Vaccine 31S (2013) K83–K87

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Review

A systematic review of validated methods for identifying transverse myelitis using administrative or claims data

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ARTICLE INFO

Article history:
Received 28 November 2012
Received in revised form 7 February 2013
Accepted 26 March 2013

Keywords:
Transverse myelitis
Administrative database
ICD-9
Positive predictive value

ABSTRACT

Purpose: To identify and assess billing, procedural, or diagnostic code algorithms used to identify transverse myelitis in administrative databases.
Methods: We searched the MEDLINE database from 1991 to September 2012 using controlled vocabulary and key terms related to transverse myelitis. We also searched the reference lists of included studies. Two investigators independently assessed the full text of studies against pre-determined inclusion criteria. Two reviewers independently extracted data regarding participant and algorithm characteristics.
Results: Three studies met criteria for inclusion in this review. The only algorithm based solely on administrative claims data with a reported positive predictive value included five ICD-9 codes (codes 341.20, 341.21, 341.22, 323.8, 323.9). The positive predictive value for physician-diagnosed acute transverse myelitis was 62%.
Conclusions: More research is needed to establish an accurate algorithm to identify transverse myelitis in large administrative databases using diagnosis and/or procedure codes. Use of standardized consensus definitions, clear description for algorithm selection, and reporting of validation procedure and results would be most beneficial.

Contents

Abbreviations: ATM, acute transverse myelitis; CSF, cerebrospinal fluid; ICD, International Classification of Diseases; KPNC, Kaiser Permanente Northern California; MRI, magnetic resonance imaging; N, number; NR, not reported; PPV, positive predictive value; TM, transverse myelitis.

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http://dx.doi.org/10.1016/j.vaccine.2013.03.074

1. Introduction

Mini-Sentinel, a pilot project sponsored by the United States Food and Drug Administration (FDA), aims to inform and facilitate the development of an active surveillance system, the Sentinel System, for monitoring the safety of FDA-regulated medical products. Mini-Sentinel is one facet of the Sentinel Initiative, an FDA effort to develop a national electronic system that will complement existing methods of safety surveillance. A first step in developing the Sentinel system is an attempt at understanding the validity of algorithms (i.e., combinations of billing, procedural, pharmacy, or diagnosis codes) for identifying health outcomes of interest in administrative and claims data, hereafter administrative data. As part of Mini-Sentinel, the Post-Licensure Rapid Immunization Safety Monitoring (PRISM) program intends to establish mechanisms for conducting vaccine safety research using healthcare claims data [1,2].

In order to conduct vaccine research in administrative data effectively, accurate methods of identifying events of interest need to be developed. This may include using multiple codes sequentially or simultaneously as indicators that a clinical event has occurred. Therefore, this project aims to identify existing studies in which specific codes or sets of codes typically used for administrative purposes (e.g., ICD-9 codes) are able to capture clinical events (health outcomes of interest) accurately. PRISM program collaborators selected health outcomes of interest using an expert elicitation process through which investigators developed a list of candidate outcomes based on input from global vaccine safety experts. A panel of five vaccine experts then prioritized the list via an iterative process using criteria including clinical severity, public health importance, incidence, and relevance [3]. The particular health event of interest in this paper is transverse myelitis.

1.1. Transverse myelitis as a health outcome of interest

Transverse myelitis is a severe neurological disorder where one third of affected individuals acquire a permanent severe disability [4,5]. Clinically, the disorder is characterized by acute or subacute onset of sensory, motor or autonomic dysfunction due to demyelination of the spinal cord. Symptoms are usually bilateral; however atypical presentations can also occur. The causes are highly variable and often not identified (30% are idiopathic). Infection precedes approximately 50% of cases [4]. The condition may also occur as the presenting sign of an underlying systemic autoimmune disorder, such as multiple sclerosis. Case reports have implicated a variety of vaccines, with the condition developing subsequent to vaccination [4]. All age groups are affected, but there tends to be a bimodal increased incidence during the second and fourth decade of life. There does not appear to be any predisposition based on geographic location, familial history, ethnicity or gender. Reported incidence rates have varied from 1.34 to 4.6 cases per million per year [4].

Confirmation of the diagnosis is made with clinical history and examination, usually including the identification of a clear sensory level below which sensory changes occur, along with findings on magnetic resonance imaging (MRI). Spinal cord lesions typically enhance with intravenous gadolinium and often span at least two vertebrae. MRI is also important in ruling out other causes of cord compression that may need acute surgical intervention [5].

In the 2011 Institute of Medicine review of adverse effects of vaccines, the potential for a causal relationship between transverse myelitis and eight different vaccines (measles, mumps, and rubella; varicella; influenza; Hepatitis A and B; human papillomavirus; diphtheria toxoid, tetanus toxoid, and acellular pertussis-containing vaccines; meningococcal vaccine) was assessed via literature review [6]. The Committee's epidemiologic assessment (assessment of the weight of evidence from the epidemiologic literature) of the evidence for cases of transverse myelitis associated with each vaccine was "weak." Similarly, the Committee's mechanistic assessment (assessment of the weight of evidence from the biological and clinical literature) was "weak" or "lacking." The report's consensus was that the current evidence was inadequate to accept or reject a causal relationship. Case reports of transverse myelitis occurring after vaccination have been reported [6], yet whether these were truly causally related to the vaccine or merely coincidental occurrences is uncertain. Thus, further epidemiologic evidence is needed to properly assess the potential association with vaccination.

2. Materials and methods

As described fully in the accompanying methods paper by McPheeters et al. [7], we developed a search strategy over a period of several months. Building on prior Mini-Sentinel approaches to searching [1], we expanded those approaches and tested the need to assess gray literature, including via Google Scholar, which did not yield any citations beyond the traditional search. Therefore, the final search strategy was executed in MEDLINE via the PubMed interface. The strategy is outlined in Appendix A. We limited searches to the last 21 years (1991 to September 2012) and required that included studies address transverse myelitis; use an administrative database reporting data from the United States or Canada; and clearly define an algorithm to identify cases of transverse myelitis. We also noted whether studies reported validation of the algorithm (e.g., via chart review or independent diagnosis). We searched the reference lists of included studies. Two investigators independently assessed the full text of each study against our inclusion criteria with disagreements resolved via a third reviewer or discussion to reach consensus. These investigators included a pediatrician with fellowship training in vaccine safety and an epidemiologist with research training.

One investigator extracted data regarding the study population, outcome studied, algorithms used, validation procedure, and validity statistics. A second reviewer and lead author of the review independently verified the accuracy of the data extraction. The lead author also contacted study investigators to request unpublished data for those studies indicating additional case-finding methods that were not fully detailed.

The lead author also independently considered methodologic elements in included studies by assessing whether: (1) all case data were validated or only a random sample; (2) authors reported the percentage of records that were sought but not obtained; (3) authors using multiple codes to identify the outcome of interest validated individual codes; (4) authors reported predictive or sensitivity measures or presented enough data that such measures could be calculated; (5) authors presented the representativeness of their sample and therefore the generalizability of the results. We summarized results of included studies qualitatively and report key characteristics below.

3. Results

3.1. Study population

Our searches identified 47 potential citations of which 3 met our inclusion criteria (Fig. 1). Table 1 summarizes study characteristics, and Appendix B includes a list of studies not meeting our review criteria with reasons for exclusion. All studies were conducted in the United States. One study by Schulz et al. reports data collected from the Thomas Jefferson University Hospital