Herpes Zoster and Postherpetic Neuralgia Surveillance Using Structured Electronic Data

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OBJECTIVE: To develop electronic algorithms for rapid, automated surveillance for herpes zoster and postherpetic neuralgia (PHN) using codified electronic health data.

PATIENTS AND METHODS: We attempted to identify every case of herpes zoster and PHN arising between January 1 and December 31, 2008, within the electronic medical record of a 560,000-patient ambulatory practice using an array of diagnosis codes; intervals between herpes zoster encounters; and prescriptions for analgesics, anticonvulsants, and antidepressants. We assessed the sensitivity and positive predictive value (PPV) of each screening criterion by medical record review and then integrated multiple criteria into combination algorithms to optimize sensitivity and PPV. We applied the optimized algorithms to the practice's historical data spanning January 1, 1996, to December 31, 2008, to assess for changes in the annual incidence of PHN.

RESULTS: The *International Classification of Diseases, Ninth Revision*, code 053 detected herpes zoster with 98% sensitivity and 93% PPV. A combination algorithm including diagnosis codes, visit intervals, and prescriptions detected PHN with 86% sensitivity and 78% PPV. Between 1996 and 2008, the age- and sex-adjusted annual incidence of PHN rose from 0.18 to 0.47 cases per 1000 patients, and the proportion of herpes zoster patients progressing to PHN rose from 5.4% to 17.6%.

CONCLUSION: Novel algorithms incorporating multiple streams of electronic health data can reasonably detect herpes zoster and PHN. These algorithms could facilitate meaningful public health surveillance using electronic health data. The incidence of PHN may be increasing.

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CI = confidence interval; ICD-9 = *International Classification of Diseases, Ninth Revision*; PHN = postherpetic neuralgia; PPV = positive predictive value

Herpes zoster is an acute, painful neurocutaneous disease caused by reactivation of latent varicella-zoster virus in nerve ganglia after an episode of varicella (chickenpox). It affects up to 1 million Americans per year and carries a lifetime risk of 15% to 30%.¹⁻⁴ The acute pain of herpes zoster gradually resolves for most patients, but a substantial fraction experience persistent pain, termed *postherpetic neuralgia* (PHN). The risk of PHN ranges from 6.5% to 18% in retrospective studies to 30% in prospective studies.⁴⁻⁸ Postherpetic neuralgia is associated with impaired emotional well-being, poor sleep, decreased social function, and difficulty carrying out activities of daily living.⁹⁻¹¹

The incidence of herpes zoster appears to be rising^{12,13} but for unclear reasons: aging of the population, increasing prevalence of immunosuppression, and decreasing exposure to wild-type virus are presumably increasing disease risk,

whereas varicella and zoster vaccine programs likely are decreasing risk.^{8,14-18} The relative contribution of each of these, as well as unrecognized additional factors, is unknown.¹⁹

Ongoing uncertainty about zoster biology and continuing changes in the population risk profile compel timely and efficient surveillance to quantify disease burden and assess the impact of vaccination programs. However, existing methods for herpes zoster and PHN surveillance are limited. Physicians are not required to report herpes zoster or PHN to public health agencies. Instead, zoster prevalence data come from periodic assessments of diagnosis registries or administrative databases,

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typically using *International Classification of Diseases, Ninth Revision* (ICD-9) codes. The positive predictive value (PPV) of the ICD-9 code 053 for herpes zoster is good (84%-94%),^{4,20,21} but there are 2 important limitations: (1) the sensitivity of ICD-9 codes for herpes zoster has not been defined, and (2) ICD-9 codes are not useful for identifying PHN because there is no specific code for PHN. The latter is a critical limitation because pain is the major morbidity associated with herpes zoster.^{9,22,23}

Despite these limitations, electronic health record and insurance claims data remain attractive sources for surveillance because they have the potential to provide rich, timely, continuous data on disease burden and vaccine effectiveness in very large populations. Effective electronic surveillance tools could also facilitate efficient case finding for treatment investigations and risk factor analyses. Therefore, we sought to develop accurate methods for herpes zoster and PHN surveillance using structured electronic data. We hypothesized that integrating the herpes zoster ICD-9 with codes for related diagnoses, pertinent laboratory tests, visit history, and

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prescriptions into combination algorithms might improve accuracy. We report on the development of optimized surveillance algorithms for herpes zoster and PHN and apply these algorithms to historical electronic health record data from a large ambulatory practice to assess for changes in the incidence of herpes zoster and PHN during a 12-year period.

PATIENTS AND METHODS

We used the following approach to develop herpes zoster and PHN surveillance algorithms: (1) define a population at risk; (2) attempt to identify every case within the population using broad search criteria including ICD-9 codes, laboratory tests, prescriptions, and intervals between visits; (3) review representative samples of records for every criterion; (4) calculate sensitivity and PPV for each criterion; and (5) refine and combine the most promising criteria into combination algorithms optimized for sensitivity and PPV.

SETTING AND POPULATION

Study patients were drawn from Harvard Vanguard Medical Associates, an ambulatory practice group that provides primary and specialty care to more than 550,000 patients in eastern Massachusetts. We included patients of all ages and both sexes. Patients were identified using demographic, encounter, laboratory, and prescription data extracted from the practice's electronic health record (EpicCare, Epic Systems, Verona, WI). All data from ambulatory office visits and telephone encounters were included. The Institutional Review Board of Harvard Pilgrim Health Care Institute approved the study.

SEARCH CRITERIA FOR HERPES ZOSTER

We attempted to identify all patients with an initial episode of herpes zoster between January 1 and December 31, 2008. We flagged all patients with (1) ICD-9 053 (herpes zoster). We sought additional potential cases *without* an ICD-9 053 as follows: (2) ICD-9 782.1 (rash) and a prescription for an antiviral medication within 0 to 14 days, (3) ICD-9 052.7 to 052.9 (varicella) in a patient older than 50 years, (4) ICD-9 054 (herpes simplex) in a patient older than 50 years, or (5) a laboratory test for herpes zoster (culture, direct fluorescence antigen, polymerase chain reaction, or serum IgM). We excluded patients with ICD-9 053 within the preceding 12 months to prevent attributing cases from 2007 to 2008. We randomly selected 100 records flagged by the first criterion and at least 50 records flagged by each of the other criteria for review.

CHART REVIEW CRITERIA FOR HERPES ZOSTER

A definite case of herpes zoster was defined as a patient with a dermatomal vesicular rash in which herpes zoster

was the treating physician's primary diagnosis, the patient was managed in a manner consistent with herpes zoster (by medications or observation), and no alternative diagnoses emerged from diagnostic testing or subsequent events. A possible case of herpes zoster was defined as clinical suspicion of herpes zoster in a patient with an atypical clinical presentation (eg, rash crossing the midline, absence of vesicles) and no alternative diagnosis suggested by diagnostic testing or subsequent events. The reviewer used a standard data abstraction form to evaluate charts and assign a designation. The study infectious disease physician (M. K.) resolved unclear cases. Sensitivity and PPV for each criterion were calculated with correction for the selective sampling strategy.

SEARCH CRITERIA FOR PHN

We nested the search for PHN among patients aged 20 years or older with an ICD-9 for herpes zoster (053) during calendar year 2008. Search criteria included (1) new prescription for an analgesic 0 to 60 days after ICD-9 053 in patients without an analgesic prescription in the preceding year, (2) new prescription for an anticonvulsant 0 to 60 days after ICD-9 053 in patients without an anticonvulsant prescription in the preceding 2 years, (3) new prescription for an antidepressant 0 to 60 days after ICD-9 053 in patients without an antidepressant prescription in the preceding year, (4) ICD-9 053.1x (herpes zoster with nervous system complications), (5) ICD-9 729.2 (unspecified neuralgia) 0 to 180 days after ICD-9 053 in patients without ICD-9 729.2 in the preceding 2 years, (6) ICD-9 338 (acute and chronic pain) 0 to 180 days after ICD-9 053 in patients without ICD-9 338 in the preceding 2 years, (7) ICD-9 780.96 (generalized pain) 0 to 180 days after ICD-9 053 in patients without ICD-9 780.96 in the preceding 2 years, and (8) 2 or more instances of ICD-9 053 within a 1-year period. Although PHN is defined as pain 30 days or more or 90 days or more after herpes zoster, these search criteria include time intervals of less than 30 days from initial zoster encounter because patients may only see a physician some time after zoster onset and because physicians generally prescribe treatments for severe symptoms before patients technically fulfill PHN criteria. Data from preceding and subsequent years were queried as needed to apply time-dependent criteria. We did not require evidence of continuous attendance at the host medical practice when applying criteria that included time spans.

CHART REVIEW CRITERIA FOR PHN

We randomly sampled at least 50% of records flagged by each criterion for full text review. Charts were assessed for persistent pain attributable to herpes zoster 30 days or more and 90 days or more after the onset of herpes zoster. We

TABLE 1. **Characteristics of All Practice Patients and Those With Herpes Zoster and PHN, Harvard Vanguard Medical Associates, Calendar Year 2008^a**

	All patients (n=559,339)	Herpes zoster (n=2089)	PHN (n=237)
Sex (%)			
Male	41	38	37
Female	59	62	63
Age group, y (%)			
<20	27	7	0
20-39	27	18	4
40-59	30	36	29
60-79	13	30	47
≥80	3	8	20
Comorbidities (%) ^b			
None	--	84	61
Diabetes	--	6	19
Cancer	--	8	14
HIV	--	<1	<1
End-stage renal disease	--	<1	<1
Corticosteroids	--	3	3
Other ^c	--	1	3

^a HIV = human immunodeficiency virus; PHN = postherpetic neuralgia.

^b Percentages are based on a sample of 100 patients with herpes zoster and 159 patients with PHN. Age and sex distributions for "All patients" and for "Herpes zoster" were directly calculated from the full patient population.

^c Immunosuppressive medications other than corticosteroids, hypogammaglobulinemia.

required explicit reference to ongoing pain or renewal of a pain medication prescribed for zoster as evidence of persistent pain. We assessed the completeness of PHN capture by the 8 screening criteria by reviewing 100 random charts selected by ICD-9 053 alone.

SENSITIVITY AND PPV CALCULATIONS

We calculated sensitivity and PPV for each PHN criterion. Many records were flagged by more than 1 criterion, leading to oversampling of patients meeting multiple criteria. Oversampled patients were more likely to have PHN; hence, the proportion of sampled patients with PHN overestimates PPV. We corrected for oversampling bias by first calculating the number of flagged (F_i) and sampled (S_i) patients for all $i=1, \dots, 256$ possible combinations of the 8 screening criteria. Within each of these 256 strata, reviewed patients were true random samples. We had at least 1 sampled patient for each strata with $F_i > 0$. We projected the total number of PHN cases (PHN_i) among the flagged patients as $E(PHN_i) = F_i * phn_i / S_i$, in which phn_i is the number of PHN cases among the sampled patients. For each of the $k=1, \dots, 8$ criteria, we then summed the number of flagged patients and the expected number of true cases; the ratio of these 2 sums is the estimated PPV. That is, $PPV_k = E(PHN_k) / F_k$, in which F_k is the number of patients flagged by criterion k and $E(PHN_k)$ is the estimated number of PHN cases among those patients. We estimated sensitivity by dividing

$E(PHN_k)$, the estimated number of PHN cases among patients with criterion k , with $\sum_k E(PHN_k)$, the estimated total number of PHN cases in the population.

DEVELOPING AN OPTIMIZED COMBINATION ALGORITHM FOR PHN

We combined criteria to maximize sensitivity and PPV for PHN. We focused this optimization on the detection of persistent pain 30 days or more after herpes zoster rather than 90 days or more to maximize power and minimize misclassification bias. Ascertaining the presence of persistent pain through retrospective chart review is progressively less reliable with increasing passage of time because patients are less likely to seek attention and physicians are less likely to document stable, chronic pain compared with acute, escalating pain. Criteria with high PPVs were selectively favored as combination components. We tried to improve criteria with low PPVs by combining them with other criteria using "AND" statements. We maximized sensitivity by combining multiple high PPV criteria using "OR" statements. Finally, we adjusted the time intervals between encounters to further enhance sensitivity and PPV.

HISTORICAL INCIDENCE OF HERPES ZOSTER AND PHN

We applied the final algorithms to Harvard Vanguard Medical Associates electronic health record data spanning January 1, 1996, to December 31, 2008, to explore trends in herpes zoster and PHN incidence over time. The population at risk each year was defined as all individuals of any age with 1 or more encounters in Harvard Vanguard Medical Associates during the calendar year. Incidence rates for each year were corrected for age and sex distribution relative to the 2000 US census. Temporal trends for disease incidence as well as percentage of herpes zoster cases progressing to PHN were estimated by standard linear regression using SAS version 9.2 (SAS Institute, Cary, NC).

RESULTS

HERPES ZOSTER

During calendar year 2008, the study practice provided care to 559,339 patients. Patients' characteristics are presented in Table 1. The total number of patients flagged by each criterion; the number of records reviewed; and their breakdown into definite, possible, and false-positive cases are shown in Table 2 along with the estimated sensitivity and PPV for each criterion. Altogether, the criteria flagged 3106 patients. Of these, 2089 had an ICD-9 code for herpes zoster (053). On review, 88 of 100 sampled patients (88%) had definite disease, and 5 (5%) had possible disease (93% PPV for definite or possible herpes zoster). The remaining criteria were designed to find herpes zoster patients with-

TABLE 2. Search Criteria for Herpes Zoster With Sensitivity and PPV for Definite and Possible Cases, Harvard Vanguard Medical Associates, Calendar Year 2008^a

	Flagged	Health records reviewed	Definite case ^b	Possible case ^b	False-positive case ^b	Definite herpes virus		Definite or possible herpes virus	
						Sensitivity ^c (%)	PPV (%)	Sensitivity ^c (%)	PPV (%)
ICD-9 for herpes zoster (053) primary or secondary diagnosis ^d	2089	100	88	5	7	99.3	88	97.5	93
ICD-9 for herpes zoster (053) primary diagnosis ^d	^e	85	78	3	4	89.0	92	85.9	95
ICD-9 for rash (782.1) AND prescription for antiviral ^f within 0-14 d NOT ICD-9 = 053 within -90 to +90 d	56	56	3	7	46	0.2	5	0.5	18
ICD-9 for varicella (052.7 or 052.8 or 052.9) AND age ≥50 y NOT ICD-9 = 053 within -90 to +90 d	11	11	4	0	7	0.2	36	0.2	36
ICD-9 for herpes simplex (054) AND age ≥50 y NOT ICD-9 = 053 within -90 to +90 d	785	50	0	1	49	0.0	0	0.8	2
Laboratory test for herpes zoster ^g NOT ICD-9 = 053 within -90 to +90 d	165	50	2	4	44	0.4	4	1.0	12

^a ICD-9 = *International Classification of Diseases, Ninth Revision*; PPV = positive predictive value.

^b Count of cases from among the health records selected for review.

^c Figures for sensitivity are corrected for variable sampling weights.

^d Physicians designate a single ICD-9 code as the primary diagnosis at each encounter; all other ICD-9 codes for the encounter are designated as secondary diagnoses.

^e Health records with diagnosis for herpes zoster in the first position (primary diagnosis) were sought from among those with an ICD-9 for herpes zoster in any position.

^f Acyclovir, valacyclovir, or famciclovir.

^g Culture, direct fluorescence antigen, polymerase chain reaction, or IgM serologic testing.

out an ICD-9 053. On review of 167 of these patients, 9 had definite and 12 had possible herpes zoster. After adjustment for sampling, the net sensitivity of ICD-9 053 was 99.3% for definite herpes zoster and 97.5% for definite or possible herpes zoster.

PHN SCREENING CRITERIA

Given the 97.5% sensitivity of ICD-9 code 053 for herpes zoster, we nested the search for PHN among patients with this code during calendar year 2008. We limited the search to individuals aged 20 years or older to focus on the population at greatest risk of PHN. This reduced the potential study population from 2089 to 1940 patients. Screening criteria for PHN flagged 765 individuals (39%). Numbers of patients flagged by each PHN screening criterion, records reviewed, confirmed cases of PHN, projected cases of PHN for the criterion in the full population, and sampling-adjusted estimates for sensitivity and PPV are reported in Table 3. The sampling strategy yielded 430 records for review. Of these, 159 (37%) met the primary case definition for PHN (persistent pain ≥30 days after herpes zoster). After correction for oversampling of patients flagged by multiple criteria, we estimated 237 cases of PHN in the total study population (incidence rate, 12.2% for calendar year 2008). Of the 100 records randomly selected on the basis of an ICD-9 for herpes zoster alone, 31 were flagged by 1 or more screening criteria for PHN. Of

the remaining 69 patients, none had PHN, affirming that screening criteria were capturing all cases. Therefore, we used the estimate of 237 cases of PHN as the denominator for all sensitivity calculations.

OPTIMIZED ALGORITHM FOR IDENTIFYING PHN

Figure 1 depicts the impact on accuracy of varying the minimum interval between first and last visits with an ICD-9 code for herpes zoster (search criterion 8 in Table 3). A visit interval of 21 days or more has a sensitivity of 69% and PPV of 58%. We tried to improve PPV by combining this visit interval with various additional criteria as depicted in Table 4. An optimized algorithm consisting of 2 or more visits with an ICD-9 for herpes zoster 21 days or more apart AND a new prescription for an analgesic, antidepressant, or anticonvulsant; OR an ICD-9 code for herpes zoster with nervous system complications; OR an ICD-9 for neuralgia within 180 days of a visit for herpes zoster had a sensitivity of 86% and PPV of 78%.

HISTORICAL INCIDENCE OF HERPES ZOSTER AND PHN

Figure 2 depicts the estimated annual incidence of herpes zoster and PHN between 1996 and 2008 derived from applying the optimized algorithms to historical electronic medical record data. Incidences are corrected for age and sex distribution relative to US Census 2000 figures. The incidence of herpes zoster remained stable (annual increase,

TABLE 3. Number of Health Records Flagged, Reviewed, and Found to Have PHN, and Sensitivity and PPV by Search Criteria for PHN in Patients 20 Years of Age or Older, Harvard Vanguard Medical Associates, Calendar Year 2008

Criterion	Flagged	Reviewed	PHN ≥ 30 d after zoster onset				PHN ≥ 90 d after zoster onset			
			PHN (≥ 30 d)	Projected PHN	Sensitivity (%)	PPV (%)	PHN (≥ 90 d)	Projected PHN	Sensitivity (%)	PPV (%)
1. New Rx for analgesic within 0-60 d of zoster ICD-9	464	246	70	96	41	21	35	42	38	9
2. New Rx for anticonvulsant within 0-60 d of zoster ICD-9	205	136	88	118	50	58	47	62	55	30
3. New Rx for antidepressant within 0-60 d of zoster ICD-9	115	85	42	48	20	42	25	28	25	24
4. ICD-9 for zoster with nervous system complications (053.1x)	166	114	96	140	59	84	48	76	68	46
5. ICD-9 for zoster followed by ICD-9 729.2 (neuralgia unspecified) within 180 d	23	23	19	19	8.0	83	11	11	10	48
6. ICD-9 for zoster followed by ICD-9 338.x (acute and chronic pain) within 180 d	13	13	6	6	2.5	46	2	3	3	23
7. ICD-9 for zoster followed by ICD-9 780.96 (generalized pain) within 180 d	0	...	...	...	...	...	...	...	...	...
8. Two or more visits with ICD-9 for zoster ≥ 7 d apart	511	252	138	182	77	36	72	90	80	18
≥ 14 d apart	350	207	132	173	73	49	68	86	77	25
≥ 21 d apart	279	186	127	163	69	58	66	82	73	29
≥ 30 d apart	219	168	114	135	57	62	64	77	69	35
≥ 60 d apart	138	119	76	84	35	61	53	59	53	43
≥ 90 d apart	104	98	59	62	26	60	49	52	46	50
≥ 180 d apart	43	42	21	21	8.9	49	15	15	13	35
Any of the above criteria	765	430	159	237	100	31	82	112	100	15

ICD-9 = International Classification of Diseases, Ninth Revision; PHN = postherpetic neuralgia; PPV = positive predictive value; Rx = prescription.

0.020 cases per 1000 patients; 95% confidence interval [CI], -0.062 to 0.103) during this period, but the annual incidence of PHN increased by 0.024 cases per 1000 pa-

tients (95% CI, 0.015 to 0.033) per year. The proportion of herpes zoster cases with PHN rose by 0.7% (95% CI, 0.4%-1.0%) per year.

FIGURE 1. Impact of varying the minimum interval from 0 to 90 days between the first and last visits with an International Classification of Diseases, Ninth Revision, code for herpes zoster (053) on sensitivity and positive predictive value for postherpetic neuralgia.

TABLE 4. Number of Health Records Flagged, Reviewed, and Found to Have PHN, and Estimated Sensitivity and PPV by Combination Equations for Detection of PHN in Patients 20 Years of Age or Older, Harvard Vanguard Medical Associates, Calendar Year 2008

Criterion	Flagged	Reviewed	PHN ≥ 30 d after zoster onset				PHN ≥ 90 d after zoster onset			
			PHN (≥ 30 d)	Projected PHN	Sensitivity (%)	PPV (%)	PHN (≥ 90 d)	Projected PHN	Sensitivity (%)	PPV (%)
Two or more visits with zoster ICD-9 ≥ 21 d apart	279	186	127	163	69	58	66	82	73	29
Two or more visits with zoster ICD-9 ≥ 21 d apart AND new Rx for analgesic within 60 d	98	74	59	78	33	80	31	36	32	37
Two or more visits with zoster ICD-9 ≥ 21 d apart AND new Rx for anticonvulsant within 60 d	96	76	72	91	38	95	39	50	45	52
Two or more visits with zoster ICD-9 ≥ 21 d apart AND new Rx for antidepressant within 60 d	50	43	35	37	16	74	21	23	21	46
Two or more visits with zoster ICD-9 ≥ 21 d apart AND new Rx for anticonvulsant or antidepressant within 60 d	123	97	86	107	45	87	48	60	54	49
Two or more visits with zoster ICD-9 ≥ 21 d apart AND new Rx for anticonvulsant or antidepressant or analgesic within 60 d	169	129	108	140	59	83	56	69	62	41
ICD-9 053.1x (herpes zoster with nervous system complications) OR ICD-9 729.2 (neuralgia) within 180 d of a visit with zoster ICD-9	179	127	105	148	62	83	55	82	73	46
Two or more visits with zoster ICD-9 ≥ 1 d apart OR ICD-9 053.1x (herpes zoster with nervous system complications) OR ICD-9 338.x (acute and chronic pain) OR ICD-9 729.2 (neuralgia) within 180 d of a visit with zoster ICD-9	755	321	152	221	93	29	81	111	99	15
Two or more visits with zoster ICD-9 ≥ 21 d apart OR ICD-9 053.1x (herpes zoster with nervous system complications) OR ICD-9 729.2 (neuralgia) within 180 d of a visit with zoster ICD-9	352	222	147	214	90	61	80	109	97	31
Two or more visits with zoster ICD-9 ≥ 14 d apart AND new Rx for anticonvulsant or antidepressant or analgesic within 60 d OR ICD-9 053.1x (herpes zoster with nervous system complications) OR ICD-9 729.2 (neuralgia) within 180 d of a visit with zoster ICD-9	296	195	140	205	87	69	75	103	92	35
Two or more visits with zoster ICD-9 ≥ 21 d apart AND new Rx for anticonvulsant or antidepressant or analgesic within 60 d OR ICD-9 053.1x (herpes zoster with nervous system complications) OR ICD-9 729.2 (neuralgia) within 180 d of a visit with zoster ICD-9	261	180	139	203	86	78	75	102	91	39
Two or more visits with zoster ICD-9 ≥ 28 d apart AND new Rx for anticonvulsant or antidepressant or analgesic within 60 d OR ICD-9 053.1x (herpes zoster with nervous system complications) OR ICD-9 729.2 (neuralgia) within 180 d of a visit with zoster ICD-9	243	175	138	193	81	79	74	99	88	41

ICD-9 = International Classification of Diseases, Ninth Revision; PHN = postherpetic neuralgia; PPV = positive predictive value; Rx = prescription.

DISCUSSION

This study demonstrates the feasibility of herpes zoster and PHN surveillance using structured electronic health data. To our knowledge, this is the first investigation to estimate sen-

sitivity for ICD-9 code 053 by seeking additional cases of herpes zoster plausibly miscoded as something other than herpes zoster. Our sensitivity estimate of 97.5% and PPV of 93% suggest that the ICD-9 code for herpes zoster misses few cases and constitutes a reasonable case-finding strategy.

FIGURE 2. Annual incidence of herpes zoster, annual incidence of postherpetic neuralgia, and percentage of patients with herpes zoster who developed postherpetic neuralgia in Harvard Vanguard Medical Associates, 1996-2008. Figure is adjusted for age and sex relative to US Census 2000.

This investigation is also the first to develop a means to conduct surveillance for PHN using codified electronic health data and to estimate changes in the incidence of PHN over time. A combination equation including multiple ICD-9 codes, intervals between visits, and medication prescriptions detected PHN with a sensitivity of 86% and a PPV of 78%. The estimated 12.9% age- and sex-adjusted incidence of PHN in this study is consistent with other retrospective, chart-review-based studies.^{4-8,24,25} If our algorithm is affirmed, national estimates of PHN incidence may now be possible to obtain by applying electronic algorithms to large national data sets of codified data, such as Medicare.

Exploratory application of the PHN identification algorithm to 12 years of historical data suggests that the age-adjusted percentage of patients with herpes zoster who develop PHN may be increasing. This is biologically plausible if one posits rising prevalence of immunosuppressive conditions and/or treatments over time or waning immunity because of less periodic boosting from natural varicella infections. However, the historical projections in this study should be interpreted with caution. We used data from a single provider group in a single metropolitan area, and the incidence of herpes zoster and PHN may vary by geography and provider organization. In addition, we did not adjust for all possible confounders, and it is possible that temporal changes in coding, prescribing, or care-seeking patterns compromised PHN algorithm performance.

We did attempt to design the PHN algorithm to minimize these possible sources of error by (1) rooting the algorithm on the principle of multiple visits (an aspect of PHN that is likely consistent over time and space), (2) demonstrating that the sensitivity and PPV of the algorithm are stable over a wide range of reasonable visit intervals, (3) making the list of eligible drug classes as well as specific agents very broad to accommodate different prescribing patterns, and (4) including many “OR” conditions in the algorithm to accommodate different coding patterns. It is reassuring that the 5.4% to 17.6% range of PHN frequencies in this study is consistent with the 6.5% to 18% range of PHN frequencies reported in the literature.^{4-8,24,25}

Researchers and public health practitioners can select different versions of the PHN algorithm, depending on the data available to them (diagnosis codes alone with or without medication prescriptions) and the question they seek to answer. Researchers seeking patients for risk factor analysis may select algorithms that maximize sensitivity followed by confirmatory chart reviews or interviews. Public health officials intent on consistent case-finding methodology over time may favor algorithms that maximize PPV.

We elected to focus algorithm optimization on persistent pain 30 days or more after zoster onset rather than 90 days or more to maximize power and minimize misclassification bias. There is no consensus on what duration of pain constitutes PHN,²⁶ but retrospective chart reviews tend to be less reliable for longer windows of pain. Chart documen-

tation declines as patients establish stable pain regimens that no longer require repeated physician visits, seek second opinions and alternative therapies outside the primary practice, resign themselves to pain, or develop new health concerns that displace pain as the focus of their visits. The algorithms' estimated PPVs for PHN at 90 days or more are likely underestimates due to false-negative misclassifications of PHN secondary to incomplete documentation. It might be possible to improve the PPV for pain 90 days or more after zoster onset by optimizing algorithms for this specific outcome, but determining the algorithms' true performance will require prospective, active assessment of PHN rather than retrospective medical record reviews.

As with all retrospective methods based on administrative data and/or medical record review, algorithms likely underestimate the incidence of herpes zoster and PHN because they are limited to patients who seek care and charts with adequate coded data to trigger the algorithms. Survey data do suggest that 95% of patients with zoster see a physician; however, it is possible that some seek care in an emergency department or from physicians outside of their primary practice.²⁷ Important clinical data generated outside of the primary practice can be missing in up to 8% of patient encounters.²⁸ The algorithms will also miss cases if physicians select none of the algorithms' diagnosis codes, opt not to prescribe any of the medications in the search criteria, prescribe by telephone and fail to document in the electronic record, or recommend over-the-counter agents such as capsaicin in lieu of prescription medications. These scenarios seem rare because we did not find any cases missed by the search criteria when reviewing a random set of 100 unselected patients with herpes zoster. Conversely, the denominator estimates are subject to overestimation from patients leaving the practice and underestimation from individuals deferring care visits for prolonged periods.

CONCLUSION

Surveillance algorithms incorporating structured electronic data can accurately detect herpes zoster and PHN. The portability of our algorithms to new data sets and time periods requires further study, but if their performance is confirmed, they have potential to facilitate streamlined, timely, automated surveillance using large administrative databases or electronic health record data.^{29,30} Surveillance algorithms are promising tools to monitor the changing epidemiology of herpes zoster and PHN.

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