Contact, travel, and transmission: The impact of winter holidays on influenza dynamics in the United States

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Abstract

Background: The seasonality of influenza is thought to vary according to environmental factors and human behavior. During winter holidays, potential disease-causing contact and travel deviate from typical patterns, and we aim to understand these changes on age-specific and spatial flu transmission.

Methods: We characterized the changes to transmission and epidemic trajectories among children and adults in a spatial context before, during, and after the winter holidays among aggregated physician medical claims in the United States from 2001 to 2009 and among synthetic data simulated from a deterministic, age-specific spatial metapopulation model.

Results: Winter holidays reduced flu transmission and delayed the trajectory of flu season epidemics. The holiday period itself observed a shift in relative risk of disease from children towards adults. Model results indicated that holidays delay epidemic peaks and synchronize incidence across locations, and contact reductions from school closures rather than age-specific mixing and travel produce these observed holiday dynamics.

Conclusions: Winter holidays delay seasonal influenza epidemic peaks due to changes in contact patterns. These findings may improve the future design of influenza intervention strategies, such as the proper timing and duration of school closures, and the spatial and demographic allocation of vaccines.

Keywords: influenza, age patterns, travel patterns, epidemiology, winter holidays, United States

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1   Introduction

Influenza epidemics are characterized by large variation in disease burden across seasons and across locations within a given season [1]. While we do not fully understand what drives this variation, contact and travel patterns have been observed to influence local and global influenza transmission [2, 3, 4, 5]. Winter holidays alter typical contact and travel patterns through school closures and holiday travel and occur early in typical flu seasons in temperate climates, yet the measurement and the subsequent effects of these temporary behavioral changes on seasonal flu remain poorly understood.

Consideration of age group patterns is an important component to understanding the transmission and relative disease burden of influenza. Empirical contact surveys have illustrated that individuals tend most to associate with others in a similar age group and school-aged children tend to have the greatest number of potential disease-causing contacts [6, 7]. Additionally, modeling studies have demonstrated that social mixing by age is sufficient to capture much of the heterogeneity in contact across populations [8]. In large population settings, school-aged children are thought to drive local transmission of flu due to their large number of contacts, while adults are thought to seed flu in different locations due to their global mobility [3, 4, 9].

Since schools and school-aged children are of particular importance for influenza transmission, temporary school closures are commonly considered as a reactive intervention in pandemic and severe flu seasons [10, 11]. However, empirical studies of the effect of these interventions varies from no significant effect on flu transmission, to reducing transmission by 29% in children alone [12, 13, 14]. Due to these mixed results, the impact on children and the subsequent trickle-down effects to other age groups remains unclear. While school holidays have similarities to closures, they occur at predetermined times and induce changes to both contact and travel patterns. In the United States, the Christmas holiday occurs in late December and U.S. epidemics typically start in December and peak in February; changes in flu transmission during the winter holidays could crucially affect the resulting flu epidemic [15]. The number of contacts between children decreases as children are out of school for the holiday [16], and mixed results suggest that winter school holidays reduce or delay the risk of influenza among school-aged children by 33-42% [17, 18] and periods around the holidays experience high variability in ILI across seasons [19].

Local and global travel are mechanisms by which respiratory pathogens are commonly thought to spread, and travel patterns have long been studied to understand the spatial spread of diseases. Winter holidays are characterized by increases in visits to friends and family that cause deviations

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33 from typical travel patterns, and in the U.S., there are notable increases in travel among children

34 and in the volume of long-distance travel [20, 21]. Human movement is tied to the phylogeographic

35 spread of influenza viruses [22], and substantial evidence suggests that travel can influence the spatial

36 spread and timing of influenza epidemics [3, 23, 24, 25, 4, 26]. However, travel restrictions have been

37 shown to produce little to no effect on the spread of pandemic influenza [27, 28, 29]

38   Our work aims to determine the impact of changing contact and travel patterns during winter

39 holidays on influenza transmission and the resulting epidemic trajectories. With U.S. medical claims

40 data, we examine changes in flu transmission during and after the holidays, and characterize common

41 patterns in the rates of influenza-like illness among school-aged children and working-aged adults

42 during the holiday period across multiple flu seasons. To understand the mechanisms behind these

43 empirical patterns, we create a parsimonious age-specific spatial metapopulation model to study

44 the interactions among child and adult populations and the importance of human travel in spatial

45 spread. Using the model, we examine two hypotheses that may work independently or in concert: 1)

46 holiday changes to travel patterns temporarily synchronize epidemics across locations (subpopulation

47 dynamics) [30, 31], or 2) holiday reductions in contact patterns damp transmission to such low

48 levels that all epidemics 'reset' to the beginning of their trajectories, thus creating an appearance of

49 synchrony [18, 17]. Using a combination of empirical and theoretical approaches, our work highlights

50 the significant role of the holidays on shaping influenza seasonal dynamics, and has implications for

51 influenza control through vaccination prioritization and school closures.

Methods

53 We used reports of influenza-like illness (ILI) to explore spatial and age-specific patterns of seasonal

54 influenza activity around the winter holidays in the United States. Motivated by these empirical

55 observations, we then tested hypotheses about the mechanisms that may be driving holiday flu

56 dynamics through a simple epidemiological model. Here, we introduce the empirical data, mathe-

57 matical model structure, and the measures through which we characterized spatial and age-specific

58 epidemiological patterns with the empirical and simulated data. (More details are available in the

59 SM sections S1 and S2).

Medical claims data

61 Weekly visits for ILI and any diagnosis from October 2001 to May 2009 were obtained from a records-

62 level database of CMS-1500 US medical claims managed by IMS Health and aggregated to three-

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63 digit U.S. zipcode prefixes (zip3s), where ILI was derived from a set of International Classification

64 of Diseases, Ninth Revision (ICD-9) codes and validated at multiple geographic scales, as described

65 elsewhere [32]. To account for temporal variation in health care-seeking (e.g., doctor's office closures,

66 lower probability of seeking care for illness during holidays), weekly ILI visits were divided by weekly

67 all-cause patient visits (i.e. a visit is included regardless of its purpose) in the medical claims database

68 and standardized by population size to calculate an *ILI incidence ratio* (See SM section S1.1, Figure

69 S1) [32]. For age-specific analyses, we calculate ILI incidence ratios for individuals 5-19 years old

70 to represent children and for individuals 20-69 years old to represent adults. The epidemic period

71 was defined as October through March, and 'before', 'during' and 'after' periods of the holiday were

72 defined as two week periods, with the "during" period beginning at the Christmas holiday.

73 To understand the effect of the winter holidays on flu transmission in the empirical data, we

74 estimated the effective reproductive number (R_t), the average number of secondary cases generated

75 by each infected individual under the conditions at time t, over weekly periods during the eight flu

76 seasons from 2001-2002 through 2008-2009. (Details on the calculation of R_t can be found in SM

77 section S1.3).

Metapopulation model

79 We used an epidemiological model to simulate flu epidemics with and without holiday-associated

80 behavioral changes to contact and travel patterns. Our model was adapted from an age-specific

81 metapopulation model that 1) incorporates contact between children and adults, and 2) is spatially

82 divided into metropolitan areas linked through air traffic flows [4, 33]. Infection followed an SIR

83 (Susceptible, Infected, Recovered) disease progression, and the entire population was assumed to

84 be susceptible at the start of an outbreak. Each model run was seeded with one child infection in

85 a single spatial area. Disease spread deterministically and in discrete time steps according to age-

86 specific contact patterns, and infection reached additional metro areas through travel. All model

87 results shown are an average across all possible seeds. (Details on the demographic and travel data

88 used to parameterize the model can be found in SM section S2.)

Experimental design

90 To mimic holiday-associated behaviors in the model, we altered age-specific contact and travel

91 parameters during a predetermined 14-day holiday period (See SM section 2.3). We identified the

92 holiday period based on the average number of days between Christmas and the epidemic peak in the

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93 national empirical data, and the 'before', 'during' and 'after' periods of the holiday were defined as
94 two week periods, with the "during" period beginning at the holiday. We also carried out sensitivity
95 analyses to compare epidemiological patterns when holiday period contact rates and timing were
96 altered (See SM sections S3.2 and S3.3). In the *school closure model*, we altered each value of the
97 baseline contact matrix according to empirical survey data that reported age-specific contact rates
98 during school holidays. Specifically, during the holiday period, the total contact rate was reduced
99 in both age groups and the rate of child to adult contact increased proportional to the total number
100 of child contacts [16]. In the *travel model*, during the holiday period, we altered the travel-based
101 connectivity between metropolitan areas based on air traffic patterns from December 2005, and by
102 increasing the fraction of child travelers, r, to 15% [20]. Generally speaking, holiday travel observed
103 a greater volume of travelers pushed through fewer locations than baseline travel (See SM section
104 S2.4). The *holiday model* combined the changes associated with both the school closure and travel
105 models.

Results

107 We first explore empirical patterns of influenza burden and transmission during and after the holiday
108 period in the United States across multiple flu seasons. We then consider results from an age-specific
109 spatial metapopulation model to systematically understand the impact of holiday-related school
110 closures and changes to travel patterns on the spatial and age-specific spread of influenza.

Characterizing empirical influenza patterns during the holidays

112 Here, we report age-specific and spatial patterns of influenza transmission based on U.S. medical
113 claims data for influenza-like illness (ILI) during the months around the Christmas holiday, after
114 having corrected for variation in reporting rates. (See Methods for details.)

115   During the weeks following Christmas, we observed temporary reductions in U.S. flu activity
116 across eight seasons, even after accounting for holiday-associated reductions in healthcare-seeking
117 (Figures 1A and S1). Flu transmission, as measured by the mean effective reproductive number
118 (R_t) (see Methods for further details), decreased by approximately 15% (reduction from $R_t \sim 1.1$
119 to ~ 0.9) in most seasons and fell below the epidemic threshold $(R_t = 1)$ immediately following
120 Christmas. Within a few weeks, flu transmission exceeded the epidemic threshold and rebounded to
121 pre-holiday levels (Figure 1B). These patterns were observed consistently within our study period,
122 including the notably early 2003-04 flu season. This pattern was also observed across smaller spatial

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123 regions, specifically across zipcodes sharing the first three digits (zip3) in the United States (Figure

124 S2). Analysis of viral surveillance data on influenza-positive laboratory confirmations verified that

125 influenza was indeed circulating around the Christmas holiday for each season in our study period,

126 so decreases in ILI and R_t may be attributed to influenza dynamics; similarly, we did not investigate

127 Thanksgiving holiday dynamics because influenza circulation was quite limited during this period

128 (Figure S3).

129 We also examined weekly ILI medical claims for school-aged children (5-19 years of age) and

130 adults (20-69 years of age) from November through January. Across the eight flu seasons, both

131 children and adults experienced temporary declines and recoveries around the Christmas holiday

132 (Figure 2A). However, the changes in incidence patterns were not synchronous in the two age groups,

133 with adults experiencing a reduction only after the holiday. To examine the differential impact on

134 the two age groups, we examined relative risk of ILI activity between children and adults. We

135 observed that risk of disease was shifted towards adults during and after the holiday, and that these

136 dynamics coincided with the temporary reductions in flu activity and flu transmission (Figure 2B).

137 We posit that these patterns may be driven by altered interaction patterns due to children being

138 home from school or families (rather than business travelers) traveling for the holidays.

139 To investigate the spatial patterns of influenza spread during the holiday period, we characterized

140 the peak timing and synchrony of ILI reports across zip3s in the medical claims data. We observed

141 that the timing and variation of seasonal influenza peaks across zip3s in the United States is compa-

142 rable for most seasons, occurring an average of five weeks after the holiday period; the early 2003-04

143 is an exception with the holiday period occurring after the epidemic peak in a majority of locations

144 (Figure 3A). Additionally, the distribution of incidence across zip3 areas showed little variation from

145 the periods before to after the holidays (Figure 3B). We hypothesize that these patterns may be

146 driven by increased travel that homogenizes and synchronizes influenza risk across the country.

Exploring the mechanisms behind holiday flu dynamics

148 Informed by the empirical patterns observed in our data, we sought to identify the impact of specific

149 behavior changes expected to occur during the holiday period. We hypothesized that two potential

150 mechanisms influenced the age-specific and spatial patterns of influenza spread around the holidays:

151 school closures and travel. As these mechanisms both lead to changes in individual-level and large-

152 scale contact patterns during the holidays, we studied their impact on holiday flu dynamics in a

153 controlled manner through the use of a mathematical model. We compared the results from three

154 models with holiday-associated behavioral changes to a baseline model, where no behavioral changes

155 were implemented. The holiday models implemented behavioral changes as follows: 1) increased

156 fraction of child travelers and changes to travel volume and connectivity, according to data on

157 altered holiday travel patterns ("travel"), 2) reduced overall number of potential disease-causing

158 contacts for children and adults, and a greater proportion of child to adult mixing, corresponding

159 to a holiday school closure informed by data ("school closure"), and 3) both of the above scenarios

160 together ("holiday"). (See Methods and SM section S2 for details).

161 The baseline model results followed an epidemic trajectory with a single peak, while the holiday

162 model epidemics had similar dynamics to the empirical data, illustrating a temporary drop and

163 recovery of flu activity during and after the holiday period with a larger epidemic peak that followed

164 (Figure 4A). The travel model produced results similar to the baseline model, while the school closure

165 model results is largely comparable to the holiday model. As with the empirical data, children always

166 had greater risk of flu than adults, and the risk shifted towards adults with the school closure and

167 holiday models (Figure 4B). No such shift was observed for the baseline and travel simulations.

168 Despite the differences in dynamics, the total epidemic sizes were comparable for all four models

169 (Table S3).

170 To characterize the spatio-temporal dynamics in the model, we considered peak timing and

171 synchrony in model epidemic results. Peak timing of influenza epidemics across spatial areas is

172 shown to be early in the baseline and travel models, and shifted to a later time in the school

173 closure and holiday models (Figure 5A). The baseline model also highlights spatial variability in

174 peak timing across metro areas, with lower variability in the holiday and school closure models.

175 We then compared the distribution of flu incidence before, during, and after the holiday periods to

176 characterize the trajectory of the model epidemics. The baseline model showed increasing disease

177 incidence from before to after the holiday period, as the baseline epidemic is uninterrupted by the

178 holiday. We also observed that the baseline and travel models appear to show spatial asynchrony,

179 illustrated by the large variance in the distribution of flu incidence across locations, compared with

180 the relatively low variance (spatial synchrony) of the school closure and holiday models (Figure 5B).

181 To further explore the sensitivity of holiday dynamics to changes in individual-level contact

182 patterns, we considered models in which the overall number of contacts was reduced for children

183 and adults (to match that of the "school closure" model), but the proportion of contact within

184 and between age groups was not altered. We found that this new model ("partial school closure")

185 produced epidemic dynamics and spatial synchrony patterns matching those of the school closure

186 model (Figure S6). We also explored the sensitivity of our results to the timing of the holiday period,

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187 and found that later holidays (occurring during the growth phase or at the epidemic peak) did not
188 impact the overall dynamics, age-specific patterns, or spatial synchrony outcomes reported above
189 (Figures S8, S10, S11), but did result in multiple epidemic peaks due to the resetting of the epidemic
190 trajectory.

Discussion

192 In this study, we have considered the impact of winter holiday periods in the United States on in-
193 fluenza transmission. We have observed that these periods are associated with temporary reductions
194 in rates of influenza-like illness, especially among children, at both national and local scales, after
195 controlling for temporal variation in reporting. These observations corroborate previous empirical
196 studies that report reduced flu transmission during the winter holidays in Argentina [17] and in
197 Arizona [18]. Additionally, we observed that the holidays may alter the synchrony of ILI incidence
198 across locations, even for seasons marked by early peaks (occurring before the holiday period).

199 These empirical patterns are descriptive of the dynamics of influenza during the holiday period,
200 but questions about the mechanisms driving these patterns remain. Our study used an age-specific
201 spatial metapopulation model to compare outcomes with and without temporary, holiday-associated
202 changes in contact and travel. This model framework allowed us to determine which behavioral
203 change drives observed holiday epidemic dynamics and the impact of holiday timing on epidemic
204 outcomes. We found that holiday-associated changes to age-specific contact patterns reproduced
205 many of the patterns observed in our empirical data. In the model, holiday contact patterns were
206 responsible for causing temporary reductions in flu activity during the holiday period, shifting the
207 risk of disease from children to adults, pushing the epidemic peak later in time, and increasing the
208 synchrony in flu incidence during the holiday period. However, total epidemic sizes were not affected
209 (in contrast to the work of [34]). Our analysis also illustrated that the age shift in burden and spatial
210 synchronization caused by holiday periods was insensitive to the timing of the holiday period during
211 the epidemic, but that later holiday periods did result in multiple peaks (as experienced in the 2009
212 H1N1 pandemic [34].) On the other hand, the empirical patterns from the 2003-2004 early flu season
213 highlight that a holiday period arriving well after an epidemic peak results in minimal impact on
214 epidemic dynamics.

215 In comparing the effects of two purported mechanisms driving holiday dynamics —school closure
216 and increased travel —we were surprised to find that changes due to school closure explained nearly
217 all of the delay in peak timing and increase in spatial synchrony in our model. Travel restrictions

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218 have been shown to produce little to no effect on the spread of pandemic influenza [27, 28, 29],
219 and our study adds to this literature on the minimal effect of holiday-related travel re-routing on
220 spatial influenza transmission. While holiday travel is more commonly linked with seeding and
221 synchronizing flu in multiple locations [24], we found that school closures, and more specifically,
222 reductions in the average number of holiday contacts and not the changes in mixing among age
223 groups, could in fact create a dampening and synchronizing spatial effect (See SM section S3.1).
224 Thus our study lends model-based support to the success of school closures, specifically when they
225 are effectively implemented and timed early during the epidemic [10].

226 In both empirical and modeling analyses, evidence suggested that children and adults have
227 staggered, temporary dips in reported ILI after the winter holidays; the reduction was later and
228 smaller in magnitude for adults, supporting results that holiday effects are delayed by one week
229 among other age groups relative to children [17], that children are the primary drivers of household
230 transmission [35, 36], and that children experience the greatest disease burden when populations are
231 naive to new strains of influenza and adults are more affected in subsequent seasons or epidemic waves
232 [37, 38]. Nevertheless, the timing of the overall epidemic peak was shifted equally in the holiday
233 model for both children and adults; this suggests that while children may experience greater flu
234 burden and local transmission due to their high contact rates [39, 40, 8, 6], they do not necessarily
235 lead the epidemic wave [41, 5]. Finally, we observed that holiday-associated behavioral changes
236 consistently increased the risk of disease among adults relative to that among children. Our previous
237 work leveraged the consistency of this temporary change to detect early warning signals of seasonal
238 influenza severity [1], and future work could examine how this early flu testbed might signal other
239 actionable epidemiological information about the flu season.

240 While our holiday model parameters are indeed based on empirical survey data, we have limited
241 knowledge about holiday-associated behavioral changes to contact and travel patterns at a pop-
242 ulation scale [42, 20, 21, 43]. There are no counterfactual scenarios to observe system behavior
243 in the absence of holidays, but future studies could address this limitation by comparing seasonal
244 flu dynamics across locations with different holiday timings (e.g., different national holidays across
245 countries or different closure timings across school districts). The average holiday travel changes
246 in our model may also not have captured non-routine travel and local travel patterns that have
247 been shown previously to synchronize and spread local epidemics [2, 3, 4], nor did they consider the
248 individual identities of travelers, which additionally slows the speed of epidemic waves [44]. Addi-
249 tionally, flu transmission and ILI reporting were conflated in the model, as the effects of holiday
250 interventions in the model were observed immediately. Future work may account for delays in timing

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251 between holiday-associated transmission and reporting (e.g., flu incubation period, time delay before

252 seeking care for ILI) by incorporating these mechanisms into a revised model, or with the use of

253 empirical data at a finer temporal scale. Seasonal environmental fluctuations like temperature and

254 humidity, both of which are hypothesized to modulate influenza transmission and survival, were also

255 not considered among our epidemic impacts [15, 45, 46, 47]. If winter holidays are indeed pushing

256 U.S. epidemics later into the winter as our results demonstrate, environmental conditions may be

257 more favorable to flu transmission. Future work should extend the examination of the link between

258 environmental factors and holiday-induced shifts in peak timing [48, 49, 50]. Additionally, we ac-

259 knowledge that populations poorly captured by medical claims data (e.g., uninsured individuals)

260 may engage in systematically different holiday-associated behaviors than other populations, as lack

261 of health insurance and financial barriers may be correlated with holiday activities [51, 52]. Future

262 studies with U.S. medical claims may better represent the entire population, as the Affordable Care

263 Act has substantially expanded insurance coverage among adults [53, 54].

Footnote page

Supporting Material

Additional Document with detailed descriptions about data processing, model parameters, sensitivity analyses, and supporting evidence.

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Conflicts of interest

The authors declare no conflicts of interest.

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Authors' contributions

AE parsed the medical claims data, assembled the demographic and contact data, performed analyses, interpreted the results, and wrote the first draft of the manuscript. ECL assembled all other data and performed analyses. CV interpreted the results and edited the manuscript. SB and ECL jointly conceived and designed the study, guided the analysis, interpreted the results, and edited the manuscript. All authors read and approved the final manuscript.

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Figures

Figure 1: **Decreases in transmission are observed following Christmas. A)** National ILI incidence ratio (ILI cases per total visits per 100,000 population) calculated using weekly ILI medical claims data over time in weeks from the first week in November to the last week in January for flu seasons from 2001 to 2009. The week of Christmas is marked with the vertical dotted line. **B)** National daily effective reproductive number (R_t) over time from November to January for flu seasons from 2001 to 2009. R_t was calculated over seven-day windows using ILI medical claims data adjusted for health care facility closures and for care-seeking. The date of Christmas is marked with the dashed line.
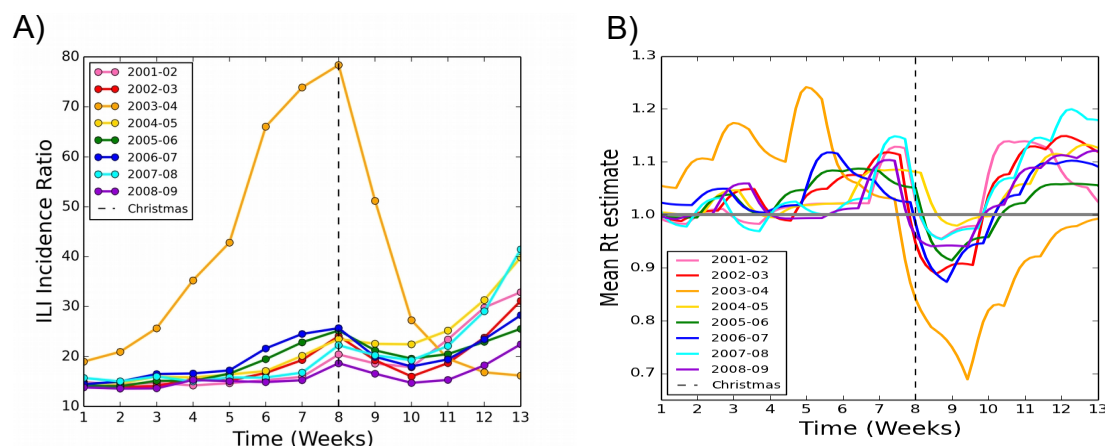

Figure 2: **The impact of the holidays varies by age group. A)** Age-specific ILI incidence ratio calculated from weekly ILI medical claims data from November to January for flu seasons from 2001 to 2009 among school children and adults. The week of Christmas is denoted by the vertical dotted line. **B)** ILI incidence ratio relative risk between school children and adults calculated over time in weeks from November to January medical claims data for flu seasons 2001-2009. The week of Christmas is denoted by the dashed line. A relative risk greater than 1 indicates a greater risk toward children, less than 1 indicating greater risk toward adults.
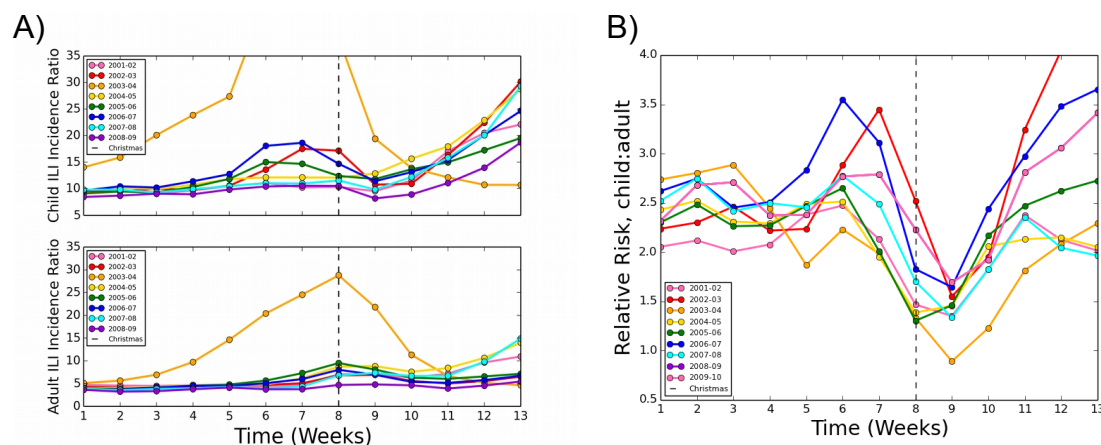

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Figure 3: **Peak timing and spatial synchrony in empirical data. A)** Distribution of weeks to peak across all zip3s, where the flu period endures from October to March. Distributions are compared across eight flu seasons in the study period. The horizontal dashed lines highlight the holiday period. **B)** Distributions of ILI reports across all zip3s averaged for the two week durations defined as 'before', 'during', and 'after' the holiday periods. Distributions are compared across eight flu seasons in the study period. A small number of outlying data points are not depicted here.
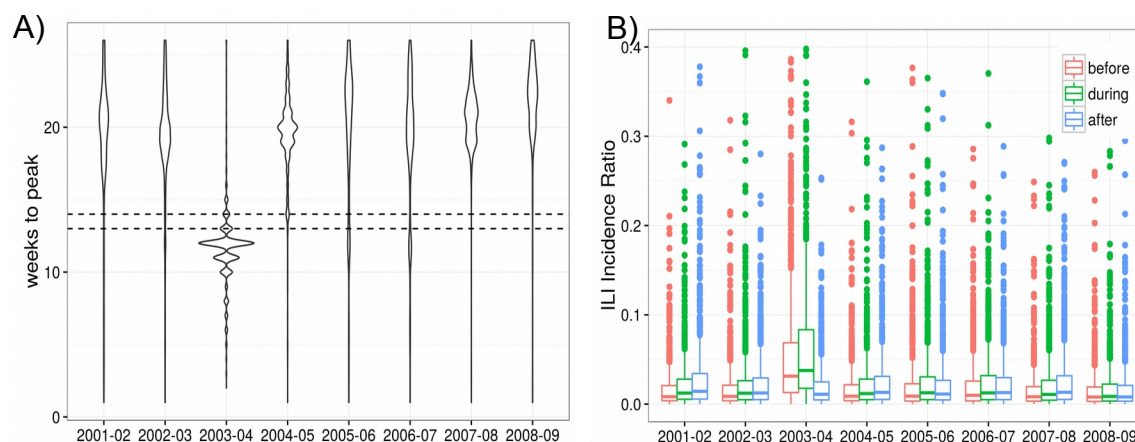

Figure 4: **Changes to contact patterns appear to drive holiday-associated dynamics in model simulations. A)** Total flu incidence per 10,000 population over time, averaged across all model runs. **B)** Relative risk of disease from children to adults across all locations, averaged across all model runs. Epidemic trajectories for the baseline (no changes during the holiday period), travel only, school closure only, and full holiday (travel and school closure changes) interventions are compared, and the holiday period is demarcated by the dashed black lines. The purple line shadows the green line in both figures.
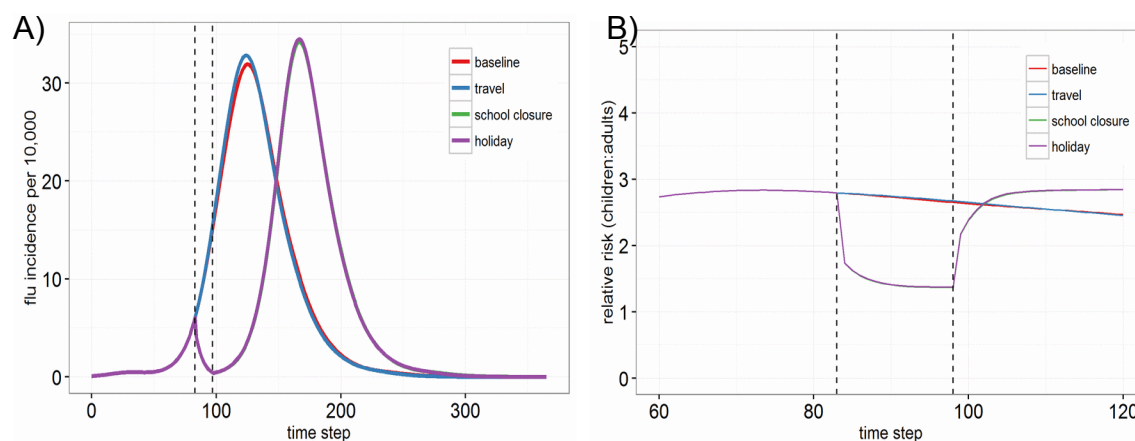
Figure 5: **Holiday-associated behavioral changes delay peak timing and increase the synchrony of epidemics across locations in model simulations. A)** Distribution of time steps (days) to peak across all metro areas, averaged across all model runs. Distributions across metros are compared for the baseline, travel only, contact only, and full holiday models, and the holiday period is demarcated by the horizontal black lines. **B)** Distributions of flu incidence across all metro areas averaged for the two week durations defined as 'before', 'during', and 'after' the holiday periods, averaged across all model runs. Distributions are compared for the baseline, travel only, school closure only, and full holiday interventions.