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Review

A systematic review of validated methods to capture stillbirth and spontaneous abortion using administrative or claims data

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ABSTRACT

Purpose: To identify and assess diagnosis, procedure and pharmacy dispensing codes used to identify stillbirths and spontaneous abortion in administrative and claims databases from the United States or Canada.
Methods: We searched the MEDLINE database from 1991 to September 2012 using controlled vocabulary and key terms related to stillbirth or spontaneous abortion. We also searched the reference lists of included studies. Two investigators independently assessed the full text of studies against predetermined inclusion criteria. Two reviewers independently extracted data regarding participant and algorithm characteristics and assessed each study's methodological rigor using a pre-defined approach.
Results: Ten publications addressing stillbirth and four addressing spontaneous abortion met our inclusion criteria. The International Classification of Diseases, Ninth Revision (ICD-9) codes most commonly used in algorithms for stillbirth were those for intrauterine death (656.4) and stillborn outcomes of delivery (V27.1, V27.3-V27.4, and V27.6-V27.7). Papers identifying spontaneous abortion used codes for missed abortion and spontaneous abortion: 632, 634.*x*, as well as V27.0–V27.7. Only two studies identifying stillbirth reported validation of algorithms. The overall positive predictive value of the algorithms was high (99%–100%), and one study reported an algorithm with 86% sensitivity. However, the predictive value of individual codes was not assessed and study populations were limited to specific geographic areas.
Conclusions: Additional validation studies with a nationally representative sample are needed to confirm the optimal algorithm to identify stillbirths or spontaneous abortion in administrative and claims databases.'

Contents

Abbreviations: NR, not reported; PPV, positive predictive value; RA, rheumatoid arthritis; SAB, spontaneous abortion.

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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 [1,2]. 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.

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 together – or sets of codes – as indications that a clinical event has occurred, which may or may not be vaccine related. There is significant potential to over or underestimate clinical event rates if the codes used to identify them are either too specific (thus missing events) or too sensitive (potentially picking up cases that are not in fact the condition of interest). Therefore, this project aims to identify existing studies in which specific codes or sets of codes typically used for administrative purposes (e.g., International Classification of Diseases [ICD]) are able to capture clinical events (health outcomes of interest) accurately. Mini-Sentinel uses data from the United States. Therefore, the focus of this work is on databases from the U.S. or Canada, thought to be most generalizable to Mini-Sentinel's focus.

Mini-Sentinel 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 and using criteria including clinical severity, public health importance, incidence, and relevance [3]. One category of health outcomes of interest is pregnancy related outcomes, which could affect either the mother or fetus; in this review, we focus on stillbirth and spontaneous abortion, both of which would be considered fetal outcomes.

Fetal deaths include both spontaneous abortions (miscarriages) and stillbirths, which are commonly referred to as intrauterine fetal deaths/demises (IUFDs). The differentiation between spontaneous abortion and stillbirth is made by gestational age, birth weight, or a combination of the two. The most common cut points for reporting stillbirth in the United States are gestational age $\geq$ 20 weeks' gestation and a fetal weight of $\geq$ 350 grams [4]. Approximately 1 in 160 pregnancies in the United States ends in stillbirth [5]. The most common causes of stillbirth are obstetric complications (e.g., placental abruption, multiple gestation, preterm labor) and placental abnormalities. The etiology of stillbirth cannot be identified in approximately 25% of cases [6].

In the United States, spontaneous abortion is the loss of the embryo or fetus (terminology varies by gestational age) between conception and the point at which the death would be considered a stillbirth. The particular number of gestational weeks used as the upper bound for identifying spontaneous abortion varies by study and by country, in some cases as low as 20 weeks or as high as 24 weeks. The definition may also include a fetal weight cut-off, typically 350–500 grams [7]. Spontaneous abortion occurs in about 10–15% of recognized pregnancies and an unknown proportion of unrecognized pregnancies, although estimates are that up to 60% of conceptions end spontaneously prior to clinical recognition [8]. The etiology of fetal loss is multifactorial; up to about 50% have a recognized chromosomal abnormality, with no definitive cause for the rest. Risk factors include having had a prior miscarriage, as well as maternal age and anatomic abnormalities [8].

The Centers for Disease Control and Prevention (CDC) currently recommends two vaccines for pregnancy women: influenza and tetanus, diphtheria, and pertussis (Tdap). Influenza vaccination is recommended for all women who will be pregnant at any time during flu season and can be given at any point during pregnancy; current coverage rates, however, remain below 50% [9]. There are more than 6.5 million pregnancies per year in the United States [10]; thus more than 2 million women receive the influenza vaccine annually, despite this less than optimal vaccination rate. The extent of recommended vaccination during pregnancy makes safety surveillance a key priority for this vulnerable population.

The CDC currently recommends against vaccinating pregnant women with measles-mumps-rubella (MMR), live influenza, varicella, and zoster. Human papillomavirus vaccine is not contraindicated, but is not recommended. Despite the fact that these vaccines are not recommended during pregnancy, unintentional exposure may occur if women are vaccinated before becoming aware they are pregnant. Thus, there are an unknown number of women exposed to a variety of vaccines during pregnancy other than influenza and Tdap.

Despite wide exposure, there are few empirical data on the risks associated with vaccination in pregnancy. Studies have found the incidence of stillbirth in women who received rubella [11,12], human papillomavirus [13], and influenza A (H1N1) [14] vaccines to be comparable to the general population. Risk of morbidity associated with influenza in pregnancy outweighs risks associated with vaccination and some research suggests that incidence of stillbirth in H1N1 vaccinated women is lower than nonvaccinated women [15–17]. Nonetheless, for most vaccines, research is currently insufficient to assess risk in pregnancy because pregnant women are actively excluded from vaccine clinical trials. As a result, post-licensure safety surveillance is a critical safety net to detect unexpected issues. Surveillance via administrative data provides a viable method of developing an empirical evidence base on the association of vaccines and pregnancy outcomes.

2. Materials and methods

A detailed description of the methods for the project can be found in the accompanying paper by McPheeters et al. [18]. Briefly, we conducted two searches of the MEDLINE database via the PubMed interface using the strategies outlined in Appendix A. We developed the search strategy by building on prior Mini-Sentinel approaches to searching [1]. We expanded those approaches and tested the need to assess grey literature, including via Google Scholar, which did not yield any citations beyond the traditional search. We limited searches to the last 21 years (1991 to September 2012) and required that included studies address stillbirth or spontaneous abortion; use an administrative database reporting data from the US or Canada; and clearly define an algorithm to identify cases of stillbirth or spontaneous abortion. We also tracked whether studies reported validation of the algorithm (e.g., via chart review or independent diagnosis). To ensure completeness of the search, 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.

One investigator also extracted data regarding the study population, outcome studied, algorithms used, validation procedure, and validity statistics. A second reviewer independently verified the accuracy of the data extracted. The first author also extracted data on elements including the population sampled and sampling methods, methods for locating cases, and methods for validating the accuracy of diagnoses in cases located to inform the writing of the report. We summarized results of studies qualitatively and report key characteristics below.