IDENTIFICATION OF ADVERSE EVENTS RELATED TO CENTRAL VENOUS CATHETERS USING TWO SEMIAUTOMATED METHODS TO REVIEW FREE TEXT COMPUTERIZED MEDICAL RECORDS

by

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I have read the thesis of Janet Frances Elizabeth Penz in its final form and have found that (1) its format, citations, and bibliographic style are consistent and acceptable; (2) its illustrative materials including figures, tables, and charts are in place; and (3) the final manuscript is satisfactory to the supervisory committee and is ready for submission to The Graduate School.

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ABSTRACT

Methods for surveillance of adverse events in clinical settings are limited by cost, technology, and appropriate data availability. Manual chart review is the gold standard methodology against which any new technology must be compared at this time. In this study, two methods for semiautomated review of text records within the Veterans Administration database are utilized to identify adverse events related to the placement of central venous catheters (CVCs) and compared to a sample of manually reviewed records. A phrase-matching algorithm was found to be a sensitive but relatively nonspecific method, whereas a Medical Language Processing program (MedLEE from Columbia University) was significantly more specific but less sensitive. Positive predictive values for each method estimated the CVC-associated adverse event rate at this institution to be 6.4 and 6.1%, respectively. Using both methods together results in acceptable sensitivity and specificity (72.0% and 80.1%, respectively). All methods including manual chart review are clearly limited by incomplete or inaccurate clinician documentation. The automated methods are additionally more likely to be negatively affected by spelling errors, abbreviations and use of proprietary brand names to identify specific catheters.

A secondary finding related to administrative data (ICD-9 and CPT codes) used to identify intensive care unit patients in whom a CVC was placed. An estimate of the completeness of this administrative data was made by determining a minimum number of
patients in which CVCs must have been placed for vascular and cardiac surgical cases and comparing this to those found by searching administrative data. Administrative data identified only 11% of patients who certainly must have had a CVC placed. This suggests that other methods, including automated methods such as phrase matching, may be more sensitive than administrative data in patients with devices.
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LIST OF ABBREVIATIONS

CPT – Current Procedural Terminology
CVC – Central venous catheter
FDA – Food and Drug Administration
ICD – International Classification of Diseases
MLP – Medical Language Processing
NLP – Natural Language Processing
NLU – Natural Language Understanding
PMA – Phrase-Matching Algorithm
SGML - Standard Generalized Markup Language
SLC VAMC – Salt Lake City Veterans Administration Medical Center
UMLS - Unified Medical Language System
VHA - Veterans Health Administration
W3C - World Wide Web Consortium
XML – Extensible Markup Language
1. INTRODUCTION

1.1 Medical Device Adverse Events

Since the Institute of Medicine (IOM) released its landmark reports “To Err is Human” (1) and “Crossing the Quality Chasm,” (2) there has been a great deal of attention focused on studying and preventing medical errors and adverse events. Patients in an intensive care setting are at particular risk for adverse events due to the acuity of their underlying illnesses and the frequent requirement for invasive procedures such as CVCs (Central Venous Catheters) for fluid therapy and hemodynamic monitoring. Unfortunately, these are also the same patients that are least able to tolerate complications. A device-related adverse event that might be relatively minor in a healthier individual could easily prove fatal to a patient in the intensive care unit.

Methods for studying adverse events have employed many different strategies and recently have incorporated the use of computer technology (3-5). Overall, the most common methodology for studying adverse events has historically involved retrospective chart review. Unfortunately, this is a very time consuming, labor intensive, and expensive research technique. The advent of computerized medical records has allowed the possibility of new tools for retrospective epidemiological and quality assurance activities, ongoing and prospective surveillance, and potentially the prevention of adverse events through alerting and decision support mechanisms. One technology, Natural Language Processing (NLP), shows promise in its ability to “read and understand” text
based files including patient records (6). Although simpler, phrase matching is another method amenable to automation that can sift through text records looking for specific word combinations that may reflect clinical scenarios.

Because the use of text-based technologies is a novel approach to medical device adverse event surveillance, it is logical to begin with a relatively simple model of an adverse event. Many devices are highly complex in their usage and the range of associated adverse events is considerable. The choice of CVCs as devices to study using text-based technologies was based on their limited number of common associated adverse events and, therefore, a relatively limited number of ways in which these events can be described in the patient record.

1.2 Central Venous Catheters

Central venous catheters are medical devices commonly used in intensive care settings that are used to provide reliable intravenous access for fluid therapy, a route for drugs that must be administered via large veins, access for hemodialysis, and for hemodynamic monitoring. It is estimated that over 5 000 000 of these catheters are placed every year in the US (7). In essence, a CVC is a long intravenous catheter that is placed by one of several methods: percutaneously, radiologically guided, or via a surgical approach ("cut-down"). They can be placed in any of the body’s major veins including the jugular, subclavian, femoral, and lumbar veins and take advantage of these veins’ relatively large size and high venous blood flow. This venous flow rate is critically important in the administration of certain solutions which may be damaging to endothelium (surface lining the lumen of the vein) if not rapidly diluted in a large blood volume.
There are a number of known complications of CVCs including pneumothorax, chylothorax, bleeding, infection, cardiac dysrhythmias, catheter occlusion, deep venous thrombosis, pulmonary embolism, venous air embolism, catheter malposition, arterial injury, nerve injury, cardiac tamponade, and death. Early complications include bleeding, pneumothorax (due to accidental puncture of the lung during catheter placement), catheter malposition, injury of nearby structures (arteries and nerves), and cardiac tamponade (blood filling the pericardium, and preventing normal heart function after perforation of the inferior vena cava or right atrium by the catheter tip). In some series the early complication rate (excluding infection and deep venous thrombosis) has been reported to be as high as 10% (8). Longer term problems including infection and thromboembolic complications have been well studied in certain patient populations (particularly in oncologic patient with long term catheters) (9), however events such as dysrhythmias, occlusion, and mechanical dysfunction are not as well reviewed in the literature. Indwelling catheters have a risk for developing complications at rates dependent upon several factors: whether or not the catheter is cuffed and tunneled (10), patient diagnoses and their associated use of a catheter (dialysis for renal failure, total parenteral nutrition for gastroenterologic failure, chemotherapy for cancer, etc.), and the specific types of catheter used (11).

The Food and Drug Administration (FDA) serves a regulatory role in medical device studies and approval of devices for clinical use (12). Additionally the FDA monitors already approved device use and their associated complications through a voluntary reporting program, and this allows compilation of some information regarding CVC related adverse events. Deaths represent approximately 2% of complications
reported to the FDA and are most commonly related to cardiac tamponade or perforation (13). In contrast to these unusual but catastrophic complications, infection is a common and frequently studied adverse event. Although not typically fatal, each CVC related infection in a critically ill patient has been estimated to add up to $40,000 to the cost of patient care per episode (14). Additionally, infection represents the most common adverse event in these catheters, occurring in up to 30% of patients in some settings. The cost of infection alone can be conservatively extrapolated to an annual healthcare cost of hundreds of millions of dollars. Clearly, CVC related adverse events are a significant source of morbidity, mortality, and healthcare expense that warrant further evaluation in order to improve care in patients requiring these devices. The identification of these adverse events, then, is the first step in understanding the factors predisposing to complications and ultimately in preventing such adverse events.

1.3 Natural Language Processing

Natural Language Processing (NLP) is a subfield of artificial intelligence and is closely related to computational linguistics. Two of NLP’s main goals are to allow authors to use free text and then to apply computerized methods in order to extract the information from within these free text records. Free text has the advantage of being highly expressive and natural for human users and is often preferred by these users over structured data entry because of its greater ease of use. The disadvantages are that it can be complex, ambiguous, and difficult to translate into coded and computable data. In order to use the information within free text documents, an NLP program must be able to recognize and disambiguate words. For example, if the word “can” appears in text, does it refer to a noun or a verb? To obtain meaning from sentences not only must the words
be recognized and understood but the syntax and semantics of the arrangement of the
words also must be somehow made computable. This is a rich area of ongoing research
involving such subfields as knowledge representation, part of speech tagging, and
probabilistic parsing and processing methods.

Medical Language Processing (MLP), a medical subfield of NLP, has been
studied for its ability to extract information from a number of clinical sources including
discharge summaries and radiology reports. Hripcsak et al. (6) demonstrated that Natural
Language Processing could detect clinical conditions in chest x-rays with a consistency
that was indistinguishable from that of physicians reviewing the same reports.

Automated coding of clinical concepts into UMLS (Unified Medical Language
System) was demonstrated using MedLEE at Columbia University (15). Recently Bates
et al. (3) reported that event monitoring and natural language processing tools could
detect certain types of adverse events including nosocomial infections, adverse drug
events, and patient falls.

MedLEE uses a sophisticated combination of utility modules to process text
information. Input text is preprocessed, parsed, converted into regular phrases, mapped
and then encoded to a controlled medical terminology (32).

The efficient use of NLP tools to find adverse events is dependent upon the
existence of a computerized electronic medical record (EMR). At the very minimum,
patient and encounter specific free text files must be available for evaluation with these
tools. The Veterans Health Administration (VHA), part of the US Department of Veteran
Affairs, has one of the world’s largest EMR systems that is integrated into clinical
practice. As such, the VHA has the ability to provide a tremendous amount of narrative
clinical information for study using technologies such as NLP. Additionally, the VHA has multiple sites with varying levels of care from primary outpatient to highly specialized inpatient care typical of academic tertiary or quaternary care centers. This allows great potential for studies related to quality assurance covering all types of adult medical care. The use of NLP will be a novel approach to studying medical device adverse events at the VHA.

1.4 Phrase-Matching Algorithms

Simple word, phrase or pattern matching algorithms are familiar to anyone using Internet based search engines or document text searching in word processing programs. Searching large pieces of text for specific strings is a very common task that is made possible by the existence of electronic data. Regular expressions are important tools in text data manipulation and are extensively used in programming languages. These expressions may allow a highly specific search for matching text or can be created to be very general with the use of wildcards or multiple possible matching characters or words. For example, Figure 1 demonstrates a very simple regular expression that searches for either “central venous catheter” or “central line” located within 15 words of either “infection” or “sepsis”. Some possible matching phrases identified by this regular expression are shown below the regular expression. The use of wildcard characters could allow many variations of a root word to be included in the searching expression. The regular expression element <pneumothora[A-Za-z]{1,3}> could match “pneumothorax” and “pneumothoraces” and even words with typing errors such as “pneumothoraxes” and “pneumothorades,” which may be advantageous.
Regular expression

\((\text{central venous catheter|central line})\{?:\W++\w++\}\{0,15\}\W++(\text{infection|sepsis})\)

Examples of matching phrases

The central venous catheter was complicated by a Staph infection. The central line developed purulence at the subclavian entrance site the se antibiotics were started to treat the infection. The left internal jugular central line was thought to be the source of his Gram positive sepsis.

Regular expression

\((\text{infection|sepsis})\{?:\W++\w++\}\{0,15\}\W++(\text{central venous catheter|central line})\)

Examples of matching phrases

A Staph sepsis thought to be caused by the subclavian central line. The infection manifest by fever and bacteremia was found to be related to the left D central venous catheter placed in the operating room. His sepsis improved after removal of the central line.

Figure 1. A simplified regular expression and examples of phrases that would match the regular expression. The regular expression specifies that one of the two phrases relating to CVCs must be located between 0 and 15 words of one of the adverse event phrases (infection or sepsis). Note that a second regular expression must be used to capture sentences in which the adverse event and CVC phrases are reversed in order.
In 1986, the International Standards Organization (ISO) adopted a standard for describing documents and formatting called Standard Generalized Markup Language (SGML). This language is a highly sophisticated system that is particularly useful for cataloging and indexing data. However, SGML is also so complex that it is impractical for use in many applications. In 1998, the World Wide Web Consortium (W3C) created version 1.0 of the Extensible Markup Language (XML) specification that was designed to provide much of the power and flexibility of SGML but in a considerably simpler format primarily for Web based purposes. Stated goals of XML are that it will support a variety of different applications, that it should be easy to write programs that can process XML documents, and that the documents are human readable. Most Internet browsers, and many text-based applications, are now compatible with XML. MedLEE, a MLP program created at Columbia University and used for processing a variety of free text medical documents, is able to produce marked up clinical notes in XML which can then be used by other applications that can take advantage of the XML structure.

XQuery is a W3C specified query language that takes advantage of the structure of XML documents to retrieve and interpret the information stored within the documents. XQuery’s functionality for querying XML documents is somewhat analogous to that of SQL for relational databases. Although XQuery is a relatively young query language, there are now numerous commercial and open source applications that will support and facilitate its use, often in user-friendly graphical user interfaces.
1.6 Study Objectives

The overall objectives of this study are to:

1. Identify individual instances of central venous catheter (CVC) related adverse events in the Salt Lake City Veterans Administration Medical Center surgical intensive care unit using manual chart review from a subset of records enriched for the presence of possible adverse events.

2. Optimize a Natural Language Processing program and a phrase-matching algorithm to detect CVC related adverse events from text records.

3. Compare the accuracy of NLP and phrase-matching detection of CVC related adverse events to that obtained by manual chart review.

4. Estimate the incidence of CVC related adverse events in the Salt Lake City Veterans Administration Medical Center surgical intensive care unit and compare to known incidences reported in the literature.

5. Assess the feasibility of text based semiautomated methods as a technology for quality assurance activities related to medical device adverse events.
2. METHODS

This study consisted of the multiple steps that are described separately. First, an assessment of the administrative data used in this study was performed. Second, development of the phrase-matching algorithms and optimization of both semiautomated methods was necessary. Next, it was necessary to identify the study patients and appropriate text records. Finally, a sample of records enriched for the likelihood of containing evidence of a CVC related adverse event allowed creation of a manually reviewed reference standard. The results of both semiautomated methods were then compared to the reference standard. Additionally, a combination of the two semiautomated methods was employed and similarly compared to the reference standard. From calculated positive predictive values an estimate of the incidence of CVC related adverse events could be made. Figures 2, 3, and 4 outline this process and sections 2.1-2.4 describe these methods in detail.

2.1 Assessment of Administrative Data

The retrospective period included all candidate records from the beginning of utilization of electronic notes in 1999 until Dec 2004 in order to give the maximum number of patient records. Administrative data were collected as described below in section 2.3.1. This provided only 365 records, and in 49 of these there was no evidence in the text of a CVC being placed so these were excluded (the original goal was 400). In only 56 records was there a procedure note documenting the placement of a CVC.
Collection of typical phrases associated with CVC related adverse events

Phrase-matching algorithm

Partialy simulated data set

Improved phrase-matching algorithm

Optimized phrase-matching algorithm

MedLEE

Partially simulated data set

Improved preprocessing for MedLEE

Optimized preprocessing for MedLEE

Figure 2. Optimization of a phrase-matching algorithm (PMA) and a preprocessing method for MedLEE. Using a Medical Intensive Care Unit note set with the addition of simulated CVC related adverse events, both the PMA and the MedLEE preprocessing method were iteratively improved to enhance both sensitivity and specificity.
Figure 3. Creation of a reference standard and comparison to both semiautomated methods (MedLEE and PMA). Comparison of the semiautomated method results to the reference standard allowed a determination of sensitivity, specificity, positive and negative predictive values of those methods. The positive predictive values could then be used to estimate the number of adverse events in the sample of 316 records.
He developed about a 50% left-sided PTX during the attempted central venous catheter placement that required a chest tube (placed by gen surg) for a day.

Figure 4. Example of XML output generated for text containing a CVC related adverse event. Note that parsing is based upon the recognized elements of the sentence.
The small number of applicable patient records seemed very surprising given the volume of complex, high acuity procedures performed at the Salt Lake City VAMC. In order to assess the completeness of the administrative data the number of the collected records was compared to the numbers of patients undergoing certain surgical procedures. All cardiac (primarily coronary artery bypass and valve replacement procedures) and aortic surgeries will have central lines placed perioperatively for hemodynamic monitoring and the administration of fluids and vasoactive pharmacotherapeutic agents. A subset of the patients collected using administrative data and having a cardiac or aortic operation was compared to data obtained from the SLC VAMC Department of Surgery.

2.2 Optimization of a Phrase-Matching Algorithm and NLP Program for Identifying Adverse Events Related to CVCs

As shown in Figure 2 the optimization of both semiautomated methods required an iterative process. The text used for the optimization process consisted of 30 records extracted from the Medical Intensive Care Unit at the Salt Lake City VAMC from November 2001 to September 2004. The phrase collection procedure noted the general language including abbreviations and local lexicon used by physicians and nurses in their daily progress notes relating to CVCs. Additionally, three general surgeons were polled for expressions that were common descriptors for CVCs or CVC related adverse events. Finally, the UMLS Metathesaurus was searched for synonymous phrases for CVCs and associated adverse events. This created a pool of words and phrases that could be combined in regular expressions to search text (these regular expressions are given in Appendix A). Perl-compatible regular expressions were used exclusively in the PMA procedures. The 30 MICU records were then altered to add expressions relating to CVC
adverse events and the phrase-matching program was run. Whenever the program failed to pick up a simulated adverse event, the regular expression search was modified. A score was determined based upon an assigned value for matching a specific regular expression pattern (Table 1). In the test sample the maximum distance between a CVC phrase and an adverse event phrase was 15 words and this was taken to be the broadest likely match interval. A slightly narrower interval of 10 words was then chosen to reflect phrases with an even closer association of the concepts. A total of five points per record was found to be an appropriate threshold in order to identify at least 90% of events in this test data set.

The text utility used for file searching with regular expressions was PowerGrep ©, (JGsoft, Muang, Ubonratchathani, Thailand). A second step was implemented whereby each of the simulated events was changed to use negation, such as “no evidence of pneumothorax.” While this was simple to do, it created an additional problem in that a record that generally contains notes from a multiple day hospitalization may include both a phrase indicating the lack of an adverse event in one note. However, it is possible that later in the same day or in subsequent days a positive adverse event may occur. This

Table 1. Assigned scores for phrases matching defined patterns reflecting probable CVC related adverse events. Linking phrases would include {related to, due to, complicated by, etc.}

<table>
<thead>
<tr>
<th>Phrase pattern</th>
<th>Assigned value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVC phrase -- located within 15 words -- adverse event phrase</td>
<td>1</td>
</tr>
<tr>
<td>Adverse event phrase -- located within 15 words -- CVC phrase</td>
<td>1</td>
</tr>
<tr>
<td>CVC phrase -- located within 10 words -- adverse event phrase</td>
<td>2</td>
</tr>
<tr>
<td>Adverse event phrase -- located within 10 words -- CVC phrase</td>
<td>2</td>
</tr>
<tr>
<td>CVC phrase -- located within 10 words -- linking phrase* -- located within 10 words -- adverse event phrase</td>
<td>3</td>
</tr>
<tr>
<td>Adverse event phrase -- located within 10 words -- linking phrase -- located within 10 words -- CVC phrase</td>
<td>3</td>
</tr>
</tbody>
</table>
creates an ambiguous situation such that it is unclear if the negative phrase reflects the lack of an adverse event throughout the hospitalization or simply at one point in time. Because the records contained text from multiple days that were processed as a single large text file it was not directly possible to determine the temporal relationship of a negative and a positive phrase. Therefore, to maximize the sensitivity of the utility, negation phrases were not used.

The optimization of MedLEE involved primarily preprocessing to improve MedLEE's performance. The program was licensed from Columbia University with the rights to use but not alter the program. MedLEE was installed with a predefined lexicon on a local workstation using a Solaris 10 platform. When the MICU records were initially processed by MedLEE there were several observations noted that affected the functioning of the program. First, any XML reserved symbols occurring within the records required replacement (e.g., "<" with "less than", ">" with "greater than", "&" with "and", etc.). Additionally, symbols such as $, #, % and * would cause the program to fail and these were also replaced. The next difficulty encountered was that the MedLEE lexicon did not include most abbreviations and common proprietary names for CVCs. This was treated by replacing all of these designations with the generic term "central venous catheter" which MedLEE recognized as a medical device entity. Only a substitution of synonyms occurred in this process; no other changes were made that would alter either the syntax or semantics of the original sentence. Finally, the file structure of the records was somewhat problematic in two ways. MedLEE is designed to parse a well-structured medical note following a relatively standard format. For example, one broadly useful mode in the program was designed to process discharge summaries
that contain fairly typical headings such as admission history, past medical history, medications, physical examination, hospital course, discharge plan, etc. It was unclear how well MedLEE would process the large text files made up of multiple days notes of different types (progress notes, nursing notes, procedure and operative notes, discharge summaries). A preprocessing program was used to divide the record into individual notes, have MedLEE parse and process each note and the reconstitute the subsequent XML output. A test record consisting of 10 individual notes was subjected to this process and the output was compared to that of the record processed by MedLEE in its entirety as a single text file. There were slight variations in the beginning and end of the XML output document reflecting the overall structure of the note; however, the elements of interest within the note were unchanged at the level of sentence structure. Figure 4 demonstrates typical XML output from MedLEE with the associated original text. Based on the results of this test all records smaller than 220 Kb were processed by MedLEE as a single file. Any record larger than 220 Kb was divided into smaller sections keeping all notes intact, and after processing the output XML documents were re-associated.

2.3 Sample Selection

2.3.1 Identification of a group of appropriate patient records based on specific inclusion criteria relating to the patient’s treating medical service and/or hospital ward plus the presence of a CVC

Patients’ records were selected from the Salt Lake City Veterans Administration Medical Center database using the following criteria:
1. Admission between June 1999 and December 2004 to the Surgical Intensive Care Unit (SICU) or admission to the Medical Intensive Care Unit (MICU) with patient care provided by a surgical team.

2. Placement of at least one CVC.

CPT or ICD-9 procedure codes were used to identify patients having had a CVC placed (shown in Table 2). The ICD-9 code of 3893 included both CVCs and Peripherally Inserted Central Catheters (PICCs), however. A total of 49 patients with PICCs were excluded from the patient group due to the significantly different technical aspects and risk profiles of these catheters.

These criteria resulted in 316 patient records being selected. This appeared to be a surprisingly small number given the hospital volume and acuity, which would tend to indicate a more frequent need for central venous catheterization. Additional data was then collected to corroborate the assumption that the use of administrative data would not provide an accurate sample of all patients having had CVCs placed.

The characteristics of the records were fairly uniform, consisting of partially templated notes with large free text descriptive entries. The average size of a record was

Table 2. Administrative data used to identify patients in which CVCs were placed.

<table>
<thead>
<tr>
<th>Code System</th>
<th>Code Number</th>
<th>Description</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICD-9CM</td>
<td>3893</td>
<td>Venous Catheterization NEC</td>
<td></td>
</tr>
<tr>
<td>ICD-9CM</td>
<td>3895</td>
<td>Venous Catheter for Renal Dialysis</td>
<td></td>
</tr>
<tr>
<td>CPT5</td>
<td>36489</td>
<td>Percutaneous placement of central venous line (age 2 and over)</td>
<td></td>
</tr>
<tr>
<td>CPT5</td>
<td>36491</td>
<td>Placement of central venous line via cutdown (age 2 and over)</td>
<td></td>
</tr>
<tr>
<td>CPT5</td>
<td>36530</td>
<td>Insertion of implantable infusion pump</td>
<td></td>
</tr>
<tr>
<td>CPT5</td>
<td>36533</td>
<td>Placement of implantable venous access device, with or without reservoir</td>
<td></td>
</tr>
</tbody>
</table>
reflecting an average of 15,000 words. Entry of radiologic and laboratory data into the progress notes was often accomplished by the authors by simply cutting and pasting from the respective portions of the patient record. The notes included in the patient records were daily physician progress notes, consultation notes, nursing notes, procedure notes, operative reports and discharge summaries. The smallest was 15 Kb and had about 10 physician and nursing notes representing 2 days of hospitalization. There were also several very large records (>1 Mb) and representing over 6 weeks of notes. Several records in the manually reviewed sample had evidence of multiple lines being placed. The notes of each record were converted from a database into a single large plain text file for ease of management and to maintain the temporal relationship of events during the hospitalization. The maintenance of the temporal relationship may be critical in assessing causality of an adverse event to a device (for example, a pneumothorax that occurs one day before a CVC is placed cannot be due to the CVC).

2.3.2 Assessment of the completeness of administrative data for identification of patients with CVCs

Certain surgical procedures require the placement of a CVC at the time of anesthesia in order to provide safe monitoring throughout the operation. Any cardiovascular operation such as a coronary artery bypass or a cardiac valve replacement and any open aortic vascular procedure will fall into this category. Additionally, each of these patients will be admitted to the SICU (or MICU under the care of the surgical team) unless they die intraoperatively. The incidence of this rare event is less than 0.1% (16) and it will be assumed that all patients survived surgery at least long enough for post-
operative admission to an intensive care unit. The SLC VAMC Department of Surgery was able to provide the total number of these cases performed during the study period from June 1999 to December 2004. This total could then be compared to the total number of vascular and cardiac patients identified using administrative data.

2.4 Development of a Manually Reviewed Reference Standard

In order for a reference standard to be created a subset of patient records was collected by subjecting the entire 316 records to the phrase-matching algorithm. The matching files were scored based on presumptive likelihood for the presence of an adverse event (this is described in detail in section 2.4.1). Thirty records were randomly selected from a group of 49 with the highest scores and were assumed to be enriched for adverse events. An additional 10 records that scored 0 were taken to be extremely unlikely to have evidence of a CVC related adverse event. These were included in order to ensure the presence of records truly negative for adverse events.

This subset of 40 records was then manually reviewed by two physicians with at least two years of surgical training. The review format used a structured implicit review using a data form (Appendix B). There was generally insufficient information in the record for a physician to determine with certainty the presence of an adverse event. For example, specific criteria for the diagnosis of a catheter related infection would include positive blood cultures drawn through the catheter, positive catheter tip cultures and signs and symptoms of infection. Most records did not contain explicit information on details such as culture results in order for the reviewers to determine the appropriateness of the clinicians’ diagnoses based on rigid diagnostic criteria. Therefore, the reviewers were instructed to use only the language of the clinician notes in order to draw conclusions
regarding the presence of absence of adverse events and then assess the likelihood of the event. Specific data collected included the number of distinct CVCs clearly documented in the record, any potential adverse events listed in Table 3, and an assessment of the probability of the event occurring and being due to the CVC (possible, highly likely, certain).

Table 3. Descriptions of adverse events provided as a guide for structured implicit review.

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>Clearly related to the CVC and requiring antibiotic therapy and/or catheter removal.</td>
</tr>
<tr>
<td>Thrombosis or embolus</td>
<td>Resulting in local venous occlusion or distal embolization</td>
</tr>
<tr>
<td>Bleeding</td>
<td>Including external bleeding, hematoma, hemothorax, cardiac tamponade.</td>
</tr>
<tr>
<td>Mechanical malfunction</td>
<td>Anything that hinders normal function of the catheter such as kinking, occlusion, inability to use all ports, etc.</td>
</tr>
<tr>
<td>Malposition</td>
<td>Location of the catheter anywhere other than intended and resulting in need for catheter removal or diminished functionality (such as inability to transduce central venous pressure or infuse hyperosmolar fluids because of a peripheral venous location).</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>Ipsilateral pneumothorax temporally related to placement of the catheter.</td>
</tr>
<tr>
<td>Cardiac dysrhythmia</td>
<td>This must be clearly related to the catheter. For example, a short run of ventricular tachycardia that begins with advancement of the guide wire and resolves with retraction of the wire would be typical.</td>
</tr>
<tr>
<td>Other</td>
<td>Many uncommon adverse events have been attributed to CVCs and this category would include diagnoses such as chylothorax, nerve injury, bowel injury, and death.</td>
</tr>
</tbody>
</table>
After these 40 records were evaluated by two physician reviewers, the results were compared. Any records in which there was a disagreement regarding the presence or absence of an adverse event were then reviewed by a third reviewer (a Board certified surgeon). A simple majority of the three assessments was used to make the final determination regarding the presence of CVC related adverse event. Any differences in the number of CVCs determined to be present in the record by the reviewers were resolved by taking a mean of the two or three (when applicable) counts.

2.5 Application of the Two Semiautomated Methods to the Included Patient Records and Estimation of the Incidence of CVC Related Adverse Events

All 316 records were subjected to MedLEE, the phrase-matching algorithm and a method combining both MedLEE and a modified phrase-matching algorithm.

2.5.1 Phrase-matching

Phrase-matching was performed for each regular expression using PowerGrep© and each positive record was noted. Records were assigned a score based on the expected likelihood of the regular expression to be specific for the adverse event. The scoring system used is described in Table 1. A particular adverse event was considered likely if the score for the phrases relating to that event was greater than 5. The event was considered possible if the score was 3-5 and negative if less than 3. Note that all phrase matching required assessing the regular expression both forwards and backwards. For example, 1 point would be awarded if the record matched the pattern “CVC – maximum 15 intervening words – adverse event phrase” and an additional point given for matching
"adverse event phrase - maximum 15 intervening words – CVC". Both possible (score > 3) and likely (score > 5) records were considered to be positive for the purposes of selecting records with this method.

2.5.2 MedLEE

Records processed with MedLEE resulted in XML output files that could then be searched for adverse events associated with CVCs using XQuery. XMLSpy© provided the XQuery engine for the search process that utilized the XML structure of the output files. The basic XQuery format was:

Xquery version "1.0";

doc("outFile.xml")//sentence/structured[device[@v= "venous catheter"]]/problem

where problem could be specified as any of the adverse events of interest and outFile.xml is an XML documented generated by MedLEE from any of the patient records. This provided an association of adverse events with the specific files.

The results for each of the manually reviewed records could then be compared to that produced by the semiautomated methods. This comparison would allow calculation of sensitivity and specificity, as well as positive and negative predictive values. The numbers of positive records generated along with their respective positive predictive values could then estimate the incidence of CVC related adverse events.

2.5.3 Combination method

After the running both semiautomated methods it appeared that MedLEE would likely have better specificity than sensitivity and that the opposite was likely for the
phrase-matching. In some cases, one method would identify an event when the other did not. Two attempts at refinement utilizing both methods together were performed. The first involved selecting records with the phrase-matching algorithm first and then processing these with MedLEE. The second used a selection process with the phrase-matching algorithm but with a more selective scoring (that is, only likely records in which the score was > 5 were considered positive) and added those results to the MedLEE positive while omitting duplicates. This created a combination set of those records only found by phrase-matching plus those only found by MedLEE plus those found by both methods. This process is shown diagrammatically in Figure 5.

2.6 Statistical Analyses

Agreement between experts in the manual review portion of the study was evaluated with a Kappa statistic. The phrase-matching algorithm, MedLEE and combined methods were assessed for sensitivity, specificity, and positive/negative predictive values when compared to the manual reviewer created reference standard. Chi square was used to compare the results of each method to that of manual review. Estimates of CVC related adverse event rates were determined from the number of positive records found by each method and the respective positive predictive value. Confidence limits were calculated for each rate using the method of Bliss (17).
Figure 5. Creation of a combined method. Positive records from MedLEE and those from a phrase-matching algorithm modified to increase specificity were combined with a goal of increasing sensitivity.
3. RESULTS

3.1 Assessment of Administrative Data

The number of patients with CVCs seemed surprisingly low and this led to a confirmatory step to assess the completeness of the administrative data. The data collected by the SLC VAMC Department of Surgery were based on physician surgical activity rather than on billing codes for small procedures that may be done as part of the total patient care.

Between 1999 and 2004, there were 197 aortic and 1223 cardiac cases (total 1423). In the sample generated using administrative data there were 163 vascular and cardiac patients. This suggests that administrative data only captured 11.5% of these patients that must have had central lines placed.

3.2 Manual Review of Subset of Records Enriched for CVC Related Adverse Events

Each of the 40 records randomly selected from the phrase matching procedure (30 with possible events, 10 probably without events) were reviewed by two physicians. The total number of distinct central lines found in the 40 reviewed records was 76. The reviewers' agreement was reasonably good with a Kappa of 0.668.

In the cases where there was disagreement a third reviewer served as a tie breaker and then these results formed the reference standard against which to compare the results produced by the phrase matching algorithm and MedLEE.
3.3 Comparison of Semiautomated Methods with the Reference Standard

Each of the semiautomated methods was compared to the manually reviewed reference standard allowing a determination of sensitivity, specificity, positive predictive value (PPV) and negative (NPV) predictive value. Positives are considered true positives when an automated result correlates to a manually reviewed determination of at least a possible adverse event. These are summarized in Figure 6. Different levels of certainty

![Figure 6](image)

Figure 6. Sensitivity, specificity, and positive/negative predictive values for each of the three methods. Error bars represent 90% confidence intervals.
were not included in the statistical analysis because of the resultant decrease in power. This made the data dichotomous with results being either the presence or absence of a CVC related adverse event.

While sensitivity, specificity and PPV are measures familiar to most physicians and biomedical scientists, precision and recall are commonly used in information retrieval domains. These values are defined as follows:

- **Sensitivity** = $\frac{TP}{TP+FN}$
- **Specificity** = $\frac{TN}{TN+FP}$
- **PPV** = $\frac{TP}{TP+FP}$

Recall = \textit{ratio of the number of relevant records retrieved to the total number of relevant records in the database} = $\frac{TP}{TP+FP}$. Note that this is the same as PPV.

Precision = \textit{ratio of the number of relevant records retrieved to the total number of irrelevant and relevant records retrieved} = $\frac{TP}{TP+FN}$. Note that this is the same as sensitivity.

One advantage of using these values is that they facilitate the calculation of an additional metric, the F measure. The F measure combines precision and recall and is considered to be a highly useful measure of system performance. A factor, $\beta$, allows weighting of the effects imparted by precision and recall. F is defined as follows:

$$ F = \frac{(1+\beta^2)PR}{\beta^2P + R} = \frac{(1+\beta^2)}{\beta^2 + \frac{1}{R}P} $$

(Equation 1)
The most commonly applied form of the F measure is referred to as F1 (or a balanced F) in which precision and recall are equally weighted (that is, $\beta = 1$). Then, F can be simplified, as shown below:

$$F1 = \frac{2PR}{P+R}$$  \hspace{1cm} (Equation 2)

Figure 7 demonstrates the calculated precision and recall for each method. Note that the combined method maintains high recall with only a slight decrement in precision. Weighting can favor precision ($\beta < 1$) or recall ($\beta > 1$). Applications of weighting are further reviewed in the Discussion section. Figure 8 demonstrates the calculated F measures for each semiautomated method. A balanced F, weighting precision and recall equally, is compared to F measures weighted to favor either precision or recall. Not surprisingly, when F is weighted towards precision (or effectively weighted towards sensitivity) the PMA shows the highest measure. Conversely, when the weighting is towards recall, MedLEE shows a higher measure. The combined method is equal to or better than either individual method regardless of the weighting of the F measure.

### 3.4 Adverse Events Estimated by Each Method

Table 6 shows the total number of adverse events found in the entire sample of 316 records and using the positive predictive value for each method an estimate of the total number of true adverse events can be estimated. A range from 6 to 10% was found by the 3 methods. This is similar to rates reported by other authors for CVC related adverse events (8, 14). Based on these results all three of these methods appear to be useful for producing such estimates.
Figure 7. Precision and recall calculated for each semiautomated method.
Figure 8. Comparison of F measures calculated for each semiautomated method. Weighting is shown for balanced F, and towards precision or recall.

Table 6. Estimation of adverse events based upon the positive predictive value of each method and the number of adverse events found in the entire 316 records.

<table>
<thead>
<tr>
<th></th>
<th>Phrase matching</th>
<th>MedLEE</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total found by method</td>
<td>50</td>
<td>28</td>
<td>51</td>
</tr>
<tr>
<td>PPV</td>
<td>41.0%</td>
<td>70.5%</td>
<td>64.3%</td>
</tr>
<tr>
<td>Estimate of positive</td>
<td>20.5</td>
<td>19.6</td>
<td>32.7</td>
</tr>
<tr>
<td>records (out of 316)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estimate of adverse</td>
<td>6.3 %</td>
<td>6.11%</td>
<td>10.7%</td>
</tr>
<tr>
<td>event rate</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
3.5 Failure of Automated Results

The results of both MedLEE and the phrase-matching algorithm were evaluated in comparison to the reviewers' identification of adverse events in order to determine the reason that each method failed in cases with false positives or negatives. Reasons common to both methods were spelling errors in the text of the notes. MedLEE additionally had greater difficulty interpreting local abbreviations such as "infn" or "infx" for infection. Human reviewers have clearly more ability to interpret the clinical situation even when the spelling and grammar in the documentation was imperfect.

False positives were also seen in both methods. In many cases in the phrase-matching method, a false positive was generated when physicians documented risks of procedures discussed with the patient. For example, if the physician writes that the "risks of bleeding, infection, thrombosis and death were discussed and consent for CVC placement was obtained" then the phrase-matching algorithm will identify bleeding, infection, thrombosis and death as actual occurrences. MedLEE handled the concept of procedural risk without difficulty but had somewhat similar problems when phrases often associated with CVCs were used in proximity to a CVC synonym. Figure 9 demonstrates one such example in which XQuery generates a positive result because the catheter is mentioned close to a concept of sepsis. In this case, however, sepsis was in the reason for placing the catheter to allow hemodynamic monitoring rather than a complication of infection of the catheter.
His PA cath numbers are appealing septic again with SVR in the 300's and hypotension.
4. DISCUSSION

This study demonstrates that semiautomated methods can identify CVC related adverse events with reasonable reliability approaching that of human reviewer. That the human reviewers differed on the presence or absence of adverse events and on the numbers of catheters recognized may simply reflect the large amount of data to be read and processed. Reviewers may tend to skim the text reports and many details that are not emphasized in the report. This is exemplified by the fact that both reviewers failed to detect any CVCs in 3 of 40 manually reviewed records. In each case the notation indicating the presence of a CVC was a single phrase, typically in the Plan section of the physician note, such as “D/C TLC” (discontinue or remove the triple lumen catheter). The average size of a record was 156 Kb or the equivalent of approximately 14 pages and so it is not surprising that brief mentions of this sort might go unnoticed. On the other hand, it also seems likely that a significant adverse event would receive considerably more mention in the record, possibly repeated over a period of several days since most adverse events result in requirement of some additional or alternate treatment. Examples would include a multiple day course of antibiotics for a CVC related infection or a chest tube and daily chest X-rays for a pneumothorax. This effect may tend to underestimate the total number of uncomplicated catheters by manual review. It is conceivable that automated methods may be beneficial in identifying such instances that do not attract the attention of human reviewers.
Specificity was considerably lower in the phrase-matching algorithm than MedLEE or the combined method. Several factors may account for this. The inability to use negation was likely a significant contributor. The primary difficulty with using methods to detect negation in this study was due to the desire to maintain the notes in chronological order within a single large file representing a period within a patient's hospitalization. The advantage to this approach is that the detection of multiple CVCs in a single patient hospitalization would be facilitated and that a description of one adverse event in multiple days' notes would not be interpreted as multiple events. The disadvantage is that an adverse event phrase that is negated in one note does not exclude the possibility of that event actually occurring in preceding or subsequent notes. It then becomes difficult to determine which case is true. For example, a note may discuss a possible CVC related infection in one note, determine that an alternate site accounts for the clinical signs of infection in the next day's note and then a week later another note may document a confirmed CVC related infection.

Spelling errors and abbreviations were a clear source of error for all automated methods. All typical abbreviations encountered in the training data were incorporated into the preprocessing step for MedLEE and in the regular expressions for the phrase-matching algorithm. In spite of this, it was apparent on re-evaluating the semiautomated methods' performance on the manually reviewed records that spelling and abbreviation accounted for many false negatives. This may be a problem peculiar to systems like that at the SLC VAMC where clinician-typed notes vary widely in their spelling accuracy and use of standardized abbreviations. Possible ways to address this problem would include
dictation and professional transcription and real-time spell checking using a dictionary with locally defined abbreviations and terms.

The accuracy of MedLEE, phrase-matching, and the combined semiautomated method was similar to other reported uses of electronic methods for adverse event detection. Bates et al. (3) reported a sensitivity of 69%, specificity of 48% and PPV of 52% in his study using an electronic tool to screen discharge summaries for 11 adverse event categories including failure of medical management, hospital incurred trauma and adverse drug events. A study that evaluated MedLEE for its ability to detect adverse events from discharge summaries (18) demonstrated a sensitivity of 28%, a specificity of 98.5% and a PPV of 45%. The combined method reported here achieved a sensitivity of 72%, a specificity of 80.8 and a PPV 64.3%. That these numbers are generally somewhat higher than those reported by Bates et al. and Melton and Hripcsak (18) likely reflects the much narrower clinical scope of adverse events being studied in this study. It would seem logical that it is easier to develop a method to detect possible permutations of text-based descriptions of adverse events when the specific types of adverse events are relatively few in number as is the case with CVC related complications. However, it is notable that the quality of the text data was also substantially different. The VA data used in this study included physician entered notes with a high frequency of spelling and grammatical errors that may limit the success of automated methods whereas both studies by Bates et al. (3) and Melton and Hripcsak (18) used discharge summaries that are likely to have been professionally transcribed.

Other authors have reported results of test-based utilities to identify adverse events in hospital discharge summaries. Melton and Hripcsak (18) used Natural
Language Processing to detect a broad range of different adverse events. Similarly, Murff et al. (19) used discharge summaries to identify a variety of events by association with "trigger" words. This is somewhat analogous to the concept of the phrase-matching algorithm. Figure 10 compares the Melton's and Murff's reported results with those obtained from this study.

Utilizing F measures to assess the performance of these methods resulted in interesting results. Although a balanced F ($\beta = 1$) is most commonly applied in other

![Figure 10. Sensitivity, specificity and PPV of different text based methods. Two methods reported in the literature are compared to the results obtained from this study (PMA, MedLEE, Combined). The values for the former two methods are reported in Murff et al. (19) and Melton et al. (18).](image-url)
general, non-medical information retrieval tasks the weighting of $\beta$ is controversial. Some authors feel that performance is optimized by weighting towards precision (20); however, at least one study suggests the opposite (21). In a medical case where the text is searched for the purpose of adverse event surveillance or early identification of adverse events with the goal of intervening and minimizing harm, a different weighting may be appropriate. For example, if the goal of surveillance is to minimize review by humans and a PPV of 50% is considered acceptable (that is, two records reviewed for each true positive adverse event) then methods placing more emphasis on sensitivity or recall would be appropriate.

This study estimated the overall incidence of CVC related adverse events to be 6-10% over the life of the catheter. It is important to point out that in SLC VAMC SICU patient population the life of a CVC may be highly variable. Uncomplicated CVCs placed routinely for intra-operative hemodynamic monitoring may be removed within 48 hours of placement. On the other hand, long-term hemodialysis access may remain in place for months. Some studies in which routine surveillance is performed for infection or thrombosis report very high rates of these adverse events (8, 22, 23) of up to 30%. The study by Timsit et al. (22) is interesting in that the patient population was admitted to an intensive care unit and surveillance allowed detection of many asymptomatic or clinically unapparent cases of thrombosis. Schwarz et al. reported on tunneled catheters in an oncologic patient population and noted rates of 17.6 infections, 8.1 thrombotic complications, 6.9 catheter breakage and 3.5 displacement per 1000 catheter days (11). The estimate found by automated methods in this study appears to be well within the range of incidences reported in the literature.
An additional issue that presents difficulties when trying to compare these results to those in the literature relates to the frequent inability to determine the length of patient exposure to risk from the CVC. In other words, in the SLC VAMC patient records it is generally impossible to determine how long a catheter is in place. This may not be of significance in adverse events such as pneumothorax or injury to adjacent structures which most commonly occur at the time of catheter insertion but are clearly important in thrombosis and infection which occur at a rate per catheter day (24). Only 56 records documented the CVC placement with a procedure note. In the manually reviewed sample of 40 records there were 76 distinct CVCs found (and at least 3 not found). Because these reviewed records were enriched for the possibility of an adverse event, they may reflect a patient group with a higher overall acuity. Therefore, the ratio of 76 lines/40 records is likely to overestimate the ratio in the remainder of the study patients. However, at the very minimum there must be \((316 - 40) + 76 = 352\) CVCs in the 316 patient records. This suggests that at most \(56/352 = 15.9\%\) of CVC placements are documented in the patient record. This poor documentation would certainly a limiting factor in development of a surveillance system that relies upon textual signals. CVCs placed with greater technical difficulty are more likely to have adverse events and this potentially predictive information may be lost without a procedure note. Additionally, the procedure note clearly identifies the date of insertion, which would be the most reliable data on which to determine the length of patient exposure to long term risks.

It may be possible to improve these automated methods in with different strategies. Spelling errors and abbreviations unrecognized by the methods may be addressed with a modification of the preprocessing step. Conversely, the same result
may be accomplished by directly altering the regular expressions in the phrase-matching algorithm or adding to the NLP program's lexicon. If both methods were to be used together as in our combined method, it would be more elegant to use a preprocessing step.

The assessment of the accuracy of administrative data for identification of patients with CVCs suggests that only 11% of patients with CVCs may be detected with this method. Whether a sample produced by administrative data creates bias in our study patients is unknown. It is conceivable that a clerk reviewing a chart for billable procedures and diagnoses may be more likely to miss the uncomplicated cases. This would suggest that our sample might have selection bias towards patients with adverse events and thus overestimate the incidence of these events. On the other hand, CVCs that are placed as surgical procedures (this would include implanted long-term venous access devices for chemotherapy, renal dialysis and total parenteral nutrition) are more likely to be included in administrative data as typically all procedures performed in the operating room will generate a billable CPT code. Short term CVCs placed as part of anesthesia care or in a patient ward may not trigger a billing charge and may not be represented in administrative data. This possibility would tend to overestimate CVCs placed in the highly controlled and sterile conditions of the operating room. The ready availability of additional technology such as ultrasound and fluoroscopy may also decrease the mechanical risks of the procedure. Interestingly, the incidence found in this study was well within the range reported by other authors and so these are unlikely to be large effects.
The potential of these methods for surveillance purposes and possibly for integration into an electronic medical record system containing alerting and other decision support capabilities is substantial. From a technical standpoint these methods could be relatively easily integrated into such a system. The methods could be further modified to identify other types of adverse events by using a methodology similar to that described here to gather phrases that could indicate the presence of such an event. In this particular example of CVC related adverse events the PPVs found (ranging from 41% for the PMA to 70% for MedLEE) were certainly high enough to be useful for surveillance purposes. Assuming that human reviewers are used to confirm adverse events, they would only need to read about two records for every case of CVC related adverse events. Given that the frequency of adverse events estimated at the SLC VAMC was 6-11%, the methods could markedly reduce the number of negative charts for the reviewers to process.
5. CONCLUSIONS

Identification of adverse events plays an important role in quality assurance activities and in the development of methods that can ameliorate the time and economic burden of manual review are potentially of great benefit. This study demonstrates that it is possible to create semiautomated methods that can retrospectively identify CVC related adverse events with sufficient sensitivity and specificity for surveillance purposes. In addition, using such methods in systems designed for early or real-time identification of factors associated with the risk of developing adverse events may allow prevention of these events. While surveillance for quality assurance purposes is certainly an important function, the potential use in preventing harm from devices with a certain intrinsic risk is a very exciting application of the technology. Considerable work remains to be done to unequivocally demonstrate the feasibility, effectiveness and value of such an application.
APPENDIX A

REGULAR EXPRESSIONS USED FOR IDENTIFYING CVCs
AND CVC RELATED ADVERSE EVENTS

A.1 CVC Phrases

(central venous catheter|central line|cvl|CVC|subclavian line| sc line| SC line| rsc | RSC |
lsc | LSC| ij | rj|lij|internal jugular line|femoral line|single lumen|double lumen|triple
lumen|TLC|cordis|hickman|broviak|port-a-cath|dialysis cath[A-Za-z]{0,6}|central venous
catheterization |vascath|permacath|duoflow|mahurkar|shiley|line related

A.2 CVC + Adverse Event

(central venous catheter|central line|cvl|CVC|subclavian line| sc line| SC line| rsc | RSC |
lsc | LSC| ij | rj|lij|internal jugular line|femoral line|single lumen|double lumen|triple
lumen|TLC|cordis|hickman|broviak|port-a-cath|dialysis cath[A-Za-z]{0,6}|central venous
catheterization |vascath|permacath|duoflow|mahurkar|shiley|line related)(?:\\W++\\w++){0,15}(\\W++(pneumothora[A-Za-z]{1,3}|hemothora[A-Za-z]{1,3}|bloody effusion|clot|htx|rhtx|hhtx|bleed into chest|hemorrhage into chest|bleed into
pleura|hemorrhage into pleura|hematoma|lung
down|ptx|rptx|lptx|pneumo(?!p|n)|Bleeding|acute anemia|hemorrhage|blood
loss|infection|inf|infx|sepsis|abnormal position|displaced|tip in artery| tip in
brachiocephalic|tip in jugular|tip in ventricle|tip in atrium|not in position|not in
svc|Tachyarrhythmia|vt|ventricular tachycardia|couplet|premature beats|pvc's|premature
ventricular complex[A-Za-z]{0,2}|Thombosis|thrombus|thrombi|embolus|emboli[A-Za-z]{0,6}|thromboemboli[A-Za-z]{0,6}|clot|Kink|occlusion|occluded|block|obstructed|failure to place|could not place|not access|Demise|die|die[s|d]|expired|multiple attempt|attempted multiple|multiple pass|unable to)

A.3 Adverse Event + CVC
(pneumothora[A-Za-z]{1,3}|hemothora[A-Za-z]{1,3}|bloody
effusion|clot|htx|rhtx|htx|bleed into chest|hemorrhage into chest|bleed into
pleural|hemorrhage into pleural|hematoma|lung
down|ptx|rptx|lptx|pneumo?(?!p)n|Bleeding|acute anemia|hemorrhage|blood
loss|infection|infl|infx|sepsis|abnormal position|displaced|tip in artery|tip in
brachiocephalic|tip in jugular|tip in ventricle|tip in atrium|not in position|not in
cvc|Tachyarrhythmia|vt|ventricular tachycardia|couplet|premature beats|pvc’s|premature
ventricular complex[A-Za-z]{0,2}|Thombosis|thrombus|thrombi|embolus|emboli[A-Za-z]{0,6}|thromboemboli[A-Za-z]{0,6}|clot|Kink|occlusion|occluded|block|obstructed|failure to place|could not place|not access|Demise|die|die[s|d]|expired|multiple attempt|attempted multiple|multiple pass)(?!\W++\w++){0,15}\W++(central venous catheter|central line|civ|CVC|subclavian
line|sc line|SC line|rsc|RSC|lsc|LSC|i|ij|internal jugular line|femoral line|single
lumen|double lumen|triple lumen|TLC|cordis|hickman|broviak|port-a-cath|dialysis
cath[A-Za-z]{0,6}|central venous catheterization
|vascath|permacath|duoflow|mahurkar|shiley|line related)
A. 4 CVC + Linker + Adverse Event

(central venous catheter|central line|cath|CVC|subclavian line|sc line|SC line|rsc |RSC |lsc |LSC| ij |rij|lij|internal jugular line|femoral line|single lumen|double lumen|triple lumen|TLC|cordis|hickman|broviak|port-a-cath|dialysis cath[A-Za-z]{0,6}|central venous catheterization |vascath|permacath|duoflow|mahurkar|shiley|line related)(?:\W++\w++) {0,15}\W++(related to|related|line related|due to|cause|source|associated|complicated[A-Za-z]{0,5}|adverse|secondary to)(?:\W++\w++) {0,15}\W++(pneumothorax[A-Za-z]{1,3}|hemothorax[A-Za-z]{1,3}|bloody effusion|clot|htx|rhtx|hxtx|bleed into chest|hemothage into chest|bleed into pleura|hemothage into pleural|hemorrhage into chest|hemorrhage into chest|bleed into pleural|hemorrhage into pleural|lung
down|ptx|rptx|lptx|pneumothorax(?!p/n)|Bleeding|acute anemia|hemothage|blood loss|infection|sepsis|infn|infx|abnormal position|displaced|tip in artery|tip in brachiocephalic|tip in jugular|tip in ventricle|tip in atrium|not in position|not in svc|Tachyarrhythmia|vt|ventricular tachycardia|couplet|premature beats|pvc’s|premature ventricular complex[A-Za-z]{0,2}|Thrombosis|thrombus|thrombi|embolus|emboli[A-Za-z]{0,6}|thromboemboli[A-Za-z]{0,6}|clot|Kink|occlusion|occluded|block|obstructed|failure to place|could not place|could not access|Demise|die|die[s|d|expired|multiple attempt|attempted multiple|multiple pass)

A.5 Adverse Event +Linker + CVC

(pneumothorax[A-Za-z]{1,3}|hemothorax[A-Za-z]{1,3}|bloody effusion|clot|htx|rhtx|hxtx|bleed into chest|hemothage into chest|bleed into pleura|hemothage into pleural|hematomalung
down|ptx|rptx|lptx|pneumo(?|p|n)|Bleeding|acute anemia|hemorrhage|blood loss|infection|sepsis|inf|infx|abnormal position|displaced|tip in artery|tip in brachiocephalic|tip in jugular|tip in ventricle|tip in atrium|not in position|not in svc|Tachyarrhythmia|vt|ventricular tachycardia|couplet|premature beats|pvc's|premature ventricular complex[A-Za-z\{0,2\}]|Thombosis|thrombus|thrombi|embolus|emboli[A-Za-z\{0,6\}]|thromboemboli[A-Za-z\{0,6\}]|clot|Kink|occlusion|occluded|block|obstructed|failure to place|could not place|could not access|Demise|die|die[s|d]|expired|multiple attempt|attempted multiple|multiple pass)(?:\W++\w++)\{0,15\}\W++(related to|related|line related|due to|cause|source|associated|complicat[A-Za-z\{0,5\}]|adverse|secondary to)(?:\W++\w++)\{0,15\}\W++(central venous catheter|central line|cvl|CVC|subclavian line|sc line|SC line|sc line|rsc | RSC | lsc | LSC | ij | rjj|lij|internal jugular line|femoral line|single lumen|double lumen|triple lumen|TLC | cordis|hickman|broviak|port-a-cath|dialysis cath[A-Za-z\{0,6\}]|central venous catheterization |vascath|perm cath|duoflow|mahurkar|shiley|line related)(?:\W++\w++)\{0,15\}\W++(absence of|no evidence|no findings|no suggestion|nothing to suggest|exclude|without [evidence|any evidence|indication|any indication|sign|any sign]|negative for|rule[s|d]
out\(\text{risk}\)\(?\backslash W^+\backslash w^+\{0,15\}\backslash W^+\)\(\text{pneumothora}[A-Za-z]\{1,3\}\)\(\text{hemothora}[A-Za-z]\{1,3\}\)\(\text{bloody effusion}\)\(\text{clot}\)\(\text{rthx}\)\(\text{lhtx}\)\(\text{bleed into chest}\)\(\text{hemorrhage into chest}\)\(\text{bleed into pleura}\)\(\text{hemorrhage into pleura}\)\(\text{hematoma}\)\(\text{lung}\)

down\(\backslash\text{ptx}\)\(\backslash\text{rptx}\)\(\backslash\text{lptx}\)\(\text{pneumo}(?!p/n)\)\(\text{Bleeding}\)\(\text{acute anemia}\)\(\text{hemorrhage}\)\(\text{blood loss}\)\(\text{infection}\)\(\text{sepsis}\)\(\text{abnormal position}\)\(\text{displaced}\)\(\text{tip in artery}\)\(\text{tip in brachiocephalic}\)

\(\text{tip in jugular}\)\(\text{tip in ventricle}\)\(\text{tip in atrium}\)\(\text{not in position}\)\(\text{not in svc}\)\(\text{Tachyarrhythmia}\)\(\text{vt}\)\(\text{ventricular tachycardia}\)\(\text{couplet}\)\(\text{premature beats}\)\(\text{pvc's}\)\(\text{premature ventricular complex}[A-Za-z]\{0,2\}\)\(\text{Thrombosis}\)\(\text{thrombus}\)\(\text{thrombi}\)\(\text{embolus}\)\(\text{emboli}[A-Za-z]\{0,6\}\)\(\text{thromboemboli}[A-Za-z]\{0,6\}\)\(\text{clot}\)\(\text{Kink}\)\(\text{occlusion}\)\(\text{occluded}\)\(\text{block}\)\(\text{obstructed}\)\(\text{failure to place}\)\(\text{could not place}\)\(\text{could not access}\)\(\text{Demise}\)\(\text{die}\)\(\text{die}[s/d]\)\(\text{expired}\)\(\text{multiple attempt}\)\(\text{attempted multiple}\)\(\text{multiple}\)\(\text{multiple pass}\)

\(\text{pneumothora}[A-Za-z]\{1,3\}\)\(\text{hemothora}[A-Za-z]\{1,3\}\)\(\text{bloody effusion}\)\(\text{clot}\)\(\text{rthx}\)\(\text{lhtx}\)\(\text{bleed into chest}\)\(\text{hemorrhage into chest}\)\(\text{bleed into pleura}\)\(\text{hemorrhage into pleura}\)\(\text{hematoma}\)\(\text{lung}\)

down\(\backslash\text{ptx}\)\(\backslash\text{rptx}\)\(\backslash\text{lptx}\)\(\text{pneumo}(?!p/n)\)\(\text{Bleeding}\)\(\text{acute anemia}\)\(\text{hemorrhage}\)\(\text{blood loss}\)\(\text{infection}\)\(\text{sepsis}\)\(\text{abnormal position}\)\(\text{displaced}\)\(\text{tip in artery}\)\(\text{tip in brachiocephalic}\)

\(\text{tip in jugular}\)\(\text{tip in ventricle}\)\(\text{tip in atrium}\)\(\text{not in position}\)\(\text{not in svc}\)\(\text{Tachyarrhythmia}\)\(\text{vt}\)\(\text{ventricular tachycardia}\)\(\text{couplet}\)\(\text{premature beats}\)\(\text{pvc's}\)\(\text{premature ventricular complex}[A-Za-z]\{0,2\}\)\(\text{Thrombosis}\)\(\text{thrombus}\)\(\text{thrombi}\)\(\text{embolus}\)\(\text{emboli}[A-Za-z]\{0,6\}\)\(\text{thromboemboli}[A-Za-z]\{0,6\}\)\(\text{clot}\)\(\text{Kink}\)\(\text{occlusion}\)\(\text{occluded}\)\(\text{block}\)\(\text{obstructed}\)\(\text{failure to place}\)\(\text{could not place}\)\(\text{could not access}\)\(\text{Demise}\)\(\text{die}\)\(\text{die}[s/d]\)\(\text{expired}\)\(\text{multiple attempt}\)\(\text{attempted multiple}\)\(\text{multiple}\)\(\text{multiple pass}\)
place|could not access|Demise| die | die[s|d]|expired|multiple attempt|attempted
multiple|multiple pass)(?:\W++\w++){0,15}\W++(absence of |no evidence|no findings|no
suggestion|nothing to suggest|exclude|without [evidence|any evidence|indication|any
indication|sign|any sign] | negative for|rule[s|d]
out|risk})(?:\W++\w++){0,15}\W++(central venous catheter|central
line|cv|CVC|subclavian line| sc line| SC line| rsc | RSC | lsc | LSC| ij | rij|lij|internal
jugular line|femoral line|single lumen|double lumen|triple
lumen|TLC|cordis|hickman|broviak|port-a-cath|dialysis cath[A-Za-z]{0,6}|central venous
catheterization|vascath|permacath|duoflow|mahurkar|shiley|line related)
APPENDIX B

DATA COLLECTION USING A STRUCTURED IMPLICIT REVIEW

The following information was gathered during the manual review portion of the study. Highly specific information was requested to determine the number of CVCs per record, the number and type of adverse events and a judgment regarding the causality of the adverse event relative to the CVCs placed.
Assessing Adverse Events Related to Central Venous Catheters (CVC's)

Is there evidence that a central line has been placed in the record?  
Y  N

Is there evidence of multiple central lines in this record?  
Y  N

If there are multiple lines, how many are clearly evident?  

Please mark each new line insertion with a red pen on the record.

Is there evidence of at least one adverse event related to CVC's?  
Y  N

Indicate the number of distinct CVC related adverse events in the table below. (If there are two line infections and one DVT in the same record then write 2 beside infection and 1 beside Thrombosis/embolus). If there are none, draw a line through the boxes on the right side. For any occurrences indicate the certainty that an event occurred using the following key:

- Possible  P
- High likelihood/probable  H
- Certain/confirmed  C

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Distinct occurrences</th>
<th>Degree of certainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombosis/embolus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bleeding - including external bleeding, hemothorax, cardiac tamponade, hematomas etc</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mechanical malfunction - for example, kinking, occlusion, inability to use all ports, anything that hinders normal function of the catheter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malposition - location of the catheter anywhere other than intended and resulting in removal or diminished functionality (such as inability to infuse hyperosmolar fluids because of a peripheral vein location)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumothorax</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac dysrhythmia - must be clearly related to the catheter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other - examples might include chylothorax, nerve injury, bowel injury, death</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Please list:
REFERENCES


