DOI:10.1111/irv.12097
www.influenzajournal.com

Original Article

Does outpatient laboratory testing represent influenza burden and distribution in a rural state?

Deborah L. Thompson,[a] Joan Baumbach,[a] Jessica Jungk,[a,b] C. Mack Sewell,[a,c] Chad Smelser,[a] Michael Landen[a]

[a]New Mexico Department of Health, Santa Fe, NM, USA. [b]University of Kansas Medical Center, Kansas City, KS, USA. [c]Wyoming Workforce Services Department, Cheyenne, WY, USA.
Correspondence: Joan Baumbach, MD, MPH, MS, New Mexico Department of Health, 1190 St. Francis Drive, Suite N-1350, Santa Fe, NM 87505, USA.
E-mail: joan.baumbach@state.nm.us

Accepted 18 January 2013. Published online 17 March 2013.

Background Laboratory testing results are often used to monitor influenza illness in populations, but results may not be representative of illness burden and distribution, especially in populations that are geographically, socioeconomically, and racially/ethnically diverse.

Objectives Descriptive epidemiology and chi-square analyses using demographic, geographic, and medical condition prevalence comparisons were employed to assess whether a group of individuals with outpatient laboratory-confirmed influenza illness during September–November 2009 represented the burden and distribution of influenza illness in New Mexico (NM).

Patients/Methods The outpatient group was identified via random selection from those with positive influenza tests at NM laboratories. Comparison groups included those with laboratory-confirmed H1N1-related influenza hospitalization and death identified via prospective active statewide surveillance, those with self-reported influenza-like illness (ILI) identified through random digit dialing, and the NM population.

Results This analysis included 334 individuals with outpatient laboratory-confirmed influenza, 888 individuals with laboratory-confirmed H1N1-related hospitalization, 39 individuals with laboratory-confirmed H1N1-related death, 334 individuals with ILI, and NM population data (N = 2 036 112). The outpatient laboratory-confirmed group had a different distribution of demographic and geographic factors, as well as prevalence of certain medical conditions as compared to the groups of laboratory-confirmed H1N1-related hospitalization and death, the ILI group, and the NM population.

Conclusions The outpatient laboratory-confirmed group may reflect provider testing practices and potentially healthcare-seeking behavior and access to care, rather than influenza burden and distribution in NM during the H1N1 pandemic.

Keywords Epidemiology, H1N1, influenza, laboratory testing, outpatient.

Please cite this paper as: Thompson *et al.* (2013) Does outpatient laboratory testing represent influenza burden and distribution in a rural state? Influenza and Other Respiratory Viruses 7(5), 686–693.

Introduction

Laboratory testing results are often used to monitor influenza illness in populations, but results may not be representative of illness burden and distribution, especially in populations that are geographically, socioeconomically, and racially/ethnically diverse. In particular, surveillance via laboratory testing may be subject to bias or limitations because of the dependence on healthcare-seeking behavior among those with symptoms.[1–3] Even among individuals receiving health care, testing may not be performed or may be performed using rapid tests that do not require formal laboratory submission.[1,4]

During the 2009 influenza A (H1N1) pandemic, enhanced surveillance was conducted in New Mexico to monitor the burden, distribution, and severity of influenza illness. This surveillance included prospective active statewide surveillance of laboratory-confirmed H1N1-related hospitalizations and deaths. Populations at risk of severe influenza outcomes were identified through this surveillance mechanism. Due to a need to better understand the risk factors for severe H1N1-related outcomes, subsequent efforts were made to conduct a case–control study to assess risk factors for hospitalization. Two control groups were identified for case–control purposes, including an outpatient laboratory-confirmed group and an influenza-like illness (ILI) group. The initial descriptive findings from the case–control groups raised concern about whether outpatient laboratory testing adequately represented the burden and distribution of influenza illness in New Mexico.

The objective of this analysis is to assess whether outpatient laboratory-confirmed influenza illness represented

the burden and distribution of influenza illness in New Mexico during the H1N1 pandemic.

Methods

Ethics statement

The Institutional Review Board at New Mexico State University approved the original case–control study and this analysis. Verbal informed consent was obtained from all interviewed outpatients (laboratory-confirmed and ILI) or their proxies. Data on laboratory-confirmed influenza hospitalizations and deaths were collected without informed consent as part of the public health response to the H1N1 pandemic and were reportable to New Mexico Department of Health (NMDOH) pursuant to state law.

Study design and population

Descriptive epidemiology and chi-square analyses were used to compare the outpatient laboratory-confirmed group with the groups of those with laboratory-confirmed H1N1-related influenza hospitalization, laboratory-confirmed H1N1-related death, those with ILI, and the New Mexico population. The outpatient laboratory-confirmed group consisted of New Mexico residents who had a positive influenza laboratory test performed at either the NMDOH public health laboratory or a large New Mexico-based clinical reference laboratory during September 2009–November 2009 and who were not hospitalized during that time period. Positive laboratory tests included real-time polymerase chain reaction (RT-PCR), culture, and direct fluorescent antibody. Individuals in the outpatient laboratory-confirmed group were randomly selected for interview from a list of outpatients with positive influenza tests provided by the two laboratories. Of the 1628 outpatients with a positive influenza test at either laboratory during the study period, 1034 were randomly called and interviews were completed with 334 outpatient laboratory-confirmed individuals. The remaining 594 outpatients were not called due to time and resource limitations.

The ILI group included New Mexico residents who had self-reported ILI (defined as subjective or measured fever with cough and/or sore throat) during September 2009–November 2009 and who were not hospitalized during that time period. Influenza-like illness households were identified via random digit dialing. Individuals in households were asked about which members of specified household groups (i.e., adult females, adult males, girls under 18 years of age, and boys under 18 years of age) had ILI. The number of individuals in each of these groups was recorded in a computer-assisted telephone interview (CATI) system. If more than one household member had ILI, then the CATI system randomly selected an individual from one of the household groups using a randomization scheme based on birth order. The interview was then conducted with this individual or his/her proxy. Of the 7707 telephone numbers called, 375 households were identified with at least one member meeting the ILI group criteria and interviews were completed with 334 ILI individuals. Recruitment for both the outpatient laboratory-confirmed and ILI groups occurred between 7 June 2010 and 1 August 2010.

The group of individuals with laboratory-confirmed hospitalization was defined as New Mexico residents admitted to a hospital with laboratory-confirmed influenza between 14 September 2009 and 25 November 2009, and was identified through prospective statewide active surveillance, which was designed to capture all H1N1-related hospitalizations in the state. This active surveillance included written dissemination by NMDOH of comprehensive inclusion criteria for influenza testing of hospitalized patients and follow-up of positive results. This time frame was chosen to correspond to active surveillance at NMDOH and to capture the peak of H1N1-related hospitalizations in the state. Prior to 12 October 2009, laboratory confirmation was defined as RT-PCR or culture positive for H1N1. On 12 October 2009, this definition was expanded to include any positive influenza test (rapid test through enzyme immunoassay, direct or indirect fluorescent antibody, culture, or RT-PCR) to reflect the fact that at the time 99% of circulating influenza viruses in the USA were H1N1.[5]

The group of individuals with laboratory-confirmed death was defined as New Mexico residents whose death occurred between 14 September 2009 and 25 November 2009, and who had any positive influenza test in the time frame around their death. This group included individuals hospitalized with a positive influenza test who subsequently died as well as individuals who were not hospitalized. Influenza-related deaths were also identified through laboratory testing performed by the New Mexico Office of the Medical Investigator.

Data collection

Data on laboratory-confirmed hospitalizations and deaths were collected using a standardized medical record abstraction form completed by hospital or NMDOH staffs that included information on demographics, height, weight, and underlying medical conditions. Data on the outpatient laboratory-confirmed and ILI groups were collected by computer-assisted telephone interviews, which were conducted by trained interviewers using a standardized interview script. Questions were worded to correspond closely to the laboratory-confirmed hospitalization and death medical record abstraction form. Proxy interviews were conducted for those individuals aged 18 years or younger. Interviews were conducted in English (94%) and Spanish (6%). Race/ethnicity data for all groups were collected using standardized ethnicity (Hispanic or non-Hispanic)

and race (American Indian, Asian, Black or African American, Native Hawaiian or other Pacific Islander, White) questions. Race/ethnicity data were gathered from medical records for those among the laboratory-confirmed hospitalization and death groups and were self-reported for those in the outpatient laboratory-confirmed and ILI groups. Data on New Mexico population demographics were obtained for 2009 from the Bureau of Business and Economic Research through the New Mexico Indicator-Based Information System.[6]

Analysis

Descriptive epidemiology comparisons and chi-square analyses were performed using demographic factors (age group, sex, race/ethnicity, county median household income), geographic factors (rurality of residence and geographic region), and medical condition prevalence (asthma, diabetes, and obesity). For all groups, county median household income estimates from the US Census Bureau were used as a proxy for socioeconomic status.[7] For all groups, rurality of residence was determined based on the Office of Management and Budget definitions for non-metro and metro counties.[8] New Mexico counties were grouped into regions in the state (Central, Northeast, Northwest, Southeast, and Southwest) to facilitate geographic comparisons. Medical conditions were chosen based on Advisory Committee on Immunization Practices guidelines for those at high risk of complications and the ability to obtain standardized statewide prevalence estimates.[9] Data on prevalence of medical conditions and obesity among the New Mexico population were obtained from the 2009 New Mexico Behavioral Risk Factor Surveillance System through the New Mexico Indicator-Based Information System.[10] The data available from this system only provided information for medical conditions and obesity on those aged 18 years and older; therefore, comparisons by medical conditions and obesity were limited to adults. For the laboratory-confirmed hospitalization and death and outpatient groups, and ILI group, the authors assessed obesity using body mass index (BMI), which was calculated for all non-pregnant participants aged ≥ 18 years who had height and weight reported. For participants between 18 and 20 years of age, calculated BMI values were compared with BMI-for-age percentiles.[11] Participants with BMI-for-age values greater than or equal to the 95th percentile were classified as obese. Participants over 20 years of age were classified as obese if the calculated BMI value was ≥ 30.

Analysis was also performed to better understand any potential impact on the data due to broadening the laboratory-confirmed definition for the hospitalization group on 12 October 2009. This group was divided into before October 12th and on/after October 12th subsections, and comparisons were made using chi-square analysis by age, sex, race/ethnicity, medical conditions, and region.

Comparisons were also made to assess potential differences between those in the ILI group who sought care and those in the outpatient laboratory-confirmed group. Interview question data were reviewed to identify which ILI individuals sought care. Chi-square analysis was used to compare these two groups by age, sex, race/ethnicity, medical conditions, and region. Descriptive and chi-square analyses were conducted using SAS® 9.2 and 9.3 (SAS Institute, Cary, NC, USA).

Results

Interviews were completed for 334 individuals in the outpatient laboratory-confirmed influenza group and 334 individuals in the ILI group with illness during September–November 2009 (Table 1). There were 888 laboratory-confirmed influenza-related hospitalizations and 39 laboratory-confirmed influenza-related deaths in New Mexico between 14 September 2009 and 25 November 2009. The estimated total New Mexico population in 2009 was 2 036 112.

There were statistically significant differences for the age group variable between the outpatient laboratory group and the following groups: ILI group (chi-square $P < 0{\cdot}0001$), hospitalization group ($P < 0{\cdot}0001$), and the death group ($P < 0{\cdot}0001$). The outpatient laboratory-confirmed group had a higher percent of individuals in the 5- to 24-year age group (61%) as compared to the ILI group (28%), the hospitalization group (28%), the death group (18%), and the New Mexico population (28%). The outpatient laboratory-confirmed group also had a higher percent of individuals in the 0- to 4-year age group (15%) as compared to all other groups except the hospitalization group (21%). In contrast, the outpatient laboratory-confirmed group had lower percentages of those in the age groups of 25–49, 50–64, and 65+ years. There were no statistically significant differences by sex between the outpatient laboratory-confirmed group and the other comparison groups. There were statistically significant differences by the race/ethnicity variable between the outpatient laboratory group and the following groups: ILI (chi-square $P < 0{\cdot}0001$), hospitalization ($P < 0{\cdot}0001$), and death ($P = 0{\cdot}004$). The outpatient laboratory-confirmed group had a lower percent of American Indians (4%) as compared to the New Mexico population (11%), despite American Indians having proportionally higher representation among the hospitalization group (19%) and the death group (18%). Non-Hispanic Whites appeared under-represented in the outpatient laboratory-confirmed group (28%) as compared to the ILI group (43%), the death group (36%), and the New Mexico population

Table 1. Characteristics of outpatient laboratory-confirmed influenza group, influenza-like illness group, laboratory-confirmed influenza hospitalization group, laboratory-confirmed influenza death group, and New Mexico population by categorical variables

Characteristics	No. (%)				
	Outpatient laboratory-confirmed influenza group (n = 334)	Influenza like-illness group (n = 334)	Laboratory-confirmed influenza hospitalization group (n = 888)	Laboratory-confirmed influenza death group (n = 39)	New Mexico population* (N = 2 036 112)
Age group (years)					
0–4	50 (15)	26 (8)	185 (21)	3 (8)	143 646 (7)
5–24	204 (61)	94 (28)	251 (28)	7 (18)	575 175 (28)
25–49	56 (17)	74 (22)	213 (24)	8 (21)	659 482 (32)
50–64	21 (6)	88 (26)	146 (16)	15 (38)	391 132 (19)
≥65	3 (1)	50 (15)	93 (10)	6 (15)	266 677 (13)
Unknown	0 (0)	2 (1)	0 (0)	0 (0)	0 (0)
Sex					
Female	181 (54)	199 (60)	450 (51)	15 (38)	1 030 153 (51)
Male	153 (46)	135 (40)	438 (49)	24 (62)	1 005 960 (49)
Race/ethnicity					
American Indian	14 (4)	31 (9)	166 (19)	7 (18)	218 337 (11)
Asian/Pacific Islander	5 (2)	3 (1)	11 (1)	0 (0)	35 119 (2)
Black	10 (3)	8 (2)	26 (3)	0 (0)	55 226 (3)
Hispanic	207 (62)	143 (43)	432 (49)	18 (46)	841 506 (41)
Non-Hispanic white	92 (28)	145 (43)	218 (25)	14 (36)	885 925 (44)
Unknown	6 (2)	4 (1)	35 (4)	0 (0)	0 (0)
County median household annual income**					
≤$36 238	19 (6)	69 (21)	150 (17)	8 (21)	402 188 (20)
>$36 238	314 (94)	265 (79)	738 (83)	31 (79)	1 633 925 (80)
Unable to classify	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Rurality of residence***					
Rural: Non-metro county	59 (18)	135 (40)	372 (42)	12 (31)	687 406 (34)
Urban: OMB metro county	275 (82)	199 (60)	516 (58)	27 (69)	1 348 706 (66)
Unable to classify	4 (1)	2 (1)	4 (0)	0 (0)	0 (0)
Obese (BMI only)†	34/115 (30)	66/212 (31)	165/321 (51)	3/12 (25)	2207/8532 (26)
High-risk medical condition†					
Asthma	25/117 (21)	39/222 (18)	125/505 (25)	3/28 (11)	787/8788 (9)
Diabetes	18/117 (15)	43/222 (19)	137/502 (27)	10/28 (36)	1038/8832 (12)
Region					
Central	174 (52)	52 (16)	221 (25)	13 (33)	652 152 (32)
Northeast	23 (7)	67 (20)	113 (13)	4 (10)	291 105 (14)
Northwest	78 (23)	111 (33)	208 (23)	8 (21)	430 482 (21)
Southeast	29 (9)	48 (14)	134 (15)	8 (21)	262 463 (13)
Southwest	29 (9)	56 (17)	212 (24)	6 (15)	399 911 (20)
Unknown	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)

*2009 New Mexico population data from New Mexico Department of Health Indicator-Based Information System for Public Health Web site. Available at: http://ibis.health.state.nm.us/query/selection/pop/PopSelection.html. Accessed 10 April 2012.

**Small-area income and poverty estimates, state and county estimates for 2008. US Census Bureau Web site. Available at: http://www.census.gov/did/www/saipe/data/statecounty/data/2008.html. Updated 18 November 2009. Accessed 26 March 2010.

***Rural definition based on Office of Management and Budget (OMB) metro counties. Available at: http://www.ers.usda.gov/datafiles/Rural_Definitions/StateLevel_Maps/NM.pdf. Accessed 16 February 2012.

†Data for those aged 18 years and older. Data for New Mexico population from New Mexico Department of Health Indicator-Based Information System for Public Health Web site. Available at: http://ibis.health.state.nm.us/query/selection/brfss/BRFSSSelection.html. Accessed 16 February 2012.

(44%). In contrast, the outpatient laboratory-confirmed group had a higher percent of Hispanic individuals (62%) as compared to all other groups and the New Mexico population (41%).

There were also statistically significant differences for the county median household income variable between the outpatient laboratory group and the following groups: ILI (chi-square $P < 0{\cdot}0001$), hospitalization ($P < 0{\cdot}0001$), and

death ($P = 0{\cdot}0008$). Similarly, analyses by the rurality of residence variable showed statistically significant differences between the outpatient laboratory group and the following groups: ILI (chi-square $P < 0{\cdot}0001$), hospitalization ($P < 0{\cdot}0001$), and death ($P = 0{\cdot}049$). The outpatient laboratory-confirmed group had a higher percent of individuals in the higher-income category (94%) and the urban residence classification (82%) as compared to all other groups and the New Mexico population (80% and 66%, respectively). Obesity classification based on BMI for those aged 18 years and older revealed a statistically significant difference only between the outpatient laboratory-confirmed group and the hospitalization group ($P < 0{\cdot}0001$). Of note, only 34% of laboratory-confirmed individuals had complete data for BMI, which was much lower than the ILI group (64%) but similar to the hospitalization (36%) and death groups (31%). Based on those aged 18 years and older, there were no statistically significant differences for the asthma variable between the outpatient laboratory-confirmed group and other groups. However, there was a statistically significant difference between those aged 18 years and older for the diabetes variable between the outpatient laboratory-confirmed group, and the hospitalization group ($P = 0{\cdot}007$) and death group ($P = 0{\cdot}01$). Specifically, the outpatient group had a lower percentage of diabetes (15%) than the hospitalization group (27%) and the death group (36%). The outpatient group had a higher percentage of those with diabetes (15%) than the New Mexico population estimates for diabetes (9%). There were also statistically significant differences by the geographic region variable between the outpatient laboratory group and the following groups: ILI (chi-square $P < 0{\cdot}0001$), hospitalization ($P < 0{\cdot}0001$), and death ($P = 0{\cdot}046$). Specifically, the outpatient laboratory-confirmed group had a higher percent living in the Central region (52%) as compared to the ILI group (16%), the hospitalization group (25%), the death group (33%), and the New Mexico population (32%).

Results from the hospitalization group sub-analysis based on the October 12th broadening of the laboratory-confirmed hospitalized revealed no statistically significant difference between the before October 12th and on/after October 12th groups by sex, asthma, or obesity variables. There were statistically significant differences by race/ethnicity (chi-square $P = 0{\cdot}003$), age group ($P = 0{\cdot}003$), region ($P = 0{\cdot}008$), and diabetes ($P = 0{\cdot}02$). Within the before October 12th group, 24·4% of individuals were American Indian, while in the on/after October 12th group, only 15·9% of individuals were American Indian. This was also reflected in regional differences with greatest difference between groups being seen in the Northwest region (29·0% before October 12th versus 19·5% on/after October 12th), which is the area of the state with the highest percentage of American Indian residence. Age group comparisons revealed that the 5- to 24-year-old group represented 34·4% of the before October 12th hospitalization group and 23·9% of the on/after October 12th hospitalization group. The 25- to 49-year-old group represented 19·5% of the before October 12th group and 27·2% of the on/after October 12th group.

Results from the ILI who sought care sub-analysis revealed that 79·2% of those aged ≤ 24 years sought care, while only 52·4% of those in the older age groups sought care. Comparisons between the ILI group who sought care and the outpatient laboratory-confirmed group showed statistically significant differences between these two groups for the following variables: age group (chi-square $P < 0{\cdot}0001$), race/ethnicity ($P = 0{\cdot}001$), and region ($P < 0{\cdot}0001$). Specifically, the 5- to 24-year age group had a higher representation in the outpatient laboratory group as compared to the ILI who sought care group (61·1% versus 34·5%, respectively). Hispanics had a higher representation in the outpatient laboratory group as compared to the ILI who sought care group (63·1% versus 47·6%, respectively), while American Indians had a lower representation in the outpatient laboratory group as compared to the ILI who sought care group (4·3% versus 10·8%, respectively). Regional differences revealed a much higher percent of the outpatient laboratory group living in the Central region as compared to the ILI who sought care group (52·3% versus 13·0%, respectively). There were no statistically significant differences by gender, asthma, diabetes, or obesity.

Discussion

Descriptive epidemiology and chi-square analyses were used to assess whether a group of individuals with outpatient laboratory-confirmed influenza illness during the fall of 2009 represented the burden and distribution of influenza illness in New Mexico. The outpatient laboratory-confirmed group appeared skewed from the other groups with regard to overall distribution of demographics, income, rural/urban location of residence, region of residence in New Mexico, and certain medical conditions. While the laboratory-confirmed hospitalization group and death group represented a measure of influenza severity, these groups also provided evidence that influenza was widely distributed across the state with regard to age group, region of residence, and rural/urban residence locations in a way that more closely mirrored the New Mexico population distribution. The hospitalization and death groups also provided evidence that certain populations, such as American Indians, were disproportionately affected by influenza, which was not reflected in the outpatient laboratory-confirmed group. Evidence from the literature also supports that American Indians and indigenous populations were disproportionately affected during the 2009 H1N1 pandemic [12–14] as well as

during previous pandemics. In the hospitalization group sub-analysis of the October 12th broadening of the laboratory-confirmed hospitalization definition, both the race/ethnicity and regional differences favored higher percentages of American Indians in the before October 12th group. It is possible that American Indians and other individuals in the Northwest region were affected by and/or tested more often for influenza earlier in the study period. This could have resulted in an underestimate of the burden on American Indians by having a more limited influenza hospitalization definition earlier in the study period. If so, the race/ethnicity and regional differences between the outpatient laboratory group and the hospitalization group may be even greater than shown in this study. Furthermore, the ILI group demonstrated that viral illness during the fall of 2009 was broadly distributed across New Mexico and largely mirrored the distribution of the New Mexico population, which was not reflected in the outpatient laboratory-confirmed group. Similarly, national surveillance data in the USA indicated that the geographic spread of influenza was widespread across most states during the fall of 2009 and peaked during the time frame evaluated in this study.[15]

The outpatient laboratory-confirmed group represented higher levels of younger individuals (<24 years) and those living in wealthier, more central, and urban regions within the state as compared to other comparison groups and the New Mexico population. The outpatient laboratory-confirmed group appeared to represent biased testing practices and might also represent access to care disparities, which might illustrate problems with the healthcare system rather than the burden and distribution of influenza illness in New Mexico. However, there might be clinical and public health reasons for what took place with respect to testing practices. High-risk groups for influenza illness complications were identified based on certain medical conditions (e.g., asthma),[9] and younger age groups were noted to be disproportionately affected by H1N1 illness.[15–17] Individuals with high-risk conditions and younger age groups therefore might have sought outpatient care more frequently as well as been tested more frequently when they did seek care. Data from the Behavioral Risk Factor Surveillance System in New Mexico during September–November 2009 indicate that among those with ILI, about twice as many children sought care (62·6%) as compared to adults (31·2%).[18] These findings are similar to the comparison in this study between younger and older age groups within the ILI who sought care group. This difference in healthcare-seeking behavior would have provided children with a greater opportunity for influenza testing as compared to adults. Comparison data from this study between those with ILI who sought care and those with outpatient laboratory-confirmed influenza showed significant differences based on demographic factors. Based on this information, it does not appear that the outpatient laboratory group solely represents a difference in persons seeking care but also may represent testing practices and other unidentified factors. In addition, beginning in September 2009 and throughout the study period, influenza testing was strongly encouraged and available at no cost through the New Mexico state public health laboratory for all hospitalized individuals with potential influenza illness and for all deaths suspicious of influenza. Recommendations for outpatient testing were not emphasized as clearly or strongly, and no cost testing was only available on a limited basis through the state public health laboratory. Statewide laboratory reporting of all positive influenza tests during the pandemic may have been more representative and useable for control groups for the case–control studies and/or for surveillance purposes. However, during the pandemic, this type of reporting was not feasible due to the time and resources that would have been needed to operationalize this level of reporting. This would have been too great a burden on both laboratories and NMDOH during the pandemic.

Despite potential reasons for the outpatient laboratory testing patterns, considerable resources were used to design and collect data for the original case–control study, which then did not yield a representative outpatient laboratory-confirmed control group. While there have been studies evaluating methods for selecting control groups and attempts to assess the magnitude of biases due to control group selection, these have been limited for influenza and have largely been focused on biases in influenza vaccine efficacy estimates derived from case–control studies.[4,19,20] Specifically, it has been noted that biases in case–control studies tend to underestimate true vaccine effectiveness.[19,20] There are implications for the lack of representativeness of outpatient laboratory-confirmed groups for either surveillance or control group purposes. These include the potential of skewed situational awareness and influenza epidemiology, which could lead to suboptimal prevention and treatment policy decisions (e.g., recommendations for prioritizing risk groups) and inappropriate allocation of prevention and treatment resources (e.g., allocation of vaccine and medications). Further examination of influenza control and surveillance group selection is necessary to identify and understand the effect that biased control and surveillance groups may have on case–control study and epidemiologic findings.

The strengths of this analysis included that comparisons were made between the outpatient laboratory-confirmed group and several different groups obtained both by active population-based surveillance (i.e., the hospitalization and death groups) and by population-based sampling (i.e., ILI group) as well as overall New Mexico population.

Limitations include that the outpatient laboratory-confirmed group was derived from data from two New Mexico laboratories. While these laboratories were the two

primary laboratories performing influenza testing during the fall of 2009, they do not represent all laboratories in the state or account for office-based testing. Also, the income, rural/urban residence location, and regions in New Mexico were based on county-level data rather than on individual-level data. The hospitalization subgroup analysis finding that the 5- to 24-year-old age group had higher representation in the before October 12th subgroup could indicate an underestimate for this group during the time of the more limited laboratory-confirmed definition. This could have resulted in an overestimate of the difference for this age group between the outpatient laboratory group and the hospitalization group. In addition, individuals in the ILI group might not all represent influenza illness but may represent other viral or non-viral illness. Furthermore, recall bias may have been a factor for the outpatient laboratory-confirmed group and ILI group as interviews were conducted during the summer of 2010. Finally, the medical condition and obesity comparisons were limited to adults due to the availability of population-based data.

Conclusion

This analysis highlights potential implications for both public health surveillance and case–control study control group selection. Reliance on outpatient laboratory-confirmed groups for surveillance or control group purposes should be undertaken with caution due to potential biases in testing practices, healthcare-seeking behavior, or other unidentified factors. Instead, a population-based approach that provides some degree of laboratory-confirmation should be considered for both surveillance and control group selection purposes in order to more accurately capture the burden and distribution of influenza illness.

Acknowledgements

We would like to thank Wayne Honey from the NMDOH Injury and Behavioral Epidemiology Bureau Survey Unit for his contributions to analysis of the influenza-like illness data from the New Mexico Behavioral Risk Factor Surveillance System. We would also like to thank the NMDOH Injury and Behavioral Epidemiology Bureau Survey Unit, NMDOH Infectious Disease Epidemiology Bureau, NMDOH Bureau of Vital Records and Health Statistics, the New Mexico Office of the Medical Investigator, New Mexico hospital infection preventionists, TriCore Reference Laboratories, the New Mexico Department of Health Scientific Laboratory Division, and New Mexico Department of Health Emerging Infections Program for their contributions to data collection. This work was supported by funding from the American Reinvestment and Recovery Act and the New Mexico Department of Health.

References

1 Achonu C, Rosella L, Gubbay JB, *et al.* Seroprevalence of pandemic influenza H1N1 in Ontario from January 2009-May 2010. PLoS One 2011; 6:e26427.
2 Brooks-Pollock E, Tilston N, Edmunds WJ, Earnes KTD. Using an online survey of healthcare-seeking behavior to estimate the magnitude and severity of the 2009 H1N1v influenza epidemic in England. BMC Infect Dis 2011; 11:68.
3 Centers for Disease Control and Prevention. Self-reported influenza-like illness during the 2009 H1N1 influenza pandemic – United States, September 2009-March 2010. MMWR Morb Mortal Wkly Rep 2011; 60:37–41.
4 Orenstein EW, De Serres G, Haber MJ, *et al.* Methodologic issues regarding the use of three observational study designs to assess influenza vaccine effectiveness. Int J Epidemiol 2007; 36: 623–631.
5 Finelli L, Brammer L, Blanton L, *et al.* Update: influenza activity—United States, April–August 2009. MMWR Morb Mortal Wkly Rep 2009; 58:1009–1012.
6 New Mexico Department of Health. Indicator-Based Information System for Public Health Web site. Available at: http://ibis.health.state.nm.us/query/selection/pop/PopSelection.html (Accessed 10 April 2012).
7 Small area income and poverty estimates, state and county estimates for 2008. US Census Bureau Web site. Available at: http://www.census.gov/did/www/saipe/data/statecounty/data/2008.html. Updated 18 November 2009. (Accessed 26 March 2010).
8 Rural definition based on Office of Management and Budget (OMB) metro counties. Available at: http://www.ers.usda.gov/datafiles/Rural_Definitions/StateLevel_Maps/NM.pdf (Accessed 16 February 2012).
9 Centers for Disease Control and Prevention. Prevention and Control of Influenza with Vaccine. Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010. MMWR Morb Mortal Wkly Rep 2010; 50(rr08):1–62.
10 New Mexico Department of Health. Indicator-Based Information System for Public Health Web site. Available at: http://ibis.health.state.nm.us/query/selection/brfss/BRFSSSelection.html (Accessed 16 February 2012).
11 CDC growth charts, Percentile data files with LMS values. Centers for Disease Control and Prevention Web site. Available at: http://www.cdc.gov/growthcharts/percentile_data_files.htm. Updated 4 August 2009 (Accessed 1 April 2010).
12 Castrodale L, McLaughlin J, Komatsu K, *et al.* Deaths related to 2009 pandemic influenza A (H1N1) among American Indian/Alaska Natives—12 States, 2009. MMWR Morb Mortal Wkly Rep 2009; 58:1341–1344.
13 Wenger JD, Castrodale LJ, Bruden DL *et al.* 2009 pandemic influenza A H1N1 in Alaska: temporal and geographic characteristics of spread and increased risk of hospitalization among Alaska Native and Asian/Pacific Islander people. Clin Infect Dis 2011;52(Suppl 1): S189–S197.
14 Zarychanski R, Stuart TL, Kumar A, *et al.* Correlates of severe disease in patients with 2009 pandemic influenza (H1N1) virus infection. CMAJ 2010; 10:257–264.
15 Brammer L, Blanton L, Epperson S, *et al.* Surveillance for influenza during the 2009 Influenza A (H1N1) pandemic – United States, April 2009- March 2010. Clin Infect Dis 2011; 52(Suppl. 1):S27–S35.
16 Fowlkes A, Arguin P, Biggerstaff M, *et al.* Epidemiology of 2009 pandemic Influenza A (H1N1) deaths in the United States, April-July 2009. Clin Infect Dis 2011; 52(Suppl. 1):S60–S68.

17 Jain S, Kamimoto L, Bramley A, *et al.* Hospitalized patients with 2009 H1N1 influenza in the United States, April-June 2009. N Engl J Med 2009; 361:1935–1944.

18 New Mexico Department of Health in collaboration with Centers for Disease Control and Prevention (CDC). Behavioral Risk Factor Surveillance System Survey Data. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2009.

19 Ferdinands JM, Shay DK. Magnitude of potential biases in a simulated case-control study of the effectiveness of influenza vaccination. Clin Infect Dis 2012; 54:25–32.

20 Uphoff H, an der Heiden M, Schweiger B, *et al.* Effectiveness of the AS03-adjuvanted vaccine against pandemic influenza virus A (H1N1) 2009 – a comparison of two methods; Germany, 2009–10. PLoS One 2011; 6:e19932.