



BRIEF REPORT

Outpatient urticaria diagnosis codes have limited predictive value for same-day influenza vaccine adverse event detection

Kristen M. Moore^a, April Duddy^a, Grace M. Lee^a, Priscilla Velentgas^a, Dale R. Burwen^b,
Richard Platt^a, Jeffrey S. Brown^{a,*}

^aDepartment of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care, Boston, MA, USA

^bDivision of Epidemiology, Office of Biostatistics and Epidemiology, Center for Biologics Evaluation and Research, Food and Drug Administration, Rockville, MD, USA

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Abstract

Objectives: To assess the predictive value of claims-based outpatient urticaria diagnosis codes to identify potential vaccine-related adverse events (AEs) when recorded on the same day as influenza vaccination.

Study Design and Setting: Health plan members with outpatient claims for influenza vaccination and urticaria on the same day between October 1, 2002, and December 31, 2007, were eligible for inclusion. Electronic medical records (EMRs) for 50 eligible patients with the most recent visits of interest occurring at a large group practice were sampled for review.

Results: EMRs were available and reviewed for 42 of 50 patients. An influenza vaccination was confirmed in all reviewed medical charts. Urticaria occurring on the day of influenza vaccination was confirmed for 40% of participants (17/42); 3 confirmed urticaria diagnoses were potential AEs and 14 urticaria events occurred before vaccination. Among those with unconfirmed diagnoses, 17 had no evidence of urticaria on physical examination on the day of interest (4 had evidence of a nonurticarial rash and 13 had no evidence of rash on examination) and 8 had insufficient information to make a clinical determination.

Conclusion: Outpatient diagnosis codes for urticaria found in health insurance claims data are limited in their predictive value to identify same-day vaccine AEs. © 2009 Elsevier Inc. All rights reserved.

Keywords: Diagnosis code; Urticaria; Vaccine safety surveillance; Influenza vaccine; Predictive value; Claims databases

1. Introduction

Rapid spread of novel influenza A (H1N1) virus infection (“pandemic swine flu”) will likely result in the widespread use of a novel influenza vaccine in a large population [1,2], underscoring the need for active postmarketing vaccine safety surveillance to rapidly identify potential adverse events (AEs).

Routinely collected administrative claims and medical encounter data contain rich information that is useful in various types of epidemiologic research, including outcome and quality of care assessments, therapeutics safety, disease surveillance, and comparative effectiveness research [3–8]. They have also been used for active postmarketing drug [9] and vaccine safety surveillance [10–14] to complement existing passive AE reporting programs, such as the Vaccine Adverse Event Reporting System (VAERS), which rely on voluntary submission and can be limited by factors such

as underreporting [15,16]. Although promising, use of administrative claims database and electronic medical record (EMR) data for postmarketing safety surveillance relies heavily on the accuracy and predictive value of recorded diagnosis and procedure codes to identify AEs after drug or vaccine exposure.

Urticaria is a common vaccine AE that can occur within minutes after vaccination [17] and is therefore often monitored in influenza vaccine safety studies [13,18,19]. In a recent influenza vaccine safety pilot project, concerns were raised about potential misclassification of outcomes, specifically urticaria, when recorded on the same day as vaccination, that is, day 0 or same-day events, and the extent to which such coding identifies a preexisting condition or a potential vaccine-related AE [14]. The predictive value of outpatient day 0 events has been questioned previously in the literature [19,20]; however, definitive studies have not been conducted.

We conducted a medical chart review to assess the positive predictive value of outpatient urticaria diagnosis codes

* Corresponding author. Tel.: +617-509-9986; fax: +617-859-8112.

E-mail address: jeff_brown@harvardpilgrim.org (J.S. Brown).

What is new?

Outpatient diagnosis codes for urticaria found in health insurance claims data are insufficient to distinguish between a same-day vaccine adverse event and a preexisting condition. Additionally, to our knowledge, no medical record validation of urticaria has been published previously. Researchers should be cautious in using administrative claims data to distinguish same-day exposure and outcome events for vaccine safety surveillance; some outcomes may be appropriate for same-day analysis (e.g., syncope, anaphylaxis); however, others may not.

recorded in administrative claims on the same day as influenza vaccination to identify potential AEs.

2. Methods

Study participants were identified through Harvard Pilgrim Health Care's (HPHC) administrative claims data warehouse. HPHC is a not-for-profit health plan serving the New England area. Health plan members were eligible for inclusion if they (1) received primary care at Harvard Vanguard Medical Associates, a large, multi-specialty medical group practice with EMRs; (2) had a claim for an outpatient visit with both an ICD-9 diagnosis code for urticaria (708.0, 708.1, or 708.9) and a CPT-4 procedure code for influenza vaccination (90655–90660) recorded on the same day between October 1, 2002, and December 31, 2007; and (3) were at least 6 months old on the visit of interest. Members who received either trivalent influenza vaccine or live attenuated influenza vaccine were eligible for inclusion. Urticaria diagnosis codes were chosen to match inclusion criteria of prior published influenza vaccine safety studies [13,14].

Fifty-one health plan members met the inclusion criteria. Among them, EMR review was limited to the 50 members with the most recent visits of interest. Information on exposure (influenza vaccination) and outcome (urticaria event), including the temporal relationship between them, was abstracted from the EMR by a physician experienced in vaccine safety research (G.M.L.).

The HPHC Human Subjects Committee approved the study protocol. A HIPAA Waiver of Authorization was also obtained through the HPHC Privacy Board.

3. Results

3.1. Study population characteristics

Of the 50 members selected for chart review, 42 (84%) had an EMR available for review. The remaining eight patients received care outside of the group practice on the day of

interest, resulting in encounters for which medical records were unavailable. Among those with available data, 31% were younger than 5 years and 19% were older than 65 years, 64% were female, and 81% had a diagnosis code for unspecified urticaria (Table 1). Compared with those with available EMRs, a greater proportion of patients with unavailable data had a diagnosis of allergic urticaria (63% vs. 12%).

3.2. Exposure and outcome misclassification

Influenza vaccination on the day of interest was confirmed in all 42 patients with available data (Fig. 1).

Medical chart review confirmed urticaria on the day of vaccination for 40% (17/42) of members with an available EMR (Table 2); 59% were younger than 18 years. Among the 25 unconfirmed diagnoses, EMRs for 17 (68%) patients contained no evidence to indicate a day 0 urticaria event. Of these 17 patients, 4 had evidence of a nonurticarial rash and 13 had reported a history of urticaria but had a normal skin examination at the visit. For the remaining eight unconfirmed diagnoses, presence of urticaria could not be determined because of lack of a documented skin examination (five patients), incomplete EMR (two patients), and a telephone encounter to self-report a "rash" potentially related to drug exposure (one patient).

3.3. Temporal relationship between vaccination and urticaria

Among the patients with a confirmed day 0 urticaria event, 18% (3/17) had urticaria documented on physical

Table 1
Characteristics of study cohort

Characteristic	Patients with available medical records (N = 42) N (%) ^a	Patients with unavailable medical records (N = 8) N (%)
Age		
6 mo–4 yr	13 (31)	2 (25)
5–17 yr	4 (10)	2 (25)
18–64 yr	17 (40)	3 (38)
> 64 yr	8 (19)	1 (13)
Sex		
Male	15 (36)	3 (38)
Female	27 (64)	5 (63)
Year of vaccination		
2002	2 (5)	0 (0)
2003	3 (7)	1 (13)
2004	8 (19)	1 (13)
2005	5 (12)	4 (50)
2006	13 (31)	2 (25)
2007	11 (26)	0 (0)
ICD-9 diagnosis code		
708.0 (allergic urticaria)	5 (12)	5 (63)
708.1 (idiopathic urticaria)	3 (7)	1 (13)
708.9 (unspecified urticaria)	34 (81)	2 (25)

^a Percents may add to >100 due to rounding.

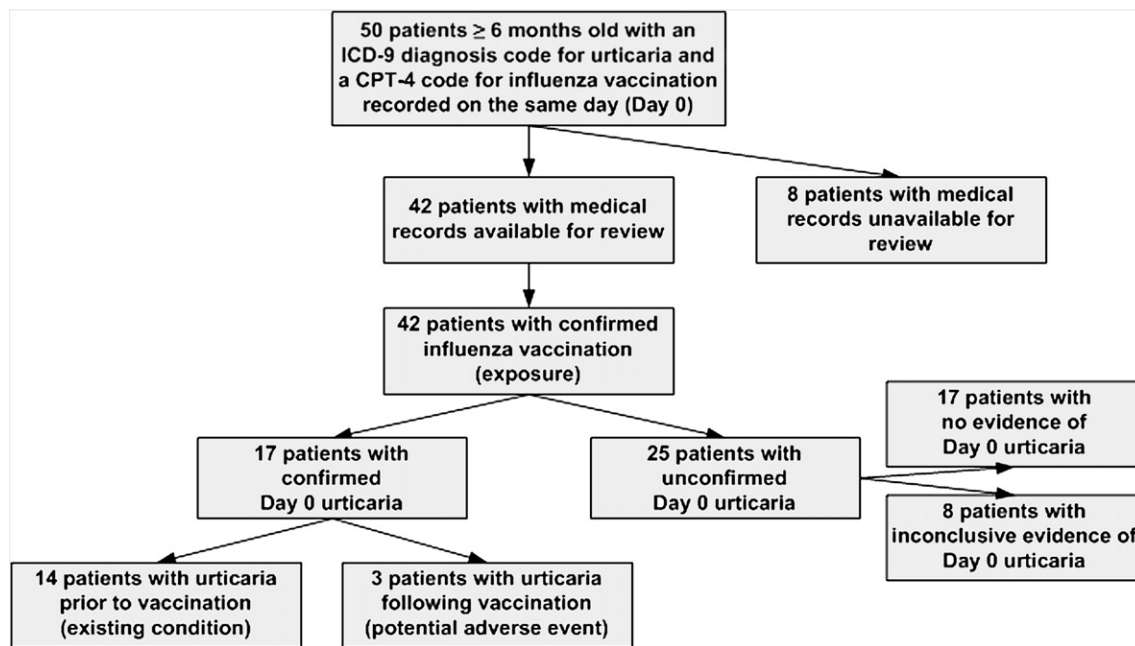


Fig. 1. Flowchart of exposure and outcomes among study participants.

examination after influenza vaccination, indicating a potential vaccine-related AE (Fig. 1); these visits occurred in 2003 ($n = 1$) and 2007 ($n = 2$). The age of these patients ranged from 4 to 12 years, and two received an additional vaccine on the day of interest. Two had an ICD-9 diagnosis code for unspecified urticaria (708.9) and one for allergic urticaria (708.0). The remaining 14 patients with a confirmed day 0 urticaria event had evidence of urticaria present on skin examination but with onset before vaccination. Most of these EMRs provided no definitive cause for the event, although viral illness, stress, and drug exposure were mentioned as potential triggers.

4. Discussion

Our medical chart review found that only 3 of 42 day 0 outpatient urticaria diagnoses were confirmed as potential vaccine-related AEs. The remaining events were instead found to represent a nonurticarial rash, history of urticaria that resolved before the visit, urticaria on the day of vaccination but before vaccine administration, or

there was insufficient evidence to determine presence of urticaria. These findings suggest that in the context of vaccine safety surveillance using administrative claims data, the predictive value of same-day outpatient ICD-9 diagnosis codes can be limited, potentially resulting in signals of excess risk that may not persist on chart review.

In addition to misclassification, the ability of outpatient diagnosis codes to identify AEs can be further influenced by a number of factors. For relatively mild conditions, such as urticaria, it has been hypothesized that the likelihood of returning for medical care is reduced when patients are informed of common side effects (“expected symptoms effect”) [19]. Furthermore, it is unknown whether age may impact the likelihood of seeking follow-up care, an important consideration given that all of our confirmed AEs occurred in children. Additional information in the EMR, such as visit time stamps, may provide valuable supplemental data to determine temporal relationships between exposure and outcome. Likewise, variables that may not be easily measured using administrative data, such as clinical workflow of a medical practice, can also affect the likelihood of capturing mild day 0 AEs. Furthermore, limitations in the predictive value of outpatient events may not be limited to same-day events. We found multiple instances where providers used the code for unspecified urticaria (708.9) to document either a past acute condition or a chronic condition. The ICD-9 diagnosis code for chronic urticaria (708.8) was intentionally excluded from this study because such events would not be considered a potential AE, regardless of the number of days after vaccination it was recorded in the EMR.

Table 2
Validation of same-day outpatient urticaria diagnosis codes

Diagnosis (ICD-9 code)	Confirmed urticaria event ($N = 17$)	Unconfirmed urticaria event ($N = 25$)
	N (%)	N (%)
Allergic urticaria (708.0)	1 (6)	4 (16)
Idiopathic urticaria (708.1)	1 (6)	2 (8)
Unspecified urticaria (708.9)	15 (88)	19 (76)

Given these potential limitations, prior published studies have chosen to exclude same-day events to optimize the specificity of outcome definitions [13,18,19]. However, exclusion of day 0 events could underestimate the risk of true AEs with rapid onset after vaccination. Although our findings generally support the exclusion of same-day outpatient events for urticaria identified in administrative claims data, careful consideration should be given to balancing the need for enhanced sensitivity in cases of serious acute events, such as anaphylaxis or myocardial infarction, vs. better specificity when considering mild, frequent AEs.

The generalizability of this study is limited by the small sample size and our reliance on a population drawn from members of a single health insurer, all of whom received care at a single group medical practice. Furthermore, we were unable to obtain medical records for eight study participants who received care outside the group practice on the day of interest. The distribution of urticaria codes differed among these individuals compared with the participants seen within the practice. Although there is no evidence to suggest that this variation is related to an actual difference in disease distribution, diagnosis coding has been shown to vary across health systems [21]. Nevertheless, this study adds important evidence to existing literature regarding the predictive value of same-day vaccine AEs identified using health care encounter data.

This study identified limitations of the predictive value of ICD-9 diagnosis codes to distinguish between a potential vaccine AE and a preexisting condition when a day 0 event is identified in the outpatient setting using administrative claims data. Further research is needed to better assess the clinical outcomes and exposures that support inclusion or exclusion of day 0 outpatient encounters when using administrative claims data for vaccine safety surveillance.

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