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Incorporating Calendar Effects to Predict Influenza Seasonality:

A Case Study in Milwaukee, Wisconsin (2004-2009)

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OBJECTIVES

Social outings can trigger influenza transmission, especially in children and the elderly. In contrast, school closures are associated with reduced influenza incidence in school-aged children. While influenza surveillance modeling studies typically account for holidays and mass gatherings, age-specific effects of school breaks, sporting events, and nationally- and commonly-celebrated cultural observances are not fully explored. We examined the impact of school holidays, social events, and religious observances for six age groups (all ages, <5, 5-24, 25-44, 45-64, >64 years) on four influenza outcomes (tests, positives, influenza A and B) as reported by the City Health Department (MHDL) in Milwaukee, Wisconsin for 258 weeks from 16 May 2004 to 25 April 2009. Our objectives were to: 1) compare outcomes across school holidays, religious observances, federal observances, and major sporting events; 2) estimate the magnitude and direction of holiday effects; 3) estimate outcome-specific peak timing; 4) compare weekly counts around Winter and Spring breaks; 5) derive outcome-specific seasonal signatures.

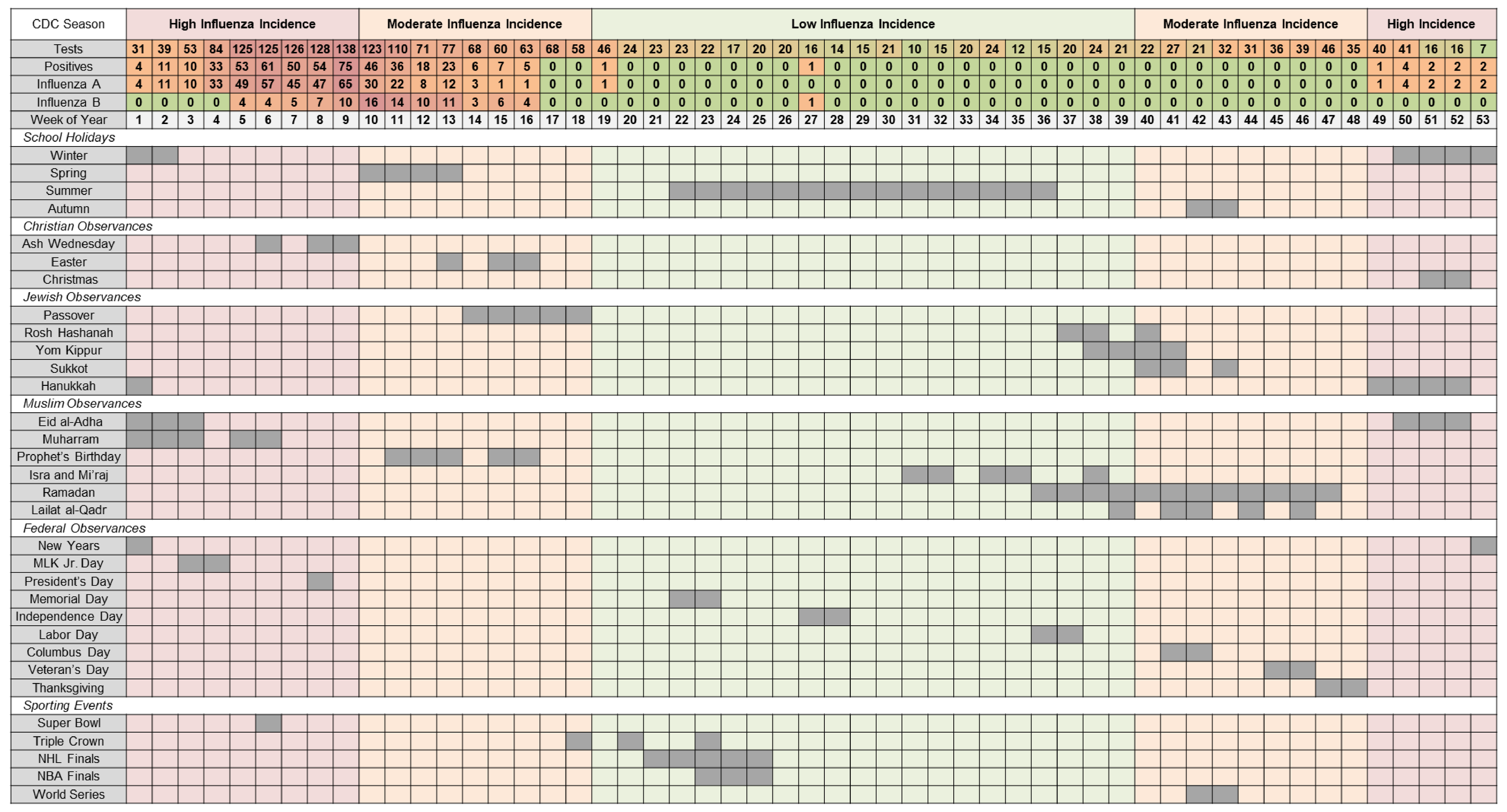

Figure 1. Total weekly counts for influenza outcomes and typical weeks of occurrence for school holidays, national holidays, religious observances, and sporting events. Influenza outcomes are defined per the CDC definition of seasonal intensities [1]. Weeks are presented in chronological order by type of holiday.

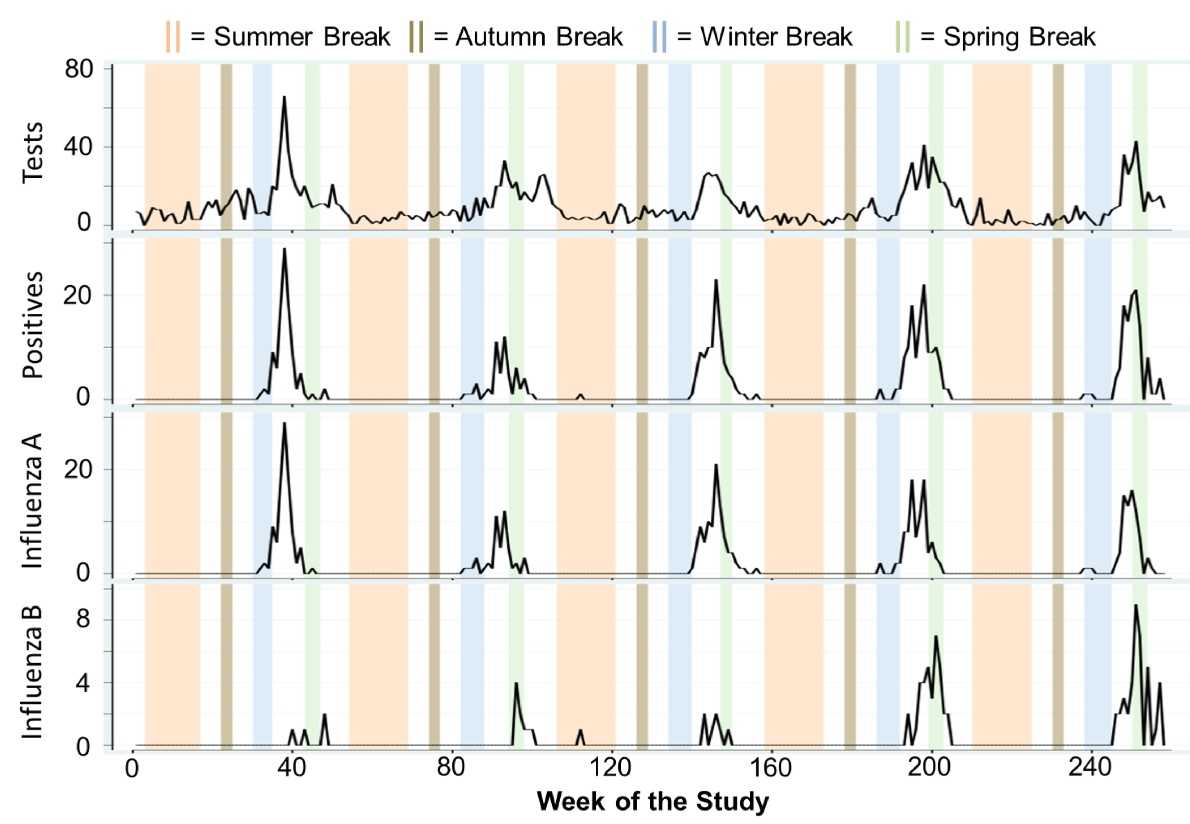

Figure 2. Weekly counts for four influenza health outcomes across all ages with superimposed school holiday occurrences

OBJECTIVE 1

We compared average weekly counts for each age group and outcome as they occurred during holiday and non-holiday time periods. Non-parametric Mann-Whitney (MW) U-tests assessed significant differences. During the 118-week school holiday period, the average number of tests was two-times lower than the 140-week school term (non-holiday) period (5.9±6.7 vs. 11.9±10.2 cases/week, p<0.005). Similarly, average weekly positives were lower for the school holiday compared to school term period (0.8±2.8 vs. 2.9±5.7 cases/week, p<0.005). In the 5-24 years age group, there are decreases in weekly tests (2.14 ± 3.63 vs 6.44 ± 7.04, p<0.005), influenza positives (0.24 ± 0.64 vs 0.18 ± 1.06, p=0.01) and both influenza types, reaching 67%, 74%, 82% and 25% declines, respectively. Similar patterns were observed in the 25-44 years age group. Figure 2 displays time series for each health outcome for all ages with school holidays superimposed.

OBJECTIVE 2

We estimated the magnitude and direction of holiday effects adjusted for meteorological conditions and seasonality using Negative Binomial Regression Models (NBRM). Models were constructed sequentially to observe the contribution of individual factors, e.g. holidays, meteorological conditions, and linear and seasonal trend components (below). Models 1-3 were used to calculate relative risk (RRs) with 95%CI. A dampening effect was defined as a significant RR<1 while amplification effects were defined as a significant RR>1.

Modeling results (Figure 3) indicate that all school holidays and Winter Break had a dampening effect (RR<1) in reported tests in all models for all ages, as well as for the 5-24 and 25-44 years age groups. For older adults, only Summer Break is associated with a reduction in average weekly tests. Spring Break appeared to show an amplification of tests (RR ranging from 1.42-3.46) in Models 1 and 2. However, these associations did not hold for any age group when we adjusted for seasonal and linear trends in Model 3.

Model 1: $ln[E(Y_t)] = \beta_0 + \beta_1 H_1$

Model 2: $ln[E(Y_t)] = \beta_0 + \beta_1 H_1 + \beta_2 D_t$

Model 3: $ln[E(Y_t)] = \beta_0 + \beta_1 H_1 + \beta_2 D_t + \beta_3 t + \beta_4(sin(2\pi\omega t)) + \beta_5(cos(2\pi\omega t))$

Model 4: $ln[E(Y_t)] = \beta_0 + \beta_3 t + \beta_4(sin(2\pi\omega t)) + \beta_5(cos(2\pi\omega t))$

Model 5: $ln[E(Y_t)] = \beta_0 + \beta_1 H_t + \beta_3 t + \beta_4(sin(2\pi\omega t)) + \beta_5(cos(2\pi\omega t))$

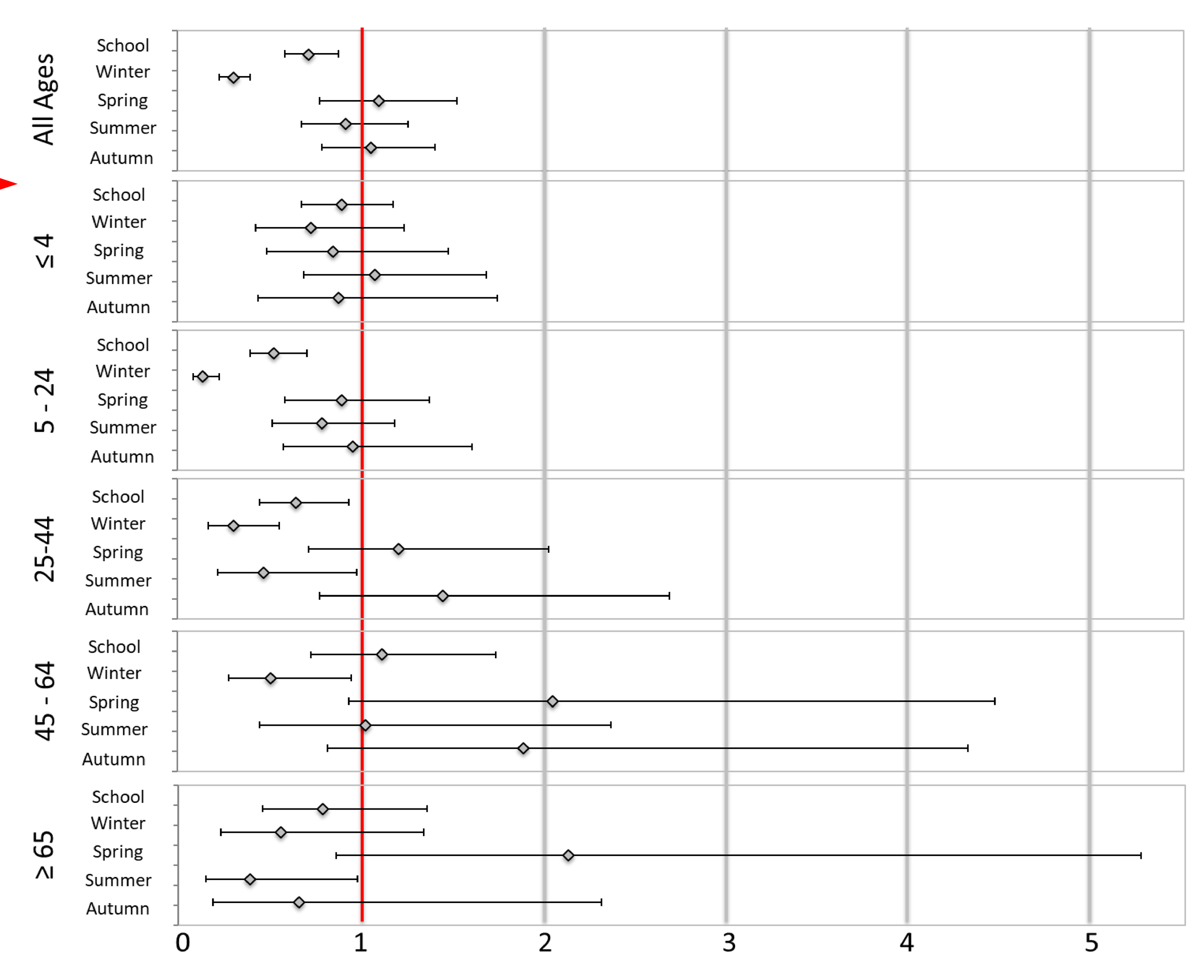

Figure 3. A forest plot of Relative Risk (RRs) calculated for all school holiday weeks (School) and each of the four individual school holiday weeks (Winter, Spring, Summer, Autumn). Analyses were performed for average weekly tests for the six age groups. RRs (with 95% CIs) were derived using Model 3.

OBJECTIVE 4

We compared weekly counts of influenza incidence around Winter and Spring Break school holiday weeks across five time periods (Figure 5). Weekly average counts with pooled standard errors were calculated for each period. The differences in average counts between adjacent time periods were tested with paired t-tests. Dampening of weekly tests, positives, and influenza A during Winter Break is evident by significant differences in counts between periods 2 and 3 (1.49 ± 1.53 vs. 14.23 ± 8.66, p<0.005) and between periods 1 and 2 (3.60 ± 2.42 vs. 1.49 ± 1.53, p=0.01) for the 5-24 years age group. Similarly, significant increases in tests (4.93 ± 2.81 vs. 22.12 ± 11.60, p<0.005), positives (0.67 ± 0.82 vs. 9.61 ± 7.16, p<0.005), and influenza A (0.67 ± 0.82 vs. 8.58 ± 6.77, p<0.005) were observed after the Winter Break for all ages. No significant changes were detected for influenza B across any age group.

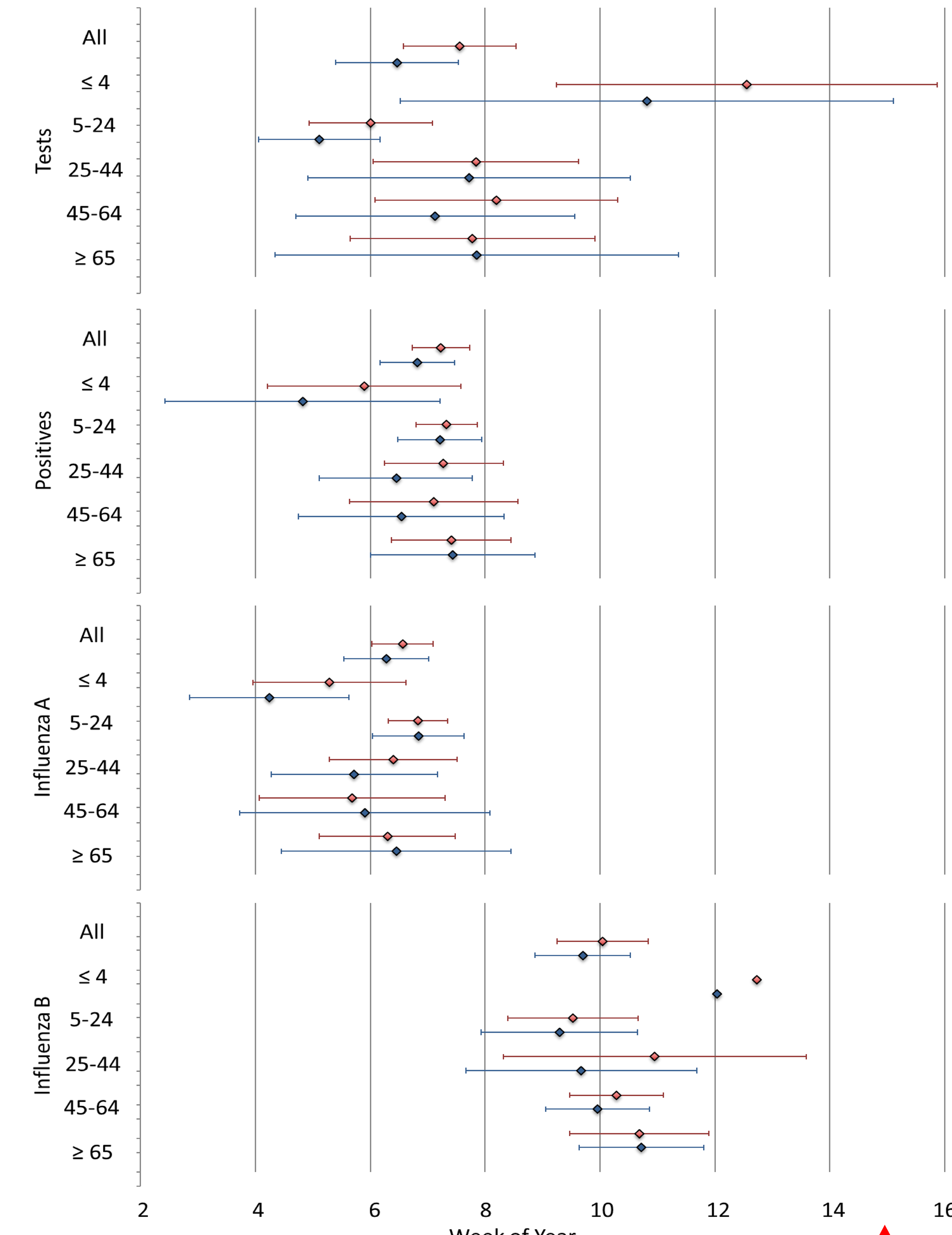

Figure 4. Peak timing estimates for six age groups (all ages, <5, 5-24, 25-44, 45-64, >64 years) on four influenza outcomes (tests, positives, influenza A and B) as calculated by Model 4 (red) and Model 5 (blue).

OBJECTIVE 3

We calculated age- and influenza outcome-specific peak timing using Model 4, derived by MacNeill and Naumova [2] with further modifications by Alarcon-Falconi [3]. We also evaluated how school holidays modify peak timing estimates using Model 5. Peak timing estimates from both models are shown in Figure 4. For all ages, influenza A peaked between the 6–7th calendar weeks right after the Winter Break and before Spring Break. Influenza B peaked between the 8–12th calendar weeks right before or during the Spring Break. The peaks for influenza A preceded influenza B by ~3.5 weeks for all ages (6.28 (5.5-7.02) vs 9.70 (8.87-10.53) calendar week) and by ~2.5 weeks for 5-24-years age group (6.84 (6.04-7.63) vs 9.29 (7.93-10.65) calendar week). While peak timing estimates for Model 5 preceded holiday-adjusted estimates from Model 4, this shift was not significant.

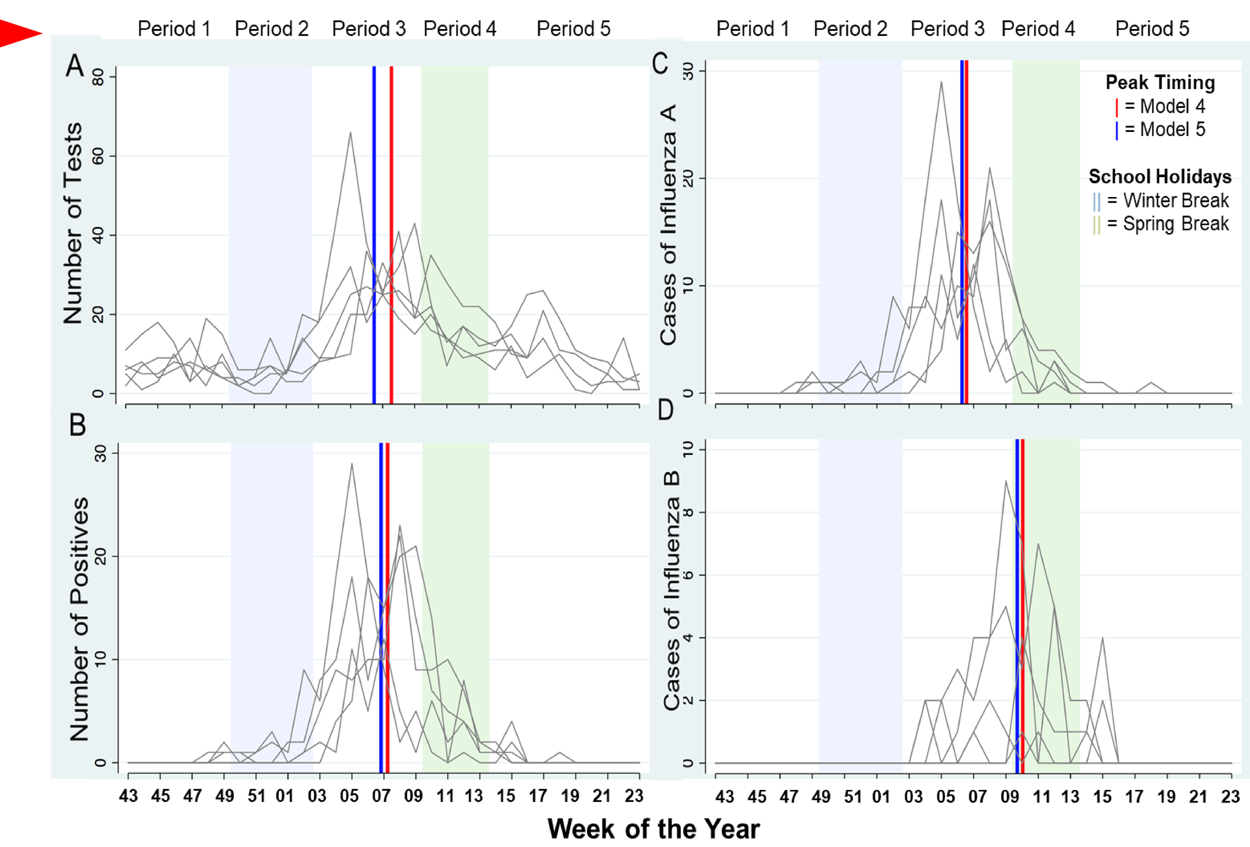

Figure 5. Weekly health outcomes (panels A-D, respectively) for all ages across each study year with superimposed peak timing estimates. The five time periods include: (1) before Winter Break (5 weeks); (2) during Winter Break (4-6 weeks); (3) between Winter and Spring Breaks (6-9 weeks); (4) during Spring Break (2-3 weeks); and (5) after Spring Break (5 weeks).

OBJECTIVE 5

We derived seasonal signature curves and plotted the predicted values from Model 5 for the interval between the 43rd to 23rd calendar week of the following year. To demonstrate the effect of Winter and Spring Breaks, we interpolated the predicted values by connecting the first and last weeks of the holiday. Signatures were derived for all ages, 5-24 years, and 45-64 years age groups for influenza tests (Figure 6). The dampening of tests during Winter Break was evident in all ages and in those 5-24 years (RR = 0.31; 95%CI = 0.22-0.41 vs RR = 0.14; 95%CI = 0.09-0.22, respectively). A significant increase in tests was observed during Spring Break in 45-64 years old adults (RR = 2.12; 95%CI = 1.14-3.96).

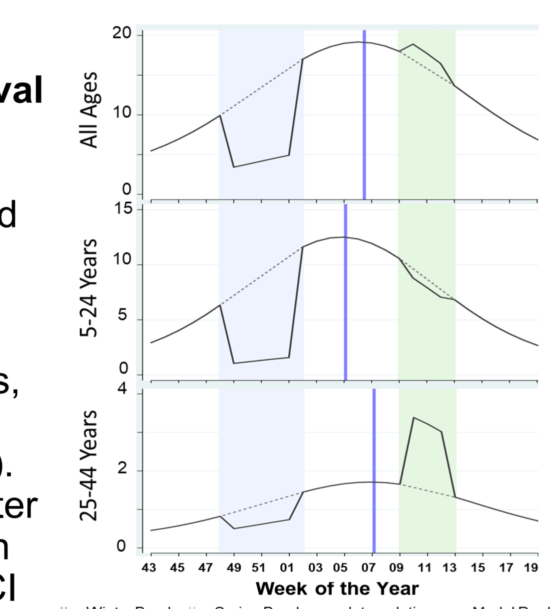

Figure 6. Seasonal signatures of weekly tests for all time periods and the all ages, 5-24 years, and 45-64 years age groups.

CONCLUSIONS

Our results show that individual holiday effects depend on the proximity of age– and influenza-specific peak timing to holiday occurrences and whether the peak precedes or succeeds the holiday. Combining individual effects into categories mask individual holiday effects. The consequence of combining individual holidays into collective holiday periods will potentially lead to misspecification.

We provided a methodology to quantify an amplification or dampening effect of a calendar event on influenza seasonal signatures. We recommend incorporating location-specific calendar effects in influenza modeling and near-term forecasts tailored to susceptible age groups and individual holidays to better predict and assess targeted intervention measures.

Further research would require a longer time series, more refined time units (daily time series), more refined age categories, and expanded to all influenza subtypes and to more diverse population groups. Further attention should be given to calendar and other temporal events that drive local social interactions and person-to-person contact. A clear methodology should also be developed to assess those effects.

ACKNOWLEDGEMENTS

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