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Declaration of interest

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The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

CRediT authorship contribution statement

Louis Yat Hin Chan: Conceptualization, Formal analysis, Investigation, Methodology, Software, Validation, Visualization, Roles/ Writing - original draft, Writing - review & editing. **Sinead E. Morris:** Investigation, Methodology, Writing - review & editing. **Melissa S. Stockwell:** Data curation, Writing - review & editing. **Natalie M. Bowman:** Data curation, Investigation, Writing - review & editing. **Edwin Asturias:** Data curation, Writing - review & editing. **Suchitra Rao:** Data curation, Writing - review & editing. **Karen Lutrick:** Data curation, Writing - review & editing. **Katherine D. Ellingson:** Data curation, Writing - review & editing. **Huong Q. Nguyen:** Data curation, Writing - review & editing. **Yvonne Maldonado:** Data curation, Writing - review & editing. **Son H. McLaren:** Data curation, Writing - review & editing. **Ellen Sano:** Data curation, Writing - review & editing. **Jessica E. Biddle:** Data curation, Writing - review & editing. **Sarah E. Smith-Jeffcoat:** Data curation, Writing - review & editing. **Matthew Biggerstaff:** Supervision, Writing - review & editing. **Melissa A. Rolfes:** Data curation, Writing - review & editing. **H. Keipp Talbot:** Data curation, Funding acquisition, Writing - review & editing. **Carlos G. Grijalva:** Data curation, Funding acquisition, Writing - review & editing. **Rebecca K. Borchering:** Conceptualization, Formal analysis, Investigation, Methodology, Supervision, Writing - review & editing. **Alexandra M. Mellis:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Supervision, Writing - original draft, Writing - review & editing.

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During the preparation of this work the authors used ChatGPT in order to enhance the clarity, coherence, and correctness of the writing, and to check for grammatical errors. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Disclaimer

The conclusions, findings, and opinions expressed by authors contributing to this article do not necessarily reflect the official position of the U.S. Department of Health and Human Services, the Public Health Service, the Centers for Disease Control and Prevention, or the authors' affiliated institutions.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.epidem.2025.100815.

Estimating the generation time for influenza transmission using household data in the United States

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Abstract

The generation time, representing the interval between infections in primary and secondary cases, is essential for understanding and predicting the transmission dynamics of seasonal influenza, including the real-time effective reproduction number (R_t). However, comprehensive generation time estimates for seasonal influenza, especially since the 2009 influenza pandemic, are lacking. We estimated the generation time utilizing data from a 7-site case-ascertained household study in the United States over two influenza seasons, 2021/2022 and 2022/2023. More than 200 individuals who tested positive for influenza and their household contacts were enrolled within 7 days of the first illness in the household. All participants were prospectively followed for 10 days, completing daily symptom diaries and collecting nasal swabs, which were then tested for influenza via RT-PCR. We analyzed these data by modifying a previously published Bayesian data augmentation approach that imputes infection times of cases to obtain both intrinsic (assuming no susceptible depletion) and realized (observed within household) generation times. We assessed the robustness of the generation time estimate by varying the incubation period, and generated estimates of the proportion of transmission occurring before symptomatic onset, the infectious period, and the latent period. We estimated a mean intrinsic generation time of 3.2 (95 % credible interval, CrI: 2.9–3.6) days, with a realized household generation time of 2.8 (95 % CrI: 2.7–3.0) days. The generation time exhibited limited sensitivity to incubation period variation. Estimates of the proportion of transmission that occurred before symptom onset, the infectious period, and the latent period were sensitive to variations in the incubation period. Our study contributes to the ongoing efforts to refine estimates of the generation time for influenza. Our estimates, derived

from recent data following the COVID-19 pandemic, are consistent with previous pre-pandemic estimates, and will be incorporated into real-time R_t estimation efforts.

Keywords

Generation interval; Serial interval; Incubation period; Pre-symptomatic transmission; Household transmission; Respiratory diseases

1. Introduction

The generation time, a crucial parameter in understanding the dynamics of infectious diseases, is defined as the time interval between infections of primary and secondary cases and reflects when most transmission is likely to happen. In the context of seasonal influenza, estimation of the generation time becomes increasingly important for predicting the trajectory of outbreaks and informed public health decision-making during an influenza season.

Estimating the generation time is challenging because few investigations can accurately detect the exact time of infection. The generation time is often inferred from the serial interval, defined as the time between symptom onsets of primary and secondary cases (Svensson, 2007), due to the practicality of observing symptom onsets rather than infections. However, this alternative measure may not always approximate the generation time due to its dependence on the incubation period, defined as the duration from infection to symptom onset, and the possibility of asymptomatic infections.

Accurate estimation of the generation time is important for predicting the real-time effective reproduction number (R_t), a metric used to describe transmission intensities through time (Gostic et al., 2020). During the 2023/2024 influenza season, the Centers for Disease Control and Prevention (CDC) estimated the current epidemic growth status for influenza infections in the U.S. as either growing or declining based on the R_t (Centers for Disease Control and Prevention, 2024a, 2024b, 2024c). For this estimate, the generation time was approximated with a serial interval from a study by Cowling et al. (Cowling et al., 2009) that utilized data collected in Hong Kong in 2007, prior to the 2009 H1N1 influenza pandemic.

To improve our understanding of seasonal influenza outbreaks, there is a need for more contemporary generation time estimates, especially following the COVID-19 pandemic. This analysis provides updated generation time estimates derived from an influenza household transmission study (Rolfes et al., 2023) conducted during the 2021/2022 and 2022/2023 influenza seasons in the U.S. We employ a model using a published Bayesian data augmentation approach (Hart, Abbott, et al., 2022; Hart et al., 2021; Hart, Miller, et al., 2022) to impute missing event times, including infections and symptom onsets of cases, and estimate generation times. We estimate both the intrinsic generation time, which assumes no susceptible depletion, as well as the realized household generation time observed within the household setting. We also estimate the serial interval. We derived estimates across the two seasons, virus types (influenza A and B), and household sizes to understand potential differences and robustness to model assumptions. These sensitivity analyses indicate the

reliability of our estimates across different data stratifications and assumptions, and provide evidence that the generation time has remained substantially unchanged over the last decade or two.

We also estimate other transmission parameters, including the proportion of transmission before symptomatic onset, the infectious period, and the latent period. This helps in assessing pre- and post-symptomatic transmission, thereby providing insights that can inform effective disease control strategies such as isolation.

2. Material and methods

2.1. Household data

Participants included in this analysis were enrolled in a 7-site case-ascertained household study, the Respiratory Virus Transmission Network – Sentinel (RVTN-S), conducted in the U.S. over two consecutive influenza seasons: 2021/2022 and 2022/2023 (Rolfes et al., 2023). After informed consent was obtained, the study enrolled individuals identified with influenza infections via polymerase chain reaction (PCR) testing and their household contacts within 7 days of the initial illness onset within the household. Households were only enrolled if the index case who first presented for clinical testing was the first symptomatic or positive person in the household, with no other members of the household symptomatic on the first day of index case symptoms. Participants, including both index cases and household contacts, were then prospectively followed for 10 days, during which they completed daily symptom diaries and collected daily nasal swabs, which were tested for influenza via RT-PCR. Approximately half of the household contacts became infected with influenza during the study period (Rolfes et al., 2023).

The dataset encompasses detailed information regarding symptoms and viral testing, including four main variables used in the model: whether individuals tested positive for influenza, their symptomatic status, dates of positive test results, and dates of symptom onset. Using the test positivity and symptomatic status, we stratified individuals into three types: symptomatic infected, asymptomatic infected, and uninfected. The unknown infection time of each individual was upper bounded by the earlier of the date of their first positive test result and their symptom onset, if available.

In the primary analysis, we excluded households with multiple co-primary cases, i.e., more than one individual exhibiting the same date of the earliest symptom onset concurrently. We also conducted analyses based on three data stratifications by season, virus type, and household size, all of which excluded households with multiple co-primary cases. To assess the potential impact of including such households, we performed a separate stratified analysis that included households both with and without multiple co-primary cases. Finally, we conducted an additional stratified analysis based on vaccination status (Supplementary material).

2.2. Modeling transmission within households

We employed a Susceptible-Exposed-Infectious-Recovered (SEIR) model, originally developed by Hart et al. (2021) for analyzing COVID-19 contact tracing data. The model

was also used in two subsequent studies of household data in the United Kingdom (Hart, Abbott, et al., 2022; Hart, Miller, et al., 2022). We modeled each household separately and assumed that all transmissions, except for primary cases infected by others in the community, occurred within households.

The SEIR model, referred to as the mechanistic model, includes compartments for asymptomatic, pre-symptomatic and symptomatic infectious stages (Hart et al., 2021). Each stage may have a different relative infectiousness, or transmission rate. Upon infection and entry into the non-infectious exposed stage, individuals may progress to become infectious through one of two pathways: either by remaining asymptomatic or by developing symptoms following a pre-symptomatic stage. Consequently, transmissions may occur before symptom onset, depending on the length of the incubation period. Additional details about the specification of parameters for the mechanistic model can be found in the Supplementary material.

2.3. Influenza-specific parameters

In adapting the model for our influenza study, we used estimates for the incubation period of influenza A from a systematic review by Lessler et al. (2009). In sensitivity analyses, we explored variations derived from parallel estimates for influenza B (Lessler et al., 2009) and for influenza A(H1N1)pdm09 (Tuite et al., 2010).

Regarding the relative infectiousness of asymptomatic infected individuals compared with symptomatic infected individuals, we assumed a value of 0.57 (i.e., asymptomatic infected individuals were 43 % less infectious than symptomatic infected individuals) based on the mean estimate from a recent study (Tsang et al., 2023), and we also conducted sensitivity analyses using values of 0.11 and 1.54 based on the corresponding 95 % credible interval (CrI).

2.4. Estimating the generation time

We estimated both intrinsic and realized generation times by integrating data augmentation Markov Chain Monte Carlo (MCMC) techniques with Bayesian inference (Hart, Abbott, et al., 2022). The intrinsic generation time assumes no depletion of susceptible individuals, providing an estimate of the time it takes for an infected individual to infect others in the community with an unlimited supply of susceptible contacts. The realized household generation time reflects the actual time interval observed within households, restricted by the depletion of susceptible individuals over time. Susceptible depletion refers to the gradual reduction in the number of individuals within a population that have not yet been infected with a virus. For example, within the SEIR framework, members may become infected, develop immunity, and subsequently be removed from the susceptible pool. Considering this distinction allows for a more thorough understanding of influenza transmission dynamics, capturing both theoretical and observed aspects of transmission.

The estimation procedure accounted for the uncertainty in determining who infected whom within a household by summing the likelihood contributions from all potential infectors, thus considering multiple possible transmission routes. The precise times of infection and symptom onset of all infected individuals were imputed as augmented data,

alongside the estimation of unknown model parameters during the MCMC iterations. The estimated parameters of the SEIR framework include the proportion of transmission before symptomatic onset, the ratio of pre-symptomatic to symptomatic transmission rates (i.e., relative infectiousness of symptomatic infected individuals before symptom onset compared to after), as well as the latent period, the pre-symptomatic infectious period, and the symptomatic infectious period. Further technical details of the statistical inference method including the likelihood function and the Bayesian data augmentation MCMC can be found in the Supplementary material and the original study (Hart, Abbott, et al., 2022).

To compare estimated parameter posterior distributions, we calculated the overlapping index, a measure of distribution similarities (Pastore, 2018; Pastore and Calcagni, 2019). A value close to 1 indicates high similarity, implying no substantial differences, while a value close to 0 indicates low similarity, implying substantial differences. We compared estimates of the generation time across multiple data stratifications and sensitivity analyses to the primary results which excluded households with multiple co-primary cases.

The model was implemented in R (version 4.3.1) with 1,000,000 Markov chain Monte Carlo iterations, discarding the initial 20 % as burn-in and obtaining posterior distributions by thinning every 100 iterations. The code for the model is available at https://github.com/CDCgov/influenza-generation_time-us.

2.5. Ethics statement

This study was reviewed and approved by the IRB at Vanderbilt University Medical Center (see 45 C.F.R. part 46.114; 21 C.F.R. part 56.114).

3. Results

3.1. The household data

During the data cleaning process, we excluded 93 individuals who did not have at least two valid PCR tests and 2 individuals who were the only household members. In the primary analysis, we further excluded 23 individuals from 6 households that had co-primary cases, resulting in a dataset that comprised 820 individuals (including primary cases and household contacts) from 246 households across both seasons (Table 1).

As shown in Table 1, more households were enrolled in the 2022/2023 season. In both seasons, influenza A viruses predominantly circulated. In the 2021/2022 season, influenza A(H3N2) virus was identified in 78 % of individuals, and influenza A(H1N1) virus was identified in 1 % of individuals. In the 2022/2023 season, the corresponding percentages were 64 % and 6 %, respectively. Since households consisting of 3 or 4 members were the majority, we stratified the data into two groups: those with 2 or 3 members, and those with 4 or greater, to ensure comparability in quantity.

Additional stratifications of the household data by vaccination status, age group, and study site are provided in Supplemental Table S1. Most individuals in the dataset were unvaccinated. School-aged children (aged 5–11 years) were the most common group to introduce infections to households as primary cases. Most of the households included in

the study were recruited from Columbia University Irving Medical Center and Vanderbilt University Medical Center.

3.2. Consistent estimates of the generation time across data stratifications and parameter assumptions

In the primary analysis, using data from both seasons and excluding households with multiple co-primary cases, we estimated a mean intrinsic generation time of 3.2 (95 % credible interval, CrI: 2.9–3.6) days (Fig. 1A, 1B and Table 2). The corresponding mean (intrinsic) serial interval was 3.2 (95 % CrI: 2.8–3.5) days, with a standard deviation (SD) of 2.2 (95 % CrI: 1.8–2.6) days. The mean realized household generation time was 2.8 (95 % CrI: 2.7–3.0) days, nearly half a day shorter than the mean intrinsic generation time.

We found no substantial differences in the mean intrinsic generation time estimates across multiple data stratifications (Fig. 1C and Supplemental Table S2). The overlapping indices for both 2021/2022 and 2022/2023 were high at 71 % and 87 %, respectively, when compared with the primary analysis above. Influenza A data showed a notable high overlapping index of 94 %, reflecting its dominance during the study period, as influenza A was identified in 83 % of individuals. Conversely, using the data exclusively from influenza B yielded a similar mean but with a wider credible interval and a lower overlapping index of 47 %. This is likely due to the smaller sample size, as influenza B was identified in only 17 % of the individuals. Upon examining household sizes, although we found slightly longer mean intrinsic and realized household generation times in smaller households compared to larger ones, the overlapping index for household sizes of 2 or 3 members and 4 or more members were moderately high at 61 % and 74 %, respectively. Incorporating households with co-primary cases remained consistent with a moderately high overlapping index of 64 %, indicating the robustness of our results to the exclusion or inclusion of multiple co-primary cases. Similarly, we found no substantial differences when stratifying by the vaccination status of primary cases and their household contacts (Supplemental Table S3).

The mean intrinsic generation time exhibited limited sensitivity to variations in the incubation period (Fig. 1D and Supplemental Table S4). In the primary analysis shown above, we used an incubation period with a mean of 1.55 days and a standard deviation (SD) of 0.66 days by fitting previously published estimates (Lessler et al., 2009) to a gamma distribution (Supplemental Fig. S2). When considering a shorter incubation period, which yielded a mean of 0.61 days and a SD of 0.25 days (Lessler et al., 2009), the mean intrinsic generation time remained unchanged with an overlapping index of 86 %. Conversely, with a longer incubation period, which yielded a mean of 4.30 days and a SD of 1.25 days (Tuite et al., 2010), the mean intrinsic generation time increased slightly with an intermediate overlapping index of 56 %.

Our estimates were not sensitive to changes in the relative infectiousness of asymptomatic infected individuals, due to the limited number of asymptomatic infected individuals in this study (Supplemental Fig. S6). We found no substantial differences in the mean intrinsic generation time estimates (Supplemental Table S4), as indicated by overlapping indices of 94 % and 97 % when using the values of 0.11 and 1.54, respectively, compared to the primary value of 0.57 (Tsang et al., 2023).

3.3. Sensitivity of other transmission parameters to the incubation period

In our sensitivity analyses, where we varied the assumed incubation period from the mean of 1.55 days and SD of 0.66 days, we found significant influences on several pre-symptomatic transmission parameters and the duration of various symptomatic infectious stages (Table 3 and Supplemental Fig. S5).

Notably, given the shorter incubation period (mean of 0.61 days and SD of 0.25 days), the proportion of transmission before symptomatic onset was lower at 3 % (95 % CrI: 0–6 %), and the ratio of pre-symptomatic to symptomatic transmission rates indicated a slightly lower relative infectiousness of symptomatic infected individuals before symptom onset compared to after. This indicates that the majority of transmission occurred after individuals developed symptoms. This was also reflected in a shorter latent period of 0.4 (95 % CrI: 0.2–0.6) days and shorter pre-symptomatic infectious period of 0.2 (95 % CrI: 0.0–0.4) days, or a longer symptomatic infectious period of 2.6 (95 % CrI: 2.3–3.0) days.

Conversely, given the longer incubation period (mean of 4.30 days and SD of 1.25 days), the proportion of transmission before symptomatic onset was higher at 76 % (95 % CrI: 65–87 %), and the ratio of pre-symptomatic to symptomatic transmission rates was also higher. This resulted in a longer latent period of 0.9 (95 % CrI: 0.2–1.6) days and pre-symptomatic infectious period of 3.4 (95 % CrI: 2.7–4.1) days, while the symptomatic infectious period was shorter at 1.2 (95 % CrI: 0.7–1.9) days.

4. Discussion

4.1. Estimates of the generation time

This study employed a Bayesian data augmentation approach (Hart et al., 2021; Hart, Abbott, et al., 2022; Hart, Miller, et al., 2022) to estimate both intrinsic and realized generation times using data collected from a U.S. household study during the post COVID-19 pandemic influenza seasons, 2021/2022 and 2022/2023. Our findings indicate that the intrinsic generation time, reflecting transmission dynamics within community settings, ranged from 2.9 to 3.6 days, while the realized household generation time, restricted to household settings, ranged from 2.7 to 3.0 days. These estimates of the generation time for influenza fall within the uncertainty bounds of pre-pandemic studies, including those that directly used viral shedding data (Carrat et al., 2008) and other contact tracing data (Fraser et al., 2009; te Beest et al., 2013; Lau et al., 2015), with estimates varying between 2 and 4 days. This suggests that there has not been substantial change since the 2009 H1N1 influenza pandemic. Additionally, the overlapping indices of more than 70 % suggested no substantial differences between the two influenza seasons.

Both seasons of this study were atypical, being the first seasons since the COVID-19 pandemic, during which immunity to influenza had potentially decreased and household transmission risks were significantly higher (Rolfes et al., 2023). The 2022/2023 season, in particular, experienced an early influenza activity peak along with RSV and COVID-19. Both seasons were dominated by influenza A(H3N2), and our analyses included parameter assumptions relevant to the virus. The generation time estimates remained similar to those from earlier studies, suggesting that virus transmission dynamics within households have

not changed substantially and may not vary widely between types. However, further work is needed to fully explore estimates for influenza that were less prevalent in this study (i.e., influenza B and A(H1N1)).

Our finding that the realized household generation time was shorter than the intrinsic generation time could be attributed to the depletion of susceptible individuals over time. As household members become infected and develop immunity, although individuals may be temporarily infectious, there are no susceptible contacts still exposed to each case. This depletion terminates transmission chains, diminishing the potential for further infections. This process, along with factors such as closer proximity of contacts and longer exposure times inherent to household settings, can increase the chance of transmission within households, leading to a shorter observed generation time.

Our updated estimates, particularly for the intrinsic generation time, may be useful for ongoing modeling efforts which require estimated generation times, such as real-time influenza R_t estimation (Centers for Disease Control and Prevention, 2024a, 2024b, 2024c; Gostic et al., 2020). Our estimates are slightly shorter than the serial interval estimated at 3.6 days (95 % confidence interval, CI: 2.9–4.3) (Cowling et al., 2009), which is currently used as a proxy for the generation time. This shorter interval suggests more rapid transmission, potentially leading to a higher estimated R_t , and emphasizes the need for prompt and effective interventions to control transmission.

4.2. Reliability of other transmission parameters

Comparing our other parameter estimates with prior research, we found the mean serial interval to be 3.2 days, within the 95 % CI of 2.9–4.3 days reported by Cowling et al. (2009). Our estimate also falls within the 3-to-4-day range of uncertainty reported in previous household studies (Cauchemez et al., 2009; Boëlle et al., 2011; Cowling et al., 2010; Levy et al., 2013; Petrie et al., 2013; Suess et al., 2012; Tsang et al., 2016; Xu et al., 2015).

We estimated a latent period of less than a day, which is shorter than the 1–3 days reported in other studies (Tuite et al., 2010; Cori et al., 2012). It is possible that this shorter latent period could be influenced by undocumented exposures outside households. For instance, both the index case and infected household member may have been exposed to influenza elsewhere, with the index case developing symptoms before the household member. Consequently, when the household member becomes sick, we attribute it to the index case within the household, but this infection could have originated from a previous exposure outside the household, which has not been accounted for in this analysis. Unfortunately, we lack data to identify the source of infection for each individual and assumed that household members were infected within their household. Nonetheless, we excluded households with multiple co-primary cases to reduce these effects and facilitate more accurate assessment of transmission dynamics within each household.

Furthermore, there was substantial uncertainty in our estimates for the symptomatic infectious period, which ranged from 1 day to 3 days for different assumed incubation periods. Likewise, there has been a wide range of estimates in earlier studies, including

those less than a day (Cori et al., 2012) and more than 3 days (Tuite et al., 2010; Cauchemez et al., 2004).

The estimates of the pre-symptomatic transmission parameters and the duration of various symptomatic stages should be interpreted with caution due to inherent uncertainty the assumed incubation period. Our estimates incorporated values from various studies based on different types or subtypes of influenza (Lessler et al., 2009; Tuite et al., 2010). This variability in the incubation period contributes to a wide range of pre-symptomatic transmission parameters. Without a reliable input for the incubation period, accurately determining these transmission dynamics becomes challenging.

4.3. Implications for preventing transmission

Understanding the proportion of transmission that occurs prior to symptoms is critical to informing effective disease control strategies and assessing the potential impact of post-symptomatic mitigation measures, such as isolation of cases. We estimated that between 3 % and 76 % of transmission may occur before a person develops symptoms. This wide range was influenced by different assumed incubation periods, which were taken from a variety of previously published estimates. Longer incubation periods yielded higher estimates of the percentage of transmission that occurred before symptoms. Similarly, estimates of individual-level pre-symptomatic transmission derived from viral kinetics data have also revealed substantial heterogeneity (Morris et al., 2024). Despite such variation, these analyses highlight that pre-symptomatic transmission of influenza does occur, aligning with findings for other respiratory pathogens like SARS-CoV-2 (Buitrago-Garcia et al., 2022).

Given the wide range of estimates for pre-symptomatic transmission, relying solely on isolation of symptomatic individuals may reduce but not eliminate influenza transmission. Although isolation measures initiated after symptom onset are likely to mitigate at least some influenza spread, given the relatively low levels of asymptomatic infection and pre-symptomatic transmission among the majority of individuals, there remains large heterogeneity (Morris et al., 2024). A layered approach, including isolation of ill or infected people, maintaining good respiratory hygiene, and promoting influenza vaccination, may be most effective to reduce transmission within households (Centers for Disease Control and Prevention, 2024a, 2024b, 2024c). This underscores the importance of vaccination as the primary recommendation to prevent influenza-associated morbidity and mortality, especially for individuals at increased risk of influenza complications.

4.4. Modeling details and limitations

While our reliance on household data might introduce limitations, such as the presence of multiple co-primary cases, sensitivity analyses confirmed the robustness of our generation time estimates to various data stratifications and model assumptions. For example, when considering the potential influence of different vaccination statuses on the generation time, we found that the vaccination status of primary cases and their household contacts did not significantly impact our estimates (Supplementary material). This may be due to similarities

in influenza viral load dynamics between infected vaccinated and unvaccinated individuals (Morris et al., 2024; Suess et al., 2012).

Although our research provides significant contributions, there are several limitations to our study. First, we did not account for potential exposures outside households. This makes determining certain transmission parameters, such as the latent period, challenging. Contact tracing data would be necessary to accurately estimate detailed transmission dynamics within and beyond households.

Second, when we excluded household members who did not have at least two valid PCR tests, some household sizes were reduced in our analysis. While this might not directly affect our generation time estimates, it could lead to an overestimation of overall infectiousness due to the absence of unobserved uninfected members.

Third, we acknowledge the potential influence of the COVID-19 pandemic on our influenza data. Generalizing these findings to pre-pandemic or post-pandemic periods should be done with caution. During the period when this study was conducted, individuals may have been more likely to adopt preventive measures against transmission within the home, such as self-isolating, practicing good respiratory and hand hygiene, wearing masks, and reducing contact with household members. Although the virological characteristics of the influenza virus might not have changed, these non-pharmaceutical interventions, alongside changes in human behavior and heightened awareness of infection control, could have impacted the spread of influenza.

5. Conclusions

Through comprehensive data collected during the 2021/2022 and 2022/2023 influenza seasons in the U.S., we provide updated estimates of the generation time, essential for informing influenza modeling and public health strategies. Despite significant changes in public behavior and preventive measures due to the COVID-19 pandemic, our study did not detect substantial changes in the generation time of influenza since the 2009 influenza pandemic. This finding is particularly significant given that the study period followed the implementation of extreme measures to prevent COVID-19, which also reduced the transmission of influenza and other respiratory infections. Our findings contribute to the understanding of influenza transmission dynamics within households and underscore the importance of ongoing research for effective outbreak management.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data sharing statement

The household data are available upon reasonable request and upon completion of required approvals. The R code for estimating the generation time is available at https://github.com/CDCgov/influenza-generation_time-us.

Data availability

Data will be made available on request.

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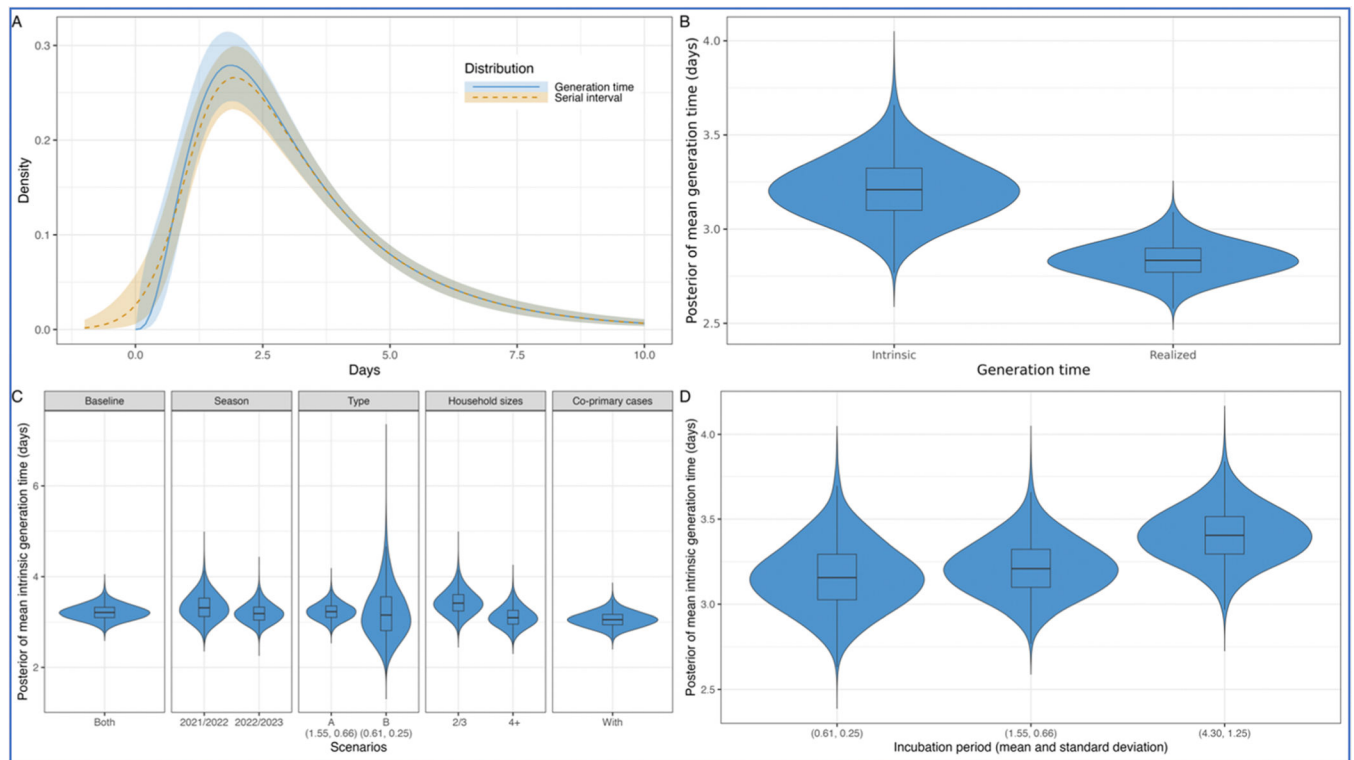
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**Fig. 1.**

(A) Distributions of the intrinsic generation time and serial interval obtained from the posterior samples. The lines represent the median, and the shaded areas denote the 95 % credible intervals (CrI). The blue color represents the intrinsic generation time distribution, while the orange color represents the serial interval distribution. (B) Posterior distributions of the mean intrinsic and realized household generation times. (C) Posterior distributions of the mean intrinsic generation time across seasons, virus types, household sizes, and with multiple co-primary cases. The incubation period, derived from influenza A, had a mean of 1.55 days and a standard deviation (SD) of 0.66 days (Lessler et al., 2009). Only for influenza B, we assumed the shorter incubation period which yielded a mean of 0.61 days and a standard deviation (SD) of 0.25 days (Lessler et al., 2009). (D) Posterior distributions of the mean intrinsic generation time estimated using the full dataset across different incubation periods.

Table 1

Characteristics of household data. The first row presents the primary analysis, along with three data stratifications by season, virus type, and household size, which all excluded households with multiple co-primary cases. The last row, as a sensitivity analysis, included households both with and without multiple co-primary cases.

Data stratifications	Number of individuals (households)	Symptomatic infected household members %	Asymptomatic infected household members %	Uninfected household members %
All data excluding households with multiple co- primary cases (primary analysis)	820 (246)	59.4 % (487/820)	7.2 % (59/820)	33.4 % (274/820)
By season				
– Season 2021/2022	308 (90)	59.4 % (183/308)	7.5 % (23/308)	33.1 % (102/308)
– Season 2022/2023	512 (156)	59.4 % (304/512)	7.0 % (36/512)	33.6 % (172/512)
By virus type				
– Influenza A	683 (209)	61.1 % (417/683)	7.5 % (51/683)	31.5 % (215/683)
– Influenza B	137 (37)	51.1 % (70/137)	5.8 % (8/137)	43.1 % (59/137)
By household size				
– Household size of 2 or 3	393 (152)	62.6 % (246/393)	5.3 % (21/393)	32.1 % (126/393)
– Household size of 4 or greater	427 (94)	56.4 % (241/427)	8.9 % (38/427)	34.7 % (148/427)
All data including households with multiple co-primary cases	843 (252)	60.3 % (508/843)	7.0 % (59/843)	32.7 % (276/843)

Table 2

Posterior mean (95 % CrIs) of estimates in the primary analysis using the full dataset. The incubation period, derived from influenza A, had a mean of 1.55 days and a standard deviation (SD) of 0.66 days (Lessler et al., 2009). The relative infectiousness of asymptomatic infected individuals compared with symptomatic infected individuals was assumed to be 0.57 (Tsang et al., 2023).

	Mean	SD
Intrinsic generation time (days)	3.2 (2.9–3.6)	2.1 (1.8–2.5)
Realized household generation time (days)	2.8 (2.7–3.0)	1.6 (1.5–1.8)
Serial interval (days)	3.2 (2.8–3.5)	2.2 (1.8–2.6)

Table 3

Posterior mean (95 % CrIs) of estimates of the generation time and transmission parameters given different assumed incubation periods. The primary incubation period, derived from influenza A, had a mean of 1.55 days and a standard deviation (SD) of 0.66 days (Lessler et al., 2009). The shorter incubation period, derived from influenza B, yielded a mean of 0.61 days with a SD of 0.25 days (Lessler et al., 2009), while the longer incubation period, derived from influenza A(H1N1)pdm09, had a mean of 4.30 days with a SD of 1.25 days (Tuite et al., 2010). The relative infectiousness of asymptomatic infected individuals compared with symptomatic infected individuals was assumed to be 0.57 (Tsang et al., 2023).

Incubation period	Shorter	Primary	Longer
Mean intrinsic generation time (days)	3.2 (2.8–3.6)	3.2 (2.9–3.6)	3.4 (3.1–3.7)
Proportion of transmission before symptomatic onset	0.03 (0.00–0.06)	0.16 (0.07–0.25)	0.76 (0.65–0.87)
Ratio of pre-symptomatic and symptomatic transmission rates	0.6 (0.1–1.7)	0.7 (0.2–1.9)	1.3 (0.5–3.2)
Latent period (days)	0.4 (0.2–0.6)	0.9 (0.2–1.4)	0.9 (0.2–1.6)
Pre-symptomatic infectious period (days)	0.2 (0.0–0.4)	0.7 (0.2–1.3)	3.4 (2.7–4.1)
Symptomatic infectious period (days)	2.6 (2.3–3.0)	2.0 (1.7–2.4)	1.2 (0.7–1.9)