MINI-SENTINEL SYSTEMATIC EVALUATION OF HEALTH OUTCOME OF INTEREST DEFINITIONS FOR STUDIES USING ADMINISTRATIVE DATA

ACUTE RESPIRATORY FAILURE REPORT

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I. EXECUTIVE SUMMARY

A. OVERVIEW OF PROJECT

The Food and Drug Administration (FDA) Mini-Sentinel contract is a pilot program that aims to conduct active surveillance to detect and refine safety signals that emerge for marketed medical products. To perform this active surveillance, it is necessary to develop and understand the validity of algorithms for identifying health outcomes of interest in administrative data. Thus, the goal of this project was to identify algorithms used to detect selected health outcomes of interest using administrative data sources and describe the performance characteristics of these algorithms as reported by the studies in which they were used. This report summarizes the process and findings of the acute respiratory failure (ARF) algorithm review.

B. SUMMARY OF FINDINGS

Only 2 studies provided codes for ARF, each using related yet different ICD-9 codes (i.e., ICD-9 codes 518.8,"other diseases of lung," and 518.81,"acute respiratory failure"). Neither study provided validation estimates.

C. RECOMMENDATION FOR ALGORITHMS AND SUGGESTION FOR FUTURE RESEARCH

Our search highlights a scarcity of literature focusing on ARF that provided validated algorithms/estimates. Research needs to be conducted on designing validation studies to test ARF algorithms, and estimating their predictive power, sensitivity, and specificity. Incorporating procedural codes in combination with diagnostic codes may aid in improving algorithm performance, particularly sensitivity, as ARF patients may be coded with other conditions such as chronic respiratory failure (CRF, ICD-9 code 518.83) and acute respiratory distress syndrome (ARDS, ICD-9 code 518.82).

II. PROJECT OBJECTIVES

The primary objective of this project was to identify studies that used validated algorithms to identify various health outcomes of interest (HOIs) using administrative data from the United States or Canada, and to summarize the results of those validation studies. If fewer than 5 validation studies were identified, a secondary objective was to identify non-validated algorithms that were used to identify the HOIs using administrative data.

III. BACKGROUND

The Food and Drug Administration (FDA) Mini-Sentinel contract is a pilot program that aims to conduct active surveillance to detect and refine safety signals that emerge for marketed medical products. In order to perform this work, the program needed to identify algorithms used to detect various health outcomes of interest using administrative data sources and identify the performance characteristics of these algorithms as measured in the studies in which they were used. The data sources of interest were limited to those from the United States or Canada to increase their relevance to the Mini-Sentinel data sources, which are all from the United States. The Mini-Sentinel Protocol Core developed a preliminary list of approximately 140 potential health outcomes of interest, based on several criteria. These criteria included: 1) previous validation studies that were identified in a textbook chapter reviewing the validity

of drug and diagnosis data used in pharmacoepidemiologic studies,[1] 2) a list of designated medical events from a proposed FDA rule on the safety-reporting requirements for human drug and biological products,[2] and 3) the Observational Medical Outcomes Partnership (OMOP)'s[i] commissioned reports on algorithms used to identify health outcomes using administrative data.[3]

From the original list of 140 HOIs, the Protocol Core worked with FDA to select 20 for which reviews of algorithms would be completed. HOIs for which OMOP had already commissioned reports were purposefully excluded in order to avoid duplication of effort.

ARF was one of the 20 HOIs selected for review. This report describes the review process and findings for the ARF definition algorithms.

IV. METHODS

A. SEARCH STRATEGY

The general search strategy was developed based on prior work by OMOP and its contractors, and modified slightly for these reports. Originally, OMOP contracted with 2 organizations to perform reviews of 10 HOIs. Because the search strategies used by each organization resulted in very different sets of articles, OMOP investigators reviewed the PubMed indexing of the articles deemed useful in final reports and developed a strategy that would identify the majority of these citations while maintaining efficiency in the number of abstracts that would need to be reviewed. Mini-Sentinel investigators made minor changes to this strategy that would result in the identification of more citations, and confirmed empirically that the majority of relevant articles from 1 set of OMOP reports (angioedema)[4, 5] would be identified using this approach. The base search strategy was then combined with PubMed terms representing the HOIs. Medical subject heading (MeSH) terms were generally preferred as HOI search terms due to their likely specificity. Text word searches were sometimes used, particularly when the MeSH search resulted in a small number of citations for review. The workgroup also searched the database of the Iowa Drug Information Service (IDIS) using a similar search strategy to identify other relevant articles that were not found in the PubMed search. For a limited number of outcomes where very few citations were identified from PubMed and IDIS searches, EMBASE searches were conducted. Search results were restricted to articles published on or after January 1, 1990.

University of Iowa investigators compiled the search results from different databases and eliminated duplicate results using a citation manager program. The results were then output into 2 sets of files, 1 containing the abstracts for review and the other for documenting abstract review results.

The search strategy and results for ARF are detailed in the Results section. The PubMed and IDIS searches were conducted on May 10, 2010.

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[i] For more information, visit the OMOP website.

B. ABSTRACT REVIEW

1. Abstract Review Methods

Each abstract was reviewed independently by 2 investigators to determine whether the full-text article should be reviewed. Exclusion criteria were documented sequentially (i.e., if exclusion criterion 1 was met, then the other criteria were not documented). If the reviewers disagreed on whether the full text should be reviewed, then it was selected for review. Inter-rater agreement on whether to include or exclude an abstract was calculated using Cohen's kappa statistic. The goal was to review any administrative database study that used data from the United States or Canada and studied the HOI, as validation components of studies are not necessarily included in the abstract and other relevant citations might be identified from the references of such studies.

2. Abstract Exclusion Criteria

1. Did not study the HOI.

2. Not an administrative database study. Eligible sources included insurance claims databases as well as other secondary databases that identify health outcomes using billing codes.

3. Data source not from the United States or Canada.

C. FULL-TEXT REVIEW

1. Full-text Review Methods

Full-text articles were reviewed independently by 2 investigators, with a goal of identifying validation studies described in the article itself or from the reference section of the article. Citations from the article's references were selected for full-text review if they were cited as a source for the HOI algorithm, or were otherwise deemed likely to be relevant. Full-text review exclusion criteria were applied sequentially, since if fewer than 5 validation studies were identified, up to 10 of the articles excluded based on the second criterion would need to be incorporated into the final report. If there was disagreement on whether a study should be included, the 2 reviewers attempted to reach consensus on inclusion by discussion. If the reviewers could not agree, a third investigator was consulted to make the final decision.

2. Full-text Exclusion Criteria

1. Poorly described HOI identification algorithm that would be difficult to operationalize.

2. No validation of outcome definition or reporting of validity statistics.

D. MINI-SENTINEL INVESTIGATOR SURVEY

Mini-Sentinel investigators were surveyed to request information on any published or unpublished studies that validated an algorithm to identify an HOI in administrative data. Studies that would not be excluded by 1 of the aforementioned criteria were included in the final report.

E. EVIDENCE TABLE CREATION

A single investigator abstracted each study for the final evidence table. The data included in the table were confirmed by a second investigator for accuracy.

F. CLINICIAN OR TOPIC-EXPERT CONSULTATION

A clinician or topic expert was consulted to review the results of the evidence table and discuss how they compare to diagnostic methods currently used in clinical practice. This included whether certain diagnostic codes used in clinical practice were missing from the algorithms, and the appropriateness of the validation definitions compared to diagnostic criteria currently used in clinical practice. A summary of this consultation is included in the results.

V. RESULTS

A. SEARCH STRATEGY AND RESULTS

The following summarizes the search results obtained from PubMed and IDIS searches. The PubMed search identified 170 citations (Table 1), and the IDIS search identified 69 citations (Table 2). The total number of unique citations from the combined searches was 204. An additional PubMed search was conducted at a later date to amend the original search strategy with names of relevant databases that were not included in the original search. This search identified 3 citations (Table 3), bringing the total number of unique citations to 207.

Table 1. PubMed Search Strategy and Results (170): Performed on 05/10/10

Search	Query	Results
#1	(acute[All Fields] AND ("respiratory insufficiency"[MeSH Terms] OR ("respiratory"[All Fields] AND "insufficiency"[All Fields]) OR "respiratory insufficiency"[All Fields] OR ("respiratory"[All Fields] AND "failure"[All Fields]) OR "respiratory failure"[All Fields]))	15438
#2	("Premier"[All] OR "Solucient"[All] OR "Cerner"[All] OR "Ingenix"[All] OR "LabRx"[All] OR "IHCIS"[All] OR "marketscan"[All] OR "market scan"[All] OR "Medstat"[All] OR "Thomson"[All] OR "pharmetrics"[All] OR "healthcore"[All] OR "united healthcare"[All] OR "UnitedHealthcare"[All] OR "UHC"[All] OR "GPRD"[All] OR "general practice research database"[All] OR "Research Database"[All] OR "Group Health"[All] OR "HCUP"[All] OR ("Healthcare Cost"[All] AND "Utilization Project"[All]) OR ("Health Care Cost"[All] AND "Utilization Project"[All]) OR "MEPS"[All] OR "Medical Expenditure Panel Survey"[All] OR "NAMCS"[All] OR "National Hospital Ambulatory Medical Care Survey"[All] OR "National Ambulatory Medical Care Survey"[All] OR "NHIS"[All] OR "National Health Interview Survey"[All] OR "Kaiser"[All] OR "HMO Research"[All] OR "Health Maintenance Organization"[All] OR "HMO"[All] OR "Cleveland Clinic"[All] OR "Lovelace"[All] OR "Department of Defense"[All] OR "Henry Ford"[All] OR ("Denmark"[All] AND "Epidemiology"[All]) OR "i3 Drug Safety"[All] OR "i3"[All] OR "Aetna"[All] OR "Humana"[All] OR "Wellpoint"[All] OR "IMS"[All] OR "Intercontinental Marketing Services"[All] OR "IMS Health"[All] OR "Geisinger"[All] OR "GE Healthcare"[All] OR "MQIC"[All] OR "PHARMO"[All] OR "Institute for Drug Outcome Research"[All] OR "Pilgrim"[All] OR "Puget Sound"[All] OR "Regenstrief"[All] OR "Saskatchewan"[All] OR "Tayside"[All] OR "MEMO"[All] OR "Medicines Monitoring Unit"[All] OR "Veterans Affairs"[All] OR "Partners Healthcare"[All] OR "Mayo Clinic"[All] OR "Rochester Epidemiology"[All] OR "Indiana Health Information Exchange"[All] OR "Indiana Health"[All] OR "Intermountain"[All] OR "THIN"[All] OR "The health	881983

		improvement network"[All] OR "blue cross"[All] OR "health partners"[All] OR "health plan"[All] OR "health services"[All] OR "Nationwide Inpatient Sample"[All] OR "National Inpatient Sample"[All] OR "medicaid"[All] OR "medicare"[All] OR "MediPlus"[All] OR "Outcome Assessment"[All] OR "insurance database"[All] OR "insurance databases"[All] OR "Data Warehouse"[All] OR "ICD-9"[All] OR "international statistical classification"[All] OR "international classification of diseases"[All] OR "ICD-10"[All] OR "Database Management Systems"[Mesh] OR "Medical Records"[Mesh] OR "Medical Records Systems, Computerized"[Mesh] OR "CPT"[All] OR "Current procedural terminology"[All] OR "drug surveillance" [All] OR ("claims"[tw] AND "administrative"[tw]) OR ("data"[tw] AND "administrative"[tw]) OR "Databases, Factual"[Mesh] OR "Databases as topic"[Mesh] OR "Medical Record Linkage"[Mesh] OR "ICD-9-CM"[All Fields] OR "ICD-10-CM"[All Fields])	
#3	#1 and #2		550
#4	("Pharmaceutical preparations/adverse effects"[Mesh] OR "Pharmaceutical preparations/contraindications"[Mesh] OR "Pharmaceutical preparations/poisoning"[Mesh] OR "Pharmaceutical preparations/therapeutic use"[Mesh] OR "Pharmaceutical preparations/toxicity"[Mesh] OR "Pharmaceutical preparations/therapy"[Mesh] OR "Pharmaceutical preparations/analysis"[Mesh] OR "Chemical actions and uses/adverse effects"[Mesh] OR "Chemical actions and uses/contraindications"[Mesh] OR "Chemical actions and uses/poisoning"[Mesh] OR "Chemical actions and uses/therapeutic use"[Mesh] OR "Chemical actions and uses/toxicity"[Mesh] OR "Chemical actions and uses/therapy"[Mesh] OR "Chemical actions and uses/analysis"[Mesh] OR "Chemical actions and uses/epidemiology"[Mesh] OR "Drug toxicity"[Mesh] OR "Diseases Category/chemically induced"[Mesh] OR "Diseases Category/drug therapy"[Mesh] OR "Diseases Category/epidemiology"[Mesh] OR "Validation Studies"[pt] OR "Validation Studies as Topic"[Mesh] OR "Sensitivity and Specificity"[Mesh] OR "Predictive Value of Tests"[Mesh] OR "Reproducibility of Results"[Mesh] OR "Predictive Value" [tw])		35821263
#5	#3 and #4		295
#6	("Clinical Trials"[pt] OR "Editorial"[pt] OR "Letter"[pt] OR "Meta-Analysis"[pt] OR "Randomized Controlled Trial"[pt] OR "Clinical Trial, Phase I"[pt] OR "Clinical Trial, Phase II"[pt] OR "Clinical Trial, Phase III"[pt] OR "Clinical Trial, Phase IV"[pt] OR "Comment"[pt] OR "Controlled Clinical Trial"[pt] OR "case reports"[pt] OR "Clinical Trials as Topic"[Mesh] OR "double-blind"[All] OR "placebo-controlled"[All] OR "pilot study"[All] OR "pilot projects"[Mesh] OR "Review"[pt] OR "Prospective Studies"[Mesh])		4546100
#7	#5 NOT #6		196
#8	("humans"[MeSH Terms] AND English[lang] AND ("1990/01/01"[PDAT] : "2010/06/1"[PDAT]))		7582731
#9	#7 and #8		170

Table 2. IDIS Search Strategy and Results (69): Performed on 05/10/10

Disease:

" FAILURE, RESPIRATORY 799.1"

NOT **Author:**

("(Editorial)" OR "Letter to Ed")

NOT **Descriptor:**

("CASE REPORT ADULT 0" or "CASE REPORT PEDIATRIC 1" or "CASE REPORT GERIATRIC 2" or "REVIEW ADULT 6" or "STUDY NON-CLINICAL 8" or "REVIEW PEDIATRIC 21" or "REVIEW GERIATRIC 23" or "STUDY RANDOMIZE ADULT 135" or "STUDY RANDOMIZE PEDIATRIC 136" or "STUDY RANDOMIZE GERIATRIC 137" or "CROSS-OVER 144" or "META-ANALYSIS 145" or "N-OF-ONE TRIAL 146" or "PRACTICE GUIDELINE 156" or "SYSTEMATIC REVIEW 161" or "ANNOTATED BIBLIOGRAPHY 167" or "PRIORITY CLIN PRACT GUIDE 168") and ("SIDE EF RESPIRATORY 79")

AND **Abstract:**

(("acute" AND "respiratory" AND "failure") OR "Premier" OR "Solucient" OR "Cerner" OR "Ingenix" OR "LabRx" OR "IHCIS" OR "marketscan" OR "market scan" OR "Medstat" OR "Thomson" OR "pharmetrics" OR "healthcore" OR "united healthcare" OR "UnitedHealthcare" OR "UHC" OR "GPRD" OR "general practice research database" OR "Research Database" OR "Group Health" OR "HCUP" OR ("Healthcare Cost" AND "Utilization Project") OR ("Health Care Cost" AND "Utilization Project") OR "MEPS" OR "Medical Expenditure Panel Survey" OR "NAMCS" OR "National Hospital Ambulatory Medical Care Survey" OR "National Ambulatory Medical Care Survey" OR "NHIS" OR "National Health Interview Survey" OR "Kaiser" OR "HMO Research" OR "Health Maintenance Organization" OR "HMO" OR "Cleveland Clinic" OR "Lovelace" OR "Department of Defense" OR "Henry Ford" OR ("Denmark" AND "Epidemiology") OR "i3 Drug Safety" OR "i3" OR "Aetna" OR "Humana" OR "Wellpoint" OR "IMS" OR "Intercontinental Marketing Services" OR "IMS Health" OR "Geisinger" OR "GE Healthcare" OR "MQIC" OR "PHARMO" OR "Institute for Drug Outcome Research" OR "Pilgrim" OR "Puget Sound" OR "Regenstrief" OR "Saskatchewan" OR "Tayside" OR "MEMO" OR "Medicines Monitoring Unit" OR "Veterans Affairs" OR "Partners Healthcare" OR "Mayo Clinic" OR "Rochester Epidemiology" OR "Indiana Health Information Exchange" OR "Indiana Health" OR "Intermountain" OR "THIN" OR "The health improvement network" OR "blue cross" OR "health partners" OR "health plan" OR "health services" OR "Nationwide Inpatient Sample" OR "National Inpatient Sample" OR "medicaid" OR "medicare" OR "MediPlus" OR "Outcome Assessment" OR "insurance database" OR "insurance databases" OR "Data Warehouse" OR "ICD-9" OR "international statistical classification" OR "international classification of diseases" OR "ICD-10" OR "Database Management Systems" OR "Medical Records Systems, Computerized" OR "CPT" OR "Current procedural terminology" OR "drug surveillance" OR ("claims" AND "administrative") OR ("data" AND "administrative") OR "Databases, Factual" OR "Databases as topic" OR "Medical Record Linkage" OR "ICD-9-CM" OR "ICD-10-CM")

Table 3. Search to Update the Original PubMed Search with Additional Database Names: Performed on 07/06/10, Results = 3

Search	Query	Results
#1	("Pharmaceutical preparations/adverse effects"[Mesh] OR "Pharmaceutical preparations/contraindications"[Mesh] OR "Pharmaceutical preparations/poisoning"[Mesh] OR "Pharmaceutical preparations/therapeutic use"[Mesh] OR "Pharmaceutical preparations/toxicity"[Mesh] OR "Pharmaceutical preparations/therapy"[Mesh] OR "Pharmaceutical preparations/analysis"[Mesh] OR "Chemical actions and uses/adverse effects"[Mesh] OR "Chemical actions and uses/contraindications"[Mesh] OR "Chemical actions and uses/poisoning"[Mesh] OR "Chemical actions and uses/therapeutic use"[Mesh] OR "Chemical actions and uses/toxicity"[Mesh] OR "Chemical actions and uses/therapy"[Mesh] OR "Chemical actions and uses/analysis"[Mesh] OR "Chemical actions and uses/epidemiology"[Mesh] OR "Drug toxicity"[Mesh] OR "Diseases Category/chemically induced"[Mesh] OR "Diseases Category/drug therapy"[Mesh] OR "Diseases Category/epidemiology"[Mesh] OR "Validation Studies"[pt] OR "Validation Studies as Topic"[Mesh] OR "Sensitivity and Specificity"[Mesh] OR "Predictive Value of Tests"[Mesh] OR "Reproducibility of Results"[Mesh] OR "Predictive Value"[tw])	1867752
#2	("Premier"[All] OR "Solucient"[All] OR "Cerner"[All] OR "Ingenix"[All] OR "LabRx"[All] OR "IHCIS"[All] OR "marketscan"[All] OR "market scan"[All] OR "Medstat"[All] OR "Thomson"[All] OR "pharmetrics"[All] OR "healthcore"[All] OR "united healthcare"[All] OR "UnitedHealthcare"[All] OR "UHC"[All] OR "GPRD"[All] OR "general practice research database"[All] OR "Research Database"[All] OR "Group Health"[All] OR "HCUP"[All] OR ("Healthcare Cost"[All] AND "Utilization Project"[All]) OR ("Health Care Cost"[All] AND "Utilization Project"[All]) OR "MEPS"[All] OR "Medical Expenditure Panel Survey"[All] OR "NAMCS"[All] OR "National Hospital Ambulatory Medical Care Survey"[All] OR "National Ambulatory Medical Care Survey"[All] OR "NHIS"[All] OR "National Health Interview Survey"[All] OR "Kaiser"[All] OR "HMO Research"[All] OR "Health Maintenance Organization"[All] OR "HMO"[All] OR "Cleveland Clinic"[All] OR "Lovelace"[All] OR "Department of Defense"[All] OR "Henry Ford"[All] OR ("Denmark"[All] AND "Epidemiology"[All]) OR "i3 Drug Safety"[All] OR "i3"[All] OR "Aetna"[All] OR "Humana"[All] OR "Wellpoint"[All] OR "IMS"[All] OR "Intercontinental Marketing Services"[All] OR "IMS Health"[All] OR "Geisinger"[All] OR "GE Healthcare"[All] OR "MQIC"[All] OR "PHARMO"[All] OR "Institute for Drug Outcome Research"[All] OR "Pilgrim"[All] OR "Puget Sound"[All] OR "Regenstrief"[All] OR "Saskatchewan"[All] OR "Tayside"[All] OR "MEMO"[All] OR "Medicines Monitoring Unit"[All] OR "Veterans Affairs"[All] OR "Partners Healthcare"[All] OR "Mayo Clinic"[All] OR "Rochester Epidemiology"[All] OR "Indiana Health Information Exchange"[All] OR "Indiana Health"[All] OR "Intermountain"[All] OR "THIN"[All] OR "The health improvement network"[All] OR "blue cross"[All] OR "health partners"[All] OR "health plan"[All] OR "health services"[All] OR "Nationwide Inpatient Sample"[All] OR "National Inpatient Sample"[All] OR "medicaid"[All] OR "medicare"[All] OR "MediPlus"[All] OR "Outcome Assessment"[All] OR "insurance database"[All] OR "insurance databases"[All] OR "Data Warehouse"[All] OR "ICD-9"[All] OR "international statistical classification"[All] OR "international classification of diseases"[All] OR "ICD-10"[All] OR "Database Management Systems"[Mesh] OR "Medical Records Systems, Computerized"[Mesh] OR "CPT"[All] OR "Current procedural terminology"[All] OR "drug surveillance"[All] OR ("claims"[tw] AND "administrative"[tw]) OR ("data"[tw] AND "administrative"[tw]) OR "Databases, Factual"[Mesh] OR "Databases as topic"[Mesh] OR "Medical Record Linkage"[Mesh] OR "ICD-9-CM"[All Fields] OR "ICD-10-CM"[All Fields]	399576
#3	("Clinical Trial"[pt] OR "Editorial"[pt] OR "Letter"[pt] OR "Meta-Analysis"[pt] OR "Randomized Controlled Trial"[pt] OR "Clinical Trial, Phase I"[pt] OR "Clinical Trial, Phase II"[pt] OR "Clinical Trial, Phase III"[pt] OR "Clinical Trial, Phase IV"[pt] OR "Comment"[pt] OR "Controlled Clinical Trial"[pt] OR "case reports"[pt] OR "Clinical Trials as Topic"[Mesh] OR "double-blind"[All] OR "placebo-controlled"[All] OR "pilot study"[All] OR "pilot projects"[Mesh] OR "Review"[pt] OR	2729582

		"Prospective Studies"[Mesh])	
	#4	#1 NOT #2	1748136
	#5	#4 NOT #3	819148
	#6	(TennCare [tiab]) OR (RAMQ [tiab]) OR (Cigna [tiab]) OR ((british columbia[tiab]) AND ((health[tiab]) OR (data[tiab]) OR (database[tiab]) OR (population[tiab]))) OR (CIHI [All Fields]) OR ((manitoba[tiab]) AND ((center for health policy[all fields]) OR (population[tiab]) OR (health insurance[tiab]))) OR ((ontario[tiab]) AND ((population[tiab]) OR (OHIP[tiab]) OR (registered persons database[tiab]) OR (health insurance [tiab]) OR (ICES[All Fields]) OR (Institute for Clinical Evaluative Sciences[All Fields]))) OR ((Alberta[tiab]) AND ((health[tiab]) OR (data[tiab]) OR (database[tiab]) OR (population[tiab]) OR (Alberta Health and Wellness[All Fields])))	5128
	#7	#5 AND #6	1579
	#8	#7 AND ((acute[All Fields] AND ("respiratory insufficiency"[MeSH Terms] OR ("respiratory"[All Fields] AND "insufficiency"[All Fields]) OR "respiratory insufficiency"[All Fields] OR ("respiratory"[All Fields] AND "failure"[All Fields]) OR "respiratory failure"[All Fields])))	3

B. ABSTRACT REVIEWS

Of the 207 abstracts reviewed, we accepted only 6 for full-text review. Because of the straightforward inclusion criteria, consisting of: 1) examination of the HOI of interest, 2) use of administrative database, and 3) study conducted in the United States or Canada, the 2 reviewers achieved perfect agreement on acceptance/rejection status (i.e., Cohen's kappa = 1). However, there was limited agreement on the reason for rejection. Among the 201 abstracts rejected, inter-rater agreement (via Cohen's kappa coefficient) was 0.39, 0.38, and 0.32 for the 3 inclusion criteria, respectively. This seemingly low agreement results from only a single rejection reason being captured in our abstract review database. These low kappa coefficients should therefore be considered a function of the different reviewers focusing on different criteria than a true lack of agreement; they also illustrate that many rejected articles fulfilled multiple exclusion criteria.

C. FULL-TEXT REVIEWS

Of the 6 full-text articles reviewed, 2 were excluded for not focusing on the HOI of interest, 1 for not using an administrative database from the US or Canada, and 1 for poorly defined algorithms. The 2 remaining studies did not report validation of the ARF coding algorithm directly in the article nor within a reference cited in the article. Cohen's kappa for agreement between reviewers on inclusion vs. exclusion of full-text articles reviewed was 1.

D. MINI-SENTINEL INVESTIGATOR SURVEY

Mini-Sentinel investigators provided no published or unpublished reports of validation studies that had been completed by their teams. They did not provide any published reports that they were familiar with but not directly involved in, either.

E. EVIDENCE INCLUDED IN TABLE

Because no validation studies were identified, 2 studies that included a coding algorithm for the HOI of interest without validation of the outcome or validity estimates were included in the evidence table. A complete list of studies with clear HOI definitions that were eligible to be selected for inclusion is available in Appendix B.

F. SUMMARY AND DISCUSSION OF ALGORITHMS AND VALIDATION

Codes Used in Algorithms. We only came across 2 studies that provided the code for ARF. ICD-9 code 518.81 (acute respiratory failure) was used by Dransfield, et al.[6] to identify ARF cases among hospitalized patients. Wu, et al.[7] used ICD-9 code 518.8 (they defined this code as Respiratory Failure) to identify respiratory failure cases among Medicare beneficiaries.

The ICD-9-CM defined the 2 codes as:

- 518.8: Other diseases of lung

- 518.81: Acute respiratory failure

  - Respiratory function fails to maintain adequate oxygen supply and carbon dioxide removal (also applicable to/known as Respiratory failure NOS)

Validation Algorithms. Neither of these 2 studies provided any validation procedure or validation estimates. Because we didn't identify any other studies that provided codes for the outcome of interest, we have included only those 2 studies in the tables.

Selected Patient Populations. Dransfield, et al.[6] used a cohort extracted from administrative data from the University of Alabama Hospital. The cohort used by Wu, et al.[7] was identified via data from a 5% national random sample of Medicare beneficiaries.

G. SUMMARY OF EXCLUDED POPULATIONS AND DIAGNOSES

As indicated in section F above, only 2 studies were identified that provided codes for ARF, neither of which included validation statistics. Another study mentioned the HOI; however, it focused narrowly on acute respiratory failure requiring mechanical ventilation (using ICD-9-CM procedural codes 96.70 [mechanical ventilation, unspecified], 96.71 [mechanical ventilation for <96 hours], or 96.72 [mechanical ventilation for >96 hours]) and was therefore excluded.[8]

One of these 2 studies with algorithms but without validation estimates used state-specific data from the University of Alabama Hospital.[6] The other implemented data from a 5% national random sample of Medicare beneficiaries.[7]

H. EVIDENCE TABLE

Table 4. Non-Validated Algorithms

Citation	Study Population and Time Period	Description of Outcome Studied	Algorithm
Dransfield, et al. 2008[6]	Patients admitted to University of Alabama Hospital whose discharge or death summaries indicated a primary diagnosis of acute exacerbation of chronic obstructive lung disease (COPD) (International Classification of Diseases, Ninth Edition [ICD-9] code 491.21) or a primary diagnosis of acute respiratory failure (518.81) and a secondary diagnosis of acute exacerbation were identified. Patients with a diagnosis of asthma (493) were excluded; 825 patients met the inclusion criteria for the study, of which 410 were males and 415 were females. The mean age for the patients was 66.5 years. The study period was October 1, 1999–September 30, 2006.	In-hospital mortality after use of β-blockers.	Acute respiratory failure: 518.81.
Wu, et al. 2003[7]	Patients over the age of 65 years who underwent total hip arthroplasty in the Medicare database were identified from the part B data using CPT codes (n=23,136; 8180 males, 14,956 females). Patients were eligible to be included if the procedure was performed by an orthopedic surgeon (part B) with an accompanying inpatient record for the same procedure (part A). Major morbidity counts at 7 and 30 days after the procedure were obtained from part B based on ICD-9 diagnosis codes, one of which corresponded to respiratory failure (ICD-9 code 518.8). The study period was 1994–1999.	Morbidity and death at 7 and 30 days after hip replacement surgery.	Respiratory failure: 518.8.

I. CLINICIAN OR TOPIC-EXPERT CONSULTATION

The literature used the following coding algorithm for ARF: ICD-9 code 518.81 (acute respiratory failure). This code was used by Dransfield, et al.[6] to identify ARF cases among hospitalized patients. Wu, et al.[7] used ICD-9 code 518.8 (other lung diseases) (although in the study they define this code as Respiratory Failure) to identify respiratory failure cases among Medicare beneficiaries. This coding algorithm is

expected to have low specificity for ARF, as it refers to a rather larger group of pulmonary-failure disorders and does not narrowly identify ARF.

We identified only 2 studies fulfilling our inclusion criteria. Wu, et al.[7] used ICD-9 code 518.8 to identify respiratory failure cases among Medicare beneficiaries. ICD-9 code 518.81 was used by Dransfield, et al.[6] to identify hospitalized patients with a primary diagnosis of ARF. In practice, one would expect the latter of these, ICD-9 code 518.81, to be commonly used to identify ARF cases, as it explicitly defines ARF. We would also expect this code to have high positive predictive value (PPV) and high specificity. ICD-9 code 518.8, however, is a less specific code referring to a group of pulmonary-failure disorders; it therefore is expected to have low specificity for ARF.

Although the PPV and specificity of ICD-9 code 518.81 are expected to be high, the sensitivity of this code may be more questionable. It is possible that patients with ARF may be coded with other conditions in administrative data. Likely examples are chronic respiratory failure (CRF, ICD-9 code 518.83) and acute respiratory distress syndrome (ARDS, ICD-9 code 518.82). CRF differs from ARF in terms of presentation, treatment, and interventions[9]; therefore, examination of procedural codes may prove beneficial in discerning between these 2 distinct types of respiratory failure. By contrast, treatments and procedures for ARDS are similar to ARF; in fact, ARDS is a possible cause of ARF.[10] Thus, examination of procedural codes may be inadequate to differentiate between these conditions. Administrative data with corresponding laboratory results, however, may prove viable in distinguishing ARF from ARDS. There is also an ICD-9 code specifying both conditions (i.e., ICD-9-CM code 518.84 – acute and chronic respiratory failure); examination of procedural codes may prove useful here as well.

Much of what is known about ARF in the US is from a study using data from the 1994 Nationwide Inpatient Sample.[11] As these are not administrative data, this article did not meet the inclusion criteria of the present study. Nevertheless, it provides an example of an ARF algorithm that implements both diagnostic and procedural codes. Diagnostic codes for acute respiratory distress or failure (ICD-9-CM 518.5, 518.81, or 518.82) in combination with a procedural code for continuous mechanical ventilation (ICD-9-CM 96.7) were used. The oft-cited US ARF incidence of 137.1 hospitalizations per 100,000 US residents aged ≥5 years was estimated via this definition.

It should be noted that in both the medical literature and in clinical practice, ARF is usually described as secondary to other diseases/abnormalities (involving the central nervous system, respiratory system, and other medical and health problems) and trauma.[9, 11] If interest lies in ARF as a result of a specific condition, we suggest that algorithm development incorporate disease/condition-specific codes in combination with ICD-9 code 518.81 (or an alternative ARF algorithm).

It is worth noting here that on October 1, 2013, medical coding in US health care settings will change from ICD-9 to ICD-10. The transition will result in business and systems changes throughout the health care industry, including health plans and health care practice and research. All HIPAA transactions, including outpatient claims with dates of service and inpatient claims with dates of discharge, will use ICD-10 codes starting in October 2013. The ICD-10 section for J96.0 (acute respiratory failure) refers to ARF.

VI. SUMMARY AND CONCLUSIONS

A. RECOMMENDATIONS FOR ALGORITHMS

We came across only 2 studies that provided codes for identifying ARF; 1 of them used ICD-9 code 518.81 (acute respiratory failure), and the other used ICD-9 code 518.8 (other diseases of lung). From the definition of the codes, we can assume that the former code is more specific than the latter; however, neither study provided any validation estimates.

The ICD-9 code 518.81 (acute respiratory failure) was used in 1 study to identify cases with a primary diagnosis of ARF. It appears to be a specific code for identifying ARF cases; however, it needs to be evaluated with validation studies. To enhance generalizability of findings in those studies, it is merited to design validation studies among different population groups and health care settings.

In the absence of validation studies, it is difficult to talk with certainty about the performance of the ARF coding algorithm. However, due to the nature of the condition and the associated diagnostic and procedural interventions, we can assume that ICD-9 code 518.81 has high PPV and specificity; however, its sensitivity may be compromised by other conditions such as CRF and ARDS. ICD-9 code 518.8 seems to be a wider and less specific code for the HOI, as it is designed to include other respiratory failures and other diseases of the lung as well. Both of these codes, however, need to be evaluated with validation studies. Although it can't yet be quantified, we expect that combining procedural codes with applicable ICD-9 diagnostic codes may improve algorithm performance.

B. SUGGESTIONS FOR FUTURE RESEARCH BASED ON EVIDENCE GAPS

Our current search highlights a scarcity of literature providing validated or non-validated algorithms for ARF that can be applied to administrative health care data. Research needs to be conducted on designing validation studies to test ARF algorithms and estimating their predictive power, sensitivity, and specificity.

VII.   REFERENCES

1. West SL, Strom BL, Poole C. Validity of pharmacoepidemiologic drug and diagnosis data. In: Strom BL, ed. *Pharmacoepidemiology*. Chichester, UK: John Wiley, 2005; 709-766.

2. Food and Drug Administration (FDA). Safety reporting requirements for human drug and biological products; proposed rule. *Federal Register.* 2003; 68(50): 12405-12497. Available at: http://www.fda.gov/OHRMS/DOCKETS/98fr/03-5204.pdf. Accessed June 4, 2010.

3. The Observational Medical Outcomes Partnership (OMOP). Health outcomes of interest. 2010. Available at: http://omop.fnih.org/HOI. Accessed June 4, 2010.

4. *Scientific American Medicine*. Lewiston, NY: ACP Medicine BC Decker Inc, 2010; Chapters II, VI, and XIV.

5. Golden WE, Cleves MA, Heard JK, Brasher R, McKinney P, Johnston JC. Frequency and recognition of angiotensin-converting enzyme inhibitor-associated angioneurotic edema. *Clin Perform Qual Health Care*. Oct-Dec 1993; 1(4): 205-207.

6. Dransfield MT, Rowe SM, Johnson JE, Bailey WC, Gerald LB. Use of beta blockers and the risk of death in hospitalised patients with acute exacerbations of COPD. *Thorax*. Apr 2008; 63(4): 301-305.

7. Wu CL, Anderson GF, Herbert R, Lietman SA, Fleisher LA. Effect of postoperative epidural analgesia on morbidity and mortality after total hip replacement surgery in medicare patients. *Reg Anesth Pain Med*. Jul-Aug 2003; 28(4): 271-278.

8. Carson SS, Cox CE, Holmes GM, Howard A, Carey TS. The changing epidemiology of mechanical ventilation: a population-based study. *J Intensive Care Med*. May-Jun 2006; 21(3): 173-182.

9. Markou NK, Myrianthefs PM, Baltopoulos GJ. Respiratory failure: an overview. *Crit Care Nurs Q*. Oct-Dec 2004; 27(4): 353-379.

10. Viegi G. Epidemiology of acute respiratory failure. *Rassegna di Patologia dell'Apparato Respiratorio*. 2008; 23: 335-338.

11. Behrendt CE. Acute respiratory failure in the United States: incidence and 31-day survival. *Chest*. Oct 2000; 118(4): 1100-1105.

VIII. APPENDICES

A. APPENDIX A: ABSTRACTS OF STUDIES INCLUDED IN EVIDENCE TABLE

Dransfield MT, Rowe SM, Johnson JE, Bailey WC, Gerald LB. Use of beta blockers and the risk of death in hospitalised patients with acute exacerbations of COPD. *Thorax*. 2008; 63(4): 301–305.

BACKGROUND: Cardiovascular disease is a major cause of death in patients with chronic obstructive pulmonary disease (COPD) and predicts hospitalisation for acute exacerbation, in-hospital death and post-discharge mortality. Although beta blockers improve cardiovascular outcomes, patients with COPD often do not receive them owing to concerns about possible adverse pulmonary effects. There are no published data about beta blocker use among inpatients with COPD exacerbations. A study was undertaken to identify factors associated with beta blocker use in this setting and to determine whether their use is associated with decreased in-hospital mortality. METHODS: Administrative data from the University of Alabama Hospital were reviewed and patients admitted between October 1999 and September 2006 with an acute exacerbation of COPD as a primary diagnosis or as a secondary diagnosis with a primary diagnosis of acute respiratory failure were identified. Demographic data, co-morbidities and medication use were recorded and subjects receiving beta blockers were compared with those who did not. Multivariate regression analysis was performed to determine predictors of in-hospital death after controlling for known covariates and the propensity to receive beta blockers. RESULTS: 825 patients met the inclusion criteria. In-hospital mortality was 5.2%. Those receiving beta blockers (n = 142) were older and more frequently had cardiovascular disease than those who did not. In multivariate analysis adjusting for potential confounders including the propensity score, beta blocker use was associated with reduced mortality (OR = 0.39; 95% CI 0.14 to 0.99). Age, length of stay, number of prior exacerbations, the presence of respiratory failure, congestive heart failure, cerebrovascular disease or liver disease also predicted in-hospital mortality (p<0.05). CONCLUSIONS: The use of beta blockers by inpatients with exacerbations of COPD is well tolerated and may be associated with reduced mortality. The potential protective effect of beta blockers in this population warrants further study.

Wu CL, Anderson GF, Herbert R, Lietman SA, Fleisher LA. Effect of postoperative epidural analgesia on morbidity and mortality after total hip replacement surgery in Medicare patients. *Regional Anesthesia and Pain Medicine*. 2003; 28(4): 271–278.

BACKGROUND AND OBJECTIVES: The effect of postoperative epidural analgesia (vs. systemic analgesia) on patient outcomes is unclear. Available randomized controlled trials (RCTs) have focused on the intraoperative period and not properly examined the effect of postoperative epidural analgesia (EA) on outcomes. METHODS: A 5% nationally random sample of Medicare beneficiaries from 1994 to 1999 was analyzed to identify patients undergoing total hip arthroplasty (Common Procedural Terminology [CPT] code 27130, 27132, 27134, 27137, 27138). Patients were divided into 2 groups depending on the presence or absence of postoperative EA based on the CPT coding (01996). The rate of major morbidity (acute myocardial infarction, deep venous thrombosis, pulmonary embolism, angina, respiratory failure, heart failure, cardiac dysrhythmias, pneumonia, pulmonary edema, sepsis, acute renal failure, paralytic ileus, acute cerebrovascular event) and death at 7 and 30 days after the procedure were compared. Multivariate regression analysis was performed to determine if the presence of postoperative (EA) had an independent effect on mortality or major morbidity. Data were reported as an odds ratio with 95% confidence intervals (CI) when appropriate. RESULTS: The unadjusted 7- and 30-day death rate was significantly lower for EA versus no EA (1.9/1000 [95% CI: 0.2-3.6] vs. 3.9/1000 [95% CI: 3.0-6.2] at 7 days [P =.04] and

5.8/1000 [95% CI: 2.9-8.7] vs. 9.9/1000 [95% CI: 8.6-11.3] at 30 days [P = 0.01]). However, multivariate regression analysis revealed that there was no difference between the groups with regard to mortality or major morbidity with the exception of an increase in deep venous thrombosis in patients who received EA. CONCLUSIONS: The use of postoperative EA was not associated a lower incidence of mortality and major morbidity in Medicare patients undergoing total hip arthroplasty. However, the results should be interpreted with caution because of limitations in using the Medicare claims data for analysis. Further trials using other properly conducted and designed studies (e.g., RCTs) would be ideal to validate these results.

B. APPENDIX B: LIST OF CITATIONS SELECTED FOR FULL-TEXT REVIEW BUT NOT INCLUDED, BY REASONS FOR EXCLUSION

1. **Studies Excluded Due to a Lack of Validation or Reporting of Validation Statistics**

   Dransfield MT, Rowe SM, Johnson JE, Bailey WC, Gerald LB. Use of beta blockers and the risk of death in hospitalised patients with acute exacerbations of COPD. *Thorax*. 2008: 63(4); 301–305.

   Wu CL, Anderson GF, Herbert R, Lietman SA, Fleisher LA. Effect of postoperative epidural analgesia on morbidity and mortality after total hip replacement surgery in Medicare patients. *Regional Anesthesia and Pain Medicine*. 2003: 28(4); 271–278.

2. **Studies Excluded Due to Poorly Defined Algorithms**

   Wijdicks EFM, Henderson RD, McClelland RL, Emergency intubation for respiratory failure in Guillain-Barre syndrome. *Archives of Neurology*. 2003; 60(7): 947–948.

3. **Other Excluded Studies – Not HOI of Interest**

   Carson SS, Cox CE, Holmes GM, Howard A, Carey TS. The changing epidemiology of mechanical ventilation: a popu*lation*-based study. *Journal of Intensive Care Medicine*. 2006; 21(3): 173–182.

   Loughlin JE, Alfredson TD, Ajene AN, Cole JA, Cook SE, Rosenberg DM, Walker AM. Risk for respiratory events in a cohort of patients receiving inhaled zanamivir: a retrospective study. *Clinical Therapeutics*. 2002; 24(11): 1786–1799.

4. **Other Excluded Studies – Not Administrative or US/Canada Data**

   Lecuyer L, Chevret S, Guidet B, Aegerter P, Martel P, Schlemmer B, Azoulay E. Case volume and mortality in haematological patients with acute respiratory failure. *The European Respiratory Journal: Official Journal of the European Society for Clinical Respiratory Physiology*. 2008; 32(3): 748–754.

C. APPENDIX C: LIST AND DEFINITIONS OF ICD OR PROCEDURAL CODES INCLUDED IN ALGORITHMS

Type of Code (e.g., ICD-9, ICD-10, CPT)	Code	Description
ICD-9	518.8	Other diseases of lung
ICD-9	518.81	Acute respiratory failure: Respiratory function fails to maintain adequate oxygen supply and carbon dioxide removal (also applicable to/known as Respiratory failure NOS)