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Predictors of Seeking Care for Influenza-Like Illness in a Novel Digital Study

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Background. Previous research has estimated that >50% of individuals experiencing influenza-like illness (ILI) do not seek health care. Understanding factors influencing care-seeking behavior for viral respiratory infections may help inform policies to improve access to care and protect public health. We used person-generated health data (PGHD) to identify factors associated with seeking care for ILI.

Methods. Two observational studies (FluStudy2020, ISP) were conducted during the United States 2019–2020 influenza season. Participants self-reported ILI symptoms using the online Evidation platform. A log-binomial regression model was used to identify factors associated with seeking care.

Results. Of 1667 participants in FluStudy2020 and 47 480 participants in ISP eligible for analysis, 518 (31.1%) and 11 426 (24.1%), respectively, sought health care. Participants were mostly female (92.2% FluStudy2020, 80.6% ISP) and aged 18–49 years (89.6% FluStudy2020, 89.8% ISP). In FluStudy2020, factors associated with seeking care included having health insurance (risk ratio [RR], 2.14; 95% CI, 1.30–3.54), more severe respiratory symptoms (RR, 1.53; 95% CI, 1.37–1.71), and comorbidities (RR, 1.37; 95% CI, 1.20–1.58). In ISP, the strongest predictor of seeking care was high symptom number (RR for 6/7 symptoms, 2.14; 95% CI, 1.93–2.38).

Conclusions. Using PGHD, we confirmed low rates of health care–seeking behavior for ILI and show that having health insurance, comorbidities, and a high symptom burden were associated with seeking health care. Reducing barriers in access to care for viral respiratory infections may lead to better disease management and contribute to protecting public health.

Keywords. care-seeking; digital study; influenza; real-world data; societal impact.

Seasonal influenza epidemics are associated with a significant disease burden, causing up to 41 million illnesses, 710 000 hospitalizations, and 21 million medical visits each year in the United States alone [1]. To allow for proper management and control of the disease, a robust understanding of annual epidemics through traditional health care–based surveillance systems, digital epidemiology approaches to surveillance, and real-world data (RWD) research studies is essential.

It is well documented that persons with influenza-like illness (ILI) are unlikely to seek care, with estimates that >50% of affected individuals do not seek health care for their ILI [2–4]. A better understanding of what influences individuals to seek care

for viral respiratory infections may help inform policies to improve access to care and protect public health. RWD research studies are vital tools in understanding epidemics of viral respiratory infections, but traditional RWD studies typically only include those individuals who seek care for their symptoms. These studies are thus unable to assess risk factors for seeking care for ILI, which may inform the management of these epidemics. This can also result in potential selection bias in RWD studies and surveillance systems, which only capture the most severe cases and may underestimate the true ILI disease burden [3, 5]. To gain a better understanding of the true burden of influenza and address this selection bias, it is necessary to develop novel ways of studying individuals with influenza, irrespective of whether they seek care, and to establish the differences between individuals who seek care and those who do not. This will elucidate potential barriers to care-seeking and may ultimately enable better management of influenza through improved access to effective treatments.

Person-generated health data (PGHD) represent a novel approach to RWD generation and have the potential to address this knowledge gap in RWD studies. PGHD can be collected from electronic surveys, applications, wearable sensors, mobile phones, and other technologies [6]. Evidation (Evidation Health, Inc.) is an online health community of 4 million members

across the United States that allows members to participate in research studies while facilitating the collection of a wide range of PGHD from participant surveys, consumer and clinical-grade applications, and wearable sensors [7]. Since 2017, the Evidation application has been used to run an ILI surveillance program that analyzes yearly influenza epidemics in the United States [8].

Using the Evidation Studies platform, we conducted 2 novel, direct-to-participant, real-world studies (FluStudy2020 and a participatory ILI surveillance program [ISP]) that utilized daily and weekly surveys, respectively, to identify a wide cohort of individuals with ILI, irrespective of whether they sought care, and to estimate the probability of participants seeking care based on baseline characteristics and ILI experience.

METHODS

Evidation Platforms and Recruitment

For both studies, participants were recruited from the Evidation consumer platform, a free application that allows members to earn compensation for completing surveys, sharing health activity data, and reading health articles [7]. For FluStudy2020, members of the Evidation consumer platform with a high probability of meeting inclusion criteria (based on data provided through normal operation of the platform, including surveys and profile information) were referred for the study. For ISP, participants were recruited directly from the Evidation platform. Individuals who indicated interest in participating in either study were then given the opportunity to enroll by providing informed consent to complete study activities and for use of their data. For ISP, Evidation members were presented with in-application prompts asking whether they had experienced ILI symptoms, and those who indicated that they had experienced symptoms were invited to provide consent and enroll in the ISP study. Members who elected to consent and enroll were then sent more detailed surveys. FluStudy2020 study activities were implemented on the Evidation studies platform, and ISP study activities were implemented on the Evidation consumer platform. A small subset of participants may have enrolled in both studies.

FluStudy2020 Study Design

FluStudy2020 was a 10-month, prospective, observational study conducted between December 2019 and November 2020 (rolling enrollment closed in February 2020) in the United States (Figure 1A). Participants were eligible to enroll if they were aged ≥18 years and lived in the United States (full inclusion and exclusion criteria are provided in Supplementary Methods 1).

At enrollment, participants completed a baseline survey that included questions on demographics, medical history and comorbidities, influenza history, and vaccination status. Following enrollment, participants completed daily surveys

for the first 120 days to report whether they had experienced ILI symptoms in the past 24 hours (Supplementary Figure 1). Symptomatic participants (answering "yes") were directed to a follow-up questionnaire to provide details on symptom severity (recorded on a 4-point scale: absent [0], mild [1], moderate [2], or severe [3]) and whether they had made a health care visit (specifically, if they had visited a health care provider [eg, doctor, nurse, practitioner, physician's assistant] at a clinic or urgent care facility), been diagnosed by a physician, or been prescribed medication. Participants were also asked where they had sought care, with the following options: primary care clinic, urgent care facility, emergency room, otolaryngology clinic, infectious disease clinic, or other. Those who met the following self-reported ILI symptom criteria—fever, ≥1 respiratory symptom (cough, nasal congestion or runny nose, or sore throat), and ≥1 systemic symptom (headache, muscle or joint ache, chills, or fatigue)—were sent an influenza diagnostic kit to confirm infection. Participants were included in the ILI population if they met the ILI symptom criteria. Participants were also issued monthly surveys on ILI complications and vaccination status (4 times across the study period), followed by bi-weekly surveys on ILI complications during study months 5–10. Data from wearable devices were also collected and analyzed; these results will be reported in a separate publication.

ISP Study Design

ISP was a prospective study conducted between November 2019 and October 2020 (Figure 1B). Participants were eligible to enroll if they were aged ≥18 years and lived in the United States (full inclusion and exclusion criteria are provided in Supplementary Methods 2).

Eligible participants completed weekly surveys to report whether they had experienced ILI symptoms in the past 7 days (including symptoms that had resolved by the time of the survey). Symptomatic participants (answering "yes") were directed to additional questions on duration of illness, symptoms, whether they sought care (specifically, if they had visited a health care provider at a clinic or urgent care facility), care outcomes, influenza diagnosis, and household characteristics (Supplementary Figure 2). As in FluStudy2020, participants were also asked where they sought care. Asymptomatic participants (answering "no") were directed to a survey on their health behaviors, which included questions on vaccination status. At the end of March 2020, additional questions related to coronavirus disease 2019 (COVID-19) were added to the survey, and participants self-reported their responses; these additional questions are detailed in Supplementary Methods 3.

Participants were included in the ILI population if they self-reported experiencing ≥1 respiratory symptom (cough, nasal congestion, or sore throat) and ≥1 systemic symptom (fever/chills/shivering, body/muscle aches, headache, or fatigue). Details of ISP's methodology have been published previously [4].
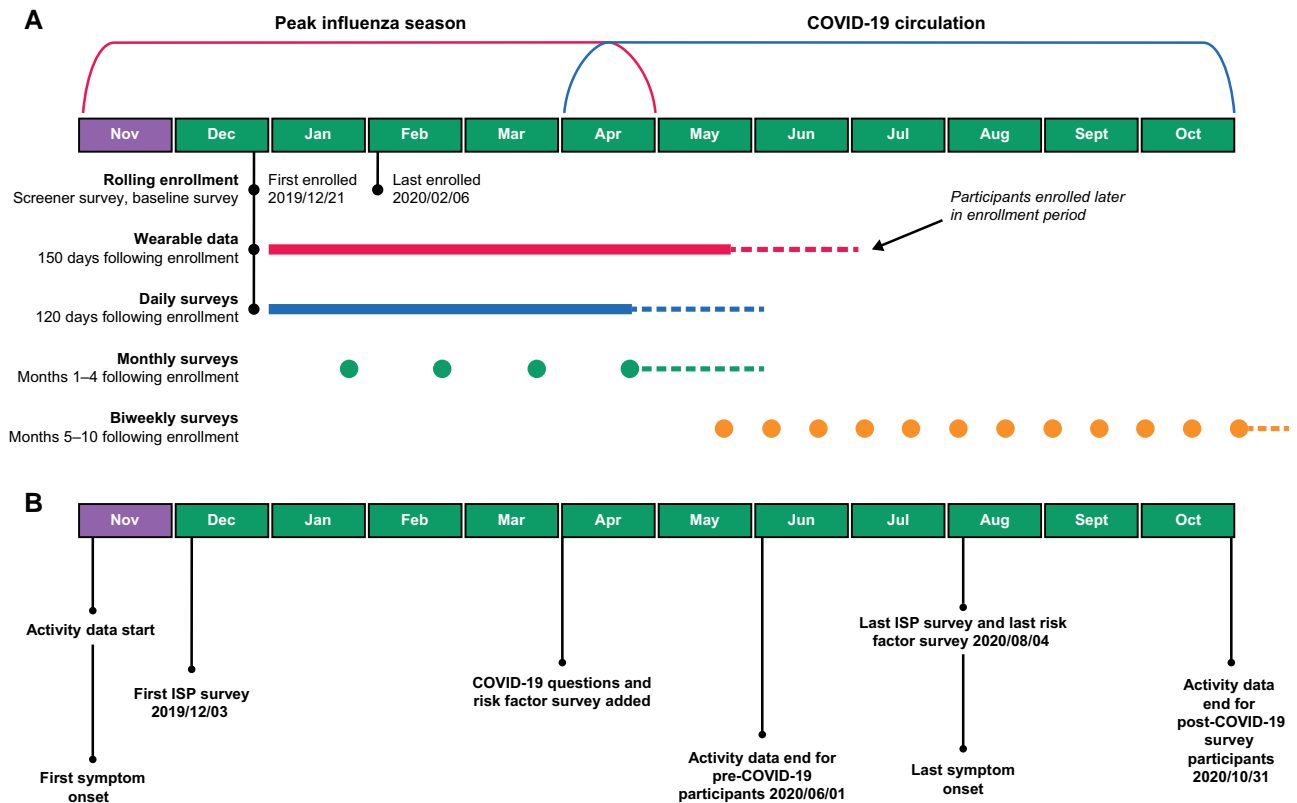
Figure 1. Study design overview. *A*, Study design for FluStudy2020. *B*, Study design for ISP. Abbreviations: COVID-19, coronavirus disease 2019; ISP, Participatory Influenza Surveillance Program.

Statistical Analyses

Two multivariable log-binomial regression analyses were conducted, 1 on the FluStudy2020 data set and 1 on the ISP data set, to measure the probability that an individual sought care based on their ILI experience and baseline characteristics (using the logbin package for R) [9]. For FluStudy2020, the independent variables were respiratory symptom severity, systemic symptom severity, health insurance status, age group, sex, education, geographic region, and having a health condition qualifying as a risk factor for influenza complications (defined as individuals with the following conditions, per US Centers for Disease Control and Prevention [CDC] guidelines: asthma, neurologic and neurodevelopment conditions, chronic lung disease, endocrine disorders, heart disease, kidney disorders, liver disorders, obesity, and weakened immune system) [10]. For ISP, the independent variables were number of symptoms experienced, age group, sex, education, geographic region, having a body mass index (BMI) >40 (classified as "severe obesity"), and existing or previous diagnosis of cancer, weakened immune system, lung conditions, or neurologic, endocrine, or heart disease. For both FluStudy2020 and ISP, to be eligible for inclusion in the analysis, participants were required to have met the aforementioned criteria for inclusion in the ILI population and to have provided data for each variable in the regression analyses. Nonbinary participants (due to a small sample size) and participants missing data on any of the predictor variables were excluded from the analysis.

For both study populations, baseline characteristics were assessed and statistically compared between the care-seeking and non-care-seeking cohorts using the Fisher exact test (categorical variables with ≥1 level with <5 observations) or the chi-square test (categorical variables where n was large). Bonferroni adjustments were applied to *P* values to correct for multiple tests (16 for FluStudy2020 and 15 for ISP). Finally, for both study populations, symptom recovery times were assessed and statistically compared between the care-seeking and non-care-seeking cohorts using Wilcoxon rank-sum tests, and Bonferroni correction was used to account for multiple testing. Adjusted *P* values <.05 were considered statistically significant.

For both studies, only 1 ILI event per individual was used for analysis. If an individual reported multiple ILI events, a single event was selected by ranking and choosing the highest-ranking event. Additional details of the criteria used to segment ILI events, for survey quality control, and to select a single ILI event are provided in Supplementary Methods 4–6.

RESULTS

FluStudy2020

Demographics and Baseline Characteristics

Overall, 10 004 participants were recruited into FluStudy2020, of whom 9925 completed ≥1 daily follow-up survey. The mean and median number of surveys completed were 114 and 104, respectively, out of a possible 120 surveys. Of these participants, 1738 met criteria to be included in the ILI population, and 1667 were eligible for inclusion in the analysis (ie, data were available for all variables in the regression analysis). Most participants were female (n = 1537, 92.2%), aged 18–49 years (n = 1494, 89.6%), and White (n = 1491, 89.4%) (Table 1). A large proportion of participants were at high risk of influenza complications (n = 762, 45.7%). Of the overall analysis population, 256 (15.4%) had a BMI categorized as severely obese (BMI >40), and 375 (22.5%) had asthma. There were 221 participants who tested positive for influenza, and of these, 55 received antiviral treatment.

Characteristics of Care-Seekers vs Non-Care-Seekers

Of the 1667 participants included in the analysis, 518 (31.1%) made a health care visit for their ILI, while the remaining 1149 (68.9%) did not. Care-seekers did not differ significantly from non-care-seekers in terms of demographic factors such as age, sex, race, or region; however, care-seekers were significantly more likely to have comorbidities associated with increased risk of influenza complications (n = 285, 55.0%, vs n = 477, 41.5%; $P < .001$). In particular, care-seekers were more likely to have asthma ($P = .07$) or endocrine disorders ($P < .001$) than non-care-seekers (Table 1).

Time from illness onset to recovery was significantly longer for care-seekers compared with non-care-seekers, with a median (interquartile range [IQR]) duration of illness of 5.0 (3.0–8.0) vs 3.0 (2.0–5.0) days, respectively ($P < .001$) (Figure 2A, left panel; Supplementary Table 1). Duration of fever was slightly longer for care-seekers than non-care-seekers (rank-sum difference $P = .001$) (Figure 2B, left panel), although the median (IQR) fever duration for both groups was 1.0 (1.0–2.0) day.

Factors Associated With Seeking Medical Care

When adjusting for measured confounders, the strongest predictor of seeking care was insurance status: Participants with health insurance were 2.14 times more likely to seek care than those without (95% CI, 1.30–3.54) (Table 2, Figure 3). Participants with any comorbidities associated with increased risk of influenza complications were also more likely to make a health care visit than those with no comorbidities (risk ratio [RR], 1.37; 95% CI, 1.20–1.58).

The probability of a participant seeking care for their ILI increased in association with respiratory and systemic symptom severity. For every unit increase in self-reported respiratory symptom severity (on a scale of 0–3: absent 0, mild 1, moderate 2, severe 3), the probability of seeking care increased by 1.53 times (95% CI, 1.37–1.71); similarly, participants with higher self-reported systemic symptom severity (on the same scale of 0–3) were more likely to seek care than those with lower symptom severity (RR, 1.22; 95% CI, 1.08–1.37) (Table 2, Figure 3).

ISP

Demographics and Baseline Characteristics

Of the 81 049 participants enrolled in ISP, 52 700 experienced ≥1 ILI during the study, and 47 480 were included in the regression analysis. In this population, 38 254 (80.6%) participants were female, 42 651 (89.8%) were aged 18–49 years, and 36 397 (76.7%) were White (Table 1). The most common comorbidities putting participants at high risk of complications were asthma (n = 12 324, 26.0%) and endocrine disorders (n = 8194, 17.3%), and 4083 (8.6%) participants had a BMI categorized as severely obese.

Characteristics of Care-Seekers vs Non-Care-Seekers

Overall, 11 426 (24.1%) participants sought medical care. Care-seekers were significantly more likely than non-care-seekers to have comorbidities associated with increased risk of influenza complications (n = 3804, 33.3%, vs n = 2011, 5.6%; $P < .001$). All comorbidities analyzed were found to be significantly more common in the care-seeking population than the non-care-seeking population (Table 1).

Of participants who sought care, 57.1% (n = 6521) reported 6–7 symptoms (from a prespecified list in the survey), vs 39.9% (n = 14 386) of those who did not seek care. Care-seekers had a longer median duration of symptoms (IQR) (9.0 [7.0–14.0] days) than non-care-seekers (7.0 [5.0–11.0] days; $P < .001$) (Figure 2A, right panel; Supplementary Table 1). Duration of fever was also longer in care-seekers than non-care-seekers (median [IQR], 4.0 [3.0–6.0] days vs 3.0 [2.0–5.0] days; $P < .001$) (Figure 2B, right panel).

Factors Associated With Seeking Medical Care

When adjusting for measured confounders, the strongest predictor of seeking care was number of symptoms: Participants experiencing 6 or 7 symptoms (considered to be most severe based on patients having between 2 and 7 symptoms) were 2.14 times more likely to seek care (95% CI, 1.93–2.38) than those with <6 symptoms (Table 2, Figure 3).

Presence of comorbidities was also associated with seeking care: Severely obese participants (RR, 1.2; 95% CI, 1.15–1.26) and those with lung conditions such as asthma and chronic lung disease (RR, 1.13; 95% CI, 1.09–1.17) were more likely to seek care than those without. Other comorbidities (such as neurologic, endocrine, or heart disease) were also associated with seeking care (RR, 1.04; 95% CI, 1.01–1.08) (Table 2, Figure 3).

Table 1. Demographics and Baseline Characteristics of Participants Included in the Regression Analyses in FluStudy2020 and ISP

No. (%)	FluStudy2020				ISP			
	Overall N = 1667	Did Not Seek Medical Care n = 1149	Sought Medical Care n = 518	P Value[a]	Overall N = 47 480	Did Not Seek Medical Care n = 36 054	Sought Medical Care n = 11 426	P Value[a]
Age	…	…	…	>.9	…	…	…	<.001
18–49 y	1494 (89.6)	1041 (90.6)	453 (87.5)		42 651 (89.8)	32 530 (90.2)	10 121 (88.6)	
50–64 y	161 (9.7)	100 (8.7)	61 (11.8)		4421 (9.3)	3231 (9.0)	1190 (10.4)	
65+ y	12 (0.7)	8 (0.7)	4 (0.8)		408 (0.9)	293 (0.8)	115 (1.0)	
Sex	…	…	…	>.9	…	…	…	<.001
Male	130 (7.8)	88 (7.7)	42 (8.1)		9226 (19.4)	7293 (20.2)	1933 (16.9)	
Female	1537 (92.2)	1061 (92.3)	476 (91.9)		38 254 (80.6)	28 761 (79.8)	9493 (83.1)	
Race	…	…	…	>.9	…	…	…	<.001
American Indian or Alaska Native	4 (0.2)	1 (0.1)	3 (0.6)		244 (0.5)	166 (0.5)	78 (0.7)	
Asian	35 (2.1)	28 (2.4)	7 (1.4)		–	–	–	
Asian or Pacific Islander	–	–	–		2264 (4.8)	1848 (5.1)	416 (3.6)	
Black or African American	59 (3.5)	38 (3.3)	21 (4.1)		1970 (4.1)	1367 (3.8)	603 (5.3)	
Hispanic or Latino	–	–	–		3388 (7.1)	2567 (7.1)	821 (7.2)	
Native Hawaiian or other Pacific Islander	3 (0.2)	2 (0.2)	1 (0.2)		–	–	–	
White	1491 (89.4)	1027 (89.4)	464 (89.6)		36 397 (76.7)	27 635 (76.6)	8762 (76.7)	
Multiple races	58 (3.5)	43 (3.7)	15 (2.9)		–	–	–	
Other	17 (1.0)	10 (0.9)	7 (1.4)		–	–	–	
Missing	–	–	–		3217 (6.8)	2471 (6.9)	746 (6.5)	
Education	…	…	…	>.9	…	…	…	.04
No college degree	507 (30.4)	356 (31.0)	151 (29.2)		20 123 (42.4)	15 293 (42.4)	4830 (42.3)	
College degree	765 (45.9)	523 (45.5)	242 (46.7)		19 471 (41.0)	14 886 (41.3)	4585 (40.1)	
Graduate degree	395 (23.7)	270 (23.5)	125 (24.1)		7886 (16.6)	5875 (16.3)	2011 (17.6)	
Health insurance status	…	…	…	.01	…	…	…	
Not insured	87 (5.2)	74 (6.4)	13 (2.5)		–	–	–	
Insured	1580 (94.8)	1075 (93.6)	505 (97.5)		–	–	–	
American region	…	…	…	>.9	…	…	…	<.001
Northeast	287 (17.2)	188 (16.4)	99 (19.1)		8266 (17.4)	6204 (17.2)	2062 (18.0)	
South	518 (31.1)	354 (30.8)	164 (31.7)		16 310 (34.4)	11 519 (31.9)	4791 (41.9)	
Midwest	552 (33.1)	383 (33.3)	169 (32.6)		12 252 (25.8)	9572 (26.5)	2680 (23.5)	
West	310 (18.6)	224 (19.5)	86 (16.6)		10 652 (22.4)	8759 (24.3)	1893 (16.6)	
CDC risk factor	…	…	…		…	…	…	
Any	762 (45.7)	477 (41.5)	285 (55.0)	<.001	5815 (12.2)	2011 (5.6)	3804 (33.3)	<.001
Asthma	375 (22.5)	236 (20.5)	139 (26.8)	.07	12 324 (26.0)	8935 (24.8)	3389 (29.7)	<.001
Neurologic and neuro-developmental conditions	6 (0.4)	6 (0.5)	0 (0.0)	>.9	1424 (3.0)	1021 (2.8)	403 (3.5)	.003
Chronic lung disease	7 (0.4)	5 (0.4)	2 (0.4)	>.9	1038 (2.2)	703 (1.9)	335 (2.9)	<.001
Endocrine disorders	209 (12.5)	117 (10.2)	92 (17.8)	<.001	8194 (17.3)	5926 (16.4)	2268 (19.8)	<.001
Heart disease	20 (1.2)	14 (1.2)	6 (1.2)	>.9	4191 (8.8)	3046 (8.4)	1145 (10.0)	<.001
Kidney disorders	11 (0.7)	7 (0.6)	4 (0.8)	>.9	–	–	–	
Liver disorders	9 (0.5)	6 (0.5)	3 (0.6)	>.9	–	–	–	
Autoimmune disease	132 (7.9)	82 (7.1)	50 (9.7)	>.9	4139 (8.7)	3002 (8.3)	1137 (10.0)	<.001
Severe obesity (BMI >40 kg/m²)	256 (15.4)	160 (13.9)	96 (18.5)	.3	4083 (8.6)	2817 (7.8)	1266 (11.1)	<.001

Dashes indicate no data collected for described variable.

Abbreviations: BMI, body mass index; CDC, Centers for Disease Control and Prevention; ISP, Participatory Influenza Surveillance Program.

[a]Bonferroni correction for multiple testing, corrected for 16 comparisons for FluStudy2020 and 15 comparisons for ISP.

Participants in the Midwest (RR, 0.87; 95% CI, 0.83–0.92) and West (RR, 0.71; 95% CI, 0.68–0.75) were less likely to seek care than those elsewhere in the United States. Additionally, participants aged ≥50 years were 1.13 times more likely to seek care (95% CI, 1.08–1.19) than those aged <50 years.

Level of education was also a predictor of seeking care: Participants with a graduate degree were 1.11 times more likely to seek care than those without a college degree (95% CI, 1.06–1.16).

DISCUSSION

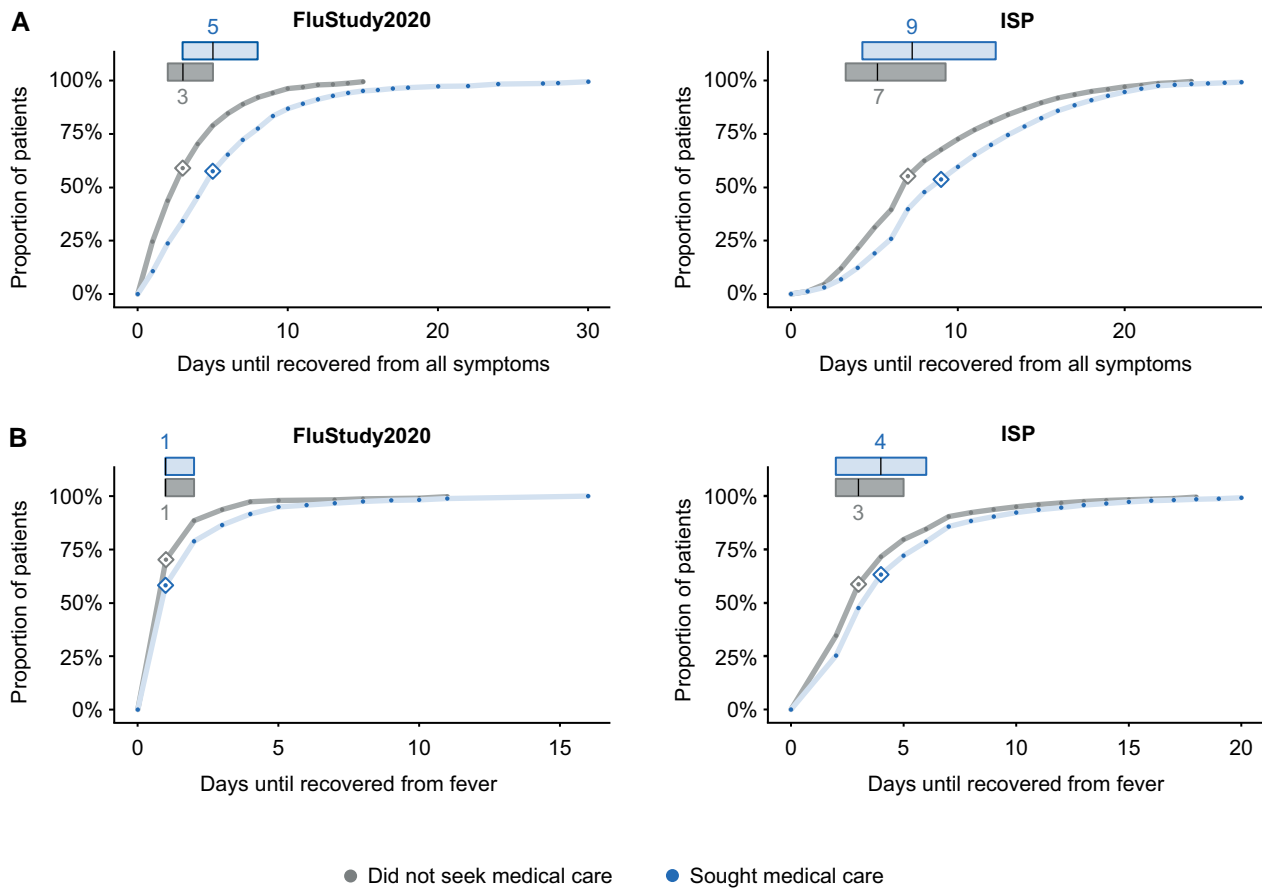Using a novel PGHD approach, we found that low proportions of participants (31.1% in FluStudy2020 vs 24.1% in ISP) sought

Figure 2. Recovery times for all symptoms and fever symptoms for care-seekers and non-care-seekers. *A*, Time to recovery from all symptoms for care-seekers and non-care-seekers in FluStudy2020 and ISP. *B*, Time to recovery from fever for care-seekers and non-care-seekers in FluStudy2020 and ISP. Lines and points show cumulative distributions, with the percentage of the population (y-axis) recovered by day n (x-axis). The diamond points on the recovery curve show the median, which is the earliest day on which ≥50% of the population is recovered. Boxplots above the recovery curve illustrate the median (center bar and text annotations) and interquartile range (boxes) recovery time for each cohort. Recovery durations exceeding the 99th percentile for each cohort–variable combination have been clipped to the 99th percentile value in this figure for readability but were not modified or excluded from the statistical analyses. Abbreviation: ISP, Participatory Influenza Surveillance Program.

care for their ILI, consistent with previous reports [2–4]. More than two-thirds of participants did not seek care and may have missed opportunities for better disease management. These individuals would also have been excluded by traditional RWD studies, which typically reference claims and medical record data collected in the clinic.

Previous studies have shown that estimates of ILI incidence based on data from clinics or hospitals do not necessarily reflect the true burden of ILI. This phenomenon is known as the "symptom iceberg," whereby the "submerged" part represents unreported symptoms and the "exposed" part reflects symptoms reported and presented to health care practitioners [11]. For example, a study in France reported that 32.6% of participants with ILI sought a consultation with a general practitioner [12]. Another study conducted in the United States across 4 influenza seasons (from 2015–2016 to 2018–2019), reported that 22.8% to 35.6% of participants sought care [5]. These results show that a large proportion of individuals with ILI do not

seek care, which may lead to systematic underestimation of the true burden of influenza on the population.

In both FluStudy2020 and ISP, we found converging evidence that care-seeking behavior was associated with various metrics of increased ILI severity. The number and severity of symptoms experienced were associated with increased likelihood of seeking care (Figure 3), and care-seekers had greater overall illness duration and fever duration than non-care-seekers (Figure 2). In fact, in ISP, the number of symptoms experienced was the strongest predictor of seeking care: participants with 6 or 7 symptoms were 2.14 times more likely to seek care than those experiencing <6 symptoms. In FluStudy2020, the strongest predictor of seeking care was insurance status: Participants with health insurance were twice as likely to seek care as those without, suggesting that lack of insurance coverage is a particularly strong barrier to individuals seeking care for ILI. Insurance status was not recorded in ISP, so we were unable to evaluate its relationship with care-seeking behaviors in this cohort.

Table 2. Regression Analysis Showing Factors Associated With Participants Seeking Medical Care for ILI Symptoms in FluStudy2020 and ISP

No. (%)	FluStudy2020			ISP		
	Relative Risk	95% CI	P Value	Relative Risk	95% CI	P Value
Respiratory symptom severity[a]	1.53	1.37–1.71	<.001			
Systemic symptom severity[a]	1.22	1.08–1.37	.001			
Number of symptoms	…	…		…	…	
2				–	–	
3–5				1.32	1.19–1.47	<.001
6–7				2.14	1.93–2.38	<.001
Health insurance status	…	…		…	…	
Not insured	–	–				
Insured	2.14	1.30–3.54	.003			
Age	…	…		…	…	
18–49 y	–	–		–	–	
50+ y	1.17	0.96–1.42	.12	1.13	1.08–1.19	<.001
Sex	…	…		…	…	
Male	–	–		–	–	
Female	0.89	0.70–1.14	.4	1.07	1.03–1.12	.002
Education	…	…		…	…	
No college degree	–	–		–	–	
College degree	1.11	0.95–1.31	.2	1.03	0.99–1.06	.2
Graduate degree	1.08	0.90–1.30	.4	1.11	1.06–1.16	<.001
American region	…	…		…	…	
Northeast	–	–		–	–	
South	0.98	0.81–1.19	.8	1.16	1.11–1.21	<.001
Midwest	0.92	0.76–1.12	.4	0.87	0.83–0.92	<.001
West	0.86	0.69–1.08	.2	0.71	0.68–0.75	<.001
CDC risk factor: any	…	…		…	…	
Absent	–	–				
Present	1.37	1.20–1.58	<.001			
CDC risk factor: cancer	…	…		…	…	
Absent				–	–	
Present				1.1	1.02–1.18	.01
CDC risk factor: severe obesity (BMI >40 kg/m^2)	…	…		…	…	
Absent				–	–	
Present				1.2	1.15–1.26	<.001
CDC risk factor: weakened immune system	…	…		…	…	
Absent				–	–	
Present				1.04	0.99–1.10	.14
CDC risk factor: lung conditions	…	…		…	…	
Absent				–	–	
Present				1.13	1.09–1.17	<.001
CDC risk factor other (neurologic, endocrine, or heart disease)	…	…		…	…	
Absent				–	–	
Present				1.04	1.01–1.08	.02
…	Null deviance = 2066; Null df = 1666; Log-likelihood = −964; AIC = 1951; BIC = 2017; Deviance = 1927; Residual df = 1655; No. Obs. = 1667			Null deviance = 52 401; Null df = 47 479; Log-likelihood = −25 186; AIC = 50 401; BIC = 50 523; Deviance = 50 373; Residual df = 47 466; No. Obs. = 47 480		

Dashes indicate the reference group for each variable, and blank spaces indicate variables that were not included in the model represented in that column. The estimated background risk of seeking care for participants who fell into the reference groups across all variables was 3% for FluStudy2020 and 13% for ISP.

Abbreviations: AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion; BMI, body mass index; CDC, Centers for Disease Control and Prevention; df, degrees of freedom; ILI, influenza-like illness; ISP, Participatory Influenza Surveillance Program.

[a]Respiratory and systemic symptom severity were self-reported on a scale of 0–3—absent (0), mild (1), moderate (2), and severe (3)—and were analyzed as continuous numeric values.

In both studies, comorbidities associated with increased risk of influenza complications as per CDC guidelines [10] were also found to be predictors of seeking care. It should be noted that the regression analyses for the 2 studies conceptualized CDC risk factors slightly differently. Due to the larger sample size in ISP, which afforded the statistical power to assess separate risk factor variables, we were able to assess risk factors with more granularity than in FluStudy2020. However, in both

Figure 3. Regression analysis showing factors associated with seeking medical care in FluStudy2020 and ISP. The reference groups for the predictor variables are as follows: health insurance, FluStudy2020 only (reference: not insured); age (reference: 18–49 years old); education (reference: no college degree); region (reference: Northeast); sex (reference: male); number of symptoms, ISP only (reference: 2 symptoms); any CDC risk factor, FluStudy2020 (risk factor absent); specific CDC risk factors, ISP only (reference: absent). [a]Risk ratios correspond to a 1-unit increase in self-reported symptom severity, ranging from 0 (absent) to 3 (severe). Abbreviation: ISP, Participatory Influenza Surveillance Program.

studies we were able to conclude that the presence of comorbidities associated with increased risk of influenza complications was predictive of seeking care. Interestingly, geographic region was a significant predictor of seeking care in ISP; participants living in the West or Midwest were less likely to seek care as compared with the Northeast. Similar results were published

in a recent study from the United States [5], which reported an association between care-seeking behavior for ILI symptoms and geographic region, as well as sex and age; this is in agreement with our data in ISP, but contrasts with our results in FluStudy2020. The reason for these differences is not clear, but could in part be attributed to the smaller sample size of FluStudy2020 relative to the ISP population or other differences between the ISP and FluStudy2020 analyses. In addition, our adjusted analyses showed a potential association between higher education and seeking care. This suggests that lack of education, which often correlates with economic barriers, both directly and by its association to other socioeconomic status factors [13], may also be a barrier to seeking care for ILI; however, this association was only statistically significant for the ISP population.

Other studies have investigated care-seeking behaviors in individuals with ILI, exploring a variety of predictors [14, 15]. In a Hong Kong–based study, significant determinants of care-seeking behavior included ILI symptoms (such as fever, cough, and shortness of breath) and diabetes, which is somewhat consistent with the predictors observed in FluStudy2020 and ISP [14]. In another study, participants with health insurance were significantly more likely to seek care than those without, which is consistent with the insurance status findings in FluStudy2020 [15]. Importantly, this highlights the economic barrier to health care access and its relevance in the context of influenza.

Seeking care is necessary to receive a diagnosis of influenza, which may lead to outcomes such as advice on self-care for symptoms, antiviral prophylaxis for exposed family members, or antiviral treatment where required [16]. Antiviral treatment has been shown to reduce influenza-related complications and mortality and provides greatest benefit when administered within 48 hours of symptom onset [17–19]. Antivirals may also reduce the duration of infectiousness, indirectly reducing the transmission of influenza; therefore, the low proportion of individuals seeking care could further contribute to the spread of influenza through missed opportunities for treatment [20, 21]. In FluStudy2020, 221 participants tested positive for influenza, and only 55 participants received an antiviral medication. However, it should be noted that participants were not informed of their test results, and care-seeking behavior was not informed by testing outcome. Additionally, there were participants who received antiviral treatment without having been tested or who were influenza negative in this study. Together, our 2 studies highlight the need to identify and address barriers to health care access, which may allow for better management of influenza.

The COVID-19 pandemic has increased societal awareness of viral respiratory illnesses, and this might influence future care-seeking behavior for ILI and attitudes about testing and treatment more broadly. Viral respiratory illnesses with pandemic potential, such as influenza, and the burden of disease complications significantly impact public health [22]. Barriers to care such as lack of health insurance present an opportunity for health policy makers to take targeted action to protect public health, especially for the most vulnerable. For instance, the US government "Test-to-Treat" initiative for COVID-19 aims to tackle barriers to access to COVID-19 testing and treatment by ensuring that high-risk patients can receive treatment regardless of insurance status [23]. Increasing access to influenza testing and treatment for patients who are at high risk of developing complications could reduce the burden of illness and hospitalizations caused by seasonal influenza epidemics.

Limitations

There were limitations to these studies: In particular, the cohorts in both studies were predominantly female, under the age of 50, and White; therefore, the results may not be generalizable to the broader influenza population. Specifically, we are not able to generalize our results to individuals 65 years or older. It is possible that both studies may be impacted by selection bias. However, a comparison of demographic characteristics between the larger Evidation platform member population and those recruited into either study was not conducted at the time that the studies were enrolling, and the relevant data from the Evidation platform population were not available at the time of analysis. Furthermore, we acknowledge the differences between the ILI definitions used in FluStudy2020 and ISP and that both differ from the CDC definition (fever defined as a temperature of ≥100°F plus a cough and/or a sore throat) [24]. The CDC definition could not be used as it required temperature measurement and thermometers were not provided to participants. Hence, sensitivity analyses with this definition could not be performed as temperature data were not collected. The ILI definitions utilized in the studies may have introduced some selection bias as they required the presence of ≥1 systemic and ≥1 respiratory symptom. This may underestimate the true burden of ILI and overestimate care-seeking behavior, as individuals with a low symptom burden may have been excluded and those with a high symptom burden (who have been shown to be more likely to seek care for their ILI) may have been selected.

An additional limitation is that the COVID-19 pandemic may have affected care-seeking behavior and incidence of influenza for a proportion of the study duration, so the cohorts observed in these studies may not be representative of a typical influenza season. However, since the majority of our ILI cases occurred before the end of February 2020, potential interference from COVID-19 is likely minimal. Additionally, some predictors of interest were not captured, specifically level of insurance coverage, distance to the clinic, and access to diagnostic tests. Future studies may consider capturing these variables.

Finally, while directly asking participants about their symptoms and care-seeking experiences allows for unique insights into the experience of individuals with ILI, self-reporting of symptoms, comorbidities, or medication use may result in measurement error if participants are unable to report accurately on their experiences.

CONCLUSIONS

Using a novel PGHD approach, we confirmed low rates of health care–seeking behavior for ILI. Individuals who do not seek care would have been excluded from most traditional RWD studies and surveillance systems and would have missed the opportunity for clinical disease management to reduce influenza-related complications. Care-seekers more frequently had health insurance, comorbidities, and a high symptom burden. Reducing barriers to care for viral respiratory infections may lead to better disease management and contribute to protecting public health.

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