WEB MATERIAL

"Utilizing Syndromic Surveillance Data for Estimating Levels of Influenza Circulation"

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Web Appendix 1

Homogeneity Criterion for Weekly Levels of Various Symptom Profiles

In this section we examine the temporal stability of the weekly rates of ILI during a period of low influenza circulation (weeks 48–5 of the 2011–2012 season). Motivated by (1), we extend the inference framework in the main body of the text to consider not just rates of ILI but also frequencies of various other *symptom profiles*. Here a symptom profile is defined as presence of a certain collection of symptoms, e.g. ILI, or fever, or lack of fever and presence of cough/sore throat. We also consider the above frequencies not just among all survey participants but also among *symptomatic* individuals, defined as those with presence of either fever, or cough or sore throat. The latter can be used towards an approach parallel to our main inference methodology, estimating symptomatic influenza incidence first by utilizing changes in the weekly distribution of symptom profiles reported by symptomatic individuals in the surveillance system (1), with full influenza incidence to be subsequently estimated by incorporating data on the share of symptomatic individuals among confirmed influenza cases.

The symptom profiles we consider are:

(a) ILI cases in the cohort (among all individuals, as in the main text)

(b) Febrile cases among the symptomatic ones

(c) Febrile cases in the cohort

(d) Nonfebrile cases with exactly one nonfebrile symptom (cough, sore throat) among the symptomatic ones

(e) Nonfebrile cases with both nonfebrile symptoms among the symptomatic ones

For each symptom profile of interest, let $C(t)$ be the number of reports of that profile for week t in a category (whole cohort, symptomatic cases) of size $N(t)$ ($t = 1,..,n$). The null hypothesis is that there is a constant population level p of that symptom profile in the chosen category of individual. Thus

$$C(t) \approx Binomial(N(t), p)$$

To test the null hypothesis, let $p' = \frac{\sum C(t)}{\sum N(t)}$ be the estimate of p, and let $p(t) = \frac{C(t)}{N(t)}$ be the observed level of the symptom profile of interest on week t. For $N(t)$ large enough, the following statistic has an approximately χ^2 distribution with $n-1$ degrees of freedom (2):

$$X = \frac{\sum N(t)(p(t) - p')^2}{p'(1-p')} \qquad \text{(W1)}$$

Web Table 1 exhibits the values of the statistic given by eq. (W1) for the 4 age groups for weeks 48–5 of the 2011–2012 season (10 weeks), and well as the corresponding (one-sided) *P* values ($P(\chi_9^2 > X)$) for symptom profiles (a)–(e).

Web Table 1: Estimate (and *P* value) for the homogeneity test statistic given by equation W1 for various symptom profiles (a)–(e) in the 4 age groups for weeks 48–5 of the 2011–2012 season

Age Group	0–19	20–49	50–60	61+
ILI incidence in the cohort	14.36 (0.11)	15.4 (0.08)	6.16 (0.72)	11.26 (0.26)
Febrile cases among symptomatic ones	10.49 (0.31)	9.75 (0.37)	16.26 (0.06)	4.26 (0.89)
Febrile incidence in the cohort	11.45 (0.25)	20.33 (**0.016**)	15.7 (0.07)	11.8 (0.22)
One nonfebrile symptom among symptomatic cases	4.28 (0.89)	7.22 (0.61)	7.83 (0.55)	17.0 (**0.049**)
Two nonfebrile symptoms among symptomatic cases	2.57 (0.97)	4.57 (0.87)	9.08 (0.43)	19.82 (**0.019**)

We see that the statistic fails to reject the null hypothesis of constant population ILI weekly incidence and constant weekly incidence of febrile cases among symptomatic ones during weeks 48–5 of the 2011–2012 season for all age groups. However weekly incidence of febrile cases in the 20–49 age group, as well as weekly prevalence of the nonfebrile cases among symptomatic cases in the 61+ age group do not accord with the null hypothesis of temporal stability.

One could, in principle, consider presence and absence of fever as the two symptom profiles for symptomatic individuals together with an estimate of the probability of being symptomatic given influenza infection to infer full influenza incidence (1), as an alternative to our main inference scheme. However, measuring two quantities of interest vs. one (percent febrile and percent symptomatic vs. percent ILI among influenza cases) is challenging with the data available to us, due to incompatibility of the Dutch and the Hong Kong data on fever (self-reported vs. measured), and due to paucity of strain-specific data (Web Appendix 3). Altogether we've deemed available data more conducive to analysis using the ILI incidence among all individuals rather than fever (and other profiles) among symptomatic cases, and we haven't pursued the latter approaches, though in principle they may be fruitful with different data.

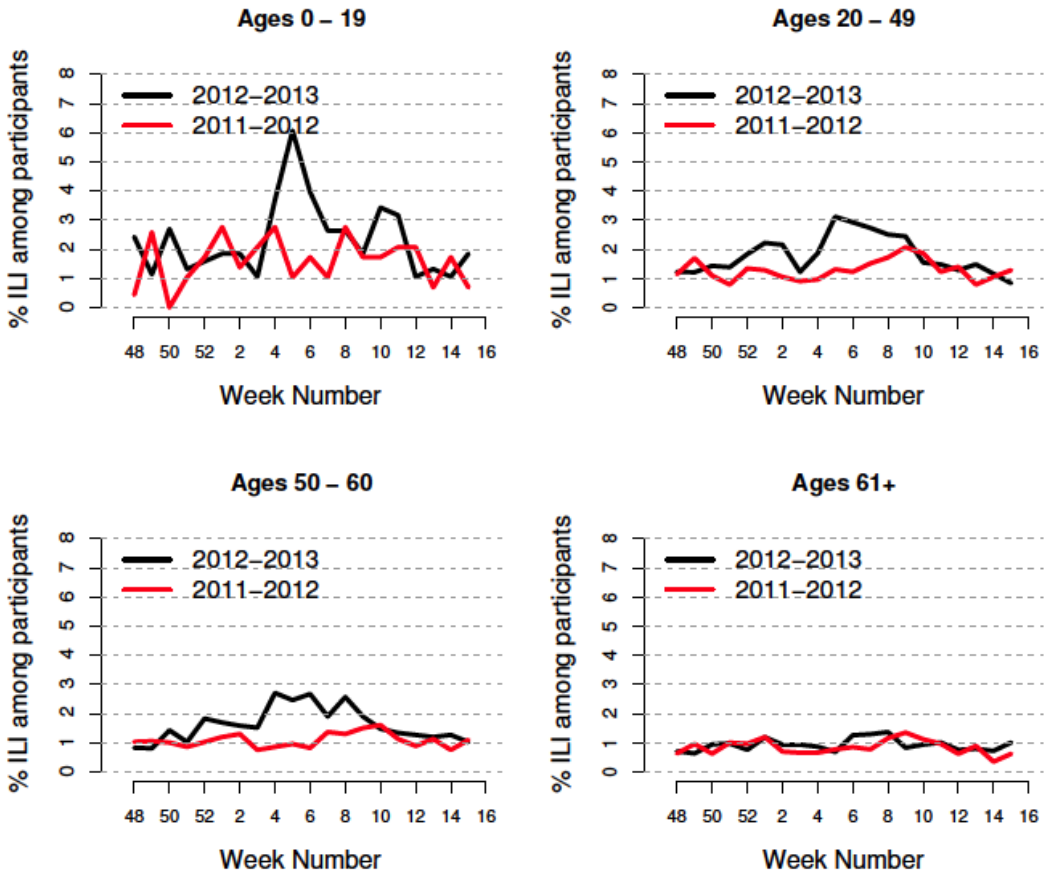
Web Appendix 2

Selection Criteria for Study Participants in the Influenzanet Data

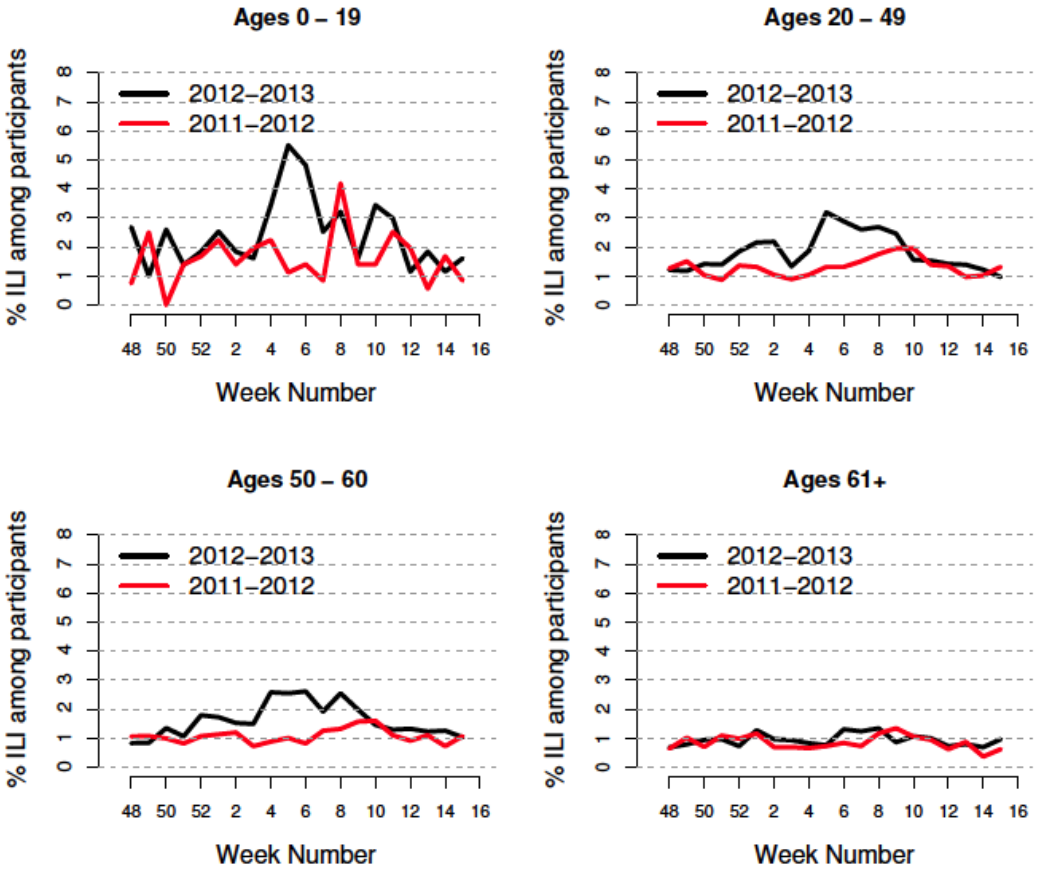
For the analysis in the main body of the text, we selected cohorts of participants in certain age groups who registered by week 50 of each season and who subsequently filled out at least 50% of weekly reports through calendar week 20 of the next year. Moreover, in measuring weekly incidence ILI we selected the denominator to be the number of individuals in the cohort, not the number of those who filled out the weekly report. Here we explore the sensitivity of the ILI incidence with regard to the threshold for the number of reports filled out, and also compared with using the weekly number of survey participants in the denominator.

Web Figures 1A–1D plot the weekly ILI incidence during the 2011–2012 and 2012–2013 seasons in the Influenzanet data for cohorts of participants who filled out reports on at least 50%, 33.33%, 25%, and 15% of weeks from the first report week to calendar week 20 (with the full cohort size in the denominator). Web Figures 2A–2D plot the corresponding incidence with the weekly number of participants in the denominator.

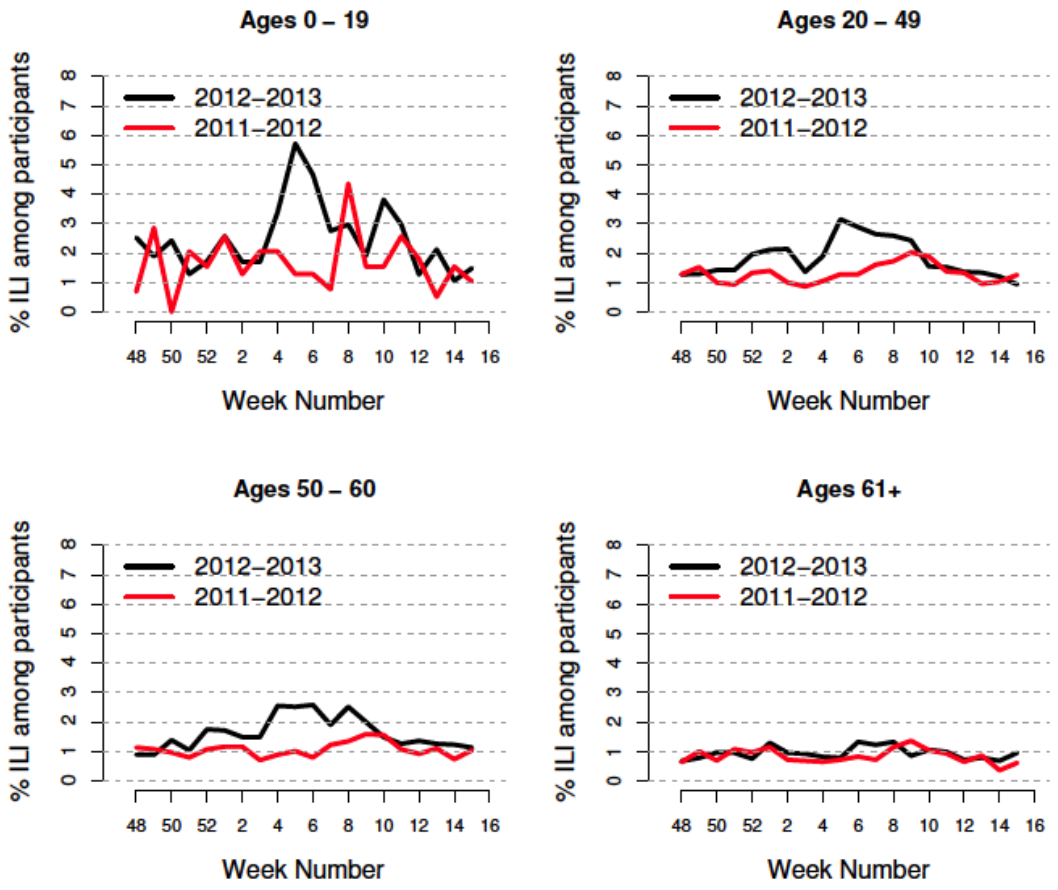
Whole cohort denominator:



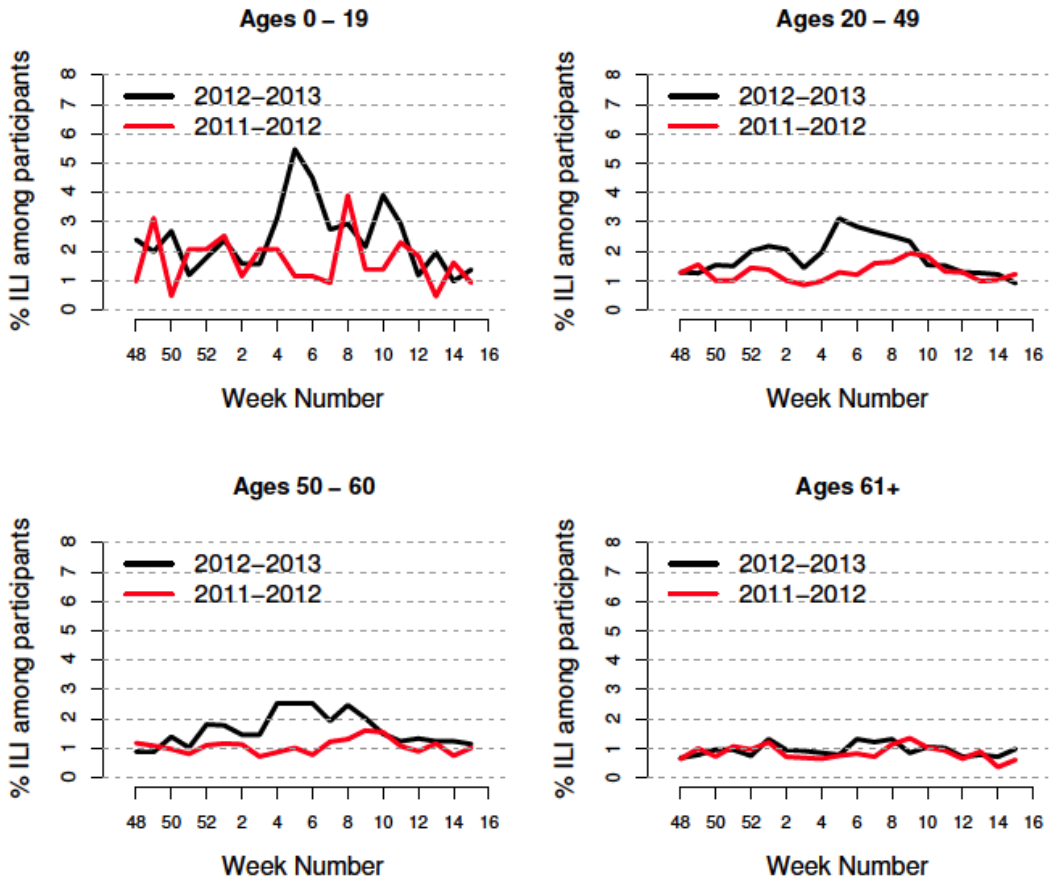
Web Figure 1A: Weekly ILI incidence for individuals reporting on at least 50% of weeks with the cohort size in the denominator.



Web Figure 1B: Weekly ILI incidence for individuals reporting on at least 33.33% of weeks with the cohort size in the denominator.

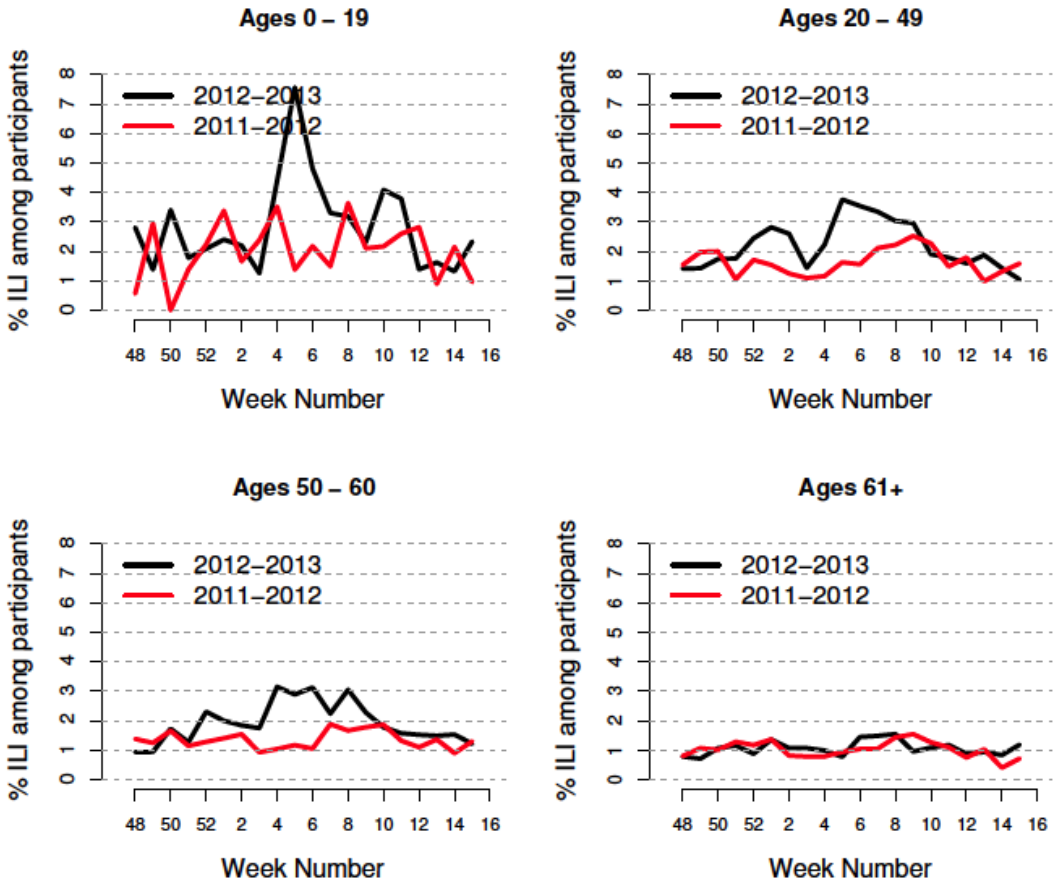


Web Figure 1C: Weekly ILI incidence for individuals reporting on at least 25% of weeks with the cohort size in the denominator.

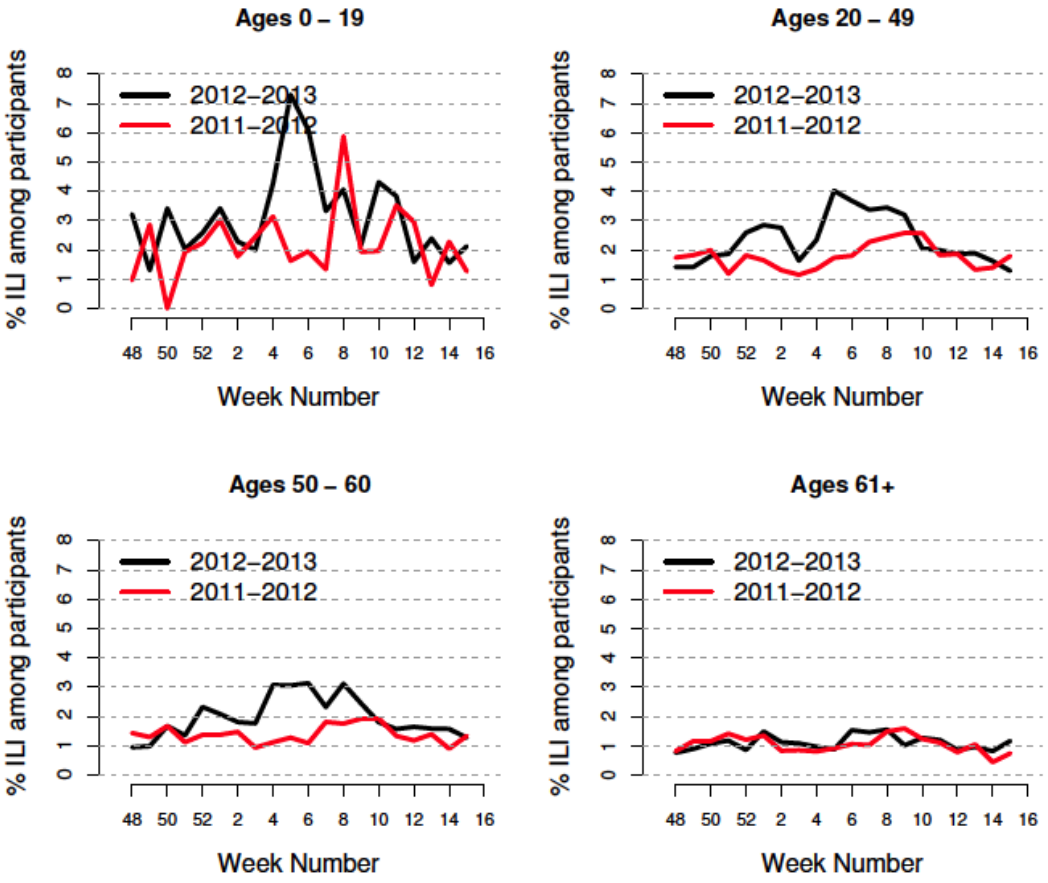


Web Figure 1D: Weekly ILI incidence for individuals reporting on at least 15% of weeks with the cohort size in the denominator.

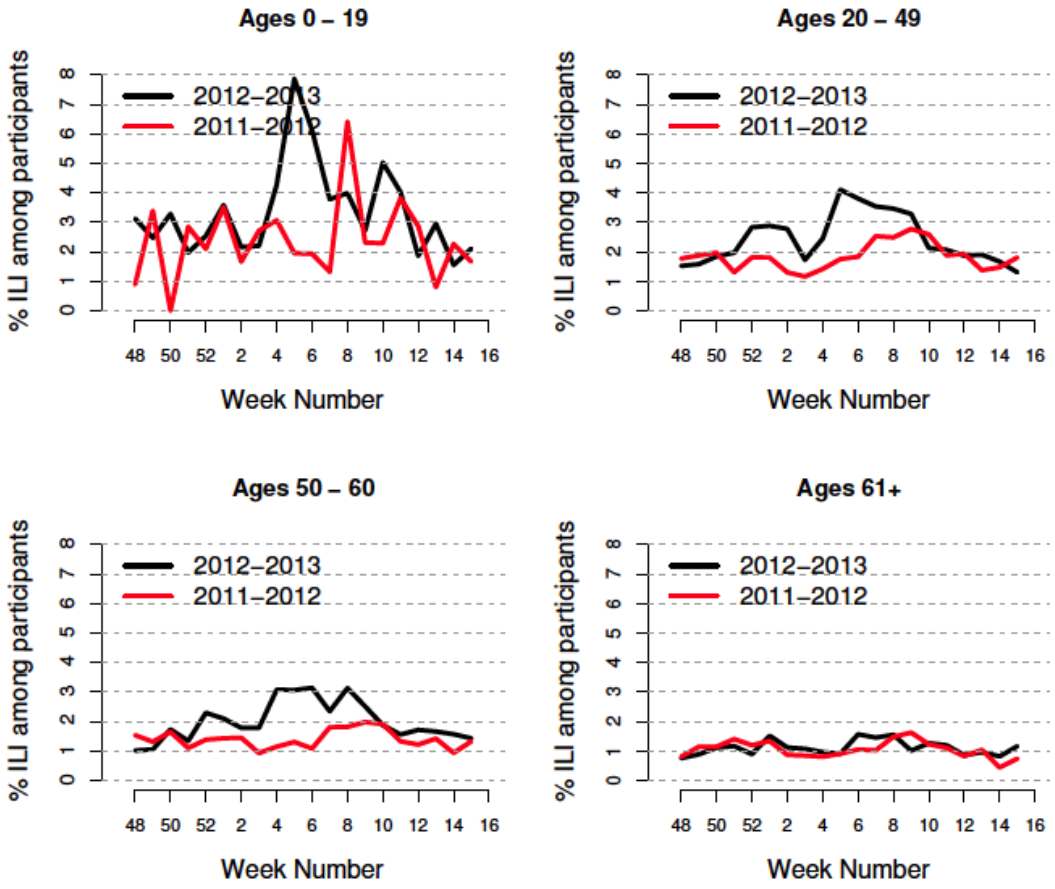
Weekly survey participants denominator:



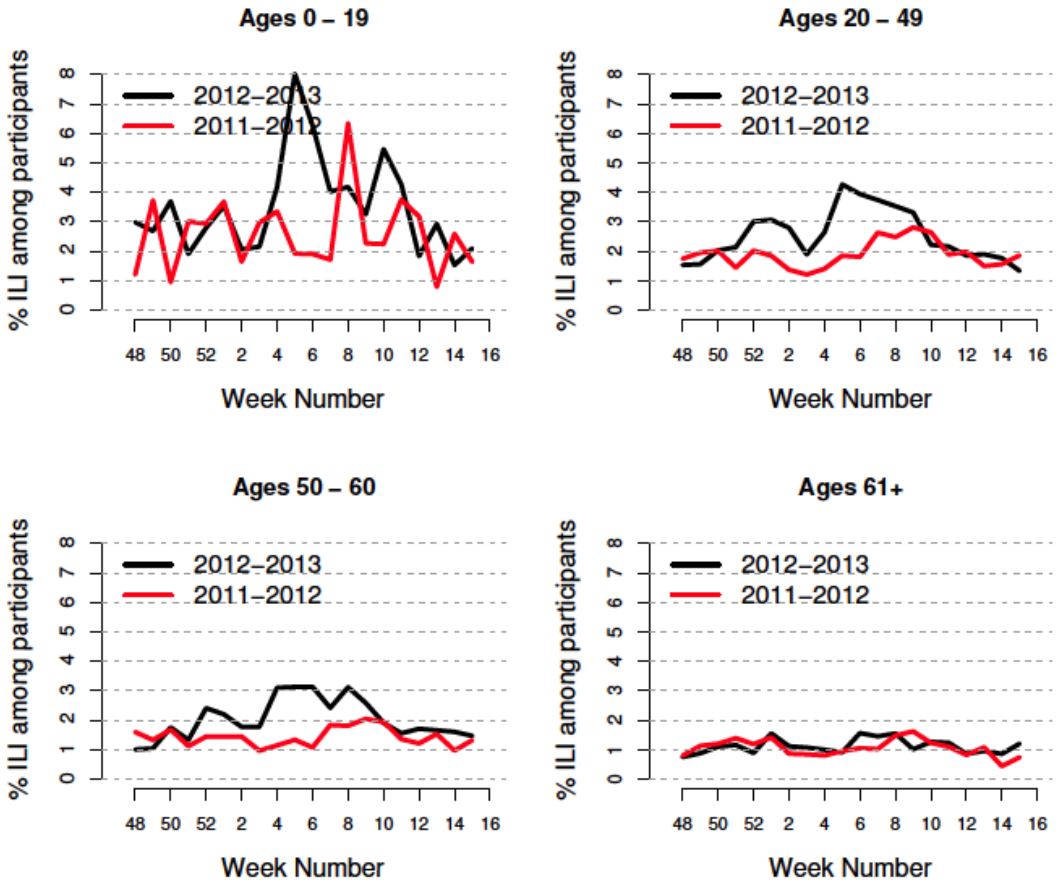
Web Figure 2A: Weekly ILI incidence for individuals reporting on at least 50% of weeks with weekly number of survey participants in the denominator.



Web Figure 2B: Weekly ILI incidence for individuals reporting on at least 33.33% of weeks with weekly number of survey participants in the denominator.



Web Figure 2C: Weekly ILI incidence for individuals reporting on at least 25% of weeks with weekly number of survey participants in the denominator.



Web Figure 2D: Weekly ILI incidence for individuals reporting on at least 15% of weeks with weekly number of survey participants in the denominator.

We see that using the number of weekly participants in the denominator produces higher ILI incidence than using the cohort size with the latter method expected to be more representative of the average number of ILI episodes experienced by cohort participants (see Methods). There is little sensitivity though to the threshold chosen, with slightly more sensitivity for the method that uses survey participants in the denominator (e.g. a gradual rise in the peak level for incidence in the 20–49 age group with lowering thresholds) that may be related to the correlation between survey participation and presence of ILI.

Web Appendix 3

Sensitivity with Respect to the Choice of the Baseline Period

In estimating influenza attack rates between weeks 51–15 of the 2012–2013 season in the main text we used weeks 48–5 of the 2011–2012 season as a baseline period due to negligible levels of influenza circulation at that time (3). Some of the reasons that made us hesitant to use the 2012–2013 data prior to the major influenza circulation period as a baseline are the small number of weeks available (weeks 48–50 of 2012), and possible biases in estimating a baseline due to the nascent influenza season and higher respiratory syncytial virus circulation levels during the 2012–2013 season compared with the 2011–2012 season (3). The latter two factors are expected to produce an upward bias for the baseline estimates, and, correspondingly, a downward bias in influenza attack rate estimates if weeks 48–50 of the 2012–2013 season are used as a baseline period. Here we give estimates of influenza attack rates between weeks 51–15 of the 2012–2013 season, with weeks 48–50 of the 2012–2013 season used as a baseline period. We also present the estimates with weeks 48–3 of the 2011–2012 season used as a baseline period. This analysis is mostly done for illustration purposes, to suggest what the estimates of the influenza attack rates during the 2012–2013 season would be if we didn't have data on ILI rates during the larger time period of little influenza circulation during the 2011–2012 season.

Web Table 2: Estimation of influenza attack rates between weeks 51–15 of the 2012–2013 season using different choices for the baseline period

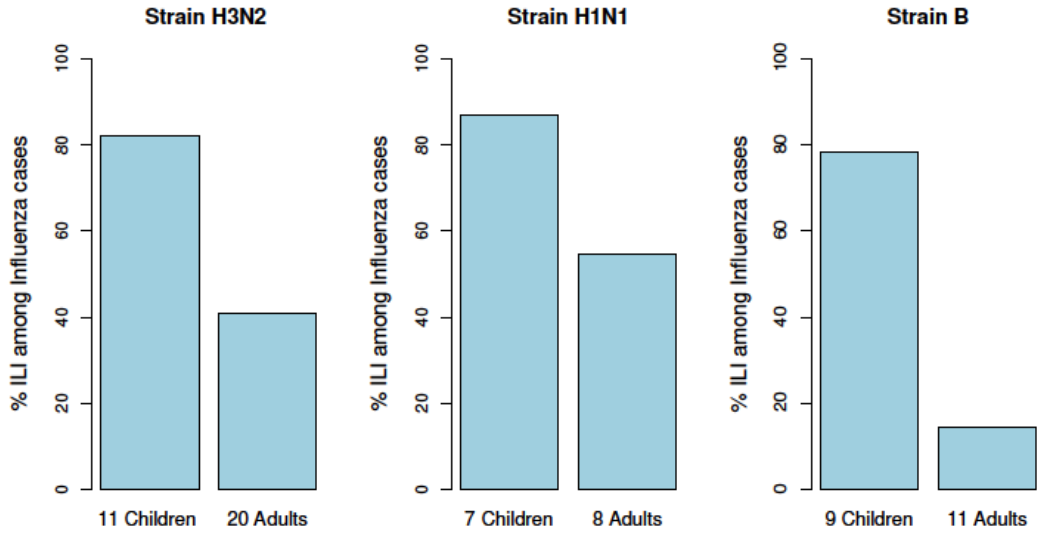
Age Group\ Baseline Period	Weeks 48–5, 2011–2012	Weeks 48–3, 2011–2012	Weeks 48–50, 2012–2013
20–49	29.2% (21.6%, 37.9%)	29% (21%, 38.1%)	23.8% (12.8%, 35.4%)
50–60	28.3% (20.7%, 36.8%)	27.4% (19.6%, 36.2%)	27.6% (16.8%, 38.6%)
61+	5.9% (0.4%, 11.8%)	4.9% (–1.3%, 11.2%)	8.1% (–0.6%, 16.4%)

Using weeks 48–50 of the 2012–2013 season as a baseline period produces a somewhat lower estimate for the 20–49 age group compared with ones obtained with the 2011–2012 baselines, perhaps due to the aforementioned biases. At the same time, availability of data for an 8-week period compared with the 10-week baseline period of little influenza circulation during the 2011–2012 season would have had a minor impact on the estimates of influenza attack rates during the 2012–2013 season.

Web Appendix 4

Strain-Specific Estimates of the Probability of Self-Reported ILI

Web Figure 3 estimates the probability of self-reported ILI (as described in the Methods) for individuals (adults and children) whose PCR-positive sample was subtyped for influenza A/H3N2, pandemic A/H1N1 and B infections. Larger, context-specific data sets are needed to improve upon the estimation of those likelihoods for finer age stratification.



Web Figure 3: Strain-specific estimates of the probability of self-reported ILI.

References

1. Goldstein E, Cowling BJ, Aiello AE, Takahashi S, King G, Lu Y, et al. Estimating incidence curves of several infections using symptom surveillance data. PloS one. 2011;6(8):e23380.
2. Agresti A. Categorical data analysis. 2nd ed. New York: Wiley-Interscience; 2002. xv, 710 p. p.
3. Virological specimen testing in the Netherlands, 2011–2012 and 2012–2013 seasons. ECDC 2013. Available from: http://www.euroflu.org/cgi-files/figures2002.cgi?year=2013&week=20&region=Netherlands&type=v&pilot=Y.