0.6%	1 0.6%
	Mixed methodologies	0 0%	2 1.3%	2 1.3%
	Nested case-control	0 0%	6 3.9%	6 3.8%
	Prospective cohort	1 50.0%	43 27.9%	44 28.2%
	Randomized controlled trial	0 0%	22 14.3%	22 14.1%
	Retrospective cohort	1 50.0%	65 42.2%	66 42.3%
Confounder control	Interrupted time-series analysis	0 0%	1 0.6%	1 0.6%
	Logistic regression	2 100.0%	123 79.9%	125 80.1%
	Mixed	0 0%	3 1.9%	3 1.9%
	Multilinear regression	0 0%	1 0.6%	1 0.6%
	Propensity matched analysis	0 0%	5 3.2%	5 3.2%
	Randomization	0 0%	21 13.6%	21 13.5%

3.1.2 Description of included studies

There were 158 studies included.[6, 7, 56-211] Table 3.1 details the methodology used by theses studies. The majority of studies (98.7%) primarily evaluated risk factors for the development of SSI. In this group I include preventive measures (e.g. peri-operative prophylactic antimicrobials or local antisepsis), as well as factors accruing before the development of SSI. In contrast, only 2 studies primarily evaluated identification factors (ones accruing after the development of SSI, such as microbiologic culture results or leukocytosis). The most common study methodologies were single-

centre involvement (90.4%), retrospective cohort design (42.3%) and confounding control by logistic regression (80.1%).

Table 3.2 describes the size of studies, SSI incidence, and the nature of surgeries and SSI's surveyed. There were over 1.5 million patients included in the 158 studies, with a median of 893 observations per study. Of these patients, 1,157,571 (75.6%) were reported in four studies performing retrospective analysis of the database of the Society of Thoracic Surgeons.[137, 164, 170, 204] Most studies reported on trigger factors for SSI in the chest, with or without inclusion of vascular graft harvest sites (e.g. radial artery or saphenous vein) (93%). Similarly, almost all studies reported trigger factors for CABG (93.7%), with or without other procedures. Only a small minority evaluated trigger factors for SSI following cardiac transplantation (3.8%).

It is difficult to determine some descriptors of the study populations. For example, gender is inconsistently reported. It is also particularly difficult to summarize patient age statistics. All studies reported on adult populations, however three included a small number of teenagers age 13-18.[125, 153, 207] Furthermore, not all studies reported an overall SSI incidence. Only 105 studies reported the number of SSI cases of all depths (total 13,082), and some of these were case-control studies where the proportion of patients with SSI was determined by study design. In 99 studies the incidence of SSI in the study group, or in the larger patient population at the study centre, was reported, and the median incidence was 5.7%.

Table 3.3 describes the SSI definitions used by these studies, and the mechanisms by which they were applied. The most commonly used definition criteria were those of the CDC (43.0% of studies), however locally-created SSI definitions were also common (41.1% of studies). Most studies reported a prospective surveillance strategy (60.8% of studies) to identify SSI cases (this does not imply that the studies were themselves prospective). Furthermore, most studies applied definition criteria universally (64.6% of studies) – i.e. by review of all patients or charts, rather than using triggering methods to concentrate surveillance. There was substantial heterogeneity in the length of surveillance (or follow-up, in clinical studies), with a large number of studies not defining the surveillance period (38.0%).

Table 3.2: Study size, surgical site infections surveyed, surgical site infection incidence, and included surgical procedures for 158 studies of potential trigger factors to identify post-cardiac surgical site infection surveillance

Total study patients (N)		Trigger Factor Goal		Total (158 studies)
		Identification (2 studies)	Risk (156 studies)	
Total study patients (N)		5590	1525545	1531135
Depth of Surgical Site Infection Included in Analysis	Superficial	0 0%	1 0.6%	1 0.6%
	Deep incisional, OS*	2 100.0%	61 39.1%	63 39.9%
	All	0 0%	94 60.3%	94 59.5%
Site of Surgical Site Infection Included in Analysis	Chest	2 100.0%	105 67.3%	107 67.7%
	Vascular Graft Harvest	0 0%	11 7.1%	11 7.0%
	Both	0 0%	40 25.6%	40 25.3%
Median incidence of all-depth surgical site infection†		0%	5.7%	5.7%
Total cases of all-depth surgical site infection (N)‡		0	13082	13082
Median incidence of deep incisional or organ/space surgical site infection††		7.4%	1.5%	1.6%
Total cases of deep incisional or organ/space surgical site infection (N)‡‡		153	9048	9201
Cardiac Surgical Procedures Included	Coronary artery bypass graft	2 100.0%	146 93.6%	148 93.7%
	Cardiac valve repair or replacement	1 50.0%	59 37.8%	60 38.0%
	Multi-procedure operations	1 50.0%	60 38.5%	61 38.6%
	Cardiac transplant	0 0%	6 3.8%	6 3.8%
	Other cardiac surgical procedures	1 50.0%	55 35.3%	56 35.4%
	Not recorded	0 0%	5 3.2%	5 3.2%

*OS = Organ/space infection; †Data from 99 studies reporting incidence of all-depth surgical site infection; ‡Data from 105 studies reporting number of surgical site infection of all depths; ††Data from 99 studies reporting incidence of deep incisional or organ/space surgical site infection; ‡‡Data from 105 studies reporting number of deep incisional or organ/space surgical site infections

Table 3.3: Surveillance strategy, definitions, and operative sites for 158 studies of potential trigger factors to identify post-cardiac surgical site infection surveillance

		Definition of Surgical Site Infection				
		ASEPSIS*	CDC†	In-house definition	Not reported	Total
Total		2 1.3%	68 43.0%	65 41.1%	23 14.6%	158 100.0%
Identification Strategy	**Prospective**	2 100.0%	53 77.9%	36 55.4%	5 21.7%	96 60.8%
	Retrospective	0 0%	11 16.2%	19 29.2%	4 17.4%	34 21.5%
	Mixed	0 0%	1 1.5%	0 0%	0 0%	1 0.6%
	Not reported	0 0%	3 4.4%	10 15.4%	14 60.9%	27 17.1%
Application of Definition Criteria	**Passive Reporting**	0 0%	0 0%	1 1.5%	1 4.3%	2 1.3%
	Triggered	0 0%	8 11.8%	8 12.3%	0 0%	16 10.1%
	Universal	2 100.0%	49 72.1%	43 66.2%	8 34.8%	102 64.6%
	Mixed	0 0%	1 1.5%	0 0%	0 0%	1 0.6%
	Not reported	0 0%	10 14.7%	13 20.0%	14 60.9%	37 23.4%
Duration of Follow-up/ Surveillance for Surgical Site Infection	**1 month or less**	0 0%	13 19.1%	5 7.7%	2 8.7%	20 12.7%
	1 to 12 months	1 50.0%	15 22.1%	20 30.8%	0 0%	36 22.8%
	12 months or more	0 0%	0 0%	0 0%	2 8.7%	2 1.3%
	Per CDC†	0 0%	28 41.2%	0 0%	0 0%	28 17.7%
	Duration of admission	1 50.0%	6 8.8%	5 7.7%	0 0%	12 7.6%
	Not defined	0 0%	6 8.8%	35 53.8%	19 82.6%	60 38.0%

*ASEPSIS = Additional treatment, Serous discharge, Erythema, Purulent discharge, Separation of deep tissues, Isolation of bacteria and duration of inpatient Stay.; †CDC = United States' Centers for Disease Control – duration of follow-up 30 days for most procedures, 365 for deep or organ/space infections following implantation of non-human derived material

3.1.3 Trigger factors reported

The 158 studies included in the systematic review reported a wide variety of potential trigger factors. There were 570 uniquely defined trigger factors, which I then grouped into 80 main trigger

themes, and 165 trigger sub-themes. Triggers fell into nine categories summarized in Table 3.4, along with the goal of the trigger (risk of SSI, versus identification). As with overall study goals (see Section 3.1.2 above), the bulk of triggers were designed to predict risk of SSI (541 [94.9%]).

Table 3.4: Trigger categories and goal of trigger for 570 trigger factors identified in systematic review of 158 studies of potential trigger factors for surveillance of post-cardiac surgical site infection

Trigger Category	Goal of Trigger		Total
	Identification	Risk	
Admission duration	0	12	12
Cardiac disease	0	49	49
Cardiac surgical procedure	0	100	100
Co-morbidity	0	170	170
Complication	2	46	48
Demographic data	0	24	24
Evidence of SSI*	27	8	35
Infection control program structure	0	2	2
Peri-operative management	0	130	130
Total	29	541	570

*SSI = Surgical site infection

After grouping triggers into themes and sub-themes, I then identified the most commonly reported themes. I evaluated the top 20 trigger themes and sub-themes in each of six classes of analysis (see Section 2.3.2 above). Collating these results, I noted 35 trigger themes (see Table 3.5). The most commonly studied trigger theme was a diagnosis of diabetes mellitus (evaluated in 102 analyses, positively associated with SSI in 50%), and the most strongly associated trigger theme was comorbid obesity (evaluated in 98 analyses, positively associated with SSI in 67.3%). Only 10 of 35 themes were significantly associated with SSI in 50% or more of analyses – obesity, post-operative infectious complication, preoperative hypoxia, surgical revision following the index operative episode, internal mammary artery grafting, hyperglycemia, comorbid lung disease, diabetes mellitus, elevated inflammatory markers (erythrocyte sedimentation rate, leukocytosis) and preoperative myocardial infarction.

Table 3.5: Trigger themes most frequently associated with cardiac surgical site infection in systematic review of the literature

Trigger Theme	Trigger Goal	Total analyses	Overall association	Studies with significant association (%)
Comorbid obesity*	Risk	98	Positive	67.3%
Complication infection	Identification	9	Positive	66.7%
Hypoxic preoperatively	Risk	5	Positive	60.0%
Revision/Resternotomy	Risk	30	Positive	60.0%
Internal mammary artery grafting	Risk	58	Positive	56.9%
Hyperglycemic	Risk	13	Positive	53.8%
Comorbid lung disease	Risk	37	Positive	51.4%
Diabetes mellitus	Risk	102	Positive	50.0%
Inflammatory markers	Identification	6	Positive	50.0%
Myocardial infarction preoperatively	Risk	10	Positive	50.0%
Unique factors	Risk	17	Positive	47.1%
Transfusion	Risk	32	Positive	46.9%
Comorbid smoking*	Risk	28	Positive	46.4%
Preoperative admission longer	Risk	11	Positive	45.5%
Non-routine postoperative instrumentation (e.g. tracheostomy)	Risk	9	Positive	44.4%
Non-caucasian ethnicity	Risk	9	Positive	44.4%
Duration of index operative episode	Risk	7	Positive	42.9%
Multiple-procedure operative episode	Risk	14	Positive	42.9%
Comorbid renal failure	Risk	35	Positive	40.0%
Coronary artery graft number greater	Risk	5	Positive	40.0%
Immunodeficiency	Risk	5	Positive	40.0%
Interactive factors	Risk	5	Positive	40.0%
Prior cardiac intervention	Risk	30	Positive	40.0%
Urgent index operative episode	Risk	5	Positive	40.0%
Wound appearance/complications*	Identification	10	Positive	40.0%
Wound therapy	Identification	5	Positive	40.0%
Cerebro- or peripheral vascular disease	Risk	43	Positive	39.5%
Duration of mechanical ventilation†	Risk	28	Positive	39.3%
Intensive care unit	Risk	18	Positive	38.9%
Older age	Risk	6	Positive	33.3%
CABG in index operative episode	Risk	7	Positive	28.6%
Infection control programs†	Risk	11	Inverse	27.3%
Female gender	Risk	8	Positive	25.0%
Comorbid heart failure	Risk	13	Positive	23.1%
Comorbid hypertension	Risk	5	Inverse	20.0%

*For these three trigger themes we could only generate crude approximation; †For these two trigger themes we could not generate any potential trigger factor

3.1.4 Selection of trigger themes

We could not use all of the trigger themes and sub-themes. Of 35 reported themes, two were considered unusable. For one theme (duration of mechanical ventilation) data were not readily available in the OHDW. The other unusable theme was the system-wide implementation of new infection prevention and control programs. We had no such system-wide changes at our centre during the study period. This left 33 usable themes, for three of which (obesity, smoking, and wound appearance /complications) I could only use ICD-10-CA codes, rather than the more detailed data more commonly used in the literature (body mass index, pack-year history, and clinical description respectively).

As Table 3.5 demonstrates, there was a paucity of "identification factors" amongst the evaluated trigger themes. Of 35 themes, 31 were risk factors for acquisition of SSI, and four were factors to identify SSI after acquisition - diagnosis of infectious complication, presence of elevated inflammatory markers, description of postoperative wound appearance/complications (dehiscence, drainage, hematoma, number and size of wounds), and application of therapy for SSI (surgical, dressings, or antibiotics). Furthermore, as noted above, I could only develop a relatively crude trigger factor for the theme wound appearance/complications.

We developed nine additional trigger themes by consensus of investigators. Four were specifically "identification" themes (involvement of the infectious diseases service in patient care, use/outcome of diagnostic radiology for SSI, prolonged postoperative admission, and readmission for care of SSI). We also defined a further five "risk" themes – rejection of cardiac transplantation, implantation of non-human-derived or prosthetic material, presence of infection or significant bacterial colonization at a locus remote to surgical site, overall health/comorbidity status of patient, and annual quarter in which index operative episode was performed.

We elaborated trigger factors from selected themes according to usage in the literature, and data available in the OHDW. Combining nine investigator created themes with 33 usable themes from the systematic review, I had 42 main trigger themes from which to elaborate specific trigger factors. From these 42 trigger themes I defined 158 unique trigger factors (see Appendix B:). Of these, 91 were trigger factors defined from 35 'risk' themes, and 67 were trigger factors defined from 7 'identification' themes.

3.2 Nested case-control study

3.2.1 Creation of study group

3.2.1.1 Preliminary identification of cases and controls

I constructed the study cohort using the OHDW. This yielded 3744 individual operative "episodes" among 3707 patients (median 1 episode per patient, range 1 to 3). Table 3.6 lists the surgical procedures undertaken during the 3744 operative episodes. The most common surgical procedure performed was CABG – either as the sole procedure (2114 episodes [56.5%]), or in combination with another procedure (765 episodes [20.4%]). The least frequently performed procedure was cardiac transplant (39 episodes [1%]).

Table 3.6: Surgical Procedures Performed in Cohort of 3744 Episodes of Cardiac Surgery at the University of Ottawa Heart Institute from July 1 2004 to June 30 2007

		Implantation of Non-Human Material		**Total** (N = 3744)
		Yes (N =1345)	**No** (N = 2399)	
Number of Cardiac Procedures (Median)		2	1	1
Cardiac Surgical Procedure	**Coronary Artery Bypass Graft**	2 0.1%	2112 88.0%	2114 56.5%
	Coronary Artery Bypass Graft/Combined Procedure	544 40.4%	221 9.2%	765 20.4%
	Cardiac Valve Repair or Replacement	398 29.6%	17 0.7%	415 11.1%
	Cardiac Valve Repair or Replacement/Combined Procedure	401 29.8%	10 0.4%	411 11.0%
	Cardiac Transplant	0 0%	9 0.4%	9 0.2%
	Cardiac Transplant/Combined Procedure	0 0%	30 1.3%	30 0.8%

I preliminarily identified cases using the records of TOH-IPCP (see Section 2.4.4). During the study period (July 1 2004 to June 30 2007), TOH-IPCP reviewed the records of 976 cardiac surgery operative episodes. Of these, 184 (18.9%) had been identified as SSI following a procedure of interest (CABG, cardiac valve repair, cardiac valve replacement, or cardiac transplant). A further 10 (1.0%) cases were confirmed as SSI following other cardiac procedures (1 insertion of a

ventricular assist device, 3 insertions of an implanted cardiac defibrillator, 1 revision of a cardiac pacemaker, 1 repair of complex congenital heart defect, 1 closure patent foramen ovale, and 3 repair or resection of thoracic aortic aneurysm). The remaining 782 (80.1%) records were falsely trigger-positive using the current trigger mechanism.

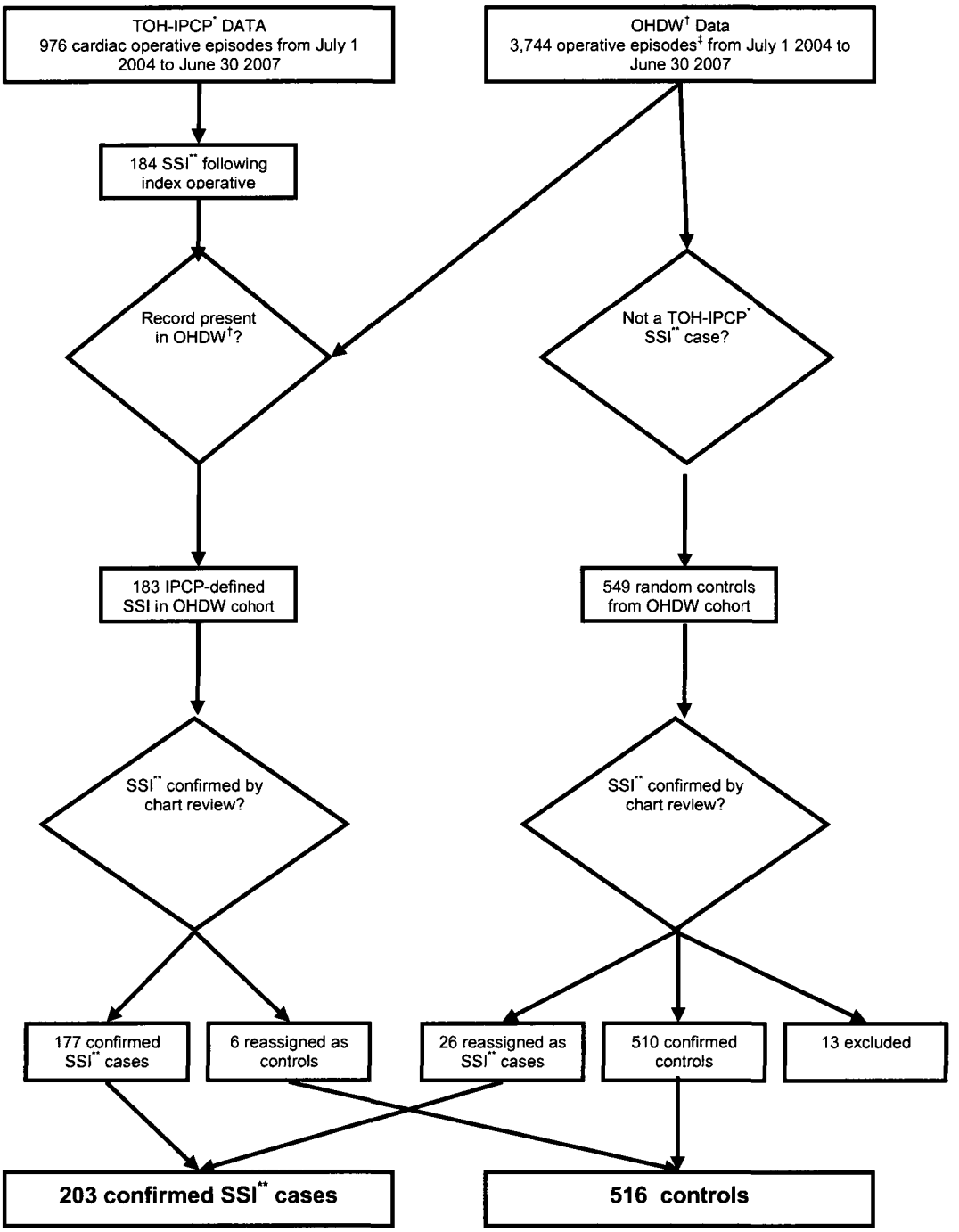
I defined these 184 SSI cases as my preliminary case group, and selected controls. Correlating TOH-IPCP data with OHDW data, I could not locate 1 of these cases in the cohort of 3744 operative episodes, leaving 183 cases in the preliminary case study group. I censored these from the cohort, and randomly selected 549 other operative episodes from the remaining 3561 in the cohort. These 549 operative episodes occurred in 547 patients, and formed the preliminary control group. One patient who had an operative episode in the case group also had an operative episode in the control group. In total the preliminary study group contained 732 operative episodes among 729 patients, where 3 patients had 2 episodes each.

3.2.1.2 Chart review and confirmation of case status.

Of 183 preliminary cases and 549 preliminary controls, I excluded 13 preliminary controls (see Figure 3.2). This included 12 operative episodes undertaken for correction of underlying endocarditis (therefore not clean surgery), and one observation where the operative episode recorded in the OHDW could not be confirmed upon chart review. Among these 13 excluded episodes were the second episodes from each of 3 patients with 2 episodes in the preliminary control group. This left 719 operative episodes among 719 patients.

Of these 719 observations, 646 (89.8%) were followed up at subsequent encounters within 14 days following a standard surveillance period – at a cardiac surgery or cardiology outpatient clinic in 340 (52.7%) instances. Clinical records were unavailable for 87 (25.6%) control observations, as they had attended the cardiac surgery outpatient clinic (see Section 2.4.3.3). Of the 73 observations not seen in follow-up within a standard surveillance period, six (8.2%) had been diagnosed with SSI during their index admission. A further 32 (43.8%) were eventually seen at the UOHI or the Ottawa Hospital at a later date (not necessarily for post-operative care). Thus, 35 control observations were seen at our centre only during the index admission, and were subsequently lost to surveillance follow-up.

Figure 3.2: Identification, selection, and confirmation of surgical site infection cases and uninfected controls from a cohort of cardiac surgery operative episodes performed at the University of Ottawa Heart Institute from July 1 2004 to June 30 2007



*TOH-IPCP – The Ottawa Hospital Infection Prevention and Control Program; †OHDW – Ottawa Hospital Data Warehouse; ‡Coronary artery bypass graft, cardiac valve repair/replace, cardiac transplant; ** SSI – surgical site infection

I found several operative episodes requiring reassignment of case or control status. I reassigned six observations from the case group to the control group. In each of these 6 observations I disagreed with the status assigned by the TOH-IPCP. I also reassigned 26 observations from the control group to the case group. Of these 26 observations, 13 had been reviewed by TOH- IPCP and deemed to be non-cases. Therefore I disagreed with the SSI status assigned by TOH-IPCP in 19 observations.

The final study group contained 203 cases of SSI (detailed in Table 3.7), and 516 uninfected controls. Of the 203 cases of SSI, 122 (60.1%) were diagnosed following discharge from the index admission at subsequent inpatient admissions, or clinic or emergency room visits. The majority (122 [60.1%]) were superficial incisional SSI's, the remainder deep incisional or organ/space (81 [39.9%]). A minority were infection in vascular graft harvest sites - 32 cases (15.8% of all cases, or 17.3% of cases having undergone CABG). Using the stratified calculation described in Section 2.4.5, the cohort-wide SSI incidence is 9.7% (95% CL 8.0%, 11.4%). The incidence of deep or organ/space SSI is 3.1% (95%CL 2.3%, 3.8%).

Table 3.7: Depth and surgical site of 203 cases of surgical site infection following cardiac surgery at the University of Ottawa Heart Institute from July 2004 to June 2007

		SSI* diagnosed after discharge from index admission		Total (N=203)
		Yes (N=122)	No (N=81)	
Depth of SSI* (Per CDC† Definition Criteria	**Superficial Incisional**	71 58.2%	51 63.0%	122 60.1%
	Deep Incisional	41 33.6%	25 30.9%	66 32.5%
	Organ/space	10 8.2%	5 6.2%	15 7.4%
Surgical site of SSI*	**Sternum/ Mediastinum**	100 82.0%	71 87.7%	171 84.2%
	Arm/Radial Artery	4 3.3%	1 1.2%	5 2.5%
	Leg/Saphenous Vein	18 14.8%	9 11.1%	27 13.3%

*SSI = Surgical site infection; †CDC: United States' Centers for Disease Control

3.2.1.3 Description of cases and controls

Table 3.8 lists the demographic and surgical data pertaining to cases and controls. The mean age was 65.36 ± 11.01 years, and males comprised the majority of both cases and controls (overall 477 [66.3%]). While some observations had as many as 7 major cardiac procedures during the index operative episode, the majority of episodes were single-procedure (487 [67.9%]). The most common procedure performed was CABG, either as the sole procedure (422 [58.7%]) or in a combined operative episode (155 [21.6%]). Only 8 operative episodes included cardiac transplantation. Similarly, only a minority of operative episodes involved implantation of non-human derived material (245 [34.1%]).

Table 3.8: Demographic factors and surgical procedures among 203 cases of surgical site infection and 516 uninfected controls following cardiac surgery at the University of Ottawa Heart Institute from July 2004 to June 2007

		Confirmed SSI*		Total (N=719)
		Yes (N=203)	No (N=516)	
Age in Years (Mean ± Standard Deviation)		64.72 ± 11.02	65.62 ± 11.00	65.36 ± 11.01
Gender	**Female**	73 36.0%	169 32.8%	242 33.7%
	Male	130 64.0%	347 67.2%	477 66.3%
Number of Cardiac Procedures (Median [Range])		1 [1, 5]	1 [1, 7]	1 [1, 7]
Cardiac Surgical Procedure	**Coronary Artery Bypass Graft**	126 62.1%	296 57.4%	422 58.7%
	Coronary Artery Bypass Graft/Combined Procedure	59 29.1%	96 18.6%	155 21.6%
	Cardiac Valve Repair or Replacement	8 3.9%	55 10.7%	63 8.8%
	Cardiac Valve Repair or Replacement/Combined Procedure	7 3.4%	64 12.4%	71 9.9%
	Cardiac Transplant	. .	2 0.4%	2 0.3%
	Cardiac Transplant/Combined Procedure	3 1.5%	3 0.6%	6 0.8%
Implantation of Non-Human Material		56 27.6%	189 36.6%	245 34.1%

* SSI = Surgical Site Infection

Table 3.9 lists operative details of the 677 (80.3%) of observations who underwent CABG, using procedure codes recorded in the OHDW. The median number of coronary artery grafts performed was 3, and 517 (89.6%) operative episodes included use of an internal mammary artery (IMA) graft. Only 2 episodes were coded as using bilateral internal mammary arteries (BIMA) (see section 3.2.3 below). A similar proportion of observations also had an excised saphenous vein or radial artery graft (511 [88.6%]). Similarly, the preponderance of index operative episodes required the use of cardiopulmonary bypass (CPB) (524 [90.8%]).

Table 3.9: Graft Type and Cardiopulmonary Bypass Pump Use in 185 Cases of SSI* and 392 Controls Undergoing CABG†

		Confirmed SSI*		Total (N=577)
		Yes (N=185)	No (N=392)	
Number of Coronary Grafts (Median)		3	2	3
Internal Mammary Artery Graft	**None**	18 9.7%	42 10.7%	60 10.4%
	Unilateral	167 90.3%	348 88.8%	515 89.3%
	Bilateral	. .	2 0.5%	2 0.3%
Excised Venous or Radial Artery Graft		170 91.9%	341 87.0%	511 88.6%
Use of CPB‡		167 90.3%	357 91.1%	524 90.8%

*SSI = Surgical Site infection; †CABG = Coronary Artery Bypass Graft; ‡CPB = Cardiopulmonary Bypass Pump

3.2.2 Derivation of electronic trigger models

3.2.2.1 Construction of initial trigger models

From the systematic review I constructed 158 trigger factors (see Appendix B:). Of these I eliminated 116 before logistic regression modelling: 13 trigger factors had data missing for 1 or more observation; 57 were positive in less than 10% of all observations, 3 were negative in less than 10% of all observations, and 43 I deemed less clinically relevant than other factors constructed with the same data elements. This left 42 trigger factors in the initial model, of which 17 did not use data from

the Health Records Abstract (HRA). From these I constructed two initial models – a larger one including HRA data, and a smaller one excluding HRA data.

3.2.2.2 Identification and management of multicollinearity

I evaluated the trigger factors in each initial model for multicollinearity. Of the 42 trigger factors in the larger model, there were 15 that exhibited significant multicollinearity. Of these, I eliminated four, transformed five (by duration of postoperative stay), and retained six. Of the five continuous variables that I transformed, four still displayed significant multicollinearity after transformation, and were eliminated. After this there were 34 trigger factors remaining in the model, (Table 3.10, Table 3.11, and Table 3.12) of which two (diagnosis in keeping with an SSI and implantation of non-human derived material) still had mild multicollinearity (tolerance 0.38 and 0.38 respectively).

There were fewer trigger factors exhibiting multicollinearity in the initial set used for the smaller (non-HRA) model. Of the 18 trigger factors initially included, six demonstrated multicollinearity. Of these, I excluded one, and transformed four by duration of postoperative stay. Despite transformation, three of these trigger factors still demonstrated multicollinearity, and I eliminated them. This left 14 trigger factors, with no further evidence of multicollinearity (Table 3.10, Table 3.11, and Table 3.12).

Table 3.10: Dichotomous trigger factors in initial logistic regression models to trigger surveillance of surgical site infection following cardiac surgery at the University of Ottawa Heart Institute

Trigger Factor	In larger model	In smaller model	SSI* Cases (N = 203)	Controls (N = 516)
Computed tomography report with mention of specific SSI terms	Yes	Yes	108 53.2%	16 3.1%
Female gender	Yes	Yes	73 35.9%	169 32.8%
Postoperative white cell count above 16 * 10e9 cells/L	Yes	Yes	102 50.2%	159 30.8%
Significant pathogen growth in culture, or any amount of polymorphonucleocytes on gram stain	Yes	Yes	189 93.1%	88 17.1%
Readmission with admitting diagnosis of SSI*	Yes	Yes	76 37.4%	5 1.0%
Readmission to emergency room/reference centre, or coded as urgent	Yes	Yes	129 63.5%	118 22.9%
Selected systemic antibiotics started on or after postoperative day 2	Yes	Yes	168 82.8%	93 18.0%
Serum glucose on day of index operative episode greater than 11.1 mmol/L	Yes	Yes	32 15.8%	44 8.5%
Preoperative creatinine greater than 106 umol/L	Yes	Yes	57 28.1%	116 22.5%
Comorbid congestive heart failure	Yes	No	106 52.2%	166 32.2%
Comorbid chronic obstructive pulmonary disease	Yes	No	38 18.7%	35 6.8%
Comorbid chronic renal failure	Yes	No	64 31.5%	88 17.1%
Comorbid cerebrovascular or peripheral vascular disease	Yes	No	26 12.8%	68 13.2%
Diagnosis of postoperative wound/graft/implant infection (definite SSI*)	Yes	No	158 77.8%	27 5.2%
Comorbid diabetes mellitus, or complication	Yes	No	118 58.1%	178 34.5%
Comorbid hypertension	Yes	No	148 72.9%	361 70.0%
Infectious disease service consulted	Yes	No	107 52.7%	31 6.0%
Myocardial infarction in index admission	Yes	No	62 30.5%	101 19.6%
Implantation of any nonhuman material	Yes	No	56 27.6%	189 36.6%
Postoperative pneumonia, urinary tract infection, or cellulitis	Yes	No	36 17.7%	60 11.6%
Resternotomy following index operative episode	Yes	No	61 30.0%	41 7.9%
Transfusion of red blood cells during index admission	Yes	No	152 74.9%	321 62.2%
Surgical revision, debridement, aspiration, or repair of damage due to SSI*	Yes	No	56 27.6%	4 0.8%
Intra- or post-operative wound complication dehiscence, hemorrhage, or operative misadventure	Yes	No	76 37.4%	115 22.3%

*SSI: Surgical Site Infection; †DM: Diabetes mellitus

Table 3.11: Categorical trigger factors in initial logistic regression models to trigger surveillance of surgical site infection following cardiac surgery at the University of Ottawa Heart Institute

Trigger Factor		In larger model	In smaller model	SSI* Cases (N = 203)	Controls (N = 516)
Interaction term for comorbid diabetes mellitus and female gender	Female, with DM†	Yes	No	46 22.7%	57 11.0%
	Female, no DM†			27 13.3%	112 21.7%
	Male, with DM†			72 35.5%	121 23.5%
	Male, no DM†			58 28.6%	226 43.8%
Yearly quarter of index operative episode	Jan-Feb-Mar	Yes	Yes	54 26.6%	134 26.0%
	Apr-May-Jun			60 29.6%	110 21.3%
	Jul-Aug-Sep			40 19.7%	141 27.3%
	Oct-Nov-Dec			49 24.1%	131 25.4%

*SSI: Surgical Site Infection; †DM: Diabetes mellitus

Table 3.12: Continuous trigger factors in initial logistic regression models to trigger surveillance of surgical site infection following cardiac surgery at the University of Ottawa Heart Institute

Trigger Factor	In larger model	In smaller model	SSI* Cases (N = 203) (Mean)	Controls (N = 516) (Mean)
Age on index admission (Years)	Yes	Yes	64.72	65.62
Number of postoperative blood cultures, transformed by postoperative stay	Yes	Yes	0.17	0.03
Days in critical care unit, transformed by postoperative stay	Yes	No	0.40	0.28
Number of principle cardiac procedures in index operative episode	Yes	No	1.49	1.47
Number of coronary bypass graft vessels	Yes	No	2.34	1.80
Preoperative stay (days)	Yes	No	3.44	3.15
Postoperative stay (days)	Yes	No	20.65	9.66
Duration of index operative episode (minutes)	Yes	No	377.95	345.99
Duration of likely systemic antibiotics (days)	No	Yes	3.41	0.37

*SSI: Surgical Site Infection

3.2.2.3 Model selection

Having eliminated multicollinearity, I then created my final models using a multistep process (see Section 2.4.6.4).

3.2.2.3.1 Model set including HRA data

The results of the initial stepwise selection procedure created 33 models, containing up to 34 potential trigger factors. Among these, the AIC-optimized model contained 12 variables (AIC = 288.355), and the IC(1) "right border" model contained 13 variables (IC(1) = 275.412). From this range of variables I constructed 10 best subsets (see Appendix C:). There was minimal heterogeneity of variable selection among these 10 models. Nine trigger factors were included in all 10 candidate models, four in 5-9 candidate models, and three in less than five. Seventeen potential trigger factors were not retained in any of the candidate logistic regression models.

The candidate model offering the lowest AIC (288.238) included twelve trigger factors: comorbid congestive heart failure; surgical revision, debridement, aspiration, or repair of damage due to SSI; computed tomography report with mention of specific SSI terms; diagnosis of postoperative wound/graft/implant infection (definite SSI); significant pathogen growth in blood, tissue, or wound culture, or rare or more polymorphs on gram stain; number of coronary bypass graft vessels; postoperative stay in days; readmission with admitting diagnosis of SSI; readmission to emergency room/reference centre, or coded as urgent; preoperative creatinine greater than 106 umol/L; selected systemic antibiotics started on or after postoperative day 2; and serum glucose on day of index operative episode greater than 11.1 mmol/L.

The AIC-optimized model performed well, but partially contradicted *a priori* expectations of association. The model displayed good explanatory power: c-statistic (area under the receiver-operator characteristic [ROC] curve) was 0.973; the Hosmer-Lemeshow Goodness-of-Fit p-value was 0.167. However, the parameter estimate was unexpectedly negative for preoperative creatinine greater than106 µmol/L (parameter estimate -0.94). As this result was opposite to the expected relationship I omitted this trigger factor from the final model. This left eleven trigger factors in the final model for this trigger mechanism.

3.2.2.3.2 Model set excluding HRA data

In the smaller model set the initial stepwise selection process created 14 models including up to 13 trigger factors. Among these, the AIC-optimized model contained 7 variables (AIC = 347.131), and the IC(1) "right border" model contained 10 variables (IC(1) = 335.843). From this range of

variables I constructed 20 best subsets (see Appendix D:). There was minimal heterogeneity of variable selection among these 20 models. Six trigger factors were included in all 20 candidate models, two in 10-19 candidate models, and four in less than 10. One trigger factor was not included in any candidate model: the yearly quarter during which the index operative episode took place.

The candidate model offering the lowest AIC (347.131) included seven trigger factors: duration of likely systemic antibiotics in days; computed tomography report with mention of specific SSI terms; significant pathogen growth in blood, tissue, or wound culture, or rare or more polymorphs on gram stain; readmission with admitting diagnosis of SSI; readmission to emergency room/reference centre, or coded as urgent; selected systemic antibiotics started on or after postoperative day 2; and female gender. There were no qualitatively unexpected parameter estimates for the seven included trigger factors. This seven-factor trigger mechanism model was identical to the AIC-optimized model produced by the initial stepwise selection strategy.

Table 3.13: Parameter estimates, odds ratio estimates and 95% confidence limits for trigger factors included in the surgical site infection surveillance electronic trigger mechanism including data from the Health Records Abstract

Trigger Factor	Parameter Estimate	Odds Ratio Estimates		
		Estimate	95% Wald Confidence Limits	
Intercept	-6.3549	.	.	.
Diagnosis of postoperative wound/graft/implant infection (definite SSI*)	2.6588	14.279	6.479	31.468
Significant pathogen growth in blood, tissue, or wound culture, or rare or more polymorphs on gram stain	2.5897	13.326	6.392	27.780
Readmission to emergency room/reference centre, or coded as urgent	1.4384	4.214	2.039	8.711
Computed tomography report with mention of specific SSI* terms	0.9334	2.543	0.971	6.663
Surgical revision, debridement, aspiration, or repair of damage due to SSI*	0.8139	2.257	0.525	9.701
Readmission with admitting diagnosis of SSI*	0.6658	1.946	0.542	6.991
Congestive heart failure	0.6583	1.932	0.987	3.780
Number of coronary artery grafts	0.6175	1.854	1.353	2.542
Selected systemic antibiotics started on or after postoperative day 2	0.3942	1.483	0.667	3.297
Serum glucose on day of index operative episode greater than 11.1 mmol/L	0.4613	1.586	0.558	4.511
Postoperative admission duration (days)	0.0130	1.013	0.994	1.033

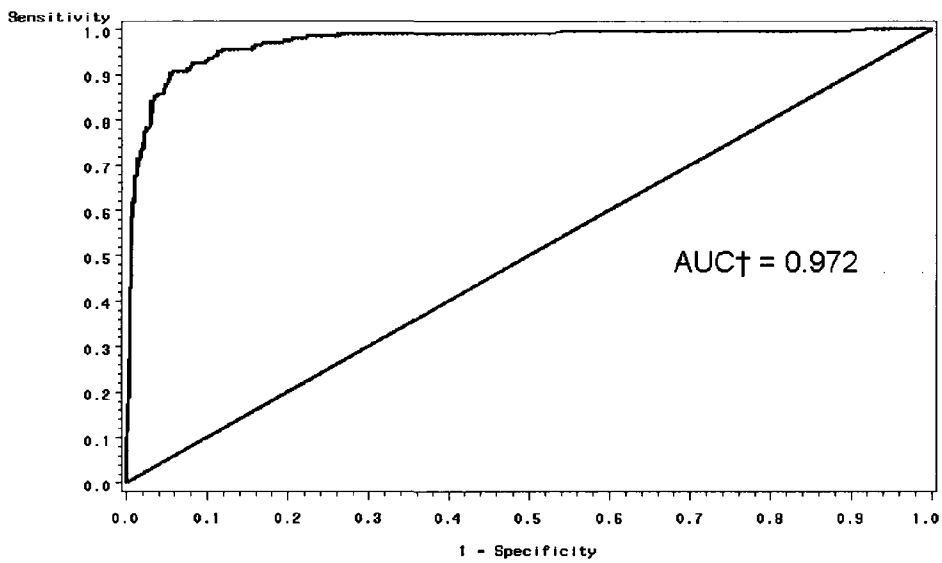
SSI: Surgical Site Infection

3.2.2.4 Evaluation of electronic trigger model estimates and goodness-of-fit

3.2.2.4.1 Model estimates and goodness-of-fit for model including HRA data

For the larger trigger mechanism, the final logistic model for the electronic trigger mechanism contained eleven trigger factors. Table 3.13 details the odds ratios and parameter estimates for the eleven trigger factors used in the model. Amongst the dichotomous trigger factors, ICD-10 code reflecting SSI and significant pathogen growth in culture/polymorphs on gram stain had the highest odds ratios, (14.279 and 13.326 respectively). The lowest odds ratio for a dichotomous trigger factor was that for serum glucose on day of index operative episode greater than 11.1 mmol/L (1.586). Increased duration of post-operative admission had an odds ratio of 1.013 for each additional day. Seven of the eleven trigger factors had odds ratio confidence limits that crossed unity. This logistic regression model displayed excellent goodness-of-fit. Figure 3.3 demonstrates the ROC for the model set including HRA data. Of note, the area under the curve (i.e. c-statistic) is 0.972.

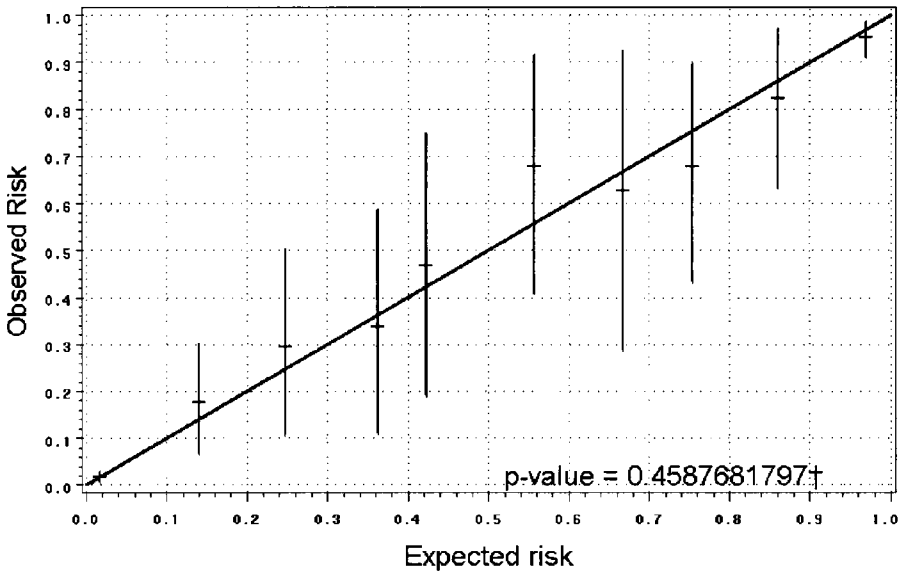
Figure 3.3: Receiver operator characteristic curve for surgical site infection surveillance electronic trigger mechanism including data from the Health Records Abstract



*HRA = Health Records Abstract; †AUC = Area under the curve

Figure 3.4 is a calibration curve, a visual analog to the Hosmer-Lemeshow goodness-of-fit test. The confidence limits all cross the line of slope = 1, and the Hosmer-Lemeshow p-value is non-significant at 0.459, indicating no significance difference between observed and expected probability of SSI.

Figure 3.4: Calibration curve for surgical site infection surveillance electronic trigger mechanism including data from the Health Records Abstract



*HRA = Health Records Abstract; †Per Hosmer-Lemeshow statistic

3.2.2.4.2 Model estimates and goodness-of-fit for model excluding HRA data

The logistic regression model excluding HRA data performed similarly to the larger model. Table 3.14 demonstrates the parameter estimates, odds ratios, and 95% confidence limits for the seven trigger factors included in the model. Much as with the larger model, review of microbiology results using TOH-IPCP criteria bears the highest odds ratio (21.428), whereas female gender bears the lowest amongst dichotomous trigger factors (1.617). Two of seven trigger factors had odds ratio estimate 95% confidence limits that crossed unity.

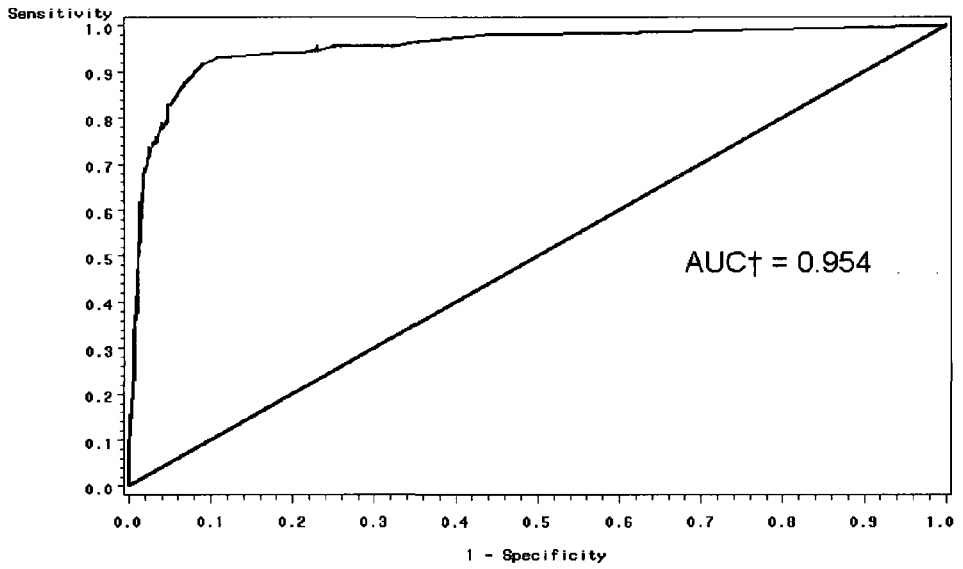
Table 3.14: Parameter estimates, odds ratio estimates and 95% confidence limits for trigger factors included in the surgical site infection surveillance electronic trigger mechanism excluding data from the Health Records Abstract

Trigger Factor	Parameter Estimate	Odds Ratio Estimates		
		Point Estimate	95% Wald Confidence Limits	
Intercept	-4.5998	.	.	.
Significant pathogen growth in blood, tissue, or wound culture, or rare or more polymorphs on gram stain	3.0647	21.428	10.939	41.973
Computed tomography report with mention of specific SSI[†] terms	1.4895	4.435	1.950	10.085
Selected systemic antibiotics started on or after postoperative day 2	1.3354	3.801	1.902	7.600
Readmission with an initial presenting diagnosis consistent with SSI[*]	1.2367	3.444	1.126	10.533
Readmission to emergency room/reference centre, or coded as urgent	1.0651	2.901	1.555	5.414
Female gender	0.4804	1.617	0.893	2.926
Duration of selected systemic antibiotics (days)	00.0958	1.101	0.952	1.272

[*]SSI: Surgical Site Infection

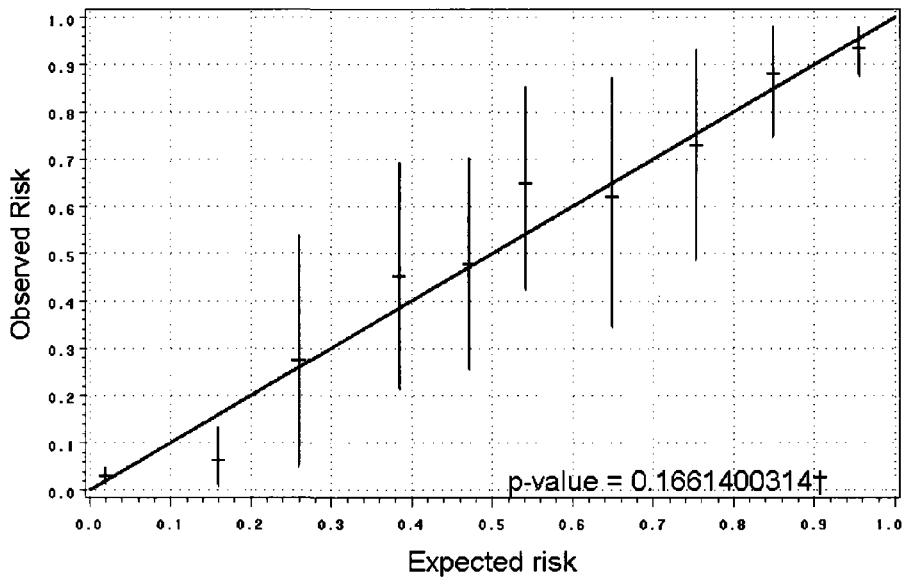
The smaller trigger mechanism model also displayed reasonable goodness-of-fit. Figure 3.5 displays the ROC for the model excluding HRA data, and the AUC is 0.954. The calibration curve in Figure 3.6 displays confidence limits crossing the line of slope = 1 for all deciles of expected risk except the second, wherein the observed risk is less than would be predicted. In this decile were two observations believed to likely be true SSI, but classed as controls as chart review could not confirm the date of onset within the standard surveillance period. Despite this one decile, the overall Hosmer-Lemeshow p-value is 0.166, indicating no significant difference between observed and expected risk.

Figure 3.5: Receiver operator characteristic curve for surgical site infection surveillance electronic trigger mechanism excluding data from the Health Records Abstract



*HRA = Health Records Abstract; †AUC = Area under the curve

Figure 3.6: Calibration curve for surgical site infection surveillance electronic trigger mechanism excluding data from the Health Records Abstract



*HRA = Health Records Abstract; †Per Hosmer-Lemeshow statistic

3.2.2.5 Dichotomization, and comparison to current trigger mechanism

3.2.2.5.1 Accuracy of current trigger mechanism

As expected, the current trigger mechanism has reasonable sensitivity and specificity, with poor positive predictive value. Table 3.15 is a two-by-two table of the outcome of the current TOH-IPCP trigger mechanism for surveillance, against SSI status as confirmed by chart review. The TPR (i.e. sensitivity) is 0.936, and the FPR (1 – specificity) is 0.167. For post-discharge SSI, the TPR was 0.926. Using the estimated cohort-wide SSI prevalence of 9.7% (see Sections 2.4.6.7 and 3.2.1.2), the estimated PPV is 0.38 (95% CL 0.33, 0.42).

Table 3.15: Two-by-two table of the sensitivity and specificity of the current mechanism to trigger surveillance of cardiac surgical site infection, against surgical site infection status, as confirmed by chart review

Current Trigger Mechanism	**Confirmation by chart review**		
	SSI* present	**SSI* absent**	**Total**
Positive	190	86	276
Negative	13	430	443
Total	203	516	719

$Specificity_C$ = 83.3%
FPR_C[†] = 0.167
$Sensitivity_C$ = 93.6%
TPR_C[‡] = 0.936

*SSI = Surgical Site Infection; [†]FPR_C = False Positive Ratio of the current trigger; [‡]TPR_C = True Positive Ratio of the current trigger

3.2.2.5.2 Dichotomization, and relative accuracy of electronic trigger mechanism including Health Records Abstract Data

I selected a probability cut-point using the methodology in Section 2.4.6.6. Using the probabilities calculated from the logistic regression model, I identified that subset of cut-points within which sensitivity was 0.936 or higher. From that subset I selected the probability which maximized the specificity. That cut-point probability was 0.19. I therefore defined "trigger positive" for the

electronic trigger mechanism (including HRA data) as having a probability greater than or equal to 0.19. Applying that dichotomy to the study group, I identified 191 true positives, 12 false negatives, 460 true negatives, and 56 false positives. This gives a TPR of 0.941 and FPR of 0.1085 (i.e. specificity of 0.8915) (see Table 3.18). The TPR for post-discharge SSI was 0.934. Using the estimated cohort-wide SSI prevalence of 9.7% (see Sections 2.4.6.7 and 3.2.1.2), the estimated PPV is 0.48 (95% CL 0.42, 0.54).

Table 3.16: Paired two-by-two tables comparing accuracy of electronic trigger mechanism (including data from the Health Records Abstract) with The Ottawa Hospital Infection Prevention and Control Program's current mechanism to trigger cardiac surgical site infection surveillance

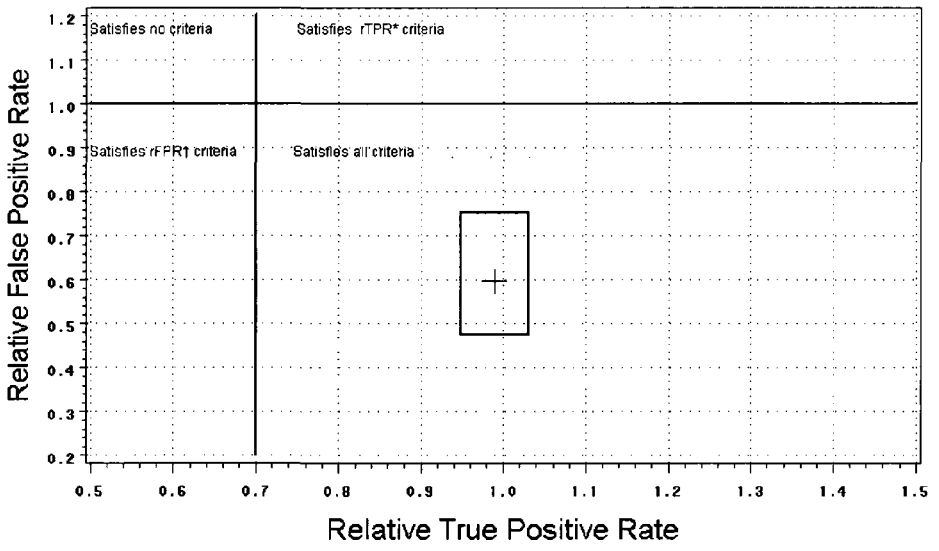
Confirmed SSI*						**No SSI***		
	CTM† +	CTM† -				CTM† +	CTM† -	
ETM‡ +	183	8	191		**ETM‡ +**	41	15	56
ETM‡ -	7	5	12		**ETM‡ -**	45	415	460
	190	13	203			86	430	516

Relative true positive ratio ($rTPR_{E:C}$) = 1.01 (0.97, 1.05)
Relative false positive ratio ($rFPR_{E:C}$) = 0.65 (0.52, 0.81)

*SSI = Surgical Site Infection; †CTM = Current Trigger Mechanism; ‡ETM = Electronic Trigger Mechanism

The accuracy of the HRA-inclusive electronic trigger mechanism compared favourably with the current TOH-IPCP trigger mechanism. Table 3.16 demonstrates that comparison in a paired two-by-two table, from which $rTPR_{E:C}$ and $rFPR_{E:C}$ are calculated. The $rTPR_{E:C}$ is 1.01 (95% CL 0.97, 1.05) and the $rFPR_{E:C}$ is 0.65 (95% CL 0.52, 0.81). The confidence limits of $rTPR_{E:C}$ and $rFPR_{E:C}$ are calculated jointly, and plotted in two dimensions in Figure 3.7. The confidence limits of $rTPR_{E:C}$ are entirely greater than 0.7 (to the right on the graph,) indicating non-inferiority of sensitivity (see Section 2.4.6.7); and the confidence limits of $rFPR_{E:C}$ are entirely less than 1.0 (below, on the graph), indicating superiority of specificity.

Figure 3.7: Plot of relative true positive rate and relative false positive rate, with joint 95% confidence limits, comparing the electronic trigger mechanism (including Health Records Abstract data) to The Ottawa Hospital Infection Prevention and Control Program's current mechanism to trigger cardiac surgical site infection surveillance



*In comparison to the current trigger mechanism; †HRA = Health Records Abstract
*rTPR = Relative True Positive Rate; †FPR = Relative False Positive Rate

3.2.2.5.3 Dichotomization, and relative accuracy of electronic trigger mechanism excluding Health Records Abstract Data

I dichotomized this model using the same mechanism as for the HRA-data-inclusive model. Using a minimum TPR of 0.936, I identified a probability cut-off of 0.18 as the level at or above which I would optimized specificity. Using this dichotomy I identified 189 true positives, 14 false negatives, 460 true negatives, and 56 false positives. The overall TPR was 0.931) and the FPR was 0.1085 (i.e. specificity of 0.8915) (see Table 3.18). For post-discharge SSI, TPR was 0.934. Using the estimated cohort-wide SSI prevalence of 9.7% (see Sections 2.4.6.7 and 3.2.1.2), the estimated PPV is 0.48 (95% CL 0.42, 0.54).

I then calculated the relative true and false positive ratios, in comparison to the current trigger mechanism. Table 3.17 shows the paired two-by-two tables, demonstrating the $rTPR_{E:C}$ is 0.99 (95% CL 0.96, 1.03) and the $rFPR_{E:C}$ is 0.65 (95% CL 0.52, 0.82). As Figure 3.8 demonstrates, the joint

confidence limits for the $rTPR_{E:C}$ and $rFPR_{E:C}$ satisfy criteria for superiority of specificity and non-inferiority of sensitivity.

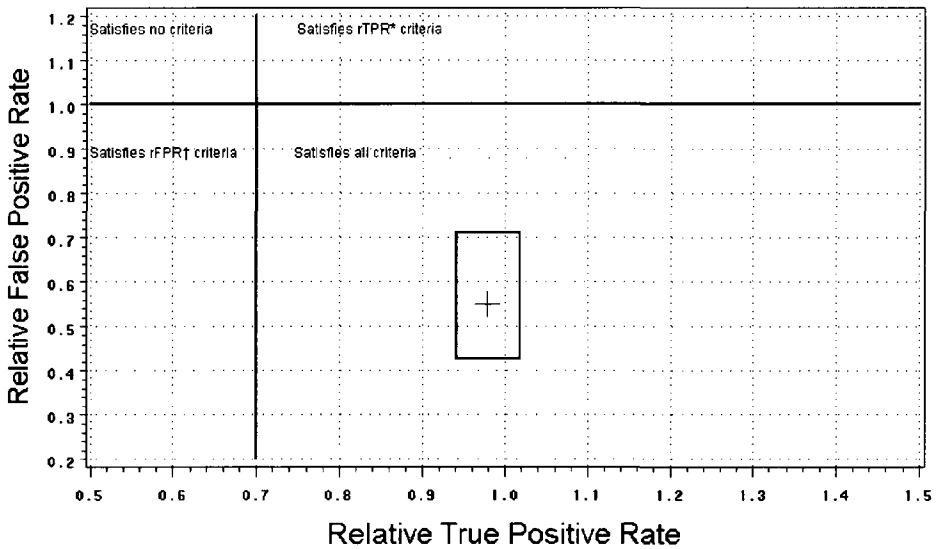
Table 3.17: Paired two-by-two tables comparing accuracy of electronic trigger mechanism (excluding data from the Health Records Abstract) with The Ottawa Hospital Infection Prevention and Control Program's current mechanism to trigger cardiac surgical site infection surveillance

Confirmed SSI*					**No SSI***			
	CTM† +	CTM† -				CTM† +	CTM† -	
ETM‡ +	184	5	189		**ETM‡ +**	39	17	56
ETM‡ -	6	8	14		**ETM‡ -**	47	413	460
	190	13	203			86	430	516

Relative true positive ratio ($rTPR_{E:C}$) = 0.99 (0.96, 1.03)
Relative false positive ratio ($rFPR_{E:C}$) = 0.65 (0.52, 0.82)

*SSI = Surgical Site Infection; †CTM = Current Trigger Mechanism; ‡ETM = Electronic Trigger Mechanism

Figure 3.8: Plot of relative true positive rate and relative false positive rate, with joint 95% confidence limits, comparing the electronic trigger mechanism (excluding Health Records Abstract data) to The Ottawa Hospital Infection Prevention and Control Program's current mechanism for cardiac surgical site infection surveillance



*In comparison to the current trigger mechanism; †HRA = Health Records Abstract
*rTPR = Relative True Positive Rate; †FPR = Relative False Positive Rate

Table 3.18: True positive rate, false positive rate, and positive predictive values of two novel electronic trigger mechanisms (including and excluding data from the Health Records Abstract) compared with The Ottawa Hospital Infection Prevention and Control Program's current trigger mechanism for cardiac surgical site infection surveillance

Trigger Mechanism	**True positive rate**	**False positive rate**	**Positive predictive value**
Current	0.936	0.167	0.38 (0.33, 0.42)
Electronic, including HRA* data	0.941	0.1085	0.48 (0.42, 0.54)
Electronic, excluding HRA* data	0.931	0.1085	0.48 (0.42, 0.54)

*HRA = Health Records Abstract

3.2.3 Accuracy of data in the Ottawa Hospital Data Warehouse

There are several data for which results from OHDW may be compared to results from chart review. Of 184 operative episodes identified as SSI cases from the TOH-IPCP records (i.e. preliminarily-defined cases), 1 (0.5%) was not located in the OHDW. The patient and admission were present, but there were no codes associated with any operative procedure recorded in the OHDW. Similarly missing were the Health Records Abstracts from 2 (0.3%) of the 719 observations in the study group (1 [0.5%] of the 203 cases, and 1 [0.2%] of the 516 controls). For four (0.56%) observations (3 cases, 1 control), the OHDW contained no listing for any of several known encounters occurring following the index surgery. Additionally, among 549 preliminary control operative episodes selected from the OHDW, there was 1 in which the recorded episode could not be confirmed on chart review.

There were a few minor errors with the recording of data pertinent to the index operative episode. In four observations (0.6%), the date of the index operation was incorrectly recorded in the OHDW – from 1 to 5 days (median 1.5 days). The nature of the surgery was accurately recorded for all procedures of interest– there was complete agreement (kappa = 1.0) between the OHDW and

chart review as to whether the patient had undergone CABG, cardiac valve repair, cardiac valve transplant, or cardiac transplant.

There was non-significant disagreement regarding the number of coronary artery grafts used during CABG. The number of coronary artery grafts could only be ascertained for 428 of 577 operative procedures including CABG (74.2%) by chart review. Among those 428, the OHDW overestimated the number of coronary artery grafts in 92 (21.5%) and underestimated the number of grafts in 145 (33.9%) (see Table 3.19). The Spearman correlation between graft number estimated from the OHDW and that obtained by chart review was 0.40 ($p = 0.0425$), moderately but significantly correlated. There was no significant difference (X^2 $p = 0.99$) in the number of misestimates of graft number between SSI cases and controls.

Table 3.19: Frequency of mis-estimation (over- or under-) of number of coronary artery graft vessels in data from the Ottawa Hospital Data Warehouse for 428 of 571 observations having undergone coronary artery bypass grafting

OHDW* estimate of number of coronary artery grafts	**Surgical site infection status**		
	Cases	**Controls**	**Total**
Overestimate	31 21.2%	61 21.6%	92
Correct	65 44.5%	126 44.7%	191
Underestimate	50 34.3%	95 33.7%	145
Total	146	282	428

*OHDW: Ottawa Hospital Data Warehouse

There was also disagreement regarding the ancillary sternotomy-based surgical procedures performed during the index operative episode. In four observations, chart review revealed the presence of an "other" procedure not recorded in the OHDW (1 aortic root enlargement, 1 ligation of an atrial appendage, 1 inspection of the atrium for suspected tumour, and 1 closure of a patent foramen ovale). There were 23 observations (3.2%) in which the OHDW contained codes indicating surgical procedures not apparent in operative reports. Most procedures were typically ancillary to the

principal cardiac surgical procedure: inter-atrial septum repair, inter-ventricular septum repair, partial excision of ascending aorta [in context of aortic valve replacement], coronary artery repair, enlargement of aortic annulus, atrial repair, thoracic ascending aortic repair, and placement of an intra-aortic balloon pump). The overall kappa for agreement between OHDW data and chart review was 0.89 (95%CL 0.85, 0.93). There was no significant difference between cases and controls in the proportion of observations with disagreements about other procedures (X^2 p=0.29).

Finally, there was some disagreement regarding the assignment of a diagnosis of SSI. As Table 3.20 demonstrates, an ICD-10 code indicating SSI was recorded in the OHDW for 185 (25.7%) of observations in the study group, of which 27 (14.6%) were false positives. The agreement between OHDW assignment of SSI diagnosis and that of gold standard chart review was moderate (kappa = 0.75 [95% CL 0.69, 0.80]).

Table 3.20: Ottawa Hospital Data Warehouse assignment of a diagnostic code indicating cardiac surgical site infection, compared to confirmation of cardiac surgical site infection by chart review

Code in OHDW* indicating SSI†	**SSI† Confirmed by Chart Review**		
	Yes	**No**	**Total**
Yes	158 85.4%	27 14.6%	185
No	45 8.4%	489 91.6%	534
Total	203	516	719

4 Discussion

4.1 Study highlights

In this two-phase study I have performed a systematic review of potential trigger factors associated with the development of SSI following cardiac surgery, and I have derived two electronic mechanisms to trigger cardiac SSI surveillance using data derived from a novel resource. The major purpose of the systematic review was to maximize the *a priori* relevance of the electronic trigger mechanisms derived in the second phase of the study. Nonetheless there are two striking findings from the systematic review: despite 22 years and156 confounder-controlled studies of risk-type trigger factors, there is still no consensus that the risk factors for cardiac surgery SSI have been adequately explored (as may be demonstrated by the 541 uniquely-defined risk factors observed, many of which are subtle variations on others); and there is a glaring paucity of confounder-controlled studies of identification-type trigger factors for SSI post-cardiac surgery – two dedicated studies, and a total of 29 factors. These findings speak to a need for a coordinated approach to investigating SSI surveillance trigger factors, with consensus definitions and more rigorous, uniform methodologies.

I believe the current study contributes to that need, by deriving two new, accurate, mechanisms for SSI surveillance triggering, using a novel but reproducible methodology that maximizes design and content validity. Our two new electronic trigger mechanisms included a larger model (that may only be applied weeks to months after the onset of SSI), and a smaller model (that may be applied in a "real-time" fashion). The logistic regression models underlying these mechanisms were constructed to maximize *a priori* probability, and both demonstrated excellent goodness-of-fit parameters (c-statistic 0.972 and 0.954). Both the large-model, and small-model, electronic trigger mechanisms were found to provide a lower false positive rate (i.e. superior specificity) and non-inferior true positive rate (i.e. sensitivity) when compared to a currently-used, labour-intensive manual trigger mechanism (FPR 0.1085, 0.1085, and 0.167 respectively; TPR 0.941, 0.931 and 0.936 respectively). These findings have the potential to standardize and automate the process of SSI surveillance triggering, and reduce the burden of manual chart review.

4.2 Comparison with other electronic trigger mechanisms

4.2.1 Healthcare-associated infection trigger mechanisms

Our surveillance trigger mechanism compares favourably with previously derived electronic trigger mechanisms (see Table 4.1). Evans and colleagues have created two different models for surveillance triggering: an early model using microbiology results, and a subsequent model using risk factors for development of hospital-acquired infection[31, 33] Both of these models were created to survey for a variety of healthcare-associated infections, including SSI among all surgical specialties. The TPR for the early model was 0.848, and for the later model was 0.636. Data were not provided to calculate FPR or PPV specifically for SSI. *Prima facie* it would appear that either of our two electronic trigger mechanisms provides superior sensitivity, however it is difficult to generalize surveillance systems addressing different surgical specialties.

4.2.2 Cardiac surgery-specific trigger mechanisms

For a more direct comparison of trigger mechanisms, I will reference the Centers for Disease Control and Prevention, Eastern Massachusetts Prevention Epicenter. This group has produced several studies evaluating automated surveillance for SSI specifically in cardiac surgery patients.

The first published mechanism by the Eastern Massachusetts Prevention Epicenter confirmed the use of antibiotic administration records in patients undergoing CABG.[40] This was a two-centre study, with a US site using automated inpatient medication records (recorded for administrative purposes), and a network of Israeli hospitals employing a prospectively collected database (including pharmacy data). The goal was to create a valid '**antibiotic interval**' – the length of time between the first and last days of antibiotic administration (not necessarily the antibiotic duration). They used a training cohort of the US patients to determine the optimal trigger antibiotic interval was nine or more days, beginning on or after the second post-operative day.

Table 4.1: Comparison of described electronic trigger mechanisms for surgical site infection surveillance

First author and year	Surgical specialty	Trigger factor data sources	Surgical patients (N)	Incidence (%)	True positive rate	False positive rate	Positive predictive value
Evans 1986 [33]	All	Laboratory	NR*	NR*	0.848	NR*	NR*
Evans 1992 [31]	All	Administrative	NR*	NR*	0.636	NR*	NR*
Yokoe 1998 [40]	Cardiac surgery	Pharmacy	4904 (USA)	5.6%†	0.95	0.15	0.28
			983 (Israel)	8.65%‡	0.87	0.18	0.31
Sands 1999 [41]	Non-obstetric Post-discharge only	Administrative Model 1	4086	2.3%‡	0.74	0.02	0.48
		Administrative Model 2			0.92	0.08	0.21
		Administrative Model 3			0.77	0.06	0.24
Sands 2003 [212]	Cardiac surgery	Administrative	1352	13%†	<0.719	NR*	0.366
Platt 2002 [213]	Cardiac surgery	Administrative	1953	NR*	NR*	NR*	0.53‡
Yokoe 2004 [38]	Cardiac surgery (obstetric & breast)	Administrative	2267 Phase 1	6.3%†	0.87	NR*	0.35
			6472 Phase 2	7.7%¤	0.93	NR*	0.36
Song 2008 [214]	Cardiac surgery	Administrative	NR*	NR*	0.811	0.354	0.203
Current study, large model§	Cardiac surgery	Data warehouse	719	9.7%¤ (8.0, 11.4%)	0.941	0.1085	0.48 (0.42, 0.54)
Current study, small model§	Cardiac surgery	Data warehouse	719	9.7%¤ (8.0, 11.4%)	0.931	0.1085	0.48 (0.42, 0.54)

*NR = Not reported; † Estimate from differential application of gold standard; ‡Calculated from universal review; ¤ Estimate based on random sample of cohort; §Large model includes health records abstract data, small model excludes

In this study, the US and Israeli centres reported similar FPR (0.15 and 0.18 respectively) and PPV (0.28 and 0.31 respectively), however the reported incidences (5.63% and 8.65%) and TPR (0.95 and 0.87) differed. I believe this reflects the differing approaches to defining SSI. The Israeli network used universal, prospective direct patient review, with post-discharge telephone interviews.

In contrast, the US centre's gold standard was their regular IPCP SSI surveillance (indirect prospective and selected retrospective review), with the additional chart review triggered by a pertinent discharge ICD-9-CM code, or the use of postoperative antibiotics – i.e. they looked for additional cases only among those who were already trigger-positive. In this respect, it is hard to judge the reliability of the estimated TPR. It is also unlikely that we would be able to apply a similar trigger mechanism at UOHI as fewer than 10% of observations in our study had an antibiotic interval of nine or more days. This in turn likely reflects the greater priority assigned by our centre to early discharge and home administration of antibiotics.

In 1999, the Massachusetts group broadened the forms of administrative data used in trigger mechanism creation, and focused on the elusive goal of a post-discharge surveillance system.[41] They used recursive partitioning to create an algorithm for use in various non-obstetric surgical specialties, specifically excluding patients with SSI diagnosed during index encounter. The data source was the billing database for a single managed care organization, containing information on diagnoses, prescription and dispensation of certain antibiotics, readmission with likely readmitting diagnosis, wound culture, OR duration, and surgical specialty. Case status was ascertained by universal chart review and patient/surgeon survey forms. By altering the datasets used, and the parameters of recursive partitioning, they created three models – two with all data sources but differing ratio of false-positive to false-negative acceptable, and one by using only in-hospital diagnoses with outpatient pharmacy data. Their three models afforded reasonable performance criteria – TPR ranged from 0.74 to 0.92, FPR ranged from 0.02 to 0.08, and PPV ranged from 0.21 to 0.48. They also created three logistic regression models, the best of which used all data types - inpatient diagnoses, outpatient diagnoses, emergency room diagnoses, prescription and dispensation of specific antibiotics, having had a wound culture, wound care procedures, and cardiothoracic or general surgery. While these trigger mechanisms provide similar measures of accuracy to our own, they were not developed or validated for surveillance during the index (i.e. initial post-operative) admission.

In a subsequent study in 2003, they addressed the issue of surveillance throughout the post-operative timeframe.[212] The trigger mechanism was a dichotomized probability calculated from the logistic regression model published in 1999, applied to a cohort of patients undergoing CABG, in the

same managed care organization. Unfortunately, they used a similar process for defining SSI as in Yokoe *et al* 1999 – either identification by regular ongoing IPCP SSI surveillance, or upon chart review of a portion of the trigger-positive patients only. Using this gold standard, the incidence was as least 13%, TPR was no more than 0.719, PPV was 0.366, and FPR was not calculable. In contrast, although we used SSI determination by our hospital's IPCP surveillance to define the initial study group, we applied gold standard to all observations – previously defined case or control, trigger positive or negative. For this reason, our TPR, FPR, and PPV are more reliably estimated.

In 2002, the Massachusetts group published a simpler trigger mechanism, based on administrative data for CABG patients from three managed care organizations.[213] The trigger mechanism was defined as the presence of any one or more of an appropriate in- or out-patient diagnostic code, procedure code for SSI investigation or management, or administration of a selected antibiotic. Again there was an issue with the application of SSI definition criteria – only a portion of the trigger-positive patients were reviewed, and they systematically excluded review among patients of one managed care plans. Trigger positivity varied from organization to organization, 22 to 33% - overall 536 of 1953 (27%) (363 [18%] when pharmacy data ignored). The trigger mechanism was most frequently positive due to outpatient criteria (e.g. diagnoses applied as outpatient or antibiotics). The estimated PPV was 0.53, however TPF, FPR, and incidence were incalculable. It is difficult to compare directly with our study, given the inability to calculate incidence and TPR.

These last two studies enjoy one advantage that we do not. By virtue of using administrative data from a managed care organization, rather than a hospital, they have access to outpatient antibiotic usage and diagnostic codes which we do not. Also of interest, patients with positive triggers were often identified seeking care at a hospital other than that where the index operative episode occurred. Again, the managed care organization database allows these data to be discovered, whereas our OHDW only applies to care at our centre. This is of some importance, as UOHI cares for patients from well beyond the Ottawa catchment area – including Nunavut, Western Quebec, and (for heart transplants) the Atlantic provinces. While we expect that patients with more severe SSI's may be transferred back to UOHI for care, many patients with SSI's are likely to be treated at other centres (see also Section 4.4.1).

The most recent publication by this group elaborates on pharmacy data used in their earliest paper, with the addition of discharge diagnoses.[38] This was again a multi-centre study, conducted in two phases – locally, and amongst six CDC Epicenters. The trigger mechanism was the presence of one or more of: a nine day antibiotic interval, beginning on or after postoperative day 2; any antibiotics upon readmission within 2 months; indicative discharge ICD-9-CM code after the index admission or; any readmission within 2 months. Again, there was a differentially-applied SSI confirmation process. In Phase 1, the gold standard was usual program of prospective (but non-direct) surveillance during index admission or re-admission, supplemented by review of charts of all trigger-positive patients not already classed as SSI. In Phase 2 they did likewise, but also randomly reviewed 200 charts to confirm accuracy of triggers, and of trigger mechanism. They extrapolated total cohort incidence from the number of SSI cases in the random review not picked up by current surveillance. We are unable to calculate FPR from this study, but TPR was 0.87 to 0.93, and PPV was 0.35 to 0.36, somewhat less than that in our study.

Song and colleagues elaborated on Yokoe *et al*'s[38] model in an attempt to supplant the formal confirmation of SSI status by patient or chart review.[214] Using a variation on the previously derived trigger mechanism consisting of five identification-type trigger factors (the chief difference from Yokoe *et al.* being the redefinition of antibiotic exposure), they defined trigger positivity by the presence of one or more trigger factors. For cardiac surgery SSI they report a TPR of 0.811 and FPR of 0.354, again somewhat poorer results than our own study. Interestingly, rather than use trigger positivity to initiate confirmatory chart review, their intent was to enumerate trigger positive patients and then calculate SSI incidence by multiplying by their established positive predictive value (PPV) of 0.203. While this method would certainly reduce required work, it has two particular disadvantages: it is reliant on a stable incidence of disease, and thus is insensitive to short-term increases in incidence (i.e. outbreaks); and it is unable to identify individual patients affected with SSI, so cannot aid in evaluation of potential risk factors.

4.3 Strengths of study

The chief advantage we enjoy in this study is the use of a novel data resource: the data warehouse. The data warehouse concept originated in business, but a number of clinical data

warehouses have been recently described.[215-220] The institutional, or enterprise, data warehouse has been posited as an obvious fit for infection control activities, including SSI surveillance.[221] However, to our knowledge there have been only two infection surveillance studies published, both for bloodstream infection.[215, 222] The data warehouse group at the Ohio State University Medical Center has explored applications for SSI, but have not yet published their results.[217] Hence, we are in a unique position.

The use of the OHDW allowed us to create a complex trigger mechanism, and likely therefore a more accurate trigger mechanism. Both our larger and smaller trigger mechanisms incorporated demographic data, diagnoses (both admitting, and discharge), laboratory and radiology results, and administrative data. Our smaller trigger mechanism also incorporated pharmacy data as well. Using these sources we were able to create trigger mechanisms offering TPR greater than 0.93, and FPR less than or equal to 0.1085. Of the previously published trigger mechanisms mentioned in Section 4.2.2, only one was able to offer similar accuracy parameters, and it too incorporated a wide variety of data – the second model reported in Sands 1999[41]. Their trigger mechanism incorporated diagnoses, pharmacy, peri-operative data, administrative data, and the use of laboratory services. The chief difference is that Sands *et al* derived all of these data from billings for services rendered, in an administrative database. Therefore they lacked the results of laboratory and radiographic testing to which the OHDW gives us access.

In addition to the novelty of our data source, our study also has a number of design features that we believe ensure the applicability of our findings. We undertook systematic review of the literature prior to selecting possible trigger factors for model inclusion, selecting those with the most consistently demonstrated association with SSI. We did additionally introduce nine potential trigger themes (approximately 20% of the total) with consensus of the investigators. These themes were drawn from the related literature (readmission following the admission for the index operative procedure[38]), from extrapolation from the epidemiology of SSI (longer postoperative stay, implantation of non-human derived material,[2, 8, 11]) or from our knowledge of local practices and concerns (the other six themes). In this manner we ensured content validity, being broadly inclusive of likely trigger factors, while maximizing the pre-test probability that potential trigger factors would have a significant association with SSI.

We also designed our model-building strategy to maximize the content validity. No single model-building strategy (and indeed, no single model) can be considered completely "correct," and over-reliance on automated Maximum Likelihood Estimate-based procedures increases the risk of model bias, particularly overfitting. By applying a semi-Bayesian approach, as described by Shtatland and colleagues,[46, 47] we used the AIC at multiple levels of model building, taking advantage of its asymptotic equivalence to the cross validation criterion to maximize internal model validity without undertaking laborious cross validation or boot-strapping.

Similarly, by excluding a seemingly useful trigger factor with non-sensical parameter estimates, we further strengthened the validity of the model[223], albeit at the possible cost of underfitting the model. We can posit no plausible explanation why patients with higher preoperative serum creatinine would be less likely to have an SSI, and this finding is at odds with the results of our systematic review, where comorbid renal failure was positively associated with the development of SSI in 40% of 35 reports. By allowing the literature to serve as a prior probability in this instance, we increase the content validity.

In taking pains to maximize content validity, we have created two potentially useful electronic trigger mechanisms. Both the larger and smaller models demonstrated compelling goodness-of-fit characteristics, and met our hypothesis criteria for superiority of specificity with non-inferiority of sensitivity. If these findings are borne out on prospective evaluation, they have the potential to improve the process of SSI surveillance both at UOHI and other centres. By automating the process of gathering trigger factor data, and by reducing the time spent on falsely trigger-positive entries, our electronic trigger mechanism will create time for ICP's to pursue their other duties – investigating healthcare-associated infection outbreaks; liaising with, and educating hospital staff on infection control issues; and implementing ongoing patient safety initiatives. Furthermore, by improving accuracy and standardization of SSI surveillance, our trigger mechanism fulfills both the writ and the intent of mandatory reporting requirements.

4.4 Weaknesses of study

4.4.1 Potential for lack of detection post-discharge

The chief concern with this study is the uncertain completeness of SSI case identification following discharge from hospital. Of 719 observations, 73 (10.2%) were not reviewed at our centre within 14 days following a standard SSI surveillance period following cardiac surgery. Furthermore, of 645 observations undergoing follow-up within this period, outpatient records were unavailable for 87 (13.5%). This is potentially problematic, as a large percentage (from 12 to 84%) of SSI are detected post-discharge from the index admission.[2] To counter these concerns, our chart review actually took into account healthcare encounters occurring after the end of standard surveillance. Although 73 observations were not seen within this period, 6 (8.2%) had been diagnosed with SSI during their index admission, and 32 returned to our centre for care at a later date. Only 35 control observations were completely lost to surveillance follow-up after discharge from the index admission. This group, plus the 87 controls for which outpatient records were unavailable, represent 17.0% of the total study group. Given any reasonable estimate of SSI incidence (e.g. 0 to 10%), it seems unlikely that we have missed a substantial number of cases.

Furthermore, it seems likely that any cases missed by our chart review are superficial incisional, rather than the more concerning deep incisional or organ/space infections. It is reported that outpatient management of SSI is the most common location for therapy of post-discharge SSI[29, 41] However the majority of the treatment measures required for deep incisional and organ/space infections (e.g. surgical debridement, initiation of intravenous antimicrobials, initiation of specialized dressing regimens), must occur in a healthcare facility, in a day unit or emergency department if not as an inpatient. Still, cases of SSI may be missed despite readmission. Platt et al reported that 48% of second hospital admissions for SSI management were to an institution other than that of the index operative episode.[213] However, our centre is the only cardiac specialty centre within a 200 kilometre radius, and regularly receives patients in transfer for care of SSI from primary and secondary care centres throughout Eastern Ontario, Northern Ontario, and Nunavut. Thus, it is likely that we will see most, if not all, deep incisional and organ/space SSI's returning to our centre for care.

Whether our electronic trigger mechanisms can detect post-discharge SSI is a different concern. This is a common issue in SSI surveillance programs, and one for which a number of detection methods have been developed. These include the electronic trigger mechanism described by Sands et al [41] (see Section 4.2.2), as well as surveys sent to surgeons and patients, and patient telephone follow-up.[224-226] As may be expected, there is no commonly accepted best practice for post-discharge SSI surveillance. Among our 203 SSI cases, there were 122 that were diagnosed or treated following discharge from the index admission. Of these, both of our electronic trigger mechanisms detected 93.4% of post-discharge cases, thus allaying this concern as well.

4.4.2 Data quality in the data warehouse

In a data warehouse there are a number of points at which data may be inaccurately recorded. Original data may be prone to vagary or error, especially free text data such as dictated reports, or admitting diagnoses; data may be erroneously recorded in the original data sources (e.g. erroneous laboratory results due to mislabeled specimens, or erroneous diagnosis codes applied retrospectively by Health Records Technologists); or they may be corrupted during uploading to the data warehouse itself. Section 3.2.3 details a number of data inaccuracies, of greater or lesser concern.

The validity of the cohort rests on the ability to detect a procedure of interest occurring in a time-frame of interest. Therefore our cohort rests on the accuracy of the health records abstract data – both the date, and the intervention code (CCI). There was at least one observation (of a known 184) that should have been in the cohort that wasn't, and one observation (in a random selection of 549) in the cohort that shouldn't have been. Happily these are small numbers in the context of overall cohort size, and we will address this issue in future work by defining the cohort using a newly-added data source, the peri-operative record. This new data source will also address the concern regarding four observations with slightly erroneous index procedure dates.

There were six observations in which whole data tables were absent. This included two missing HRA data, and four missing 'encounter' data. These data tables were likely not uploaded to the data warehouse, or not appropriately linked to the 'Patient' data table. Given the preponderance of cases affected (4, versus 2 controls), coupled with the negative-default nature of many of our

dichotomous trigger factors (i.e. defined as a negative in the absence of positive data) the likely quantitative effect would be to underestimate parameters for included trigger factors, and possibly underestimate model accuracy. It is unlikely that there was a substantial qualitative effect. Further, this form of data corruption upon upload is the focus of ongoing data accuracy surveillance, and ultimately contributes to improvement of data aggregation algorithms.

Finally, trigger factors reliant upon coded diagnoses or interventions are sometimes inaccurate. For example, there was only moderate correlation between number of coronary artery grafts as estimated from the OHDW, and as demonstrated on chart review. This stems from the fact that CCI codes are designed to specify whether a particular type of graft was used, rather than note how many. The tendency was to underestimate graft number, therefore possibly leading to underestimation of parameter values for this trigger factor, and therefore possibly underestimate model accuracy.

4.4.3 Applicability of the trigger mechanisms

There are two potential concerns regarding the application of these trigger mechanisms to surveillance activities: generalizability to other centres, and the complexity of calculating probability from a logistic regression model. Regarding the first of these, generalizability may refer to the application of these trigger mechanisms outside our centre (for which, please see Section 4.5.2 below), or their application to other surgical specialties.

It was not our intent that these trigger mechanisms would be applied to other specialties (see Section 4.5.3 below), however, arguably they may be readily adapted. In the two trigger mechanisms there is only one trigger factor that is cardiac surgery-specific ('number of coronary grafts' in the larger model), and three where alteration in coding or search terms may render them more broadly applicable ('Diagnosis of postoperative wound/graft/implant infection', 'Computed tomography report with mention of specific SSI terms' 'Surgical revision, debridement, aspiration, or repair of damage due to SSI'). These models make a logical starting point for future development.

The other potential applicability concern about our trigger mechanisms is the complexity of calculating probability from a logistic regression model. While there are superficial similarities between our trigger mechanisms and clinical decision rules, there is are important differences.

These mechanisms are intended for fully automated application (see Section 4.5.2 below), rather than for point-of-care calculation by clinicians or ICP's. In order to maximize the accuracy of the mechanisms, we have to maximize the information available from the model. For this reason we did not attempt to round parameter estimates into easily-calculated points.

A further corollary of this difference from clinical decision rules, is that our models can't be used for clinical decision making. This may seem self-evident, particularly given the use of a *diagnosis* of SSI in both trigger mechanisms. However, it also means that parameter estimates and odds ratios from our model may not be used to judge the *clinical* utility of any individual trigger factor. As one example, notice the presence of a consultation to the Infectious Diseases service. *Prima facie,* clinical assessment by Infectious Diseases is likely be associated with SSI. Furthermore, Infectious Diseases consultations were more frequent in cases (52.7%) than controls (6.0%) in our data, and yet it was retained in only a minority of the candidate models utilizing Health Records Abstract data. It seems likely that the inclusion of trigger factors noting the diagnosis or treatment of SSI confounded the relationship of Infectious Diseases consultation to SSI.

4.5 Future directions

4.5.1 Validation of electronic trigger mechanism

The critical next step in developing these trigger mechanisms is prospective validation. Although we took great pains to ensure the content validity of the models, and designed a selection strategy to mitigate the risk inherent in frequentist model-building, there is still a risk that our models are over-fitted to the data. Ideally these mechanisms will be applied to a prospective cohort of cardiac surgery patients, side-by-side with the current manual trigger mechanisms, with confirmatory chart review of all patients in the cohort. We will then compare the electronic trigger mechanism to the current manual method using the same rTPR and rFPR calculations used in this study. One key question will be observing the length of time it takes for Health Records Abstract data to become available. This will be a crucial question in deciding whether to apply our larger trigger mechanism, or the smaller one.

After prospective validation, we will examine the need for model refining. The OHDW recently added a new data source which may provide further discriminatory power. This is the peri-operative record, and it contains information on the surgical procedures performed, the wound class (see Table 1.2), and the American Society of Anesthesiologists' score. Information in this record may supplant our reliance on Health Records Abstract data, and therefore apply an electronic trigger mechanism in a more "real-time" fashion.

4.5.2 Proposed application of this electronic trigger mechanism

Assuming the model demonstrates sufficient validity on prospective evaluation, the next step will be to operationalize it, and apply it live. This will likely present challenges. The OHDW is currently a research tool, and is accessed directly only by research analysts, and administrative staff of the Ottawa Hospital. Live application will require a fully automated algorithm which is capable of accessing the OHDW. This algorithm would search the OHDW for patients who have undergone a cardiac surgical procedure of interest within a standard surveillance period, apply the trigger mechanism, calculate the probability of SSI, and generate an electronic alert if trigger-positive. This algorithm will have to activate at regular intervals, perhaps following the weekly OHDW update. Once an alert has been generated, TOH-IPCP will then perform confirmatory chart review, and summarize and report SSI incidence.

There are a few as-yet uncertain issues to be dealt with. This trigger mechanism was meant to improve the efficiency of SSI surveillance at our centre, yet it should have external applicability as well. This would require validating the trigger mechanism at another centre – one with both a data warehouse (or some other method of data aggregation across disparate sources,) and a cardiac SSI surveillance program. We are currently searching for partners in this venture. Another concern is that the individual trigger factors may need to be updated periodically. Some change every several years (e.g. ICD-10-CA will likely be replaced around 2015), and some vary with local epidemiology and practice patterns (e.g. antibiotic selection, and pathogens of importance on microbiology results). We will likely need to review this trigger mechanism every five to ten years.

4.5.3 Development of electronic trigger mechanisms for other surgical specialties

There are a number of other potential surveillance activities to which we could apply the OHDW. Currently the OHDW group is developing trigger mechanisms for medication errors, *Clostridium difficile* infections, and infections with antimicrobial-resistant organisms. Our next step will be the development of further SSI surveillance trigger factors. Three surgical specialties of note will be vascular surgery, orthopedics (including spine surgery) and obstetrics/gynecology. Ideally we will be able to develop specialized SSI surveillance trigger mechanisms for most, if not all, clean surgical specialties over the next several years.

4.6 Conclusion

We have developed two electronic mechanisms to trigger surveillance for cardiac surgical site infection, using a novel electronic data repository called a data warehouse. With these trigger mechanisms, we have demonstrated the potential to automate surveillance activities with non-inferior sensitivity, and superior specificity, compared to our current labour-intensive manual trigger mechanism.

In addition to the narrow outcome of creating these specific trigger mechanisms, we have also demonstrated the utility of the data warehouse as a tool. Using this information architecture to access clinical, administrative, pharmacy, radiologic, and laboratory data, we believe we will be able to create a number of similar trigger mechanisms to automate healthcare epidemiology surveillance acitivities, and improve the efficiency of infection control activities.

5 References

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6 Definitions

6.1 Glossary

Antibiotic interval: the length of time between the first and last days of antibiotic administration. This may include days wherein no antibiotic was administered, and therefore is distinct from the antibiotic duration.

Encounter: an inpatient admission, outpatient clinic visit, emergency room visit, UOHI Reference Centre assessment, or outpatient use of diagnostic radiology or laboratory services.

Entity: an individual data table in the Ottawa Hospital Data Warehouse derived from a particular data source – e.g. the "Patient" entity containing demographic information drawn from the hospital's patient registry database

Index encounter: the inpatient admission during which the index operative episode occurs.

Index operative episode: a trip to the operating room during which the patient undergoes coronary artery bypass grafting, cardiac valve repair or replacement, or heart transplant, and subsequent to which surgical site infection surveillance occurs.

Operative episode: a single trip to the operating room, during which one or more surgical procedures may be performed.

Reference Centre: a high-acuity outpatient urgent care assessment unit at the University of Ottawa Heart Institute

Trigger factor: a risk factor for development of surgical site infection, or identification factor noting the presence of same, which may be used to trigger surveillance efforts.

Trigger mechanism: a systematic method of assessing one or more trigger factors, as part of a surgical site infection surveillance program.

6.2 Abbreviations

95% CL: 95% Confidence Limits

AIC: Akaike Information Criterion

AUC: Area under the curve

BIMA: Bilateral internal mammary artery grafting

CABG: Coronary Artery Bypass Graft

CCI: Canadian Classification of Health Interventions

CDC: Centers for Disease Control

CPB: CardioPulmonary Bypass pump

FPR: False positive ratio

HAI: Healthcare associated infection

HRA: Health Records Abstract

ICD-10-CA: International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Canada

ICP: Infection Control Professional

IMA: Internal mammary artery grafting

MID: Minimally important difference

OHDW: the Ottawa Hospital Data Warehouse

PPV: positive predictive value

$rFPR_{E:C}$: relative false positive ratio (ratio of the electronic trigger mechanism to the current trigger mechanism)

ROC: Receiver-operator characteristic curve

$rTPR_{E:C}$: relative true positive ratio (ratio of the electronic trigger mechanism to the current trigger mechanism)

SSI: Surgical Site Infection

TOH: The Ottawa Hospital

TOH-IPCP: The Ottawa Hospital Infection Prevention and Control Program

TPR: True positive ratio

UOHI: the University of Ottawa Heart Institute

Appendix A: Standardized free text search terms, and diagnosis and procedure codes used to define potential factors to trigger cardiac surgical site infection surveillance

Trigger Factor Definitions	Search Terms or Codes Used
Microbiology Reports (Free text entry)	
'Any likely significant pathogens on wound culture'	'obacter'; 'staphylococcus aureus'; 'escherischia'; 'streptococcus'; 'pseudomonas'; 'morganella'; 'serratia'; 'stenotrophomonas'; 'klebsiella'; 'proteus'; 'providencia'; 'coagulase negative' (IF moderate polymorphs or greater on gram); 'multiple gram negative' (IF heavy growth, AND moderate polymorphs or greater on gram); 'enterococcus (IF heavy growth, AND moderate polymorphs or greater on gram)
'Any likely significant pathogens on blood culture'	'obacter'; 'staphylococcus aureus'; 'escherischia'; 'streptococcus'; 'pseudomonas'; 'morganella'; 'serratia'; 'stenotrophomonas'; 'klebsiella'; 'proteus'; 'providencia'; 'enterococcus'; 'haemophilus'; 'propionibacterium'; 'coagulase negative' (IF had non-human derived material implanted in index operative episode)
Radiology Reports (Free text entry)	
'Any CT report with mention of specific SSI terms'	'osteomyelitis'; 'sternal infection'; 'wound infection'; 'mediastinitis'; 'abscess'; 'retrosternal fluid'; 'endocariditis'; 'phlegmon'
Admitting Diagnoses (Free text entry)	
'Readmission with presumed diagnosis of SSI'	'endocarditis'; 'infect'; 'cellulitis'; 'incision'; 'wound'; 'osteomyelitis'; 'sepsis'; 'I + D'; 'abscess'; 'mediastinit'; 'debride'; 'sternal'
Pharmacy Records (Generic and Trade names, Drug Identification Numbers, Anatomic Therapeutic Chemical Classification codes, and American Hospital Formulary Service pharmacologic-therapeutic classifications for listed agents)	
'Systemic antibiotics likely for SSI started on or after post-operative day 2'	cefazolin; cephalexin; clindamycin; cloxacillin; ertapenem; imipenem; linezolid; meropenem; nafcillin; penicillin; piperacillin; rifampin; rifampicin; ticarcillin; vancomycin
'Topical antibiotics likely for SSI started on or after post-operative day 2'	bacitracin; framycetin; fucidin; fusidic; garamycin; mupirocin; neomycin; polymyxin
'Patient on immunosuppressives during index admission or surveillance period'	abatacept; abciximab; adalimumab; lemtuzumab; altretamine; amsacrine; anakinra; anti-lymphocyte; anti-thymocyte; azathioprine; basiliximab;

	bevacizumab; bleomycin; bortezomib; busulfan; capecitabine; carboplatin; carmustine; cetuximab; chlorambucil; chlormethine; cisplatin; cladribine; cyclophosphamide; cyclosporine; cytarabine; dacarbazine; daclizumab; dactinomycin; dasatinib; daunorubicin; docetaxel; doxorubicin; epirubicin; etanercept; etoposide; fludarabine; fluorouracil; gemcitabine; idarubicin; ifosfamide; imatinib; infliximab; irinotecan; leflunomide; lenalidomide; lomustine; mechlorethamine; melphalan; mercaptopurine; methotrexate; mitomycin; mitoxantrone; muromonab; mycophenolic; natalizumab; nelarabine; nilotinib; oxaliplatin; paclitaxel; panitumumab; pegaspargase; pemetrexed; pentostatin; porfimer; procarbazine; raltitrexed; rituximab; sirolimus; sorafenib; streptozocin; sunitinib; tacrolimus; temozolomide; temsirolimus; teniposide;thiotepa; tioguanine; topotecan; tositumomab; trastuzumab; triptorelin; ustekinumab; valrubicin; vinblastine; vincristine; vindesine; vinorelbine
Diagnoses (International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Canada)	
'Diagnosis of any respiratory disease'	J__
'Diagnosis of COPD, asthma, or bronchiectasis'	J4_
'Diagnosis of COPD alone'	J40; J41; J42; J43; J44
'Diagnosis of cerebrovascular disease'	F01; G45; G46; I63; I64; I65; I66; I67; Z86.7
'Diagnosis of atherosclerotic peripheral vascular disease	I70; Z95.8
'Diagnosis of hyperglycemia not otherwise specified'	R73.9
'Diagnosis of diabetes mellitus 1 or 2, or complications thereof'	E10; E11; E12; E13; E14; R73
'Diagnosis of any acute or chronic kidney disease'	I12; I13; N00-N08; N10-N19; N25;N99; O08.4; O10.2; O26.8; O90.4; O90.8; T79.5
'Diagnosis of acute or chronic renal failure'	N17-19; N25; N99; O90.4; T79.5
'Diagnosis of chronic renal failure'	N18; N19; N99; N25
'Diagnosis of heart failure, or hypertensive heart failure'	I11.0; I13.0; I13.2; I50
'Diagnosis of congestive heart failure or hypertensive heart failure'	I11.0; I13.0; I13.2; I50.0
'Diagnosis of hypertension, or associated disease'	I10-I15
'Diagnosis of HIV or AIDS'	B20; B21; B22; B23; B24
'Diagnosis of any immunosuppressed condition'	B20; B21; B22; B23; B24; D80; D81; D82; D83; D84
'Diagnosis of obesity'	E66.8; E66.9

'Diagnosis of tobacco use or dependence'	F17; Z72.0
'Diagnosis of myocardial infarction in index admission'	I21
'Postoperative pneumonia, urinary tract infection, or cellulitis'	B37.1; B44.0; J15 (not 15.7); J18; J69.0; L03 (not L03.3); N10; N30.0; N39.0; T83.5
'Organ rejection (transplant only)'	T86.2; T86.3
'Intra or postoperative wound complication dehiscence, hemorrhage, intraoperative misadventure, mechanical & other complication'	T81.0; T81.2; T81.3; T81.5; T82.0-T82.5; T82.8; T82.9; Y6_
'Diagnosis of potential postoperative wound infection or leukocytosis'	D72.8; I33; J85.3; J98.5; L03.3; M86.1; M86.9; T81.4; T82.6; T82.7
'Diagnosis of postoperative wound infection or infection due to grafts/implants (definite SSI)'	T81.4; T82.6; T82.7
Procedures (Canadian Classification of Health Interventions)	
'Dialysis performed preoperative on index admission' 'Dialysis ever performed'	1.PZ.21.^^
'Sternotomy performed in index admission, before index operative episode' 'Sternotomy performed in index admission, following index operative episode'	1.GY.^^.^^; 1.HA.52.Q^; 1.HA.8^.^^; 1.HB.87.^^; 1.HH.59.L^; 1.HH.71.^^; 1.HJ.^^.^^; 1.HM.^^.^^; 1.HN.80.L^; 1.HP.^^.^^; 1.HR.^^.^^; 1.HS.^^.^^; 1.HT.^^.^^; 1.HU.^^.^^; 1.HV.80.L^; 1.HV.90.^^; 1.HW.^^.^^; 1.HZ.09.L^; 1.HZ.55.^^; 1.HZ.85.^^; 1.IA.^^.^^; 1.IB.^^.^^; 1.IC.53.L^; 1.IC.57.^^; 1.IC.87.^^; 1.ID.^^.^^; 1.IJ.57.^^; 1.IJ.76.^^; 1.IJ.80.^^; 1.JL.^^.^^; 1.JU.^^.^^; 1.LC.^^.^^; 1.LD.^^.^^; 1.LZ.37.L^; 1.SK.^^.^^; 1.SY.^^.^^; 1.SZ.52.L^; 1.SZ.59.L^; 2.HZ.70.^^; 2.IL.70.^^;
'CABG during index operative episode'	1.IJ.76.^^
'Implantation of any nonhuman material in index operative episode'	1.HM.80.LA.XX.N; 1.HM.90.LA.XX.N; 1.HP.80.LA.XX.L; 1.HP.80.LA.XX.N; 1.HP.87.LA.XX.N; 1.HR.87.LA.XX.N; 1.HS.80.LA.FE; 1.HS.90.LA.CF; 1.HS.90.LA.XX.L; 1.HT.90.LA.XX.L; 1.HU.80.LA.FE; 1.HU.90.LA.CF; 1.HU.90.LA.XX.L; 1.HV.80.LA.FE; 1.HV.90.LA.CF.^^; 1.HV.90.LA.XX.L; 1.HV.90.LA.LA.Q; 1.HW.79.LA.XX.L; 1.HW.79.LA.XX.N; 1.HZ.53.^^; 1.HZ.54.^^; 1.IA.80.LA.XX.N; 1.IA.87.LA.XX.N; 1.IB.87.LA.XX.N; 1.IC.87.LA.XX.N; 1.ID.76.MV.XX.N; 1.ID.76.MX.XX.N; 1.IJ.6.LA.XX.N
'Any IMA graft used in index operative episode'	1.IJ.6.LA.XX.G; 1.IJ.6.LA.XX.Q; 1.IJ.6.WK.XX.Q; 1.JL.58.^^
'Tracheostomy, thoracentesis, or chest tube performed in surveillance period'	1.GJ.77.HA; 1.GJ.77.LA; 1.GZ.52.HA
'Resternotomy for bleeding in index encounter'	1.GY.13.^^
'Resternotomy for bleeding or to removing packing in index encounter'	1.GY.^^.^^

'Resternotomy or electrocautery for bleeding in index encounter'	1.GY.13.^^; 1.YS.59.^^
'Surgical revision, debridement, aspiration, or repair likely due to SSI'	1.SK.^^ (except 1.SK.35.^^); 1.SY.58.^^; 1.SY.80.^^; 1.SZ.52.^^; 1.SZ.55.^^; 1.SZ.56.^^; 1.SZ.59.^^; 1.YS.14.JA.XX.^; 1.YS.52.^^; 1.YS.55.^^ (not 1.YS.55.JA.FF); 1.YS.59.^^; 1.YS.80.^^; 1.YS.87.^^; 1.YZ.53.^^
'Packing on wound to trunk or abdo (may or may not be SSI)'	1.YS.14.JA.^^ (not 1.YS.14.JA.XX.^);
'Dressing or surgery for likely SSI (or noninfectious complication of wound)'	1.SK.^^ (except 1.SK.35.^^); 1.SY.58.^^; 1.SY.80.^^; 1.SZ.52.^^; 1.SZ.55.^^; 1.SZ.56.^^; 1.SZ.59.^^; 1.YS.14.JA.^^; 1.YS.52.^^; 1.YS.55.^^ (not 1.YS.55.JA.FF); 1.YS.59.^^; 1.YS.80.^^; 1.YS.87.^^; 1.YZ.53.^^
'Any chest Computed tomography performed (per procedures table)'	3.GT.20.^^; 3.GY.20.^^; 3.IP.20.^^

Appendix B: Themes and defined potential trigger factors to trigger surveillance of surgical site infection surveillance in post-cardiac surgery patients

Main Trigger Theme	Trigger goal	Number of Potential Triggers	Trigger Definitions
Complication infection	Identification	17	'Diagnosis of potential postoperative wound infection or leukocytosis NYD' 'Diagnosis of postoperative wound infection or infection due to grafts/implants (definite SSI)' 'Any postoperative wound cultures' 'Moderate or many PMNs on wound gram stain' 'Rare or more PMNs on gram stain' 'Few or more PMNs on gram stain' 'Any organisms on wound culture' 'Any likely significant pathogens on wound culture' 'Any blood culture done postoperative' 'Any organisms on blood culture' 'Any likely significant pathogens on blood culture' 'Any organisms on wound or blood culture' 'Any likely significant pathogens on wound or blood culture' 'Significant pathogen growth in blood tissue or wound culture, or rare or more PMN's on gram stain' 'Number of postoperative wound cultures' 'Semi-quantitative PMNs on gram' 'Number of postoperative blood cultures'
Inflammatory markers	Identification	14	'ESR performed postoperative' 'CRP performed postoperative' 'Highest post-op ESR > 10 mm/hr' 'Highest post-op ESR > 50 mm/hr' 'Highest post-op CRP > 10 mg/L' 'Highest post-op CRP > 50 mg/L' 'White cell count on 2nd postoperative day above 12.5 * 10e9 cells/L' 'Any postoperative white cell count above 16 * 10e9 cells/L' 'Highest post-op ESR (mm/hr)' 'Highest postoperative CRP (mg/L)' 'Highest post-op WBC count (10E9 cells/L)' 'Number of times WBC drawn postoperative' 'First WBC on admission for index operative episode (10E9 cells/L)' 'Highest WBC on POD2 (10E9 cells/L)'
Radiology	Identification	13	'Any chest CT performed (per procedures table)' 'Any chest CT performed (per services table)' 'Any CT report with mention of specific SSI terms' 'CT report mentioning osteomyelitis' 'CT report mentioning sternal infection' 'CT report mentioning wound infection ' 'CT report mentioning mediastinitis ' 'CT report mentioning abscess ' 'CT report mentioning retrosternal fluid' 'CT report mentioning endocarditis' 'CT report mentioning phlegmon' 'Number of chest CTs performed (per services table)' 'Highest number of terms denoting SSI in a CT report'
Wound therapy	Identification	10	'Systemic antibiotics likely for SSI started on or after POD2' 'Topical antibiotics likely for SSI started on or after POD2'

			'Systemic or topical antibiotics likely for SSI started on or after POD2' 'Nine or more days of systemic antibiotics, started on POD2 or later' 'Duration of likely systemic antibiotics in days' 'Plastic surgery service ever involved' 'Any procedures by plastic surgery service' 'Packing on wound to trunk or abdo (may or may not be SSI)' 'Surgical revision, debridement, aspiration, or repair likely due to SSI' 'Dressing or surgery for likely SSI (or noninfectious complication of wound)'
Readmission	Identification	8	'Unplanned post discharge readmission' 'Post discharge readmission coded as urgent or emergent' 'Post discharge visit to emergency or the reference centre' 'Readmission with admitting diagnosis of SSI' 'Systemic antibiotics likely for SSI started on readmission' 'Topical antibiotics likely for SSI started on readmission' 'Systemic or topical antibiotics likely for SSI started on readmission' 'Readmission to ER or Reference centre, or coded as urgent'
Infectious diseases consulted	Identification	2	'Infectious disease service ever involved' 'Post discharge outpatient ID visit'
Longer postoperative stay	Identification	2	'Postoperative stay in days' 'Total index admission in days'
Wound appearance/ complication	Identification	1	'Intra or postoperative wound complication dehiscence, hemorrhage, intraop misadventure, mechanical & other complication'
Hyperglycemic	Risk	13	'Diagnosis of hyperglycemia NOS' 'Highest glucose on day of OR > 7.1 mmol/L' 'Highest glucose on day of OR > 11.1 mmol/L' 'Last preoperative glucose on day of OR > 7.1 mmol/L' 'Last preoperative glucose on day of OR > 11.1 mmol/L' 'Highest intraoperative glucose on day of OR > 7.1 mmol/L' 'Highest intraoperative glucose on day of OR > 11.1 mmol/L' 'First postoperative glucose on day of OR > 7.1 mmol/L' 'First postoperative glucose on day of OR > 11.1 mmol/L' 'Highest glucose on day of OR (mmol/L)' 'Last preoperative glucose before OR (mmol/L)' 'Highest intraoperative glucose (mmol/L)' 'First postoperative glucose on OR day (mmol/L)'
Comorbid renal failure	Risk	11	'Diagnosis of any acute or chronic kidney disease' 'Diagnosis of acute or chronic renal failure' 'Diagnosis of chronic renal failure' 'Dialysis performed preoperative on index admission' 'Dialysis ever performed' 'First preoperative creatinine > 88 umol/L' 'First preoperative creatinine > 106 umol/L' 'Highest preoperative creatinine > 88 umol/L' 'Highest preoperative creatinine > 106 umol/L' 'Last preoperative creatinine (umol/L)' 'Highest preoperative creatinine in index admission (umol/L)'
Hypoxic preoperatively	Risk	9	'Intubated, on ECMO, or on supplemental oxygen preoperative' 'Lowest preoperative paO2 < 61 mmHg' 'Last preoperative paO2 < 61 mmHg' 'Lowest preoperative oxygen sat < 80%' 'Last preoperative oxygen sat < 80%' 'Lowest preoperative paO2 (mmHg)' 'Last preoperative paO2 (mmHg)'

			'Lowest preoperative oxygen saturation (%)' 'Last preoperative oxygen saturation (%)'
Intensive care unit	Risk	7	'Critical care service involved in surveillance period' 'ICU admission in index admission' 'CSICU admission in index admission' 'Any critical care unit admission in index admission' 'Days in ICU in index admission' 'Days in CSICU in index admission' 'Days in critical care unit in index admission'
Immunodeficiency	Risk	4	'Diagnosis of HIV or AIDS' 'Diagnosis of any immunodeficiency disease' 'Diagnosis of immunodeficiency disease or use of immunosuppressive med 'Patient on immunosuppressives during index admission or surveillance period'
Revision/ Resternotomy	Risk	4	'Resternotomy post index operative episode in index encounter' 'Resternotomy for bleeding in index encounter' 'Resternotomy for bleeding or to removing packing in index encounter' 'Resternotomy for bleeding or electrocautery for bleeding in index encounter'
Urgent index operative episode	Risk	4	'Index operative episode performed on weekend' 'Index operative episode performed from 18:00 to 07:00' 'Index operative episode performed on weekend or from 18:00 to 07:00' 'Index operative episode coded as unplanned'
Comorbid infection	Risk	3	'S. aureus species grown from preoperative surveillance swabs' 'On isolation precautions for any reason' 'Postoperative pneumonia, urinary tract infection, or cellulitis'
Overall health status	Risk	3	'Comorbidity code assigned' 'Resource intensity weight' 'Resource intensity weight (per MOH)'
Cerebro- or peripheral vascular disease	Risk	3	'Diagnosis of CVD (vascular dementia, TIA, CVA, non-infarcting occlusions 'Diagnosis of atherosclerotic PVD' 'Diagnosis of CVD or PVD'
Comorbid lung disease	Risk	3	'Diagnosis of any respiratory disease (ICD-10 section J)' 'Diagnosis of COPD, asthma, or bronchiectasis' 'Diagnosis of COPD alone'
Comorbid heart failure	Risk	2	'Diagnosis of heart failure, or hypertensive heart failure' 'Diagnosis of congestive heart failure or hypertensive heart failure"
CABG during index operative episode	Risk	2	'CABG as only principle cardiac procedure' 'CABG during index operative episode'
Multiple-procedure operative episode	Risk	2	'More than 1 principle cardiac procedure in index operative episode' 'Number of principle cardiac procedures in index operative episode'
Transfusion	Risk	2	'Any blood products transfused in index admission' 'Packed RBCs during index admission'
Time of year of OR	Risk	1	'Quarter of index operative episode'
Transplant rejection	Risk	1	'Organ rejection (transplant only)'
Implantation of non-human derived material	Risk	1	'Implantation of any nonhuman material in index operative episode'
Interactive factors	Risk	1	Female gender interacting with diabetes mellitus

Older age	Risk	1	'Age on index admission (Years)'
Comorbid hypertension	Risk	1	'Diagnosis of primary or secondary hypertension, or associated disease'
Comorbid obesity	Risk	1	'Diagnosis of obesity'
Comorbid smoking	Risk	1	'Diagnosis of tobacco use or dependence'
Non-routine postoperative instrumentation	Risk	1	'Tracheostomy, thoracentesis, or chest tube performed in surveillance period'
Coronary artery graft number greater	Risk	1	'Number of graft vessels during CABG'
Diabetes mellitus	Risk	1	'Diagnosis of DM1, DM2, HONK, DKA, diabetic complications, or hyperglycemia'
Duration of index operative episode	Risk	1	'Index operative episode duration in minutes'
Female gender	Risk	1	'Female gender'
Internal mammary artery grafting	Risk	1	'Any IMA graft used'
Myocardial infarction preoperatively	Risk	1	'Diagnosis of MI in index admission'
Non-caucasian ethnicity	Risk	1	'First language not French or English'
Preoperative admission longer	Risk	1	'Preoperative stay in days'
Prior cardiac intervention	Risk	1	'Sternotomy performed in index admission, before index operative episode'
Unique factors	Risk	1	'Resident involved in care during index admission'

Appendix C: Model descriptions, and intercepts for eighteen trigger factors included in twenty-five "candidate" logistic regression models to trigger cardiac surgical site infection surveillance, including data from the Health Records Abstract

	Number of models with trigger factor	Model1	Model2	Model3	Model4	Model5
Number of trigger factors in model		12	12	12	12	12
Akaike Information Criterion		288.3878023	289.115758	288.9993	288.2375	291.2474
Intercept		-6.330326897	-6.227346416	-6.20865	-6.30458	-6.33586
Comorbid congestive heart failure	10	0.763277991	0.740194953	0.757511	0.7377	0.75144
Surgical revision, debridement, aspiration, or repair of SSI*	10	1.249199042	1.040560382	0.984562	0.914843	1.21017
Computed tomography report mentioning specific SSI* terms	10	0.767868024	0.757024014	0.724029	0.722828	0.858545
Diagnosis of postoperative wound/graft/implant infection (definite SSI*)	10	2.943120331	3.022835385	2.805337	2.85561	2.862787
Significant pathogen growth in blood, tissue, or wound culture or; rare or more polymorphs on gram stain	10	2.654181023	2.628723581	2.577983	2.595655	2.644986
Number of coronary bypass graft vessels	10	0.623033111	0.620561658	0.613164	0.630536	0.590164
Postoperative stay (days)	10	0.021872447	0.021585893	0.019628	0.017224	0.024271
Readmission with admitting diagnosis of SSI*	10	1.029017711	0.898539417	0.943336	0.82202	0.824168
Readmission to emergency room/reference centre, or coded as urgent	10	1.379673337	1.418528467	1.401994	1.432222	1.421737
Postoperative pneumonia, urinary tract infection, or cellulitis	9	-0.285264283	-0.156956209	-0.20034		-0.49193
Preoperative creatinine greater than 106 umol/L	8	-0.863527937	-0.906708358	-0.88411	-0.93609	
Female gender	6	0.466423553				0.516184
Selected systemic antibiotics started on or after postoperative day 2	5			0.433358	0.41937	
Serum glucose on day of index operative episode greater than 11.1 mmol/L	4		0.544111865		0.534552	
Comorbid chronic renal failure	2					-0.5539
Infectious disease service consulted	1					

Bolded box indicates model with optimized Akaike Information Criterion; *SSI = Surgical site infection

Appendix C continued.

	Model6	Model7	Model8	Model9	Model10
Number of trigger factors in model	13	13	13	13	13
Akaike Information Criterion	289.3184	289.5843	290.1348	290.1295	291.9513
Intercept	-6.38984	-6.40194	-6.32384	-6.28205	-6.39235
Comorbid congestive heart failure	0.756205	0.744446	0.756391	0.736431	0.737638
Surgical revision, debridement, aspiration, or repair of SSI*	1.143566	1.190225	1.235565	0.937874	1.109883
Computed tomography report mentioning specific SSI* terms	0.732921	0.764584	0.716964	0.720545	0.806894
Diagnosis of postoperative wound/graft/implant infection (definite SSI*)	2.761528	2.986995	2.89726	2.845357	2.680751
Significant pathogen growth in blood, tissue, or wound culture or; rare or more polymorphs on gram stain	2.613375	2.663951	2.631867	2.590743	2.605563
Number of coronary bypass graft vessels	0.629397	0.637335	0.631958	0.626102	0.592501
Postoperative stay (days)	0.018252	0.020302	0.020213	0.01824	0.020626
Readmission with admitting diagnosis of SSI*	0.935274	0.909937	0.999543	0.825035	0.714485
Readmission to emergency room/reference centre, or coded as urgent	1.397598	1.411163	1.372764	1.433075	1.444648
Postoperative pneumonia, urinary tract infection, or cellulitis	-0.27856	-0.23633	-0.29496	-0.15412	-0.4839
Preoperative creatinine greater than 106 umol/L	-0.86373	-0.88917	-0.86698	-0.90744	
Female gender	0.468595	0.448703	0.454912		0.518967
Selected systemic antibiotics started on or after postoperative day 2	0.436699			0.419807	0.477446
Serum glucose on day of index operative episode greater than 11.1 mmol/L		0.505742		0.517536	
Comorbid chronic renal failure					-0.60322
Infectious disease service consulted			0.245804		

*SSI = Surgical site infection

Appendix D: Model descriptions, and intercepts for twelve trigger factors included in twenty "candidate" logistic regression models to trigger cardiac surgical site infection surveillance, excluding data from the Health Records Abstract

	Number of models with trigger factor	Model1	Model2	Model3	Model4	Model5	Model6	Model7	Model8	Model9
Number of trigger factors in model		7	7	7	7	7	8	8	8	8
Akaike Information Criterion		347.1313	348.3444	348.7768	349.6415	349.65	347.8659	348.5861	349.0681	349.1305
Intercept		-4.59979	-4.33179	-4.46631	-4.56051	-4.41111	-4.52091	-4.63067	-4.5994	-4.57472
Duration of likely systemic antibiotics (days)	20	0.0958	0.105154	0.097362	0.092949	0.092427	0.107099	0.098016	0.092504	0.095994
Computed tomography report with mention of specific SSI* terms	20	1.489536	1.452392	1.46233	1.477643	1.468199	1.467013	1.479843	1.482041	1.488643
Significant pathogen growth in blood, tissue, or wound culture or; rare or more polymorphs on gram stain	20	3.064685	3.013777	3.025962	3.021657	3.009716	3.064467	3.069265	3.055501	3.063847
Readmission with admitting diagnosis of SSI*	20	1.236662	1.326326	1.182151	1.247084	1.235509	1.318643	1.190602	1.219749	1.236025
Readmission to emergency room/reference centre, or coded as urgent	20	1.065125	1.045795	1.106346	1.074798	1.073242	1.032987	1.086834	1.052111	1.066005
Selected systemic antibiotics started on or after postoperative day 2	20	1.335377	1.411618	1.341559	1.362274	1.364382	1.379639	1.318667	1.329551	1.336224
Female gender	16	0.480424					0.475688	0.450646	0.485873	0.48146
Preoperative creatinine greater than 106 umol/L	11		-0.38157				-0.37548			
Serum glucose on day of index operative episode greater than 11.1 mmol/L	7			0.420554				0.331624		
Age on index admission (Years)	6				0.002272					-0.00039
Number of postoperative blood cultures, transformed by postoperative stay	6					0.152717			0.286098	
Postoperative white cell count above 16 * 10e9 cells/L	4									

Bolded box indicates model with optimized Akaike Information Criterion; *SSI = Surgical site infection

Appendix D continued.

	Model10	Model11	Model12	Model13	Model14	Model15	Model16	Model17	Model18	Model19	Model20
Number of trigger factors in model	8	9	9	9	9	9	10	10	10	10	10
Akaike Information Criterion	349.1312	349.2117	349.8327	349.8621	349.8597	350.5072	351.177	351.2037	351.2083	351.8239	351.8257
Intercept	-4.60028	-4.55251	-4.68469	-4.52143	-4.5271	-4.63083	-4.7205	-4.55338	-4.54837	-4.69986	-4.69366
Duration of likely systemic antibiotics (days)	0.095743	0.109587	0.106141	0.106172	0.106419	0.09436	0.108563	0.108276	0.110114	0.10464	0.105401
Computed tomography report with mention of specific SSI* terms	1.48936	1.455799	1.472632	1.465072	1.464207	1.471152	1.461767	1.452904	1.45784	1.470155	1.469741
Significant pathogen growth in blood, tissue, or wound culture or; rare or more polymorphs on gram stain	3.064597	3.070106	3.069754	3.062069	3.063257	3.05918	3.075664	3.066724	3.071091	3.066588	3.068539
Readmission with admitting diagnosis of SSI*	1.236597	1.266744	1.324591	1.313924	1.317731	1.169165	1.273193	1.259289	1.266623	1.317866	1.323718
Readmission to emergency room/reference centre, or coded as urgent	1.065262	1.056203	1.025539	1.030035	1.03471	1.0729	1.048626	1.052156	1.055208	1.020342	1.027279
Selected systemic antibiotics started on or after postoperative day 2	1.335225	1.365275	1.375519	1.377708	1.377871	1.311871	1.360733	1.362425	1.366539	1.372176	1.373547
Female gender	0.480241	0.443364	0.468596	0.476984	0.473223	0.456522	0.43591	0.445176	0.44482	0.469952	0.465838
Preoperative creatinine greater than 106 umol/L		-0.39143	-0.38719	-0.37182	-0.37713		-0.40326	-0.38633	-0.39029	-0.38263	-0.38912
Serum glucose on day of index operative episode greater than 11.1 mmol/L		0.366528				0.336547	0.366739	0.367805	0.371047		
Age on index admission (Years)			0.002609				0.002675			0.002837	0.002646
Number of postoperative blood cultures, transformed by postoperative stay				0.072397		0.320376		0.103785		0.11093	
Postoperative white cell count above 16 * 10e9 cells/L	0.001797				0.023924				-0.01784		0.025649

***SSI = Surgical site infection**