# Incorporating Equity in Influenza Vaccination Strategies: An Assessment of Neighborhood Disadvantage and Influenza Outcomes

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## Abstract

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The Centers for Disease Control and Prevention (CDC) estimates that influenza vaccinations prevented 9.8 million influenza-related illnesses, 120,000 influenza-related hospitalizations, and 7,900 influenza-related deaths in 2023 – 2024. However, influenza vaccination rates are declining and fall short of the Healthy People 2030 goal of 70%. Improving vaccination rates is important to reduce the influenza burden. In developing new strategies, public health leaders should apply lessons from COVID-19 vaccine allocation to prioritize equity in reducing respiratory infectious diseases and to prevent worsening health disparities.

One approach to assessing disparities could use the area deprivation index (ADI), a composite Census block-group score that reflects neighborhood disadvantage. To our knowledge, few studies have evaluated neighborhood disadvantage and individual influenza outcomes in a nationally representative sample. This dissertation uses data from the CDC-funded US Flu Vaccine Effectiveness (Flu VE) Network, the largest network of ambulatory vaccine effectiveness studies, to assess the association between ADI and influenza outcomes

and to conduct a cost-effectiveness analysis to inform routine vaccination programs that prioritize equitable strategies to increase vaccination rates.

In **Chapter 1**, we examine associations between area deprivation index and influenza outcomes among 2023 – 2024 US Flu VE study participants. We constructed several modified Poisson regression models with robust standard errors to estimate risk ratios (RRs) for influenza outcomes (test positivity and vaccine uptake) by two ADI categorization types: relative and percentile-based. These exploratory analyses were conducted to estimate RRs across ADI categories, examine the impact of including Network site in the models, and assess the influence of covariates on the results. In **Chapter 2**, we use a retrospective cohort design to conduct modified Poisson regression analyses adjusted for age, sex, race, ethnicity, smoking exposure, history of a high-risk condition, month of illness onset, and calculate RRs for influenza outcomes by participants' ADI quartile categories. Vaccine effectiveness by ADI quartile was also estimated. In **Chapter 3**, we analyze the cost-effectiveness of a hypothetical targeted influenza vaccination strategy to increase coverage among the most disadvantaged, using results from Chapter 2 to estimate equitable implementation. We built a decision tree model to estimate the health and economic outcomes of an intervention strategy over one year for 20 subgroups, based on disadvantage measured by ADI (4 groups, with Quartile 4 as most disadvantaged) and age (5 groups). To assess whether the intervention strategy improved equity, we calculated the incremental cost-effectiveness ratio across a range of inequality-aversion parameters, the Atkinson index, and the proportion of health benefits gained by the most disadvantaged.

We found that ADI scores varied substantially across sites, and relative quartile categorization best balanced interpretability with sufficient population sizes. Study-site adjustment was outcome-dependent: site was retained for assessing associations between ADI and vaccine uptake but excluded for test positivity, where it over-adjusted for the socioeconomic signal ADI captures. Participants in the most disadvantaged neighborhoods were the least likely

to be vaccinated and the most likely to test positive, though vaccine effectiveness did not differ significantly across quartiles. Lastly, we found the hypothetical targeted intervention was cost-effective (ICER $262/QALY against a $100,000/QALY threshold), and incorporating equity weighting strengthened the case: the equity-weighted ICER fell to $216/QALY, the Atkinson index dropped roughly 15%, and all incremental QALYs accrued to the most disadvantaged quartile.

Neighborhood disadvantage is a meaningful and measurable driver of influenza disparities in the Flu VE Network. ADI should be operationalized as relative quartiles with outcome-specific site adjustment, and influenza prevention programs should prioritize the most disadvantaged communities, where targeted vaccination is both cost-effective and equity-improving. Future analyses should incorporate state-level vaccination policy to further reduce geographic residual confounding.

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## Dedication

To people domestically and internationally who have been pierced by the injustices and systemic oppression perpetrated by the United States of America. May we all be free.

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## Introduction

The concept of this dissertation was informed by the Fundamental Cause Theory (FCT). Developed by Link and Phelan in 1995, the FCT was initially introduced to explain how socioeconomic inequalities in health outcomes persist, hypothesizing that "people and collectivities use their knowledge, money, power, prestige, and social connections to gain a health advantage".[1] In this sense, the FCT argues that health disparities are developed because individuals can access and use resources, i.e. knowledge, money, power, prestige and social connections, to gain a health advantage and protect themselves from disease. In 2015, the authors added structural racism as an additional fundamental cause, arguing it operates both by shaping access to these resources and as an independent driver of disadvantage.[2]

Previous studies have used the FCT to explain differences in respiratory virus infections, more recently COVID-19, due to the global outbreak and the notable racial and socioeconomic disparities in illness and mortality, as well as access to resources such as vaccines, that arose as a result.[3–6] The historical legacy of segregation has concentrated disadvantage and disinvestment in marginalized communities, with ripple effects that influence economic opportunities, occupational risks, housing quality, and environmental stressors, creating racial and socioeconomic disparities. These disparities are evident during stable periods and become more pronounced during crises such as pandemics, which is why sociodemographic disparities should be incorporated into analyses of respiratory disease to identify the structural changes needed to prevent worsening inequities.[7]

Since disadvantages are geographically concentrated, area-level socioeconomic status indices offer a practical way to measure socioeconomic disadvantage and vulnerability. One commonly used measure of neighborhood sociodemographic characteristics is the Area Deprivation Index (ADI), a weighted composite neighborhood score based on 17 Census variables related to income, education, employment, and housing. ADI scores have been widely used as a health policy tool and can be linked to individual- or geographically based data to

identify socioeconomic disadvantages and inform program planning, research, and policy development.[8] ADI scores are typically calculated for block groups with 600 to 3,000 people.[9] Its finer geographic unit of analysis and established use in policy make it useful for targeting neighborhood-level influenza interventions such as education, outreach, and mobile clinics.

Another widely used index is the Social Vulnerability Index (SVI). While ADI and SVI utilize the same data sources, the SVI was developed to aid in disaster management and pinpoint at-risk populations for local response and relief planning.[10] The most notable difference in calculation between ADI and SVI is the inclusion of race and ethnicity and language spoken in SVI. SVI assumes that social and economic marginalization has made all persons, except White, non-Hispanic populations, more vulnerable during disasters, while the lack of non-English translations in disaster communication further increases the risk for immigrant communities.[10] ADI's exclusion of race does not make it race-neutral in effect, but rather captures the concentrated material disadvantage that structural racism produces, while leaving race as a distinct variable to be examined alongside it rather than embedded within the exposure. For a non-emergency, seasonal respiratory virus like influenza, ADI's policy orientation and neighborhood-level granularity made it the more appropriate choice throughout this work.

Throughout all chapters, we used data from the 2023–2024 US Flu Vaccine Effectiveness Network to build on our findings. We first established a methodological base for an epidemiologic analysis, which then helped develop a model for practical economic and equity assessments of a targeted vaccination intervention strategy. In **Chapter 1**, we examine associations between area deprivation index and influenza outcomes among 2023 – 2024 US Flu VE study participants. We constructed several modified Poisson regression models with robust standard errors to estimate risk ratios (RRs) for influenza outcomes (test positivity and vaccine uptake) by two ADI categorization types: relative and percentile-based. These exploratory analyses were conducted to estimate RRs across ADI categories, examine the impact of including Network enrollment site in the models, and assess the influence of covariates on the

results. In **Chapter 2**, we use a retrospective cohort design to conduct modified Poisson regression analyses adjusted for age, sex, race, ethnicity, smoking exposure, history of a high-risk condition, month of illness onset, and calculate RRs for influenza outcomes by participants' ADI quartile categories. Vaccine effectiveness by ADI quartile was also estimated. In **Chapter 3**, we conducted a distributional cost-effectiveness analysis, drawing on results from Chapter 2, to estimate the economic and health outcomes of universal, routine pediatric and adult influenza vaccination strategies over a 1-year time horizon.

Altogether, these analyses support recommendations for the integration of socioeconomic and continual analysis of disparities in respiratory illness.

# Chapter 1: Model Building Using US Flu VE Network Data, 2023–2024, to Examine Associations Between the Area Deprivation Index and Influenza Outcomes

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*ABSTRACT*

*Introduction:* Area-level socioeconomic measures, such as the Area Deprivation Index (ADI), are widely used to assess associations between neighborhood disadvantage and health outcomes, including influenza infection and vaccination. However, no standardized method exists for categorizing ADI scores in nationally representative datasets, and prior respiratory-infection research has used binary, tertile, quartile, quintile, or decile categorizations. A related challenge is geographic confounding: US Flu Vaccine Effectiveness (Flu VE) Network analyses routinely adjust for study site, but because both site and ADI are geographically defined, adjusting for site may overcorrect for the socioeconomic disadvantage ADI aims to capture. In this first application of ADI to Network-wide data, we aimed to recommend a standardized ADI categorization and to evaluate whether study site should be retained when estimating ADI-influenza associations, improving the interpretation and reproducibility of future Network analyses.

*Methods:* We analyzed 7,898 participants enrolled across seven sites in the 2023–2024 Flu VE Network. We first characterized the variation and geographic distribution of ADI scores. Using a retrospective cohort study design, we then used modified Poisson regression models with robust standard errors to estimate unadjusted and adjusted risk ratios (RRs) for two influenza outcomes (laboratory-confirmed influenza and receipt of the seasonal vaccine) across ADI categories. Models with and without study site were compared using the Bayesian Information Criterion (BIC) and theoretical considerations, and site-stratified analyses assessed the consistency of ADI associations across sites.

*Results:* ADI scores and population characteristics differed across study sites. ADI was divided into quartiles to ensure interpretability and sufficient cell sizes. This categorization maintained the disadvantage gradient that a binary categorization would obscure while preventing the smaller categories that finer divisions might create. Participants in the most disadvantaged neighborhoods (Q4) were significantly less likely to be vaccinated than those in the least

disadvantaged (Q1) across all vaccination models. For test positivity, site adjustment attenuated the ADI association, and BIC comparisons, along with theoretical considerations, indicated that site likely serves as a proxy for ADI in this outcome. The final vaccine uptake model included site, while the test positivity model did not.

*Conclusion:* Given the post-COVID regional differences in vaccine uptake and policies, study site should be retained as a covariate when assessing ADI and influenza vaccine uptake. However, including the site in models predicting test positivity tends to weaken the ADI association, likely due to over-adjustment. Therefore, we recommend excluding it when assessing the overall impact of neighborhood disadvantage on influenza illness. Future Network analyses should also incorporate a measure of state-level vaccination policy to better capture geographic variation and reduce residual confounding.

## *INTRODUCTION*

The 2023–2024 influenza (flu) season was the first season since the COVID-19 pandemic to return to pre-pandemic intensity and seasonality. Across all age groups, the season was classified as moderate, based on rates of influenza-like illness, hospitalization and deaths.[11] Annually, influenza illness rates vary by age group and across seasons due to factors such as antigenic vaccine matching, reduced vaccine immunogenicity, the timing of influenza peaks, and behavioral differences, including vaccine uptake and healthcare-seeking behaviors.[12] Other sociodemographic factors, such as race, ethnicity, education, and income, further explain variation in influenza illness rates across groups.[13–15] While individual-level data explain how influenza affects people, area-level socioeconomic data reveal disparities and highlight where resources could be focused.

Area-level socioeconomic measures, such as the area deprivation index (ADI), have been used to assess the relationship between neighborhood disadvantage and health outcomes, including viral respiratory infections.[16–18] However, there is no single method for categorizing ADI scores on nationally representative datasets to optimally estimate the associations; prior research on ADI and respiratory infections has used binary categorization, as well as tertiles, quartiles, quintiles, or deciles.[19] This study is the first application of ADI to the US Flu Vaccine Effectiveness (Flu VE) Network-wide data. We aimed to provide recommendations for ADI categorization in this population to improve the interpretation and reproducibility of Network analyses evaluating ADI and influenza outcomes: lab-confirmed influenza and receipt of the seasonal vaccine.

Historically, Network analyses, particularly estimates of medically attended influenza vaccine effectiveness, have adjusted for study site to account for differences in clinic types, recruitment pools, and geographic variation in influenza trends.[20] However, study site lacks the granularity needed to understand how where a person lives influences influenza outcomes. As vaccination and exposure have become more geographically linked, especially after the COVID-

19 pandemic's effects on public trust in science and changes in federal and state vaccination policies, finer geographic analyses have grown increasingly important for strategic interventions.[21,22] ADI offers this level of socioeconomic granularity, but because it is also geographically defined, site and ADI may capture overlapping information, making it possible that adjusting for site could over-adjust for the socioeconomic disadvantage ADI is meant to measure.

This study had two objectives. First, to characterize the variation and geographic distribution of ADI scores across the US Flu VE Network population and to recommend a standardized categorization method. The second objective, built on the selected categorization, was to examine how estimated associations between ADI and lab-confirmed influenza and receipt of the seasonal vaccine, vary with and without study-site adjustment. Since ADI and study site are both geographically defined, we hypothesized that adjusting for site would attenuate the associations between ADI and influenza outcomes, masking the socioeconomic differences ADI is intended to capture, and therefore, anticipated that site should not be included as a covariate in future Network models assessing these relationships.

*METHODS*

We first calculated the median score and interquartile range for three ADI categorization types: binary, quartile, and quintile. Secondly, we leveraged a retrospective cohort study design using data from the US Flu VE Network to run several modified Poisson regression models with robust standard errors to estimate risk ratios (RRs) for participants' ADI categorization and influenza outcomes: flu vaccination (vaccinated/ unvaccinated) and influenza test positivity (positive/negative), adjusting for and without study site. The Centers for Disease Control and Prevention (CDC) reports seasonal influenza test positivity by age groups; we also compared models with age as a continuous variable to those adjusted for age as categorical variables that mirror the CDC's age groups. The Bayesian Information Criterion (BIC) was used alongside theoretical considerations to guide decisions about whether to retain the site variable in each

model and whether to keep age as categorical or continuous. Lastly, site-stratified analyses were conducted to examine the consistency of ADI associations across Network sites.

**Directed Acyclic Graph**

For the purposes of this study, participants' neighborhood deprivation scores were assessed to estimate associations with influenza test positivity and vaccine uptake (**Figure 1.1**). The FCT authors posited that structural racism is both a core driver of socioeconomic resources and a separate fundamental cause; this factor was explicitly isolated and integrated into the graph. Structural racism is connected to the area deprivation index and its components, especially the housing and poverty measures, which are influenced by segregationist policies such as redlining, discrimination, and biased employment practices.[2] While ADI helps identify community socioeconomic differences and resources, it may not detect all inequities, and some disparities could persist even after accounting for ADI.[23] Additional research is needed to assess the processes, policies, and practices that lead to the unequal distribution of resources, using ADI as a measure.

**Study Procedures**

The US Flu VE Network has one of the few available datasets that combines individual-level vaccination history, laboratory-confirmed influenza, and neighborhood disadvantage across multiple states. For over 20 years, the US Flu VE Network has provided clinical effectiveness estimates of licensed flu vaccines and has played a crucial role in local influenza surveillance. The Network was primarily designed to evaluate influenza vaccine effectiveness against medically-attended influenza by age group, virus type, and subtype across study sites. At baseline enrollment, participants consent to participation, complete a baseline survey, and provide nasal and/or oropharyngeal swabs for laboratory testing. Seven study sites enrolled participants: Arizona State University Tempe (Arizona); University of Michigan (Michigan); Washington University at St. Louis (Missouri); University Hospitals Cleveland (Ohio); University of Pittsburgh (Pennsylvania); Baylor Scott & White Health (Texas); Kaiser Permanente Washington (KPWA)

(Washington). For the 2023-2024 season, participants consented to have their addresses geocoded for linkage to ADI scores.

*Measures*

*Exposure (ADI categorization):* ADI scores range from 0 to 100 on a national scale, with 0 representing the lowest disadvantage and 100 representing the highest disadvantage. Studies on respiratory infections in the US have used ADI scores in multiple ways, including as a single score, as a national or state ranking, or as categorization.[24–27] We evaluated ADI as a binary variable, quartiles, quintiles, and as relative and percentile categorizations for each category.

*Outcome - Influenza Vaccination:* For the 2023–2024 season, the influenza vaccine was a quadrivalent formulation that included 2 influenza A antigens and 2 influenza B antigens: one H1N1 virus, one H3N2 virus, one B/Victoria virus, and one B/Yamagata virus.[20,28] For the purpose of the study, being vaccinated against influenza is defined as receiving any influenza vaccine after July 1, 2023. Receipt of the flu vaccine at least 14 days before illness onset was confirmed by combining data from plausible self-reports, electronic health records, and state records, and dichotomized as vaccinated and unvaccinated.

*Outcome - Influenza Test Positivity:* At enrollment, staff collect swab specimens to be tested for influenza by a Clinical Laboratory Improvement Amendments-certified laboratory. Influenza specimens that test positive undergo further testing to determine subtype and lineage. For this study, influenza-test positivity relies on laboratory-confirmed test results from the swabs to dichotomize results as positive or negative for any influenza type.

*Covariates:* The following variables were included as covariates in the study analysis: age, tobacco history and exposure, race, ethnicity, month of illness onset, enrollment site, and history of a high-risk condition. The rationale for including each variable is as follows:

*Age:* Age was included in the models as a categorical variable to align with prior vaccine effectiveness studies and vaccination recommendations, and to reflect infection trends.[20,29,30]

Children 8 years and younger are eligible to receive up to 2 doses, based on their vaccination history.[30] For the 2023 – 2024 season, people aged 18–49 and under 8 years old had the highest infection rates, while those aged 50 years and older showed the highest vaccination uptake in outpatient settings.[20]

*Tobacco history:* People with a history of tobacco use or exposure to smoke from tobacco are more susceptible to respiratory irritation and weakened immune responses, which subsequently increase the risk of influenza complications.[31,32] Research indicates that current users of tobacco are less likely to receive influenza vaccines compared to those who have never used tobacco, further raising their risk of infection and respiratory problems.[32] Finally, tobacco use and indoor environmental tobacco smoke reflect socioeconomic disparities, with lower socioeconomic groups more likely to be exposed smoke.[33]

*Race and Ethnicity:* When evaluating influenza outcomes by race and ethnicity, non-White populations bear a disproportionately higher disease burden. Additionally, one study showed that while non-White populations, specifically Black and Hispanic individuals, had higher rates of respiratory viruses, community-level racial distribution was not a major confounder of the association between an individual's race and ethnicity and the prevalence of respiratory viruses. This suggests that neighborhood disadvantage metrics may not fully account for these disparities, implying that other factors may play a more significant role.[27] Individual factors related to race and ethnicity, such as disproportionate occupational exposures, health behaviors, and access to health insurance and preventative care, are leading factors that increase susceptibility to infection.[4,27] Ultimately, these individual factors may also be linked to varying exposure caused by segregation and other types of discrimination. When considering variables such as race and ethnicity, it is vital to remember the Fundamental Cause Theory and Zelner et al.'s model, which examine how structural racism leads to downstream effects on individual and neighborhood vulnerability.[4,34] This understanding helps explain how racism perpetuates systems that contribute to disparities in infection risk, disease severity, and mortality. The inclusion of race and ethnicity

in the models aims to illuminate racial disparities but cannot fully explain or be a substitute for the measurement of structural racism.

*Month of Illness Onset:* The 2023 – 2024 influenza season was considered "moderate" across all age groups, with the CDC noting influenza activity had returned to levels experienced prior to the 2020 COVID-19 pandemic. Influenza test positivity peaked the last week of December, with a smaller peak occurring in February 2024.[11,35] Differences in the timing of vaccine uptake also exist, as influenza vaccination is generally recommended earlier in the season (i.e. starting in late September rather than in the spring). The month of illness onset is recorded in the baseline survey conducted after enrollment, in which participants are asked to specify the date their illness began. Considering the seasonal variability of influenza, including temporal and regional differences in prevalence, the month of illness onset was included in all models as it is a valuable variable for controlling for these factors.

*Inclusion of Network Enrollment Site:* Though all sites recruit in outpatient medical settings and use a standardized protocol, they differ in the types of medical organizations, the locations of their clinical sites, and the populations they serve. Additionally, there are differences across states in immunization policy and coverage. Although most insurance plans cover influenza vaccine free of charge, uninsured or underinsured adults and children can receive vaccines through healthcare providers in the public and private sectors who are enrolled to accept federal funding under Section 317.[36] Besides financial accessibility, an individual's ability to be vaccinated depends on various factors, including attitudes towards vaccination, motivation, and practical concerns, as described in the "Behavioural and Social drivers of Vaccination" (BeSD) framework.[37] In the multivariate models, it was important to include regional differences due to variations in vaccination policies, access to vaccine clinics, and regional attitudes towards the influenza vaccine. Regarding test positivity, most participating sites were in Health and Human Services Regions 5 (Midwest) and 3 (Mid-Atlantic), with the remaining three in Regions 10 (Pacific Northwest), 9 (West Coast), and 6 (South Central). Based on clinical laboratory testing, regional

differences in peak influenza activity were observed. Regions 9 and 10 experienced their peaks earliest, in mid-December, followed by peaks in the other regions: Region 3 in late December, Region 6 in late January, and Region 5 in late February.[35] Studies by the Network have previously adjusted for site in estimations of vaccine effectiveness.

*History of High-Risk Conditions:* The models were adjusted for history of at least one high-risk condition, as assessed through electronic health records and baseline enrollment surveys. We used the CDC-formulated variable used in vaccine effectiveness studies. High-risk conditions include: heart or lung disease, diabetes, cancer, and liver failure. Influenza vaccination is strongly recommended for individuals with the listed high-risk conditions, as they face a greater risk of complications from influenza.[38] Previous research has shown that these high-risk conditions vary by vaccination status, socioeconomic status, and geographical location.[39–41]

**Statistical analysis**

For these analyses, we assessed two categorization methods: relative and percentile-based. “Relative” categories were based on population distributions, such as the median for comparing high versus low in a binary category, while “percentile” categories were based on raw scores, such as scores above or below 50. We assessed categorization by its interpretability and adequate cell sizes. After selecting the ADI categorization, we ran models to evaluate the impact of including the Network enrollment site.

We ran several exploratory modified Poisson regression models with robust standard errors to estimate risk ratios (RRs) for influenza outcomes by ADI categorization. This method was selected because the two influenza outcomes were binary and sufficiently common that odds ratios would overestimate the risk ratio. Additionally, modified Poisson regression avoids potential convergence problems when log-binomial models fail. These exploratory analyses were conducted to estimate RRs across ADI categories, examine the impact of including Network enrollment site in the models, and assess the influence of covariates on the results.

Since both ADI and site are geographically dependent, a one-way ANOVA test was run first between ADI and site to determine if the average ADI scores differed across sites. We compared sets of models where influenza vaccination was the dependent variable and included all covariates, both with and without Network site. Additionally, we ran a similar set of models using test positivity as the dependent variable, again with and without Network site. The Bayesian Information Criterion (BIC) was used to compare model fit, with preference given to the model with the smallest BIC, as it balances goodness-of-fit with model complexity and reduces the risk of overfitting. Finally, we conducted site-specific analyses by stratifying the dataset by Network site. Separate modified Poisson regression models with robust standard errors were fit for each site to estimate risk ratios and corresponding 95% confidence intervals. Statistical significance is set at an alpha of 0.05, and RStudio (Version 2021.09.1) was used.

*RESULTS*

Median ADI scores and population distributions differed across the overall study population and within sites across various categorizations (**Table 1.1**). When evaluating the potential categorization of ADI, binary classification oversimplified the exposure, minimized the gradient of disadvantage, and limited our ability to distinguish meaningful associations across ADI categories. Percentile-based categorization, though informative, is more suitable with a larger, nationally representative dataset. Although all sites had a wide range of ADI scores, most sites' median scores were above 50 (**Supplemental Table 1.6**); since the study population's scores tend to cluster towards the more disadvantaged part of the national distribution, we categorized ADI based on the study population rather than national percentiles. When comparing the remaining categorization options (quintiles versus quartiles), quartiles were preferred over quintiles. Quartile categorization resolved differences within the middle 50% of the distribution while preserving adequate group sizes. Therefore, relative quartile ADI categorization was chosen as the exposure variable, with Quartile 1 representing the 25% of the study population with the

lowest ADI scores (least disadvantage), and Quartile 4 representing the highest disadvantage within the study population.

A one-way ANOVA confirmed that mean ADI scores differed significantly across sites ($p < 0.001$), and the large effect size (eta-squared = 0.334) indicated that approximately one-third of the variation in ADI scores was attributable to differences between Network sites. This substantial overlap between site and ADI raised the possibility that adjusting for site could attenuate the association between ADI and influenza outcomes, concealing the socioeconomic gradient ADI is intended to capture. To assess this directly, we fit models with and without site for each influenza outcome: vaccination status and test positivity. Models with and without site were run for each influenza outcome: vaccination status and test positivity; **Table 1.2** lists the descriptions of each model. Using vaccination history as the outcome, we first assessed the associations with ADI and vaccination (Model 1). Then, we analyzed these associations while adjusting for all covariates, including site (Model 2), excluding site (Model 3), and with age modeled as a continuous variable (Model 4). With test positivity as the outcome, we evaluated associations with ADI and test positivity (Model 5), then examined associations adjusted for all covariates, including site (Model 6), excluding site (Model 7), and with age treated as a continuous variable (Model 8).

With influenza vaccination as the outcome, the fully adjusted model (Model 4), including site and age as a continuous variable, had the lowest BIC. Although the BIC value for the model with continuous age was lower, we ran only models with age as a categorical variable, as it was considered more helpful for interpretation and comparison with other vaccine studies. For test positivity, the fully adjusted model with age as a categorical variable (Model 6) had the lowest BIC (**Table 1.2**).

Three models were run to estimate the risk ratio between ADI categorization and influenza vaccination: unadjusted, adjusted for all covariates including site, and adjusted for all covariates except site. After adjusting for site, participants in quartile 4 were 23% less likely to be vaccinated (RR = 0.77, 95% CI: 0.70-0.84) than those in quartile 1 (**Table 1.3**). When we removed site from

the adjusted covariates, the risk ratio was similar in magnitude and precision, with overlapping confidence intervals (**Table 1.3**).

Similarly, three models were run to estimate the risk ratio for test positivity by ADI category. Compared with participants in quartile 1, there was no statistical difference in the likelihood of testing positive for influenza after adjusting for site (**Table 1.3**). However, when site was removed from the adjusted covariates, participants in quartile 4 were approximately 18% more likely to test positive for influenza (RR = 1.18, 95% CI: 1.04-1.34) than participants in quartile 1. To better understand the relationship between site and test positivity, we stratified the dataset by site and ran adjusted models for each site. Among participants from Missouri, Ohio, and Washington, those in quartile 4 were more likely to test positive than those in quartile 1. Missouri was the only site where participants in quartiles 2 to 4 were statistically more likely to test positive (**Table 1.4**). There were no statistical differences between quartiles among participants in Arizona, Michigan and Texas.

*DISCUSSION*

Using the 2023–2024 Flu VE Network dataset, we analyzed the variation and distribution of ADI scores to decide on the type of ADI categorization; the relative quartile categorization was favored as the exposure variable. We estimated both unadjusted and adjusted risk ratios for laboratory-confirmed influenza and seasonal vaccine receipt across ADI quartiles and examined how including the site in the models affected these estimates. We had aimed to incorporate an area-level SES measure with ADI as the exposure; our initial reason for including the site was to account for differences in recruitment, population, and local influenza activity.

We observed that the risk ratio for receiving the seasonal influenza vaccine remained similar in magnitude and precision, with overlapping confidence intervals, whether site was included or removed. Conversely, when the outcome was test positivity, the attenuation of the aRRs following inclusion of the site suggests residual geographic confounding not fully accounted

for by the ADI. Alternatively, since the Network site may lie on the pathway between neighborhood deprivation and testing, inclusion as a covariate in the model is more likely to lead to over-adjustment, potentially underestimating the full effect of ADI. Because the recruitment protocol was consistent across sites and the association between ADI and test positivity remained significant even when using local influenza activity rather than site as a covariate, this potentially undermines the original examination.

Adjusting for site in vaccine effectiveness studies may account for variations in population types or local influenza activity. Vaccine effectiveness studies have incorporated Network site as a covariate, aligning with the test-negative design, which involves calculating the vaccination ratio among patients seeking medical care for acute respiratory illness symptoms.[20,42] Additionally, for vaccination specifically, incorporating the site may also account for state-level differences in vaccine policy (e.g., vaccination coverage among under- or uninsured individuals). Vaccine coverage is tied to the recommendations of the Advisory Committee on Immunization Practices (ACIP), a federal advisory committee that develops national guidelines for vaccine use in the U.S., which mandate that all payers, except Medicare Part B, must offer no-cost coverage for these vaccines.[43] However, in response to the 2025 initiatives by Secretary of Health and Human Services Robert F. Kennedy Jr. to limit vaccine access, states have begun expanding vaccine availability to ensure continued access, with geographic differences in policy linked to political party affiliation.[44] Already, access to primary care, including preventive vaccinations, tends to be lower in areas with higher social vulnerability. Areas with higher vulnerability also tend to have higher Medicaid enrollment and more reports of difficulty seeing a doctor because of cost, emphasizing that cost-related barriers to care are significant, with the high expense of insurance being the primary reason many people lack coverage.[45,46] Though vaccines are available to most U.S. residents at low or no cost, no-cost options are limited for the more than 26 million individuals younger than 64 years without health coverage.[46] For children, the Vaccines for Children Program

provides funding for pediatric vaccine administration. However, for adults aged 18 and older, a discretionary federal program can offer grants to states to support vaccination efforts, but it is not guaranteed.[43] As federal policies change and lead to differences in coverage among states, it becomes increasingly important to keep participants' states as a covariate in vaccination models, given the growing geopolitical variations in vaccine policy.

In contrast, when the outcome was test positivity, including site attenuated the association between ADI and test positivity. For decades, various theories have demonstrated the persistent association between SES and health disparities.[34] In 2008, Blumenshine used these theories to study influenza outbreaks, investigating how disparities in SES, race, and ethnicity could lead to differences in illness or mortality. These disparities arise from variations in exposure, infection risk, and access to timely and effective treatment.[47] Although Blumenshine modeled factors influencing pandemic influenza outbreaks, research indicates that disparities in illness related to disadvantage and race or ethnicity are present during annual flu seasons and are worsened during pandemics.[48] Since 2019, vaccination rates have remained at or below 50%, and recent influenza seasons have ranged from moderate to severe. The factors listed in **Table 1.6**, originally examined by Blumenshine and updated to include vaccination factors from the Behavioral and Social Drivers of Vaccination, could also be relevant to typical influenza seasons.[11,49–51,47]

Additionally, there could be a conceptual reason the risk ratios attenuate for test positivity but not vaccination: ADI carries socioeconomic information that overlaps heavily with site. For test positivity, site sits directly on the causal path and is dependent on measurement timing **(Figure 1.1**): neighborhood disadvantage shapes where people live and where they seek care, which determines the Network site they visit for symptoms and are swabbed for testing. Adjusting for site means conditioning on that step and is ascertained at the visit so the association attenuates. In contrast, vaccination history is fixed before the medical visit and is validated against medical records. A better understanding of the interplay of these factors, especially how neighborhood disadvantage influences them, could help identify links with influenza illness and guide targeted

interventions to lower exposure, reduce infection risk, or enhance access to treatment. To best assess disparities, it has been recommended to evaluate area-level SES status at a minimum at the Census-tract level to capture geographic diversity, particularly in densely populated urban areas.[52]

Currently, the CDC monitors national seasonal severity through multiple networks that cover various medical settings and populations, using diverse data types such as specimen tests, influenza-like illness reports, hospitalizations, and mortality.[53,54] One such network is the US FluVE Network, whose strength lies in using the gold-standard testing method (Reverse Transcription-Polymerase Chain Reaction) and detailed survey data that evaluate social determinants of health at the individual level, geocoding results to the neighborhood level.[20,55] Enhancing electronic health record data could enable real-time tracking of illnesses using patient demographics and geolocation. However, it would be necessary to incorporate methods for geocoding or evaluating an individual's SES both personally and at the neighborhood level.[54] Regardless, these Networks and electronic health record data are subject to limitations of health-seeking behaviors and cost concerns with seeking healthcare among the most disadvantaged populations. Federally qualified or community-based health centers could help identify under- or uninsured individuals, but sufficient resources must be invested to establish the necessary infrastructure. Overall, more work is needed to encourage researchers and public health organizations to incorporate an area-level SES measure, such as the ADI, when evaluating influenza outbreaks or seasonality and better understand disparities in influenza outcomes, and to reduce reporting lag, all of which remain crucial for real-time surveillance and interventions to reduce inequities in the influenza burden and severe outcomes.

Our study had several strengths. The US Flu VE Network has a standardized protocol for participant recruitment and sample collection, resulting in a well-structured cohort recruited during peak influenza seasons. Although the Network sites span 7 U.S. states, excluding Washington, median ADI scores can be grouped into 3 pairs of sites with similar scores, suggesting that greater

variation in ADI scores or the inclusion of additional geographic locations could better elucidate the association between ADI and influenza outcomes. Another limitation is that most recruitment sites are in largely urban areas and target individuals who can seek medical care for acute respiratory infections, limiting findings to those populations.

*CONCLUSION*

Through these exploratory analyses, we aimed to gain a deeper understanding of the role of site in the association between ADI and influenza outcomes. Given the significant changes in vaccine policy at both federal and state levels, we suggest including site as a covariate when examining the association between ADI and vaccine uptake; future studies could better incorporate state-level vaccine policy as a variable to minimize misclassification. Conversely, including site as a covariate in test positivity analysis attenuates the association between ADI and influenza illness. Because our goal was to evaluate socioeconomic associations across the Network, we suggest omitting site as a covariate when analyzing laboratory-confirmed influenza illness.

*TABLES AND FIGURES*

***Figure 1.1.*** *Direct acyclic graph outlining relationship between Area Deprivation Index (ADI) components and influenza outcomes*

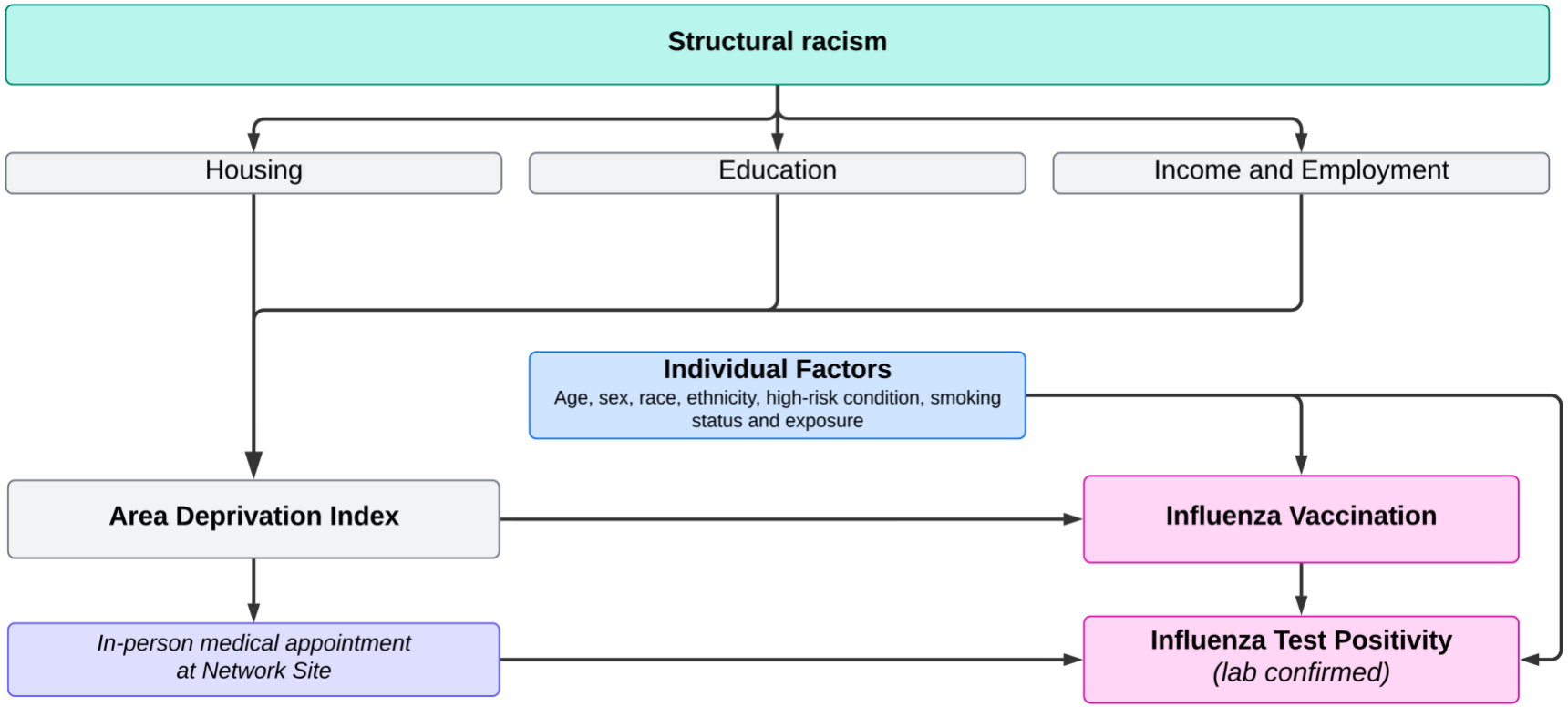

**Table 1.1.** Population size distribution, median score and interquartile range (IQR) by Area Deprivation Index categorization

| Quintile Categorization | | | | | |
|---|---|---|---|---|---|
| **Population Size Distribution** | | | | | |
| | **Quintile 1** | **Quintile 2** | **Quintile 3** | **Quintile 4** | **Quintile 5** |
| **Relative** | 1587 | 1575 | 1617 | 1551 | 1568 |
| **Percentile** | 606 | 1517 | 1777 | 1649 | 2349 |
| **Median Scores (IQR)** | | | | | |
| | **Quintile 1** | **Quintile 2** | **Quintile 3** | **Quintile 4** | **Quintile 5** |
| **Relative** | 23 (13) | 42 (13) | 60.5 (10.5) | 80 (9) | 96.5 (6) |
| **Percentile** | 12 (10) | 30 (10) | 50 (10.5) | 69.5 (9.5) | 93 (10.5) |

| Quartile Categorization | | | | |
|---|---|---|---|---|
| **Population Size Distribution** | | | | |
| | **Quartile 1** | **Quartile 2** | **Quartile 3** | **Quartile 4** |
| **Relative** | 2011 | 1958 | 1978 | 1951 |
| **Percentile** | 914 | 2058 | 2178 | 2748 |
| **Median Scores (IQR)** | | | | |
| | **Quartile 1** | **Quartile 2** | **Quartile 3** | **Quartile 4** |
| **Relative** | 25.5 (14.2) | 50 (10.5) | 72 (12) | 95 (8) |
| **Percentile** | 17 (11.9) | 38 (12.5) | 61.5 (13) | 90.8 (14) |

| Binary Categorization | | |
|---|---|---|
| **Population Size Distribution** | | |
| | **Low** | **High** |
| **Relative** | 3969 | 3929 |
| **Percentile** | 2972 | 4926 |
| **Median Scores (IQR)** | | |
| | **Low** | **High** |
| **Relative** | 38 (25) | 84 (23) |
| **Percentile** | 31 (18.5) | 78 (28.5) |

**Table 1.2.** Comparison of model performance using Bayesian Information Criterion (BIC) for influenza vaccination and test positivity, US FluVE Network 2023-2024

| | Description | BIC | Difference Compared to Unadjusted |
|---|---|---|---|
| **Outcome: Vaccination** | | | |
| Model 1 | Unadjusted | 11,859.7 | - |
| Model 2 | Adjusted with Site[1] | 11,355.8 | 503.90 |
| Model 3 | Adjusted without Site[2] | 11,386.7 | 473.00 |
| Model 4 | Adjusted with Age Continuous[2] | 11,323.3 | 536.40 |
| **Outcome: Test Positivity** | | | |
| Model 5 | Unadjusted | 9,072.2 | - |
| Model 6 | Adjusted with Site[1] | 8,771.5 | 300.70 |
| Model 7 | Adjusted without Site[2] | 8,813.2 | 259.00 |
| Model 8 | Adjusted with Age Continuous[2] | 8,797.8 | 274.40 |

[1] Models were adjusted for: Age category, assigned sex at birth (male/ female), month of illness onset, enrolled network site, smoking status and household exposure to smoke, high-risk medical condition, race and ethnicity.
[2] Models were adjusted for: Age category, assigned sex at birth (male/ female), month of illness onset, smoking status and household exposure to smoke, high-risk medical condition, race and ethnicity.

**Table 1.3.** Estimates of adjusted risk ratios and 95% confidence intervals for associations of ADI quartiles on influenza outcomes, US FluVE Network 2023-2024

| ADI Quartile [a] | Vaccination | | | | Test positivity | | | |
|---|---|---|---|---|---|---|---|---|
| | # vaccinated (%)[b] | Model 1 | Model 2[c] | Model 3[d] | # positive (%)[b] | Model 5 | Model 6[c] | Model 7[d] |
| Quartile 1 | 967 (12.2) | *Reference* | | | 380 (4.8) | *Reference* | | |
| Quartile 2 | 807 (10.2) | **0.86 (0.80, 0.92)** | **0.91 (0.85, 0.97)** | **0.90 (0.84, 0.97)** | 428 (5.4) | **1.15 (1.02, 1.31)** | 1.04 (0.91, 1.18) | 1.11 (0.98, 1.25) |
| Quartile 3 | 747 (9.5) | **0.80 (0.74, 0.85)** | **0.88 (0.82, 0.94)** | **0.86 (0.80, 0.94)** | 471 (6.0) | **1.27 (1.13, 1.43)** | 1.02 (0.90, 1.17) | **1.15 (1.02, 1.30)** |
| Quartile 4 | 542 (6.9) | **0.57 (0.53, 0.62)** | **0.77 (0.70, 0.84)** | **0.73 (0.66, 0.80)** | 579 (7.3) | **1.57 (1.4, 1.76)** | 1.03 (0.90, 1.18) | **1.18 (1.04, 1.34)** |

a. p-values < 0.05 are bolded. Only models with age as a categorical variable were shown.
b. The percentage is out of the total number of participants (N = 7898).
c. Models were adjusted for: age (category), sex, race, ethnicity, smoking exposure, history of a high-risk condition, month of illness onset and site.
d. Models were adjusted for: age (category), sex, race, ethnicity, smoking exposure, history of a high-risk condition, and month of illness onset.

**Table 1.4.** Association of ADI quartiles on influenza test positivity stratified by site, US FluVE Network 2023-2024

| | **Population** (n (% out of total)) | | | | | **Risk Ratio** (RR (95% Confidence Interval)) [a, b] | | |
|---|---|---|---|---|---|---|---|---|
| **Network Site** | **Total** | **Quartile 1** | **Quartile 2** | **Quartile 3** | **Quartile 4** | **Quartile 2**[c] | **Quartile 3** | **Quartile 4** |
| Arizona | 585 (7.4%) | 118 (1.5%) | 214 (2.7%) | 214 (2.7%) | 39 (0.5%) | 1.12 (0.77, 1.62) | 1.13 (0.76, 1.68) | 0.65 (0.29, 1.45) |
| Michigan | 527 (6.7%) | 182 (2.3%) | 122 (1.5%) | 100 (1.3%) | 123 (1.6%) | 0.83 (0.49, 1.42) | 0.92 (0.51, 1.65) | 0.96 (0.47, 1.97) |
| Missouri | 1132 (14.3%) | 127 (1.6%) | 172 (2.2%) | 290 (3.7%) | 543 (6.9%) | **2.1 (1.43, 3.09)** | **1.8 (1.24, 2.63)** | **1.99 (1.37, 2.88)** |
| Ohio | 961 (12.2%) | 121 (1.5%) | 171 (2.2%) | 209 (2.6%) | 460 (5.8%) | 1.11 (0.72, 1.7) | 1.3 (0.87, 1.95) | **1.58 (1.07, 2.33)** |
| Pennsylvania | 1310 (16.6%) | 298 (3.8%) | 277 (3.5%) | 358 (4.5%) | 377 (4.8%) | 0.77 (0.59, 1.01) | 0.92 (0.73, 1.18) | **0.71 (0.54, 0.94)** |
| Texas | 2103 (26.6%) | 147 (1.9%) | 777 (9.8%) | 774 (9.8%) | 405 (5.1%) | 1.21 (0.82, 1.78) | 1 (0.68, 1.47) | 1.07 (0.7, 1.63) |
| Washington | 1280 (16.2%) | 1018 (12.9%) | 225 (2.8%) | 33 (0.4%) | 4 (0.1%) | **0.59 (0.37, 0.94)** | 1.22 (0.52, 2.86) | **2.89 (1.14, 7.38)** |

a. p-values < 0.05 are bolded.
b. Models were adjusted for: age (category), sex, race, ethnicity, smoking exposure, history of a high-risk condition, and month of illness onset.
c. Quartile 1 was the reference group.

**Table 1.5.** Factors influencing uptake and severity of influenza illness

| |
|---|
| **Differences in exposure to influenza virus** |
| Crowding in households, medical facilities, public transportation |
| Occupational factors such as inability to work from home, dependence on childcare outside of the home |
| **Differences in susceptibility to influenza disease, once exposed to the virus** |
| Host factors, including preexisting immunity, age, other underlying diseases or conditions, smoking, nutritional status, stress |
| Perceived risk |
| Vaccination status, reflecting differences in vaccine seeking and acceptance and in vaccine availability |
| Vaccine confidence (includes perceived benefits, safety and trust) |
| Healthcare worker recommendation and trust in medical system |
| Social norms |
| Gender and race/ ethnicity equity |
| Practical issues: Ease of access, affordability (e.g. insurance coverage), availability |
| **Differences in timely effective treatment, once influenza disease has developed** |
| Access to outpatient and inpatient medical care |
| Care-seeking attitudes and behavior |
| Respect from health worker |
| Financial obstacles, including lack of adequate insurance coverage |
| Logistic obstacles, including transportation, language |
| Quality of care |
| Availability of antiviral treatments |
| Appropriate inpatient treatment |

## Supplemental Tables

**Table 1.6.** Population sizes and national ADI median, minimum and maximum scores by site

| Site | Number of Participants | Median (Interquartile Range) | Minimum | Maximum |
|---|---|---|---|---|
| *Overall* | 7898 | | | |
| Arizona | 585 | 56 (27) | 1 | 100 |
| Michigan | 527 | 54 (52) | 5 | 100 |
| Missouri | 1132 | 82.5 (37) | 5 | 100 |
| Ohio | 961 | 83 (41.5) | 8 | 100 |
| Pennsylvania | 1310 | 66 (46) | 3 | 100 |
| Texas | 2103 | 66 (29.8) | 2 | 100 |
| Washington | 1280 | 26 (20.5) | 1 | 99 |

# Chapter 2: Associations between Area Deprivation Index and Influenza Outcomes Using US Flu VE Network Data, 2023 – 2024

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**Keywords:**

neighborhood disadvantage, influenza, area deprivation index

***ABSTRACT***

*Introduction:* Measures such as the area deprivation index (ADI) are vital for public health efforts to identify socioeconomic disparities in influenza vaccine uptake and test positivity and to develop strategic interventions. This study aimed to estimate associations between influenza test positivity, vaccine uptake, and neighborhood deprivation, as measured by an ADI score.

*Methods:* The study population included participants enrolled in the 2023–2024 US Flu Vaccine Effectiveness (FluVE) Network. Participants' addresses were geocoded to FIPS codes to link data to ADI scores with baseline enrollment data, vaccination history, and laboratory-confirmed influenza test results. National ADI scores were used to create quartiles that divide the study population into four equal groups. Modified Poisson regression analyses were adjusted for age, sex, race, ethnicity, smoking exposure, history of a high-risk condition, month of illness onset, and study site. Vaccine effectiveness by ADI quartile was also estimated.

*Results:* The study population consisted of 7,898 participants. We found that participants living in the most disadvantaged neighborhoods were the least likely to be vaccinated against influenza and the highest likelihood of testing positive for influenza. Other characteristics linked to vaccination and test positivity included age and race. Those over 65 had the highest likelihood of vaccination, while children under 18 had a higher risk of testing positive. Participants who identified as Black were less likely to get vaccinated, but Asian and Black participants were more likely to have a positive test. Vaccine effectiveness did not vary significantly by ADI quartile.

*Conclusion:* Using neighborhood disadvantage is important for examining associations with influenza outcomes. This can help in designing policies that address geographic disparities and improve the allocation of influenza prevention resources.

## *INTRODUCTION*

For the 2023 – 2024 season, the Advisory Committee on Immunization Practices (ACIP) recommended routine annual influenza vaccination for all persons aged ≥6 months without contraindications.[56] The 2023 – 2024 season severity was classified as "moderate" and influenza activity was similar to levels seen prior to the COVID-19 pandemic in 2020.[11] It is estimated that during this season, vaccines prevented approximately 9.8 million influenza-related illnesses, and 7,900 influenza-related deaths in the United States.[11]

Influenza vaccines have historically been associated with decreased risk of hospitalization and death. Though the vaccine prevents severe illness and adverse outcomes across all age groups, vaccination rates have dropped compared to previous seasons. According to the National Center for Health Statistics, influenza vaccination rates for adults over 18 years have consistently remained below 50% since 2019, while rates among pediatric populations dropped to under 50% in 2020. These rates fall short of the Healthy People 2030 goal of 70% coverage among all populations.[57] Furthermore, vaccination status differed by socioeconomic factors, with the lowest flu vaccination rates among adults and children with a family income below 100% of the federal poverty level and without health insurance. Other factors, such as living in a rural setting, race and ethnicity, and education, have also been associated with vaccination uptake.[58]

Prior research assessing vaccination uptake and laboratory-confirmed test positivity by socioeconomic status has been limited to county-level estimates.[59] Strategies focusing on socioeconomic factors affecting adult and parent vaccine-seeking behaviors should be incorporated into targeted vaccination campaigns to boost vaccination rates. [60,61] However, these targeted strategies require more detailed geographic data than county-level information alone. Composite social determinants of health measures, such as the area deprivation index (ADI), are particularly important for public health departments and policymakers, as they consolidate individual factors and can identify areas where health disparities exist, helping to develop strategic

interventions at smaller geographical levels.[8,16,62,63] In particular, since the start of the COVID-19 pandemic, there has been a greater need to uplift and coordinate hyperlocal strategies to mitigate inequities in routine immunization strategies.[64] Communities disproportionately affected by lower access to and uptake of respiratory vaccines could also be at higher risk of respiratory illness due to differences in social contact, health care utilization, and absenteeism from school or work.[13,65]

We propose using a nationally representative study sample, the US Flu Vaccine Effectiveness (Flu VE) Network, to estimate the associations of neighborhood disadvantage, as measured by ADI, with influenza test positivity and vaccine uptake.[20]

## *METHODS*

We conducted a retrospective cohort study design using data from the US Flu VE Network. We ran modified Poisson regression models with robust standard errors to estimate risk ratios (RRs) for participants' ADI quartile and influenza outcomes: flu vaccination (vaccinated/ unvaccinated) and influenza test positivity (positive/negative).

### *Study Procedures & Population*

Since its founding in 2004, the US Flu VE Network has enrolled more than 95,000 pediatric and adult participants across multiple study sites to estimate the clinical effectiveness of licensed influenza vaccines and contribute to local influenza surveillance.[66] The US Flu VE Network has one of the few multi-site and nationally representative datasets that includes a standardized protocol for collecting vaccination history and laboratory-confirmed influenza test results. The Network evaluates influenza vaccine effectiveness by age group, virus type, and subtype across outpatient medical centers, urgent care centers, and emergency rooms in the United States.[66]

For the 2023 – 2024 season, the US Flu VE Network recruited participants from the following seven study sites: Arizona State University Tempe; University of Michigan; Washington University at St. Louis; University Hospitals Cleveland; University of Pittsburgh; Baylor Scott & White Health; Kaiser Permanente Washington (KPWA); and one coordinating center (Duke

University) (**Figure 2.1**). Eligible participants sought outpatient care at these study sites for an acute respiratory illness 7 days or less in duration and had a new or worsening cough. At baseline enrollment, participants consent to the study, complete a baseline survey, and provide nasal and oropharyngeal swabs for influenza laboratory testing. More detailed study enrollment protocols have been previously documented.[67] The study protocol, reviewed by CDC, was and conducted in accordance with federal law and CDC policy. All study sites comply with a memorandum of understanding and individual Institutional Review Board (IRB) protocols for data sharing. IRB review for these analyses was ceded to KPWA under the Cooperative IRB Reliance Agreement between the University of Washington and Kaiser Permanente – Washington (STUDY0002234).

MEASURES

*Exposure Ascertainment:* In the current Network, there is a concerted effort to evaluate health equity regarding influenza outcomes, including multiple social determinants of health. For the 2023-2024 season, participants consented to geocode their addresses for data linkages.

The University of Wisconsin-Madison has refined, validated, and standardized ADI to the neighborhood or Census block-group level using 17 specific U.S. Census variables and the American Community Survey (ACS) Five-Year Estimates. Census tract blocks are identified by their respective Federal Information Processing Standards (FIPS) codes, which uniquely identify geographic areas, and are assigned an ADI score calculated by the Neighborhood Atlas, a website created in 2018 to share measures of disparity at a granular level.[68,69] There are 17 socioeconomic variables included in the ADI calculation.[69]

Upon enrollment into the study, the research staff collects participants' addresses. For the 2023 – 2024 season, participants' addresses were geocoded to an 11-digit FIPS code that corresponded to their census tract. FIPS codes linked participant addresses to national and state ADI scores. The ADI scores utilized were based on the 2022 version, constructed from 2018-2022 ACS 5-year estimates and 2022 Census block groups. This version was recently updated to reduce the impact of annual sampling variations in block group-level data from the American

Community Survey.[69] For this analysis, national ADI scores were employed, ranging from 1 (least disadvantaged) to 100 (most disadvantaged). The scores were categorized into quartiles according to their distribution within the study population. For regions where FIPS codes could not be matched at the census-tract block level, the median ADI was calculated for the census tract.

*Outcomes:* There are two primary outcomes: First, receipt of 2023 - 2024 seasonal influenza vaccination was ascertained through medical records, self-report at the baseline visit, or state immunization records, and was dichotomized as vaccinated and unvaccinated. Vaccination history was verified by site staff against state immunization registries. Participants with missing vaccination records or who were vaccinated less than 2 weeks prior to enrollment were categorized as unvaccinated. Study methods for the US Flu VE Network have used similar ascertainment of vaccination.[67,70]

The second outcome, laboratory-confirmed influenza test results, relies on laboratory-confirmed test results from the swabs collected at enrollment to dichotomize results as positive or negative for any influenza type. Influenza specimens that test positive undergo further testing to determine subtype and lineage.

In addition, we also plotted fitted lines for each ADI quartile, representing a LOESS (locally weighted scatter-plot smoother) regression to evaluate trends in the proportion testing positive for influenza over time. Lastly, we estimated vaccine effectiveness against clinically attended influenza using a test-negative case-control design, as described in the US Flu VE Network, with multivariable logistic regression based on ADI.[71] The test-negative design is an observational design, similar to a case-control study, that estimates vaccine effectiveness by comparing vaccination status between test-positive cases and test-negative controls.[72] Vaccine effectiveness is calculated as $(1 - \frac{the\ odds\ of\ vaccination\ among\ test-positve\ cases}{the\ odds\ of\ vaccination\ among\ test-negative\ \ controls}) * 100$. The test-negative design works because negative tests approximate the source population, allowing effectiveness

127 estimates without a full denominator. Vaccine effectiveness was estimated against medically
128 attended outpatient influenza A and B viruses.

129 *Covariates:* Key covariates are ascertained from the baseline survey and supplemented
130 by the participant's electronic medical records, if missing. Age category (ages < 8, ages 9 – 17,
131 ages 18 – 24, ages 25 – 44, ages 45 – 64, ages 65+), assigned sex at birth (male/ female), month
132 of illness onset and enrolled network site were included as categorical variables. Additional
133 covariates include cigarette use (every day and some days/ not at all), household exposure to
134 smoke (daily and some days/ none) and having at least one high-risk medical condition such as
135 heart or lung disease, diabetes, cancer, or liver failure (yes/ no). Finally, race and ethnicity will be
136 included as covariates (Ethnicity: Non-Hispanic (NH) and Hispanic; Race: American Indian or
137 Alaska Native, Asian, Black or African American, Native Hawaiian or Pacific Islander, White or Not
138 Listed Race). We understand that race and ethnicity do not have biological origins and were
139 created to enforce a social order that structured and reinforced inequality. Racialized beliefs about
140 disease susceptibility are pervasive in epidemiologic research and medical care and are rooted
141 in the history of biological determinism that dehumanized minoritized individuals, particularly
142 Black individuals.[73–76] Given the prevalent impacts of structural racism and its varying effects on
143 different races and ethnicities, it is still helpful to identify disparities in vaccination history and test
144 positivity by race and ethnicity, and the inclusion of race and ethnicity will be used, understanding
145 that any significance is due largely to societal differences.[74,77] This information may need to be
146 explicitly included in policy to advocate for resources in under-resourced areas and is particularly
147 relevant in conjunction with the area deprivation index, which assesses neighborhood
148 socioeconomic status that may have been impacted by redlining, the history of segregation, and
149 unequal access to healthcare.[74]

150 *Statistical Analysis*: We conducted a complete case analysis for all models and excluded
151 participants who were unable to be geocoded to an ADI score, were missing an influenza outcome

or any of the covariates. Participants with missing variables were compared to the participants in the analytic dataset on all covariates, outcome and ADI score, using chi-square tests.

Descriptive statistics summarized key covariates by proportions for categorical variables and median and interquartile range for continuous variables. We fit modified Poisson regression models with robust standard errors to estimate risk ratios (RRs) for influenza outcomes by ADI quartiles. All multivariable models for influenza vaccination were adjusted for age category, sex, month of illness onset, site, exposure to smoke, high-risk medical condition, race, and ethnicity. Models for test positivity and vaccine effectiveness were adjusted for age category, sex, month of illness onset, exposure to smoke, high-risk medical condition, race, and ethnicity. Reference groups was selected based on the largest categories in the overall study population. Temporal trends in influenza test positivity, stratified by ADI quartiles and the overall population, were also plotted, showing the proportion of participants testing positive each month. The fitted lines for each quartile represent a LOESS (locally weighted scatter-plot smoother) regression used to evaluate trends over time within each quartile. Statistical significance is set at an alpha of 0.05, and RStudio (Version 2021.09.1) was used.

***RESULTS***

For the 2023 – 2024 season, 9,184 participants aged 8 months or older enrolled in US Flu VE Network study across the seven sites. After excluding participants who were unable to be geo-coded to an ADI score, had missing covariates or outcomes, or enrolled outside the official enrollment period from October 1, 2023, to April 30, 2024, a total of 7,898 participants remained (**Figure 2.2**). Though the excluded participants did not differ significantly on most variables from participants in the analytic dataset, there were statistically significant differences in site enrollment (most excluded participants were enrolled in Texas (41.0%) and Missouri (26.4%)), age (excluded participants were younger), and ethnicity. Additionally, a lower proportion of excluded participants

were vaccinated (34.1% versus 39.1%) and tested positive for influenza (12.6% versus 22.9%) compared to those in the analytic dataset.

A quarter of participants were between 25 and 44 years old (25.5%), with a median age of 34 years (interquartile range (IQR) = 14 to 57 years); the majority self-identified as White (59.8%), and 15.0% were Hispanic. The majority of participants were assigned female at birth (60.1%), and 35.0% had a history of at least one high-risk health condition. 22.8% of participants experienced illness onset in January 2024 (**Table 2.1**). The study sites in Texas and Pennsylvania across the network enrolled the most participants (2,103 and 1,310). Missouri had the highest percentage of people in Quartile 4 at 27.8%, followed by Ohio (23.6%). In contrast, half of the participants in quartile 1 were enrolled in Washington (50.6%). Among participants living in neighborhoods in the highest ADI quartile (quartile 4), a larger percentage identified as Black (63.4%), reported greater individual or household exposure to tobacco (24.2%), and were younger than participants in the other three ADI quartiles.

*Influenza Vaccination:* Overall, 3,069 (38.9%) out of 7,898 participants had a record of receiving an influenza vaccine. Almost one third of vaccinated participants (31.6%) lived in the most advantaged neighborhoods (quartile 1). After adjusting for covariates, participants living in the most disadvantaged neighborhoods (quartile 4) were 23% less likely to be vaccinated (RR: 0.77, 95% CI: 0.70–0.84, p-value < 0.001) than those living in the most advantaged neighborhoods (quartile 1). The likelihood of being vaccinated decreased with each increase in neighborhood disadvantage quartile (p-trend <0.001) (**Table 2.2**). Other characteristics associated with influenza vaccination included age, race and cigarette smoking history/ household exposure to smoke, history of a high-risk condition and month of illness onset. Participants aged 65 or older had the highest likelihood of vaccination compared with those aged 25 to 44 years, whereas those identifying as Black or Native Hawaiian/Pacific Islander had a lower likelihood than White participants.

*Influenza Test Positivity:* Among all quartiles, 1,856 participants (23.5%) out of 7,898 tested positive for influenza. Of these, 579 (31.2%) resided in the most disadvantaged neighborhoods (Q4). We first plotted trends of the proportion of test positivity by month of illness onset overall, and for each ADI quartile (**Figure 2.3**). Trends in Quartile 4 were consistently higher than other quartiles, with two peaks occurring in December 2023 and February 2024, suggesting that continuing vaccination efforts through the fall could have a particular benefit to communities in this quartile. After adjustment, participants living in the most disadvantaged neighborhoods (Q4) were more likely to test positive for influenza (RR = 1.18, 95% CI: 1.04-1.34, p-value = 0.01) than those living in quartile 1. In contrast to vaccination trends, the odds of testing positive increased with increasing neighborhood disadvantage (p-trend: 0.009) (**Table 2.3**). Higher likelihood of test positivity was associated with: children <18 years (vs participants 25-44 years); Black and Asian participants (vs White participants) and having an illness onset date between January and February 2024, compared to those in October 2023, consistent with national trends for the 2023 – 2024 influenza season. **(Table 2.3).**

*Vaccine Effectiveness (VE) by ADI Categorization:* Across all participants, VE was estimated to be 51.3% (95% CI: 44.6 – 57.2%), after adjusting for all covariates except site. VE did not substantially differ by quartile (**Figure 2.4**).

***DISCUSSION***

Using a national cohort, we found that participants living in the most disadvantaged neighborhoods had the lowest likelihood of being vaccinated against influenza and the highest risk of testing positive for influenza in ambulatory outpatient settings. We also found that VE didn't differ substantially by ADI. Increasing vaccination, which supports those particularly vulnerable to influenza, might be the most important for public health campaigns to reduce influenza infections and severe outcomes. The proportion of participants testing positive reached its peak in January

2024, aligning with clinical laboratory surveillance showing influenza levels peaking in the last week of December 2023 and remaining elevated through February 2024.[11]

Estimates from recent annual influenza seasons indicate that vaccines reduce influenza-related hospitalizations and mortality.[20,78] However, our findings and prior studies have demonstrated that people residing in disadvantaged neighborhoods have lower vaccine uptake and subsequently have a higher risk of respiratory infections.[18,65] Persistent disparities in influenza infection and hospitalizations were associated with neighborhood characteristics, including employment in essential jobs with limited sick leave, reliance on public transit, living in more crowded households, limited access to preventive and medical care, poverty, and other socioeconomic factors.[47,48] These factors lead to varying exposure levels, increase individuals' risk of infection, and contribute to higher infection rates within communities.[47,79] Disparities in infection, morbidity, and mortality related to social determinants, neighborhood disadvantage, as well as race and ethnicity, have been assessed during annual influenza seasons, with disparities widening during influenza pandemics in the United States.[48,79–81] As such, health policy should focus on protecting those most likely to experience poor influenza outcomes, such as a higher risk of infection and hospitalization, by prioritizing improvements in vaccine uptake and reducing infections in communities with high ADI scores (greater disadvantage).

We selected ADI instead of the Social Vulnerability Index (SVI) for this analysis because racial and ethnic differences in vaccine uptake and infection risk can be examined separately from the overall score, as the ADI, unlike the SVI, does not include non-White populations in its calculations. Since minoritized populations are over-represented in disadvantaged communities, it remains important to consider race and ethnicity when examining disparities in influenza outcomes. One study’s findings suggest that while SVI as a score may not be optimal for measuring or evaluating respiratory virus infection, the minority status and language subtheme within the SVI was strongly associated with respiratory viruses, suggesting that measuring minoritized populations should still be prioritized.[27] Mathematical modeling shows that policies

reducing race-based comorbidities mitigate disparities in influenza hospitalizations.[82] Higher vaccination rates among marginalized groups could equalize infection rates, especially benefiting younger adults (18 to 49 years) in Black, American Indian/Alaskan Native, and Hispanic populations. In our study, we observed that Black participants had lower likelihood of vaccination, while both Black and Pacific Islander participants showed higher risk of testing positive. Along with disparities in exposure at home and work, minoritized populations, especially Black communities, face higher allostatic load and suffer from the impacts of racial residential segregation and historical disinvestment in their neighborhoods, which negatively affect overall health and may lead to increased influenza prevalence or illness severity from a history of high-risk conditions in these communities.[83] Although ADI and SVI are helpful neighborhood metrics, employing a specific MSL score or measures of neighborhood segregation might better reveal the roots of disparities, recognizing that social determinants of health influence an individual's well-being beyond their home address.

Overall, individual behavior can only do so much to reduce influenza prevalence. Reinvestment in public health services is necessary to boost access to vaccination, encourage vaccination, and enhance awareness of protective behaviors across entire communities and populations. Though useful, targeted vaccination clinics alone are insufficient for achieving widespread, equitable vaccination.[17] ADI scores could help identify disparities to optimize resource distribution to disadvantaged communities and encourage community organizations, local governments, and healthcare providers to collaborate on implementing evidence-based approaches to boost vaccination rates. Combining strategies that increase community demand, such as outreach, patient incentives, and reminder systems, with efforts to improve access by expanding healthcare settings, providing home visits, and lowering out-of-pocket costs will yield the best outcomes.[84] Though this study focused on neighborhood disadvantage based on participants' home addresses, there is value in considering workplace interventions to increase vaccination rates and reduce influenza infections. Models have shown that adopting workplace

changes, such as improved air filtration and social distancing, significantly reduces influenza outcomes.[82] Since workers from disadvantaged neighborhoods and/ or minoritized communities may struggle to take time off or work remotely, targeted community outreach that also educates them on ways to reduce influenza exposure at work, like increased masking and vaccination, could help reduce influenza infections.[82,85] Although one study indicates that influenza vaccinations might not be cost-effective for working-age adults (roughly 18 to 65 years), workplace interventions can still reach a broad age range, helping to decrease community transmission and support employees who are most disadvantaged, have a high-risk condition and/or are unable to take sick leave for vaccination.[86] Finally, among older adults, especially those aged 65 and above, who experience much higher rates of influenza-related hospitalizations, deaths, and complications, vaccination programs that target racial and ethnic disparities in vaccine uptake due to financial and structural barriers, declining vaccine confidence, and disparities in rural areas can help prevent disproportionate outcomes.[87–89] Overall, public health investments in historically neglected communities should be prioritized to reduce influenza infection and later severe outcomes.

Our observational study had several strengths, including valid outcome measures, national representativeness, and heterogeneous ADI across multiple sites. The study's populations represent diverse geographical regions in 7 states in the United States. The Network staff responsible for participant recruitment and sample collection adhere to a systematic protocol, and data is reliably managed by a single external organization to ensure consistency across various healthcare systems. Participant data are collected on an individual basis, with vaccination history and test results documented in accordance with best practice. However, our study had some limitations. The primary limitation of this study is that the US FluVE Network recruits participants who are symptomatic and able to attend outpatient clinics, primarily in urban areas. It is possible that those who seek healthcare for acute respiratory infections differ from those who do not or cannot due to access or insurance status. Additionally, the study assessed one influenza

season. Recent seasons have seen historic highs in influenza positivity, and a multi-year study could highlight temporal trends in vaccination and infection, especially with the emergence of new variants, and differences in geographical locations. Lastly, the primary exposure used the ADI score from the Neighborhood Atlas. There are limitations to using this score, including how it is calculated and how it accounts for population sizes, as well as its use with census tracts. An updated score, such as the Reproducible Area Deprivation Index, could help minimize non-differential misclassification.

## ***CONCLUSION***

Overall, higher neighborhood disadvantage was associated with lower influenza vaccine uptake and higher test positivity but did not impact vaccine effectiveness. Future consideration should be given to employing a score that incorporates factors such as second-language proficiency, race and ethnicity, or historical segregation, and using it to implement policies that incorporate neighborhood characteristics to target vaccine resources and education. Public health investments should be focused on communities with high ADI scores to boost vaccine confidence and uptake, potentially leading to significant public health benefits, such as reduced influenza infections and severe outcomes.

***TABLES AND FIGURES***

**Figure 2.1.** Map of US Flu VE Network sites, 2022-23 Season[66]

**Figure 2.2.** Study Participant Population

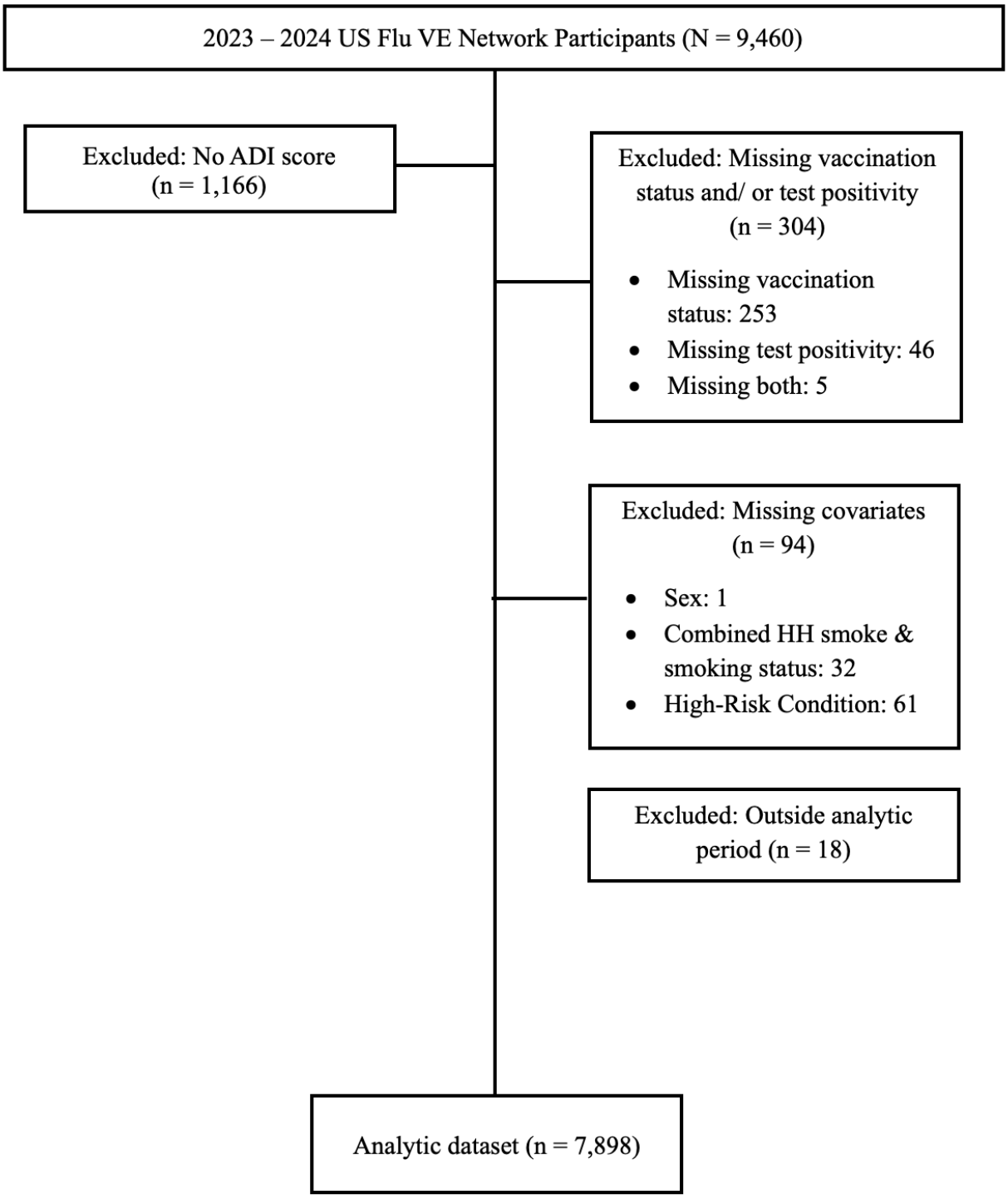

**Table 2.1.** Demographic characteristics of 2023 – 2024 US Flu VE Participants, overall and by ADI categorization[a]

| Characteristic | All (N = 7898) | Q1 (n = 2011) | Q2 (n = 1958) | Q3 (n = 1978) | Q4 (n = 1951) |
|---|---|---|---|---|---|
| **Network Site (%)*** | | | | | |
| Arizona | 585 (7.4) | 118 (5.9) | 214 (10.9) | 214 (10.8) | 39 (2.0) |
| Michigan | 527 (6.7) | 182 (9.1) | 122 (6.2) | 100 (5.1) | 123 (6.3) |
| Missouri | 1132 (14.3) | 127 (6.3) | 172 (8.8) | 290 (14.7) | 543 (27.8) |
| Ohio | 961 (12.2) | 121 (6.0) | 171 (8.7) | 209 (10.6) | 460 (23.6) |
| Pennsylvania | 1310 (16.6) | 298 (14.8) | 277 (14.1) | 358 (18.1) | 377 (19.3) |
| Texas | 2103 (26.6) | 147 (7.3) | 777 (39.7) | 774 (39.1) | 405 (20.8) |
| Washington | 1280 (16.2) | 1018 (50.6) | 225 (11.5) | 33 (1.7) | 4 (0.2) |
| **Sex (%)** | | | | | |
| Female | 4744 (60.1) | 1187 (59.1) | 1199 (61.0) | 1164 (59.7) | 1189 (60.3) |
| Male | 3154 (39.9) | 820 (40.9) | 766 (39.0) | 786 (40.3) | 783 (39.7) |
| **Age in years** [median, IQR] | 34 [14, 57] | 37 [20, 60] | 37 [18, 59] | 36 [13, 60] | 28 [8, 51] |
| **Age Category (%)*** | | | | | |
| Age <8 | 1502 (19.0) | 245 (12.2) | 336 (17.1) | 380 (19.5) | 536 (27.2) |
| Age 9 - 17 | 674 (8.5) | 147 (7.3) | 152 (7.7) | 182 (9.3) | 191 (9.7) |
| Age 18 - 24 | 727 (9.2) | 228 (11.4) | 176 (9.0) | 181 (9.3) | 147 (7.5) |
| Age 25 - 44 | 2016 (25.5) | 568 (28.3) | 518 (26.4) | 430 (22.1) | 501 (25.4) |
| Age 45 - 64 | 1683 (21.3) | 440 (21.9) | 424 (21.6) | 424 (21.7) | 393 (19.9) |
| Age 65 and Older | 1296 (16.4) | 379 (18.9) | 359 (18.3) | 353 (18.1) | 204 (10.3) |
| **Race (%)*** | | | | | |
| American Indian/ Alaskan Native | 64 (0.8) | 33 (1.7) | 17 (0.9) | 13 (0.7) | 11 (0.6) |
| Asian | 312 (4.0) | 176 (9.0) | 105 (5.5) | 53 (2.8) | 19 (1.0) |
| Black | 2146 (27.2) | 165 (8.4) | 288 (15.0) | 478 (25.6) | 1223 (63.4) |
| Multiracial | 295 (3.7) | 69 (3.5) | 69 (3.6) | 69 (3.7) | 64 (3.3) |
| Native Hawaiian/ Pacific Islander | 47 (0.6) | 29 (1.5) | 12 (0.6) | 7 (0.4) | 5 (0.3) |
| Unknown | 314 (4.0) | 1373 (70.2) | 1174 (61.3) | 971 (52.0) | 442 (22.9) |
| White | 4720 (59.8) | 110 (5.6) | 249 (13.0) | 278 (14.9) | 165 (8.6) |
| **Ethnicity (%)*** | | | | | |
| Hispanic | 1182 (15.0) | 189 (9.4) | 339 (17.3) | 405 (20.8) | 247 (12.5) |
| Non-Hispanic | 6637 (84.0) | 1796 (89.5) | 1606 (81.7) | 1526 (78.3) | 1706 (86.5) |

| | | | | | |
|---|---|---|---|---|---|
| Unknown | 79 (1.0) | 22 (1.1) | 20 (1.0) | 19 (1.0) | 19 (1.0) |
| **Smoking Exposure (%)*[a]** | | | | | |
| Exposure | 1684 (21.3) | 190 (9.5) | 240 (12.2) | 318 (16.3) | 477 (24.2) |
| None | 6214 (78.7) | 1817 (90.5) | 1725 (87.8) | 1632 (83.7) | 1495 (75.8) |
| **History of High-Risk Condition (%)*[2]** | | | | | |
| High-Risk | 2764 (35.0) | 624 (31.1) | 660 (33.6) | 743 (38.1) | 732 (37.1) |
| No High-Risk | 5134 (65.0) | 1383 (68.9) | 1305 (66.4) | 1207 (61.9) | 1240 (62.9) |
| **Month of Illness Onset (%)*** | | | | | |
| October 2023 | 429 (5.4) | 146 (7.3) | 134 (6.8) | 101 (5.1) | 48 (2.5) |
| November 2023 | 1048 (13.3) | 273 (13.6) | 317 (16.2) | 285 (14.4) | 173 (8.9) |
| December 2023 | 1670 (21.1) | 366 (18.2) | 385 (19.7) | 436 (22.0) | 483 (24.8) |
| January 2024 | 1804 (22.8) | 406 (20.2) | 464 (23.7) | 460 (23.3) | 474 (24.3) |
| February 2024 | 1467 (18.6) | 402 (20.0) | 339 (17.3) | 345 (17.4) | 381 (19.5) |
| March 2024 | 1025 (13.0) | 263 (13.1) | 234 (12.0) | 246 (12.4) | 282 (14.5) |
| April 2024 | 455 (5.8) | 155 (7.7) | 85 (4.3) | 105 (5.3) | 110 (5.6) |

a. Quartile 1 represents the lowest level of socioeconomic disadvantage (most affluent), while Quartile 4 represents the highest level of disadvantage.
*(*) p-value < 0.001*

**Table 2.2.** Association of ADI by quartiles on influenza vaccination, US FluVE Network 2023-2024

| | | Vaccination Status[a] n (% out of quartile) | | Risk Ratio[c] RR (95% Confidence Interval) | |
|---|---|---|---|---|---|
| | **n (%)** | **Vaccinated** | **Not Vaccinated** | **Unadjusted[b]** | **Adjusted[b]** |
| **Overall** | 7898 | 3063 (38.8) | 4829 (61.2) | - | - |
| **ADI Quartile** | | | | | |
| Quartile 1 | 2011 (25.5) | 967 (48.1) | 1044 (51.9) | *Reference* | |
| Quartile 2 | 1958 (24.8) | 807 (41.2) | 1151 (58.8) | **0.86 (0.80, 0.92)** | **0.91 (0.85, 0.97)** |
| Quartile 3 | 1978 (25.0) | 747 (37.8) | 1231 (62.2) | **0.80 (0.74, 0.85)** | **0.88 (0.82, 0.94)** |
| Quartile 4 | 1951 (24.7) | 542 (27.8) | 1409 (72.2) | **0.57 (0.53, 0.62)** | **0.77 (0.70, 0.84)** |

a. Vaccinated means vaccinated more than 14 days before enrollment. Vaccination status was ascertained from self-report and electronic health records.
b. Output with p-value <0.05 were bolded
c. Models were adjusted for: age (category), sex, race, ethnicity, smoking exposure, history of a high-risk condition, month of illness onset and site.

**Table 2.3.** Association of ADI by quartiles on influenza test positivity, US FluVE Network 2023-2024

| | Test Results[a] n (% out of quartile) | | Risk Ratio[c] RR (95% Confidence Interval) | |
|---|---|---|---|---|
| | **Positive** | **Negative** | **Unadjusted[b]** | **Adjusted[b]** |
| **Overall** | 1858 (23.5) | 6042 (76.5) | - | - |
| **ADI Quartile** | | | | |
| Quartile 1 | 380 (18.9) | 1631 (81.1) | *Reference* | |
| Quartile 2 | 428 (21.9) | 1530 (78.1) | **1.15 (1.02, 1.31)** | 1.11 (0.98, 1.25) |
| Quartile 3 | 471 (23.8) | 1507 (76.2) | **1.27 (1.13, 1.43)** | **1.15 (1.02, 1.30)** |
| Quartile 4 | 579 (29.7) | 1372 (70.3) | **1.57 (1.40, 1.76)** | **1.18 (1.04, 1.34)** |

a. Vaccinated means vaccinated more than 14 days before enrollment. Vaccination status was ascertained from self-report and electronic health records.
b. Output with p-value <0.05 were bolded
c. Models were adjusted for: age (category), sex, race, ethnicity, smoking exposure, history of a high-risk condition, and month of illness onset.

**Figure 2.3.** Test Positivity by Area Deprivation Index (ADI) Quartile, US FluVE Network 2023-2024

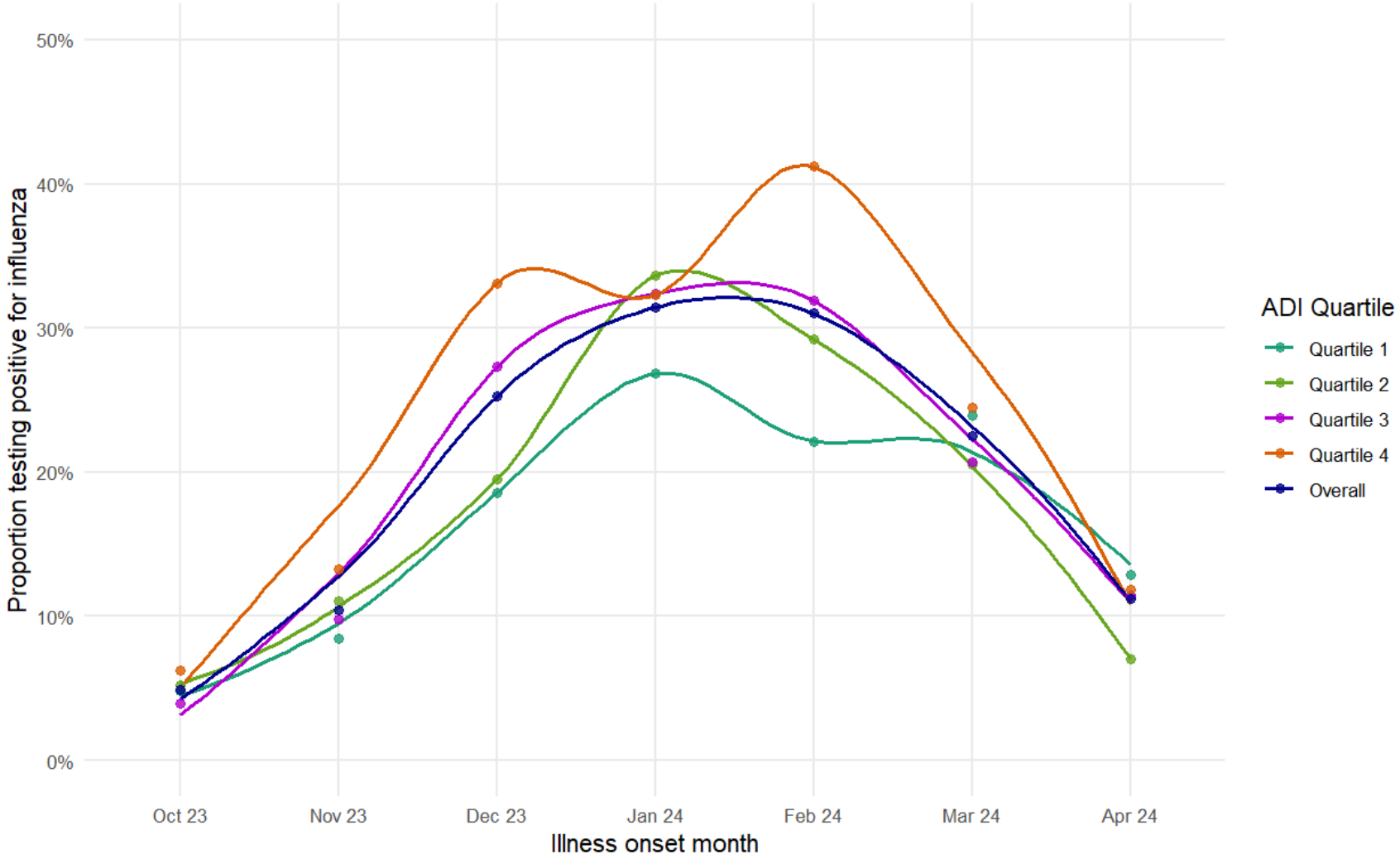


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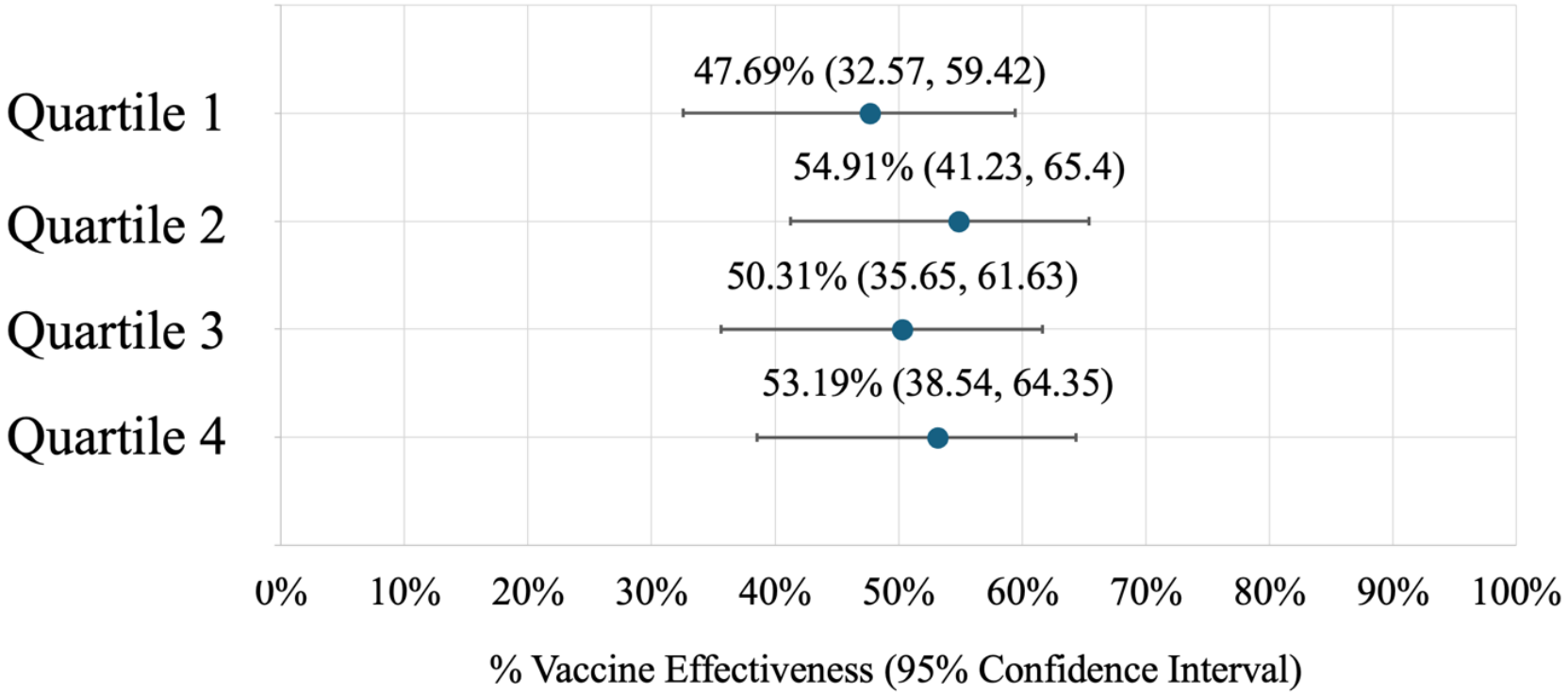
**Figure 2.4.** Vaccine Effectiveness by Area Deprivation Index (ADI) Quartile, US FluVE Network 2023-2024

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# Chapter 3. Distributional cost-effectiveness analysis of a targeted influenza vaccination intervention strategy using data from US Flu VE Network, 2023 - 2024

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**Keywords:**

neighborhood disadvantage, influenza, area deprivation index, distributional cost effectiveness analysis

*ABSTRACT*

*Introduction:* In the United States, influenza-related illness is estimated to result in nearly $30 billion in total economic losses, including both direct medical costs and indirect productivity losses. Targeted strategies to increase vaccine uptake in disadvantaged communities could help reduce inequities between disease burden and vaccination rates. The objective of this study was to construct a distributional cost-effectiveness model (DCEA) to estimate the health, cost, and equity impacts of an influenza vaccination intervention strategy. The modeled intervention strategy aimed to increase vaccine uptake among the most disadvantaged population with a vaccine voucher, financial incentive, and mailed reminders.

*Methods:* We constructed a decision tree model to estimate the health and economic outcomes of an annual influenza season for 20 subgroups by disadvantage measured by Area Deprivation Index (4 groups, with Quartile 4 (Q4) as the most disadvantaged group); and age (5 groups): 6 months–4 years, 5–17 years, 18–49 years, 50–64 years, and 65 years and older. Model input parameters were derived from the 2023 - 2024 US Flu Vaccine Effectiveness Network (Flu VE Network) dataset and published sources. The primary outcome measured was the incremental cost-effectiveness ratio (ICER), with a willingness-to-pay threshold (WTP) of $100,000 per QALY. To assess whether the intervention improved both population health and equity, we calculated additional inequality measures: the DCEA ICER using an inequality aversion parameter ($\varepsilon$) of 12.12, the Atkinson inequality index (A($\varepsilon$)), and the proportion of QALYs allocated to the most disadvantaged.

*Results:* Under the standard cost-effectiveness framework, the targeted intervention was cost-effective compared to a regular influenza season at the $100,000/QALY WTP threshold, with an incremental ICER of $262/QALY. When considering distributional weighting, the equity-weighted (DCEA) ICER decreased as inequality aversion increased, dropping from $262/QALY at ε = 0 (no aversion, like standard CEA) to $216/QALY at the estimated ε = 12.12. The

intervention provided an incremental net monetary benefit of about $160 million per 100,000 individuals (roughly $1,600 per person) at the $100,000/QALY threshold. For all $\varepsilon > 0$, the Atkinson inequality index was lower under the intervention scenario, decreasing approximately 15% at $\varepsilon = 12.12$. All additional QALYs gained were attributed to the most disadvantaged quartile (Q4), which captured 100% of the health benefits. These findings suggest that targeting the lowest socioeconomic quartile can reduce health inequality, with the case becoming stronger as inequality aversion increases.

*Conclusion:* Under the standard cost-effectiveness framework, the intervention proved cost-effective at the $100,000/QALY willingness-to-pay threshold. When equity considerations were included, the case for implementation became stronger. When the highest quartile of the area deprivation index was considered, vaccination efforts targeting the most disadvantaged neighborhoods were cost-effective and improved population health. Overall, influenza immunization programs should consider neighborhood disadvantage in prioritizing populations during influenza seasons.

*INTRODUCTION*

For the 2023–2024 United States (U.S.) influenza season, influenza-related illness caused $29 billion in total economic losses among adults, including both direct medical costs and indirect productivity losses.[90] Since the 2010 – 2011 season, the CDC's Advisory Committee on Immunization Practices has recommended yearly influenza vaccinations for all children and adults nationwide to prevent illness, complications, and death caused by the flu.[91] Though many vaccines are considered to be cost-effective, systemic inequities can hinder access to them.[86,92] Most adults get their yearly flu vaccine at medical clinics or pharmacies.[93] However, while increasing vaccination rates offers important economic and health advantages, disparities in health insurance coverage and access to primary care or vaccination sites lead to unequal vaccination rates across sociodemographic groups.[94] For the 2023–2024 influenza season, ~22% of uninsured adults received a vaccination compared to 52% of insured adults. Similarly, 39.5% of adults with income below the poverty line were vaccinated, compared to 54.2% of those earning at least $75,000.[95] These gaps result in worse health outcomes, as the likelihood of testing positive for influenza and hospitalization rates also vary by socioeconomic status.[93,96] In census tracts with high poverty levels (≥20% of residents below the federal poverty line), the age-adjusted incidence of influenza hospitalizations was 21.5 per 100,000, nearly twice that in low-poverty areas (<5% below the poverty line), at 10.9 per 100,000.[96]

Given low vaccination rates in certain populations, targeted strategies are needed to increase uptake. Though the flu vaccine is safe, reduces illness, and is cost-effective, adult vaccination rates have stalled at 45–50% over the last five years, with a further one-third of adults stating they will definitely or probably not get a vaccine.[95] Healthy People 2030 has identified improving influenza vaccination as a leading health indicator and recommends strategies focused on making vaccines available in nontraditional settings, sending vaccination reminders, and reducing costs to reduce access barriers.[57] These strategies could be further tailored to account

for socioeconomic factors influencing adults' and parents' vaccine-seeking behaviors into targeted vaccination campaigns to improve vaccination rates.[60,61] Composite social determinants of health measures like area deprivation index (ADI) are particularly important for public health departments and policymakers, as they consolidate individual factors and help identify areas of health disparities, informing the development of strategic interventions to address them.[8,63,97,98] Since the COVID-19 pandemic in 2020, there has been a growing need to support and coordinate hyperlocal efforts to reduce inequities in routine immunization strategies.[99] Being able to differentiate health disparities can better inform community-based strategies and shared decision-making to improve health outcomes, such as increasing vaccine uptake.[100,101]

Previous cost-effectiveness analyses of influenza vaccines have focused on estimating economic outcomes by age and risk status, but have not taken socioeconomic factors into account.[86,102,103] Given persistent disparities in vaccination rates and worse influenza outcomes among different socioeconomic groups, evaluating the cost-effectiveness of vaccination strategies that include social determinants measures would provide empirical evidence. This evidence could demonstrate the potential of targeted interventions for communities with the highest influenza risk, helping to reduce influenza inequalities and avoid additional costs from increased outpatient visits and hospitalizations. [104,105] This analysis focused on estimating the costs and health benefits of a new intervention designed to boost influenza vaccination among the most disadvantaged group. The overall objective of this study was to leverage a distributional cost-effectiveness model to estimate the health, cost, and equity impacts of an influenza vaccination intervention strategy targeting the most disadvantaged populations. [106]

*METHODS*

Cost-effectiveness analyses can be used to guide the allocation of limited resources to maximize health, as measured by quality-adjusted life years (QALYs).[107] However, cost-effectiveness analyses (CEAs) can mask uneven distributions of health benefits (e.g., a costly

intervention may yield health gains only among advantaged individuals) to prioritize efficiency. The distributional cost-effectiveness analysis (DCEA) framework enhances CEAs by explicitly assessing how health interventions affect equity, helping guide decisions by balancing costs, health outcomes, efficiency, and equity. The DCEA model building and cost-effectiveness analysis consist of two stages: 1) simulating baseline distributions of health, costs, and benefits for base case and intervention scenarios, and 2) evaluating whether these distributions improve overall health and reduce inequality.[106,107]

*Study Design*

We adapted a model from DeLuca et al. (2023) to construct a decision tree model and estimate the health and economic outcomes of an annual influenza season versus a targeted vaccination intervention strategy (described below) by hypothetical US cohorts (**Figure 3.1**).[86] The model included 20 subgroups stratified by disadvantage quartile, as measured by the area deprivation index (4 groups), and age (5 groups): 6 months–4 years, 5–17 years, 18–49 years, 50–64 years, and 65 years and older.[86,108] The model did not incorporate influenza transmission dynamics. A 1-year time horizon, comprising 30 weeks, simulated a hypothetical annual influenza season. A societal perspective was chosen for this economic evaluation to determine the appropriate resource allocation and to integrate direct medical costs and caregiver costs. Model input parameters were derived from the 2023 - 2024 US Flu Vaccine Effectiveness Network (Flu VE Network) dataset and published sources.

*US Flu Vaccine Effectiveness Network*

Since 2004, the Flu VE Network has provided clinical effectiveness estimates of licensed flu vaccines and has played a crucial role in local influenza surveillance.[20] For over 20 years, the Flu VE Network has enrolled over 95,000 pediatric and adult participants across multiple study sites, and collected data from baseline and follow-up surveys, immunization records, and lab-confirmed test results. For the 2023 – 2024 influenza season, 7,898 participants were enrolled at 7 study sites across the U.S., with patients recruited from outpatient medical care settings for

acute respiratory infection symptoms.[20] We used the participant dataset to estimate population distributions and influenza outcomes by neighborhood disadvantage, as measured by the area deprivation index. Participants provided consent under a Public Health Service determination or individual-level consent for primary data collection. To complete CEA, ethics approval for use of the Flu VE Network dataset was obtained from the University of Washington Human Subjects Division (STUDY0002234). Beyond that, since this analysis used only aggregate, published data, it did not require further institutional review board approval.

*Area Deprivation Index*

The Area Deprivation Index (ADI) is a composite score derived from 17 variables from the U.S. Census American Community Survey to estimate block-level socioeconomic status at the Census tract level. The variables include population-level measures of income, employment, education, household characteristics, vehicle access, poverty, and housing costs.[18,19] ADI scores are available at both state and national levels. For this analysis, Flu VE participants' addresses at the time of study enrollment were geocoded and categorized into quartiles based on national scores, which range from 1 (least disadvantaged) to 100 (most disadvantaged). Participants in Quartile 4 represent the top 25th percentile of disadvantage within the group.

*Intervention Description*

For this analysis, we focused on the impact of a hypothetical multi-component vaccination intervention targeting residents of the most disadvantaged neighborhoods (Quartile 4), delivered through mass communication strategies (mailed letters) and the distribution of vaccine vouchers with a $20 financial incentive for completion. The intervention mirrors a successful pharmacy-led partnership with local community organizations that distributed influenza vaccine vouchers nationwide, with added costs of a hypothetical informational letter and financial incentive to optimize response and vaccine uptake rates.[109,110]

*Model Structure*

The decision tree model included influenza and vaccination outcomes. During a typical influenza season, an individual in any ADI quartile and age group could experience an uncomplicated influenza illness, seek medical care, be hospitalized due to influenza, or die from influenza. Additionally, for vaccinated individuals, the following vaccine-related adverse events were recorded: injection-site reaction, systemic reaction, anaphylaxis, and Guillain-Barré syndrome.

*Model Inputs*

*i. Derived influenza-related parameters by ADI Quartile and Age Group*

Influenza-related parameters, such as probabilities of vaccination and illness, were derived from an individual-level dataset, estimated by ADI quartile and age group, and validated against published data (**Tables 3.1–3.4**). The influenza-related parameters were chosen based on influenza clinical outcomes that may be affected by differences in vaccination and infection rates, aligning with the natural progression of the disease.[13] Using the 2023–2024 US Flu Vaccine Effectiveness Network dataset, we calculated probabilities based on each participant's laboratory-confirmed influenza result, seasonal influenza vaccination status (2 groups), age group (5 groups), and ADI quartile (4 groups), for a total of calculated probabilities for up to 40 subgroups. We derived three estimates: 1) the distribution of age groups by ADI quartile (**Table 3.1**), 2) the baseline probability of influenza vaccination by age group and ADI quartile (**Table 3.1**), and 3) the probability of medically attended influenza illness by vaccination status, age group, and ADI quartile (**Tables 3.2 – 3.3**). ADI quartile served as the equity-relevant measure of socioeconomic disadvantage for the distributional cost-effectiveness analysis. The probability of influenza vaccination and corresponding 95% confidence intervals were estimated using logistic regression, with vaccination status as the outcome and an $[ADI\ Quartile\ x\ Age\ group]$ interaction term, so coverage could be estimated separately within each subgroup. Similarly, the probabilities and 95% confidence intervals for laboratory-confirmed influenza were modeled using logistic regression with an $[Vaccination\ status\ x\ Age\ group]$ interaction term to allow vaccine

effectiveness to vary across age groups; the ADI quartile was included to adjust the baseline risk of influenza for socioeconomic disadvantage. Since the US Flu VE Network population probabilities are conditional on individuals who present to outpatient medical clinics with symptomatic influenza-like illness, the predicted probabilities would exceed the general population's incidence. We used the 2023 – 2024 season CDC-estimated symptomatic influenza illness rate by age group to calibrate the US Flu VE estimates, as it measures the overall population rate (the vaccinated/unvaccinated mix at observed coverage).[111] The uncalibrated and calibrated estimates are presented in **Tables 3.2 – 3.3**. For each age group, a calibration factor was calculated by dividing the CDC estimates of cumulative influenza incidence by the model's vaccination-status-weighted population incidence (**Table 3.4**).[3] The probabilities of illness by vaccination status for each age group across all socioeconomic quartiles were multiplied by $k_a$, including the lower- and upper-bound values, to calculate probabilistic sensitivity estimates on the calibrated scale.

ii. *Other Influenza-Related Parameters*

Other influenza-related parameters, such as hospitalization and death, were were estimated based on published literature.[11,20,86,111–118] Age-specific hospitalization rates were derived from the CDC Influenza Hospitalization Surveillance Network (FluSurv-NET) for the 2023-2024 season (**Table 3.5**).[111] For each age group, the hospitalization rate was calculated as reported hospitalizations divided by the FluSurv-NET population, and then corrected following the established CDC burden-estimation methodology.[111,117] Since the model uses influenza illness estimates derived from the Flu VE Network participants, a population of medically attended symptomatic cases rather than the total population, the per-population hospitalization rate was re-expressed as the conditional probability of hospitalization given a medically attended influenza

[3] To calculate calibration factor (k) by age group (a), the following formula was used:

$$k_a = \frac{CDC-incidence_a}{[(vaccination_a * probability\ of\ flu \mid vaccination)+((1-vaccination_a) * probability\ of\ flu \mid vaccination))]}$$

case. Finally, to align hospitalization rates with published data on the association between census-tract poverty and influenza hospitalization, we used a socioeconomic status (SES) severity multiplier.[96] We set the probability of hospitalization for individuals in Quartile 4 to 1.3 times that for those in Quartile 1. Similarly, the probabilities for Quartiles 2 and 3 were adjusted using multipliers of 1.08 and 1.16 respectively, to reflect the SES gradient. Age-specific influenza death probabilities were derived from the corresponding hospitalization estimates.[111] For each age group, the hospitalization rate was adjusted for under-detection and multiplied by an age-specific ratio of deaths to hospitalizations. As with hospitalizations, the death rate was converted to the probability of death conditional on a medically attended influenza case.[111,117]

*iii. Adverse influenza-vaccine adverse reactions and utility decrements*

Probabilities of risks of adverse vaccine reactions, such as injection-site and systemic reactions, anaphylaxis, and Guillain-Barré syndrome, were based on published studies (**Table 3.6**).[86,111,112] Utility decrements were estimated to be equivalent to 1 week of influenza illness and were applied to illness, hospitalization, and vaccination side effects (**Tables 3.7)**. For all parameters, if the original source did not specify a distribution, 95% confidence intervals for influenza probabilities were derived (estimate ± 1.96 × standard error); for parameters reported only with point estimates and bounds, bounds were taken from the source. These intervals were converted to standard errors, where missing, and used to parameterize distributions for the probability inputs in the probabilistic sensitivity analysis.

*iv. Costs*

The analysis focused on direct medical costs, including over-the-counter medications, outpatient visits, hospitalizations, and vaccine administration and side effects (**Table 3.8).** Vaccination costs were calculated based on the CDC Advisory Committee on Immunization Practices' age group recommendations for the 2023 – 2024 influenza season and historical uptake rates.[119] If more than one vaccine was recommended for the age group (ex. for >65 years, the recommended vaccines are quadrivalent high-dose inactivated influenza vaccine (HD-IIV4),

quadrivalent recombinant influenza vaccine (RIV4), or quadrivalent adjuvanted inactivated influenza vaccine (aIIV4)), the cost was calculated using a weighted average of historical uptake for each vaccine type by age group.[120–122] Costs were reported in 2025 U.S. dollars, with historical costs inflated using the Consumer Price Index.[123]

*v. Intervention strategy parameters*

The weekly change in vaccine uptake due to the intervention strategy was estimated to range from 0.027% to 0.037% (**Table 3.6**), with an average of 0.32%, based on a similar influenza vaccine intervention.[113] These estimates were derived from adult populations aged 18-49 years, so we adjusted vaccine uptake by age group. Adults aged 50-64 showed moderate vaccine responsiveness, so we adjusted the estimate to 0.75 times that of the 18-49 group, with bounds of 0.7 and 0.8. Adults aged 65 had lower responsiveness, likely due to their high baseline vaccination and Medicare coverage.[93] The estimate for this group was adjusted to 0.5 times (bounds: 0.4-0.6). It was estimated that children under 18 would have lower responsiveness because parents or caregivers act as indirect decision-makers, and due to universal vaccination coverage provided by the Vaccines for Children program. As such, the estimate was adjusted by 0.75 times (bounds: 0.7 – 0.8) for 5-17 years, and 0.4 (bounds: 0.3 – 0.5) for children under 4 years. The vaccination intervention costs included mailing and printing of two reminder letters (~$1.15), a vaccine voucher (cost varied by age group), and a $20 financial incentive (**Table 3.8**). The intervention strategy costs were based on retail and published estimates and estimated per person.[110,113,124]

*Analysis*

We calculated the costs and health benefits for each scenario to calculate the incremental cost-effectiveness ratio (ICER) for each age group. **Figure 3.2** visually summarizes the calculation and inputs for the analysis. The ICER is defined as the additional cost of the intervention divided by the difference in associated health benefits (incremental cost [$] per person/QALYs gained per person), which we interpreted as a cost per health outcome gained.

The incremental cost was the per-person cost in the intervention scenario minus the cost in the base case (a usual influenza season, without equity targeting), capturing both the investment in the intervention and differences in medical costs; the incremental QALY was, similarly, the per-person QALYs in the intervention scenario minus those in the base case, summed across all four ADI quartiles even though the intervention itself was directed only at the most disadvantaged quartile (Quartile 4). Based on the 2023 Institute for Clinical and Economic Review's Value Assessment Framework, we set the willingness-to-pay threshold of $100,000 per QALY (the lower bound of the Institute's recommended range).[125] To assess whether the intervention improved both population health and reduced inequities, we compared economic and health outcomes with three measures of equity: (1) the standard ICER versus the DCEA ICER using a range of inequality aversion parameters ($\varepsilon$), (2) changes in the Atkinson inequality index (A($\varepsilon$)), and (3) the proportion of QALYs allocated to the most disadvantaged. **Table 3.9** details the specific calculation steps.

Sensitivity analysis involved modifying model parameters to identify key assumptions and examine how changes in the probabilities affected outcomes. We performed both deterministic (one-way) and probabilistic sensitivity analyses. In the one-way analysis, each parameter was varied individually within its 95% confidence interval, with results summarized in a tornado diagram that highlighted the most influential parameters. The probabilistic analysis involved running 1,000 Monte Carlo iterations, where all parameters were sampled simultaneously from their respective distributions reflecting the estimated means and standard errors. For the equity analysis, we calculated the ICER across various inequality aversion parameters (ε = 0.0, 0.5, 1.0, 3.0, 12.12, 30.0), focusing primarily on ε = 12.12, which is the median estimate for the US.[126] We reported findings in accordance with standard recommendations for cost-effectiveness analyses and the 2022 CHEERS (Consolidated Health Economic Evaluation Reporting Standards) statement and its accompanying Explanation and Elaboration document.[127,128] All US Flu VE

probabilities were derived in R (version 2026.01.2+418); the remaining calculations and analyses were performed in Excel.

*RESULTS*

The distributional cost-effectiveness analysis aimed to model an intervention to increase vaccine uptake among individuals in the most disadvantaged ADI quartile and estimate incremental costs and quality-adjusted life years over one influenza season. **Tables 3.1 – 3.8** present the key model parameters, including those derived from the Flu VE population estimates for demographic distribution, vaccination probabilities, and test positivity, as well as costs, transition probabilities, and utility decrements.

*Baseline Results*

**Table 3.10** summarizes the averted medically attended infections (MAI) comparing the base case scenario (no intervention) and the targeted intervention from a societal perspective. The intervention averted an average of 2,051 MAI (95% CI: 1645, 2483), 71 hospitalizations (95% CI: 46, 94), and 1.87 deaths per 100,000 individuals (95% CI: 0.8, 2.9) in a population in the most disadvantaged ADI quartile. Averted MAI count was highest for individuals aged 6 months – 4 years, while hospitalizations and deaths averted were the highest for individuals aged ≥ 65 years (**Table 3.10**). The estimated cost of the intervention was a one-time fee ranging from $43.33 to 58.45, including a $20 financial incentive, two mailed reminder letters, and a vaccine voucher. The intervention had incremental costs ranging from $3.77 (aged ≥65 years) to $5.52 (aged 5-17 years) per person and yielded net positive QALYs across all age groups (**Table 3.11**). QALYs gained were highest for individuals aged 6 months - 4 years (0.02 QALYs) and lowest for those aged ≥65 years (0.01 QALYs). Compared with the base case, the intervention was projected to be cost-effective across all ages at a level well below the designated $100,000/QALY. The ICER was estimated at $261.85/QALY overall: the highest ICER was for adults aged 65 years and older

($370.60/QALY), and the lowest was for children aged 6 months – 4 years ($191.84/QALY) (**Table 3.11**).

*Sensitivity Analyses*

In one-way sensitivity analyses, the net monetary benefit (NMB) was used to evaluate the intervention's cost-effectiveness by comparing its value to the WTP threshold. Under the baseline analysis, the intervention yielded an NMB of almost $1,600 per person at a willingness-to-pay threshold of $100,000/QALY (approximately $160 million per 100,000 individuals) (**Table 3.12**). The intervention was most sensitive to three parameters (**Figure 3.3, Table 3.13**): vaccine effectiveness as captured by illness in vaccinated ADI Q4 individuals (NMB swing $957), the disease burden in ADI Q4 among unvaccinated individuals ($871), and the magnitude of the intervention's effect on vaccination coverage ($484). Cost parameters, such as vaccine cost and administration, hospitalization, and the intervention delivery, had a minimal impact on NMB, each shifting it by less than $10 across their 95% confidence intervals. Probabilistic sensitivity analyses were conducted to plot the incremental cost-effectiveness plane: a graphical representation of the QALYs gained and incremental cost over 1,000 iterations (**Figure 3.4**). Across simulations the intervention consistently produced QALY gains at a small positive incremental cost (the 95% confidence interval of incremental cost lay entirely above zero), so essentially all iterations fell in the more-costly/more-effective quadrant; at a willingness-to-pay threshold of $100,000/QALY the intervention was cost-effective in essentially all simulations. The sensitivity analyses highlighted the most influential parameters and confirmed that the intervention was cost-effective compared with the base case.

*Equity Assessment*

The analysis also aimed to address a question beyond cost-effectiveness: How would the intervention affect the distribution of health gains? The targeted ADI Quartile 4 intervention required $554,882 in incremental delivery costs to boost vaccination coverage among 24,702 individuals by 7.0 percentage points (from 27.5% to 34.5%). It prevented approximately 105

influenza infections compared with the base-case scenario. Because the intervention exclusively targeted population in ADI Q4, all averted cases and the resulting health gains benefited only this quartile. Cost savings resulted in $134,918 in averted seasonal influenza-related healthcare costs, for a net incremental cost of $419,963 and a standard ICER of $262/QALY. As the inequality aversion (ε) rose from 0 to 12.12, the DCEA ICER fell from $262 to $216 per equity-weighted QALY, which was up to approximately 18% below the standard ICER (**Table 3.14**). At every value of ε, the Atkinson inequality index was lower under the intervention than under the baseline (approximately a 15% relative reduction at ε = 12.12), indicating that targeting the population in ADI Quartile 4 is projected to diminish health inequality. The intervention also produced a positive, EDE QALY impact across the full range of ε, indicating the equity-weighted population health gain persists even under strong inequality aversion (**Figure 3.5**). On average, individuals in Quartile 4 gained 0.065 QALYs per person. Although this health improvement is notable, Q4 remains behind other quartiles, being roughly 0.80 QALYs below Q1 and about 0.40 below Q3. Consequently, this gain represents only about 8% of the total gap to the highest quartile. The intervention favors Q4's progress but does not nearly close the disparity gap (**Figure 3.6**).

*DISCUSSION*

We demonstrate that a hypothetical vaccination intervention strategy focused on highly disadvantaged communities is not only cost-effective but also enhances equity by prioritizing health gains among the most vulnerable. Our findings show that using ADI stratification can guide influenza vaccination resource allocation to provide population-level health, economic, and equity advantages. This approach draws on lessons learned during the early COVID-19 pandemic (2020), when public health officials across the United States used the CDC/ATSDR Social Vulnerability Index to prioritize vaccination resources to socially vulnerable populations.[129] Under the standard cost-effectiveness framework, the influenza intervention strategy was cost-effective at the $100,000/QALY willingness-to-pay threshold. We then integrated equity into the model by

estimating costs and health benefits based on ADI quartiles, showing that the targeted intervention increased QALYs for those in the most disadvantaged quartile. We applied three measures to determine whether the intervention strategy was equitable: changes in the DCEA ICER with respect to inequality aversion parameters ($\varepsilon$), the Atkinson inequality index (A($\varepsilon$)) used to derive the equally distributed equivalent (EDE) health, and the proportion of QALYs accruing to the most disadvantaged. The DCEA ICER decreases from $262.85 to $167.34/EDE QALY as inequality aversion increases, while the Atkinson inequality index drops by about 15% (from 0.00079 to 0.00067, a difference of 0.00012) at $\varepsilon$ = 12.12. These combined results suggest that the intervention strategy is both cost-effective and promotes equity.

The development of the intervention strategy was informed by the World Health Organization's Behavioral and Social Drivers (BeSD) of vaccination framework, which outlines beliefs and experiences that influence vaccine uptake. Though many factors influence vaccination, BeSD focuses on potentially changeable individual-level factors.[49] However, the most effective strategies to increase vaccine uptake involve using various multi-component interventions, and outcomes vary by socioeconomic status and age.[109,113,130]

Due to the higher effectiveness of multi-component interventions, we developed a hypothetical intervention strategy that involved multiple strategies to identify costs. For adults 18 years and older, convenience, financial incentives, and reminders have been associated with willingness to be vaccinated against influenza.[131] Reminders alone don't fully increase vaccination coverage, but early-season reminders, combined with repeated prompts, incentives, and convenience, may improve uptake.[113] Research on adults' choices of interventions to promote influenza vaccination found that reminders and walk-in access significantly increased vaccination intent compared with requiring appointments at unfamiliar locations.[131] During the 2023–2024 influenza season, pharmacies administered nearly 11 million more influenza doses to adults than medical offices, likely due to their extended hours and greater number of locations.[132] In addition, financial incentives were associated with the highest willingness to vaccinate in the 18–64 age

group and the lowest in those 65 and older, probably because of Medicare coverage and a generally greater health-seeking behavior in the older population.[133] Financial incentives are an effective strategy for boosting influenza vaccination rates, benefiting not only individuals but also caregivers, even among those who remain unvaccinated later in the season.[113]

In contrast, during the same 2023 – 2024 season, most children 17 years and younger received an influenza vaccine at a doctor's office (59.8%), with smaller percentages at a pharmacy/other location (16.2%) and clinic (14.3%).[93] Parents and caregivers play a key role in their children's vaccination decisions; thus, efforts to change parents' attitudes on vaccines might help boost vaccination rates among children. For parents who are hesitant about vaccines, clear recommendations from healthcare providers, closely followed by parental education, improve acceptance and increase awareness of disease risks, severity, and the benefits of vaccination.[94] Reminder letters can be created to address parental concerns, enhance understanding of influenza risks, and highlight the benefits of vaccination. The hypothetical intervention strategy was crafted as a multi-level approach, including a financial incentive, an educational reminder letter, and a vaccine voucher to cover costs, especially in cases of lack of coverage, to appeal to multiple age groups.

Apart from preventing illness and adverse influenza outcomes, increasing vaccine uptake can positively impacts the US economy. The estimated economic loss for adults during the 2023–2024 season included $16 billion in direct medical costs, such as outpatient visits and hospitalizations, and $13 billion in indirect costs from productivity losses due to missed workdays, caregiving, and premature death.[90] Indirect costs particularly affect adults aged 18 to 49 years and account for nearly 40% of total indirect costs across all age groups.[134] Although this study did not explicitly estimate the cost of productivity loss, we found that the intervention avoided just over $1 million in illness-related medical costs per 100,000 individuals in ADI Quartile 4. As of May 2026, while there are no immediate reductions in vaccine coverage, a proposed $1 trillion cut to Medicaid services is set to take effect in 2027. Together with the elimination of reporting

requirements for pediatric and prenatal immunizations in 2027 and confusion over the recommended immunization schedule in 2025, these vast changes could indirectly decrease access to primary care, hinder patient education and vaccination opportunities, and make it easier for adults and caregivers to delay vaccines.[135,136] Individuals with lower socioeconomic status face increased susceptibility to influenza due to limited preventative healthcare, such as routine services and vaccines, as well as higher residential crowding, more comorbidities, and limited sick leave access.[13,14,137] These factors contribute to disparities in vaccine coverage and illness rates at the neighborhood level, highlighting a greater need for healthcare access. Understanding these area-level socioeconomic status differences can better inform policies and vaccination programs, such as the Vaccines for Adults program, which funds vaccine access for under- and uninsured adults in the US.[138]

Our study contributes to the limited research on distributional cost-effectiveness analyses of influenza vaccines. We used multi-site, nationally representative data from the US Flu VE Network to estimate influenza probabilities using laboratory-confirmed results and validated immunization histories. This approach enabled us to determine probabilities across different ADI quartiles, age groups, and vaccination statuses, helping to assess the health, economic, and equity benefits of a targeted vaccination intervention strategy. The developed model could be adapted for studies involving other populations (e.g., uninsured and non-symptomatic individuals or evaluating socioeconomic inequities using a different index, such as the social vulnerability index). The findings also have implications for both local and national policy decisions. Local public health departments should create and apply similar intervention strategies to allocate financial resources to the most disadvantaged neighborhoods. Meanwhile, national policies must emphasize the importance of healthcare coverage through Medicaid funding and establish a requirement to collect national-level data on vaccination coverage, segmented by area-level socioeconomic status (e.g., the ADI), to improve understanding and visualization of influenza-season trends.

Our study had several key strengths. Standard cost-effectiveness analyses assess an intervention's efficiency but may mask increasing inequalities, whereas DCEA clearly shows where costs and health benefits are concentrated across disadvantage quartiles. We used data collected from a single year in the US Flu VE Network, a nationally representative source that employs a standardized protocol for collecting participant information and specimens across seven sites to group populations by disadvantage quartiles. We were able to calculate probabilities for up to 40 subgroups (4 ADI quartiles, 5 age groups, and 2 vaccination statuses) using detailed data. Another strength of the study was its calibration and validation using external, publicly available data. We used external data from the CDC's estimated US Flu Disease Burden for the 2023 – 2024 influenza season and results from DeLuca (2023) to validate with the model's estimated average cases, hospitalizations, and deaths, as well as the calculated ICERs.

Despite study strengths, our study has some limitations. First, one important limitation is that the probabilities by vaccination status were derived from participants who could access outpatient medical clinics for influenza-like illness. Since a larger proportion of uninsured individuals often live in more disadvantaged areas and have lower vaccination rates, we might be underestimating the gains in QALYs or the costs. However, we aimed to reduce bias in healthcare-seeking behavior estimates by calculating illness probabilities using a test-negative design and adjusting these probabilities with CDC's seasonal data. Second, geocoding of ADI may have misclassified some participants and might lead to attenuated findings. The unit used for ADI might obscure true variation in neighborhood disadvantage. Nevertheless, our findings indicate that more precise geocoding could produce even stronger results. For this analysis, we used probabilities derived from only one influenza season. The analysis could be more robust if it incorporated estimated probabilities from other influenza seasons to accommodate the variation in influenza severity. Third, we utilized a decision tree model which does not account for influenza transmission. Future studies might consider a compartmental or agent-based model to better account for transmission within households, workplaces, and the broader population.

*CONCLUSION*

The study strongly indicates that targeted vaccination in the most disadvantaged communities is both cost-effective and promotes equity. The intervention was found to be cost-effective at a $100,000/QALY threshold, with an ICER of $262, as well as equity improving: the Atkinson inequality index was lower under the intervention at every aversion level, and all health benefits were gained by the most disadvantaged quartile. Using nationally representative, deprivation-stratified data, the modeling strategies account for both economic efficiency and equity. This distributional approach makes it explicit who benefits rather than just providing a population average. These findings offer local and state public health departments solid, transferable evidence to justify focusing resources on increasing vaccine coverage in the most disadvantaged areas.

*TABLES AND FIGURES*

**Figure 3.1.** Decision tree

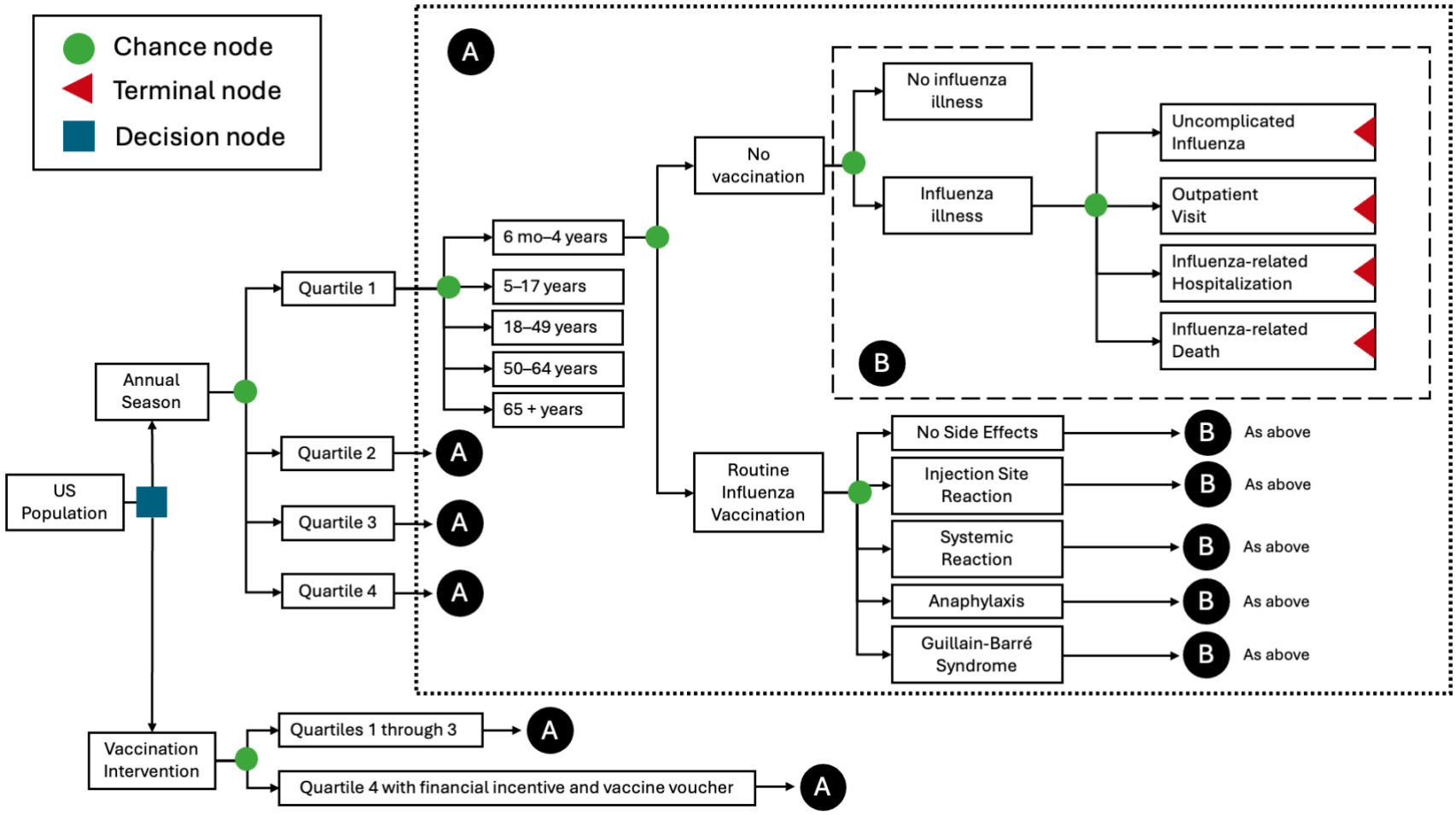


**Table 3.1.** Demographic distributions and probabilities of influenza vaccination by ADI quartile and age groups

| Variable | Base Case | Range[4] | Standard Error (SE) | Distribution Parameter 1[5] | Distribution Parameter 2[2] |
|---|---|---|---|---|---|
| **AGE DISTRIBUTIONS BY ADI QUARTILE[6]** | | | | | |
| ***Quartile 1*** | | | | | |
| 6 months-4 years | 0.072103 | 0.061596 - 0.084243 | 0.00577 | 145 | 1865 |
| 5-17 years | 0.123819 | 0.110136 - 0.138936 | 0.00734 | 249 | 1761 |
| 18-49 years | 0.436599 | 0.415063 - 0.458376 | 0.01106 | 878 | 1132 |
| 50-64 years | 0.179015 | 0.162877 - 0.196378 | 0.00855 | 360 | 1650 |
| ≥65 years | 0.188463 | 0.171971 - 0.206144 | 0.00872 | 379 | 1631 |
| ***Quartile 2*** | | | | | |
| 6 months-4 years | 0.103166 | 0.090461 - 0.117426 | 0.00678 | 207 | 1803 |
| 5-17 years | 0.146578 | 0.131604 - 0.162936 | 0.00789 | 295 | 1715 |
| 18-49 years | 0.392237 | 0.370842 - 0.414054 | 0.01089 | 788 | 1222 |
| 50-64 years | 0.175179 | 0.158982 - 0.192647 | 0.00848 | 352 | 1658 |
| ≥65 years | 0.182840 | 0.166345 - 0.200576 | 0.00862 | 368 | 1642 |
| ***Quartile 3*** | | | | | |
| 6 months-4 years | 0.131446 | 0.117267 - 0.147053 | 0.00753 | 264 | 1746 |
| 5-17 years | 0.158241 | 0.142821 - 0.174985 | 0.00814 | 318 | 1692 |
| 18-49 years | 0.344793 | 0.324166 - 0.366022 | 0.01060 | 693 | 1317 |
| 50-64 years | 0.185541 | 0.169025 - 0.203276 | 0.00867 | 373 | 1637 |
| ≥65 years | 0.179980 | 0.163675 - 0.197525 | 0.00857 | 362 | 1648 |
| ***Quartile 4*** | | | | | |
| 6 months-4 years | 0.176320 | 0.16005 - 0.193861 | 0.00850 | 354 | 1656 |
| 5-17 years | 0.192722 | 0.17583 - 0.210821 | 0.00880 | 387 | 1623 |
| 18-49 years | 0.356228 | 0.33528 - 0.377741 | 0.01068 | 716 | 1294 |
| 50-64 years | 0.170682 | 0.154638 - 0.188019 | 0.00839 | 343 | 1667 |
| ≥65 years | 0.104049 | 0.09127 - 0.118384 | 0.00681 | 209 | 1801 |

[4] 95% confidence intervals for proportions were calculated based on (estimate ± 1.96 × standard error).
[5] Utilized a beta distribution for the probabilistic sensitivity analysis. Distribution parameter 1 refers to α, distribution parameter 2 refers to β; both were calculated using the corresponding base case and SE.
[6] Proportions of age distribution were calculated based on counts of each age category within each quartile divided by the total number of participants for the corresponding quartile.

| PROBABILITY OF INFLUENZA VACCINATION BY ADI QUARTILE[7] | | | | | |
|---|---|---|---|---|---|
| ***Quartile 1*** | **Base Case** | **Range[2]** | **Standard Error (SE)** | **Distribution Parameter 1[8]** | **Distribution Parameter 2[2]** |
| 6 months-4 years | 0.434483 | 0.356188 - 0.516189 | 0.04082 | 64 | 83 |
| 5-17 years | 0.337349 | 0.281338 - 0.398331 | 0.02985 | 84 | 166 |
| 18-49 years | 0.384966 | 0.353324 - 0.417612 | 0.01640 | 338 | 541 |
| 50-64 years | 0.533333 | 0.481626 - 0.584334 | 0.02620 | 193 | 169 |
| ≥65 years | 0.767810 | 0.722630 - 0.807590 | 0.02167 | 291 | 88 |
| ***Quartile 2*** | | | | | |
| 6 months-4 years | 0.277228 | 0.219887 - 0.342948 | 0.03139 | 56 | 146 |
| 5-17 years | 0.209059 | 0.165879 - 0.259976 | 0.02400 | 60 | 226 |
| 18-49 years | 0.341146 | 0.308451 - 0.375424 | 0.01709 | 262 | 507 |
| 50-64 years | 0.533528 | 0.480554 - 0.585755 | 0.02684 | 184 | 161 |
| ≥65 years | 0.687151 | 0.637243 - 0.733069 | 0.02445 | 247 | 112 |
| ***Quartile 3*** | | | | | |
| 6 months-4 years | 0.215385 | 0.169602 - 0.269515 | 0.02549 | 56 | 203 |
| 5-17 years | 0.191693 | 0.151809 - 0.239103 | 0.02227 | 60 | 252 |
| 18-49 years | 0.348974 | 0.314102 - 0.385540 | 0.01822 | 238 | 445 |
| 50-64 years | 0.449591 | 0.399394 - 0.500836 | 0.02588 | 166 | 203 |
| ≥65 years | 0.668539 | 0.617964 - 0.715502 | 0.02488 | 239 | 118 |
| ***Quartile 4*** | | | | | |
| 6 months-4 years | 0.177326 | 0.140487 - 0.221336 | 0.02062 | 61 | 281 |
| 5-17 years | 0.138298 | 0.106948 - 0.177015 | 0.01787 | 51 | 321 |
| 18-49 years | 0.254676 | 0.223659 - 0.288397 | 0.01652 | 177 | 518 |
| 50-64 years | 0.384384 | 0.333639 - 0.437778 | 0.02657 | 128 | 206 |
| ≥65 years | 0.586207 | 0.517243 - 0.651948 | 0.03436 | 120 | 85 |

[7] Predicted probabilities were derived from 7,898 US Flu Vaccine Effectiveness Network participants enrolled in the 2023 – 2024 season. These predicted values represent the average estimated probability of influenza vaccination by ADI quartile and age group.
[8] Utilized a beta distribution for the probabilistic sensitivity analysis (PSA). Distribution parameter 1 refers to α, distribution parameter 2 refers to β; both were calculated using the corresponding base case and SE.

**Table 3.2.** Uncalibrated and calibrated probabilities of influenza illness among unvaccinated individuals, by ADI quartile and age groups

| PROBABILITY OF INFLUENZA ILLNESS BY ADI QUARTILE AMONG UNVACCINATED PARTICIPANTS (UNCALIBRATED)[9] | | | | | |
|---|---|---|---|---|---|
| ***Quartile 1*** | **Base Case** | **Range[10]** | **Standard Error (SE)** | **Distribution Parameter 1[11]** | **Distribution Parameter 2[9]** |
| 6 months-4 years | 0.237657 | 0.203672 - 0.275352 | 0.01829 | 129 | 412 |
| 5-17 years | 0.367067 | 0.329294 - 0.406547 | 0.01971 | 219 | 378 |
| 18-49 years | 0.243657 | 0.218886 - 0.270261 | 0.01311 | 261 | 811 |
| 50-64 years | 0.176317 | 0.147900 - 0.208856 | 0.01555 | 106 | 494 |
| ≥65 years | 0.143349 | 0.112185 - 0.181402 | 0.01766 | 56 | 337 |
| ***Quartile 2*** | | | | | |
| 6 months-4 years | 0.260445 | 0.225570 - 0.298632 | 0.01864 | 144 | 409 |
| 5-17 years | 0.395821 | 0.358319 - 0.434589 | 0.01946 | 250 | 381 |
| 18-49 years | 0.266818 | 0.240889 - 0.294457 | 0.01367 | 279 | 767 |
| 50-64 years | 0.194726 | 0.164406 - 0.229104 | 0.01650 | 112 | 463 |
| ≥65 years | 0.158980 | 0.125374 - 0.199539 | 0.01892 | 59 | 313 |
| ***Quartile 3*** | | | | | |
| 6 months-4 years | 0.282175 | 0.246381 - 0.320954 | 0.01902 | 158 | 401 |
| 5-17 years | 0.422395 | 0.384817 - 0.460893 | 0.01941 | 273 | 374 |
| 18-49 years | 0.288873 | 0.261567 - 0.317802 | 0.01435 | 288 | 709 |
| 50-64 years | 0.212549 | 0.181411 - 0.247416 | 0.01684 | 125 | 464 |
| ≥65 years | 0.174239 | 0.137775 - 0.217914 | 0.02044 | 60 | 283 |
| ***Quartile 4*** | | | | | |
| 6 months-4 years | 0.321285 | 0.283966 - 0.361035 | 0.01966 | 181 | 382 |
| 5-17 years | 0.468261 | 0.431293 - 0.505582 | 0.01895 | 324 | 368 |
| 18-49 years | 0.328486 | 0.300859 - 0.357354 | 0.01441 | 349 | 712 |
| 50-64 years | 0.245306 | 0.210918 - 0.283288 | 0.01846 | 133 | 409 |
| ≥65 years | 0.202611 | 0.161830 - 0.250596 | 0.02264 | 64 | 250 |

[9] Predicted probabilities were derived from 7,898 US Flu Vaccine Effectiveness Network participants enrolled in the 2023 – 2024 season. These predicted values represent the average estimated probability of influenza illness among unvaccinated participants and by ADI quartile and age group.

[10] 95% confidence intervals for proportions were calculated based on (estimate ± 1.96 × standard error).

[11] Utilized a beta distribution for the probabilistic sensitivity analysis (PSA). Distribution parameter 1 refers to α, distribution parameter 2 refers to β; both were calculated using the corresponding base case and SE.

**PROBABILITY OF INFLUENZA ILLNESS BY ADI QUARTILE AMONG UNVACCINATED PARTICIPANTS (CALIBRATED)** [12]

| ***Quartile 1*** | **Base Case** | **Range**[13] | **Standard Error (SE)** | **Distribution Parameter 1**[9] | **Distribution Parameter 2**[9] |
|---|---|---|---|---|---|
| 6 months-4 years | 0.149194 | 0.127859 – 0.172858 | 0.01148 | 144 | 819 |
| 5-17 years | 0.149232 | 0.133875 – 0.165282 | 0.00801 | 295 | 1682 |
| 18-49 years | 0.108686 | 0.097637 – 0.120553 | 0.00585 | 308 | 2525 |
| 50-64 years | 0.129587 | 0.108702 – 0.153503 | 0.01143 | 112 | 751 |
| ≥65 years | 0.044152 | 0.034553 – 0.055873 | 0.00544 | 63 | 1363 |
| ***Quartile 2*** | | | | | |
| 6 months-4 years | 0.163499 | 0.141606 – 0.187472 | 0.01170 | 163 | 835 |
| 5-17 years | 0.160921 | 0.145675 – 0.176683 | 0.00791 | 347 | 1810 |
| 18-49 years | 0.119017 | 0.107451 – 0.131346 | 0.00610 | 336 | 2485 |
| 50-64 years | 0.143117 | 0.120833 – 0.168384 | 0.01213 | 119 | 713 |
| ≥65 years | 0.048967 | 0.038616 – 0.061459 | 0.00583 | 67 | 1303 |
| ***Quartile 3*** | | | | | |
| 6 months-4 years | 0.177141 | 0.154670 – 0.201485 | 0.01194 | 181 | 840 |
| 5-17 years | 0.171725 | 0.156448 – 0.187377 | 0.00789 | 392 | 1892 |
| 18-49 years | 0.128855 | 0.116675 – 0.141759 | 0.00640 | 353 | 2387 |
| 50-64 years | 0.156216 | 0.133331 – 0.181843 | 0.01238 | 134 | 725 |
| ≥65 years | 0.053666 | 0.042435 – 0.067119 | 0.00630 | 69 | 1211 |
| ***Quartile 4*** | | | | | |
| 6 months-4 years | 0.201693 | 0.178265 – 0.226647 | 0.01234 | 213 | 843 |
| 5-17 years | 0.190372 | 0.175343 – 0.205545 | 0.00770 | 494 | 2101 |
| 18-49 years | 0.146525 | 0.134201 – 0.159402 | 0.00643 | 443 | 2582 |
| 50-64 years | 0.180292 | 0.155018 – 0.208208 | 0.01357 | 145 | 657 |
| ≥65 years | 0.062405 | 0.049845 – 0.077185 | 0.00697 | 75 | 1127 |

[12] Probabilities were calibrated to external population incidence from CDC using a calibration factor $k_a$.
[13] 95% confidence intervals for proportions were calculated based on (estimate ± 1.96 × standard error).

**Table 3.3.** Uncalibrated and calibrated probabilities of influenza illness among vaccinated participants, by ADI quartile and age groups

| PROBABILITY OF INFLUENZA ILLNESS BY ADI QUARTILE AMONG VACCINATED PARTICIPANTS (UNCALIBRATED)[14] | | | | | |
|---|---|---|---|---|---|
| ***Quartile 1*** | **Base Case** | **Range[15]** | **Standard Error (SE)** | **Distribution Parameter 1[16]** | **Distribution Parameter 2[14]** |
| **6 months-4 years** | 0.056060 | 0.034200 - 0.090582 | 0.01438 | 14 | 240 |
| **5-17 years** | 0.190420 | 0.146206 - 0.244181 | 0.02499 | 47 | 199 |
| **18-49 years** | 0.157099 | 0.134330 - 0.182911 | 0.01239 | 135 | 726 |
| **50-64 years** | 0.132351 | 0.107766 - 0.161529 | 0.01372 | 81 | 529 |
| **≥65 years** | 0.093119 | 0.075190 - 0.114792 | 0.01010 | 77 | 749 |
| ***Quartile 2*** | | | | | |
| **6 months-4 years** | 0.062871 | 0.038695 - 0.100573 | 0.01579 | 15 | 221 |
| **5-17 years** | 0.209926 | 0.162607 - 0.266630 | 0.02654 | 49 | 185 |
| **18-49 years** | 0.173924 | 0.148371 - 0.202830 | 0.01389 | 129 | 614 |
| **50-64 years** | 0.146989 | 0.120540 - 0.178066 | 0.01468 | 85 | 496 |
| **≥65 years** | 0.103937 | 0.084430 - 0.127324 | 0.01094 | 81 | 696 |
| ***Quartile 3*** | | | | | |
| **6 months-4 years** | 0.069670 | 0.042778 - 0.111497 | 0.01753 | 15 | 195 |
| **5-17 years** | 0.228744 | 0.178440 - 0.288255 | 0.02801 | 51 | 173 |
| **18-49 years** | 0.190293 | 0.163328 - 0.220536 | 0.01459 | 137 | 585 |
| **50-64 years** | 0.161317 | 0.132317 - 0.195243 | 0.01605 | 85 | 439 |
| **≥65 years** | 0.114633 | 0.093308 - 0.140078 | 0.01193 | 82 | 630 |
| ***Quartile 4*** | | | | | |
| **6 months-4 years** | 0.082720 | 0.051126 - 0.131141 | 0.02041 | 15 | 166 |
| **5-17 years** | 0.263164 | 0.207335 - 0.327809 | 0.03073 | 54 | 151 |
| **18-49 years** | 0.220581 | 0.190357 - 0.254098 | 0.01626 | 143 | 506 |
| **50-64 years** | 0.188065 | 0.155727 - 0.225326 | 0.01776 | 91 | 392 |
| **≥65 years** | 0.134885 | 0.109729 - 0.164741 | 0.01403 | 80 | 512 |

[14] Predicted probabilities were derived from 7,898 US Flu Vaccine Effectiveness Network participants enrolled in the 2023 – 2024 season. These predicted values represent the average estimated probability of influenza illness among vaccinated participants and by ADI quartile and age group.

[15] 95% confidence intervals for proportions were calculated based on (estimate ± 1.96 × standard error).

[16] Utilized a beta distribution for the probabilistic sensitivity analysis, Distribution parameter 1 refers to α, distribution parameter 2 refers to β; both were calculated using the corresponding base case and SE.

**PROBABILITY OF INFLUENZA ILLNESS BY ADI QUARTILE AMONG VACCINATED PARTICIPANTS (CALIBRATED)** [17]

| *Quartile 1* | Base Case | Range[14] | Standard Error (SE) | Distribution Parameter 1[14] | Distribution Parameter 2[14] |
|---|---|---|---|---|---|
| 6 months-4 years | 0.035193 | 0.021470 - 0.056865 | 0.00903 | 15 | 401 |
| 5-17 years | 0.077415 | 0.059440 - 0.099272 | 0.01016 | 53 | 637 |
| 18-49 years | 0.070076 | 0.059919 - 0.081590 | 0.00553 | 149 | 1982 |
| 50-64 years | 0.097274 | 0.079205 - 0.118719 | 0.01008 | 84 | 779 |
| ≥65 years | 0.028681 | 0.023159 - 0.035357 | 0.00311 | 82 | 2794 |
| ***Quartile 2*** | | | | | |
| 6 months-4 years | 0.039469 | 0.024291 - 0.063137 | 0.00991 | 15 | 370 |
| 5-17 years | 0.085346 | 0.066108 - 0.108399 | 0.01079 | 57 | 613 |
| 18-49 years | 0.077581 | 0.066183 - 0.090475 | 0.00620 | 144 | 1718 |
| 50-64 years | 0.108032 | 0.088593 - 0.130873 | 0.01079 | 89 | 738 |
| ≥65 years | 0.032013 | 0.026005 - 0.039216 | 0.00337 | 87 | 2640 |
| ***Quartile 3*** | | | | | |
| 6 months-4 years | 0.043737 | 0.026855 - 0.069994 | 0.01101 | 15 | 329 |
| 5-17 years | 0.092996 | 0.072545 - 0.117191 | 0.01139 | 60 | 589 |
| 18-49 years | 0.084882 | 0.072854 - 0.098372 | 0.00651 | 156 | 1676 |
| 50-64 years | 0.118563 | 0.097249 - 0.143497 | 0.01180 | 89 | 661 |
| ≥65 years | 0.035308 | 0.028739 - 0.043145 | 0.00367 | 89 | 2432 |
| ***Quartile 4*** | | | | | |
| 6 months-4 years | 0.051929 | 0.032095 - 0.082326 | 0.01281 | 16 | 283 |
| 5-17 years | 0.106990 | 0.084292 - 0.133271 | 0.01249 | 65 | 546 |
| 18-49 years | 0.098393 | 0.084911 - 0.113343 | 0.00725 | 166 | 1519 |
| 50-64 years | 0.138221 | 0.114454 - 0.165607 | 0.01305 | 97 | 602 |
| ≥65 years | 0.041545 | 0.033797 - 0.050741 | 0.00432 | 88 | 2042 |

[17] Probabilities were calibrated to external population incidence from CDC using a calibration factor $k_a$.

**Table 3.4.** Outlined calculation of the calibration factor based on probabilities of vaccination coverage and illness

| Quartile 1 | | | | |
|---|---|---|---|---|
| **Age Group** | **Vaccination Coverage** | **P(flu\|unvacc)[18]** | **P(flu\|vacc)** | **Population incidence[19]** |
| 6 months-4 years | 43.4% | 0.238 | 0.056 | 0.159 |
| 5-17 years | 33.7% | 0.367 | 0.190 | 0.307 |
| 18-49 years | 38.5% | 0.244 | 0.157 | 0.210 |
| 50-64 years | 53.3% | 0.176 | 0.132 | 0.153 |
| ≥65 years | 76.8% | 0.143 | 0.093 | 0.105 |
| **Quartile 2** | | | | |
| **Age Group** | **Vaccination Coverage** | **P(flu\|unvacc)** | **P(flu\|vacc)** | **Population incidence** |
| 6 months-4 years | 27.7% | 0.260 | 0.063 | 0.206 |
| 5-17 years | 20.9% | 0.396 | 0.210 | 0.357 |
| 18-49 years | 34.1% | 0.267 | 0.174 | 0.235 |
| 50-64 years | 53.4% | 0.195 | 0.147 | 0.169 |
| ≥65 years | 68.7% | 0.159 | 0.104 | 0.121 |
| **Quartile 3** | | | | |
| **Age Group** | **Vaccination Coverage** | **P(flu\|unvacc)** | **P(flu\|vacc)** | **Population incidence** |
| 6 months-4 years | 21.5% | 0.282 | 0.070 | 0.236 |
| 5-17 years | 19.2% | 0.422 | 0.229 | 0.385 |
| 18-49 years | 34.9% | 0.289 | 0.190 | 0.254 |
| 50-64 years | 45.0% | 0.213 | 0.161 | 0.190 |
| ≥65 years | 66.9% | 0.174 | 0.115 | 0.134 |
| **Quartile 4** | | | | |
| **Age Group** | **Vaccination Coverage** | **P(flu\|unvacc)** | **P(flu\|vacc)** | **Population incidence** |
| 6 months-4 years | 17.7% | 0.321 | 0.083 | 0.279 |
| 5-17 years | 13.8% | 0.468 | 0.263 | 0.440 |
| 18-49 years | 25.5% | 0.328 | 0.221 | 0.301 |
| 50-64 years | 38.4% | 0.245 | 0.188 | 0.223 |
| ≥65 years | 58.6% | 0.203 | 0.135 | 0.163 |

| **Age Group** | **Symptomatic Illness Estimates[111]** | **Population Estimates[111]** | **CDC Incidence[20]** | **Model Population Incidence[21]** | **k(a)[22]** |
|---|---|---|---|---|---|
| 6 months-4 years | 2,556,047 | 18,511,160 | 0.138 | 0.220 | 0.628 |
| 5-17 years | 8,224,211 | 54,320,701 | 0.151 | 0.372 | 0.407 |
| 18-49 years | 15,660,509 | 140,303,491 | 0.112 | 0.250 | 0.446 |
| 50-64 years | 8,444,156 | 62,531,182 | 0.135 | 0.184 | 0.735 |
| ≥65 years | 2,386,916 | 59,248,361 | 0.040 | 0.131 | 0.308 |

[18] P(flu|unvacc) = probability of influenza illness if unvaccinated; P(flu|vacc) = probability if vaccinated
[19] Population incidence calculated by [(coverage * P(flu|vacc)) + ((1 - coverage) * P(flu|unvacc)]
[20] Calculated by dividing symptomatic illness estimates by population estimates.
[21] Calculated by averaging the population incidence across quartiles.
[22] Calculated by CDC cumulative influenza incidence divided by the model population incidence.

**Table 3.5.** Probabilities of hospitalizations and death conditional on medically attended cases

| **Probability of hospitalizations due to influenza conditional on a medically attended influenza case quartile** | | | | | |
|---|---|---|---|---|---|
| **Age Group** | **Q1** | **Q2** | **Q3** | **Q4** | **Source** |
| 6 months-4 years | 0.00491 | 0.00530 | 0.00569 | 0.00643 | Influenza Hospitalization Surveillance Network (FluSurv-NET), 2025 |
| 5-17 years | 0.00217 | 0.00235 | 0.00252 | 0.00285 | |
| 18-49 years | 0.00439 | 0.00474 | 0.00509 | 0.00575 | |
| 50-64 years | 0.00828 | 0.00894 | 0.00961 | 0.01085 | |
| ≥65 years | 0.06168 | 0.06662 | 0.07155 | 0.08081 | |

| **Probability of death due to influenza conditional on a medically attended influenza case quartile** | | | | | |
|---|---|---|---|---|---|
| **Age Group** | **Q1** | **Q2** | **Q3** | **Q4** | |
| 6 months-4 years | 0.000031 | 0.000034 | 0.000036 | 0.000041 | Influenza Hospitalization Surveillance Network (FluSurv-NET), 2025 |
| 5-17 years | 0.000013 | 0.000014 | 0.000015 | 0.000017 | |
| 18-49 years | 0.000063 | 0.000068 | 0.000073 | 0.000082 | |
| 50-64 years | 0.000227 | 0.000246 | 0.000264 | 0.000298 | |
| ≥65 years | 0.002855 | 0.003083 | 0.003312 | 0.003740 | |

**Table 3.6.** Probabilities Associated with Influenza Vaccination and Illness

| Variable | Base Case | Range for Sensitivity Analysis | Type of Distribution | Distribution Parameter 1 | Distribution Parameter 2 | Source |
|---|---|---|---|---|---|---|
| ***Interventional Change in Uptake of Vaccination, Weekly[23]*** | | | | | | |
| Reference: 18-49 years | 0.00320 | 0.002700 – 0.003700 | Beta | 157 | 48855 | Chang, 2026 |
| 6 months-4 years | 0.00128 | 0.001080 – 0.001480 | Beta | 157 | 122611 | Derived |
| 5-17 years | 0.00240 | 0.002025 – 0.002775 | Beta | 157 | 65246 | |
| 50-64 years | 0.00240 | 0.002025 – 0.002775 | Beta | 157 | 65246 | |
| ≥65 years | 0.00160 | 0.001350 – 0.001850 | Beta | 157 | 98026 | |
| ***Probability of Injection Site Reaction[24]*** | | | | | | |
| 6 months-4 years | 0.00515 | 0.001 – 0.017 | Beta | 4 | 46 | DeLuca, 2023 |
| 5-17 years | 0.00165 | 0.000 – 0.002 | Beta | 4 | 46 | |
| ***Probability of Systemic Reaction*** | | | | | | |
| 6 months-4 years | 0.0115 | 0.001 – 0.025 | Beta | 5.2 | 194.8 | DeLuca, 2023; Prosser, 2006 |
| 5-17 years | 0.0035 | 0.000 – 0.008 | Beta | 5.2 | 194.8 | |
| ≥18 years | 0.011 | 0.000 – 0.044 | Beta | 0.8 | 73.2 | |
| ***Probability of Anaphylaxis*** | | | | | | |
| 6 months-17 years | 0.00000025 | 0 – 0.0000010 | Beta | 0.5 | 19.5 | DeLuca, 2023; Prosser, 2006 |
| ≥18 years | 0.00000025 | 0 – 0.0000025 | Beta | 0.1 | 3.9 | |
| ***Probability of Guillain-Barré syndrome*** | | | | | | |
| 6 months-17 years | 0.000001 | 0 – 0.000010 | Triangular | 0.000001 (most likely) | 0 (min), 0.000002 (max) | DeLuca, 2023 |
| ≥18 years | 0.000001 | 0 – 0.000002 | | 0.000001 (most likely) | 0 (min), 0.000002 (max) | |

[23] Estimated uptake based on behavioral differences related to insurance coverage, parental influence for children under 18, and lower responsiveness due to previously higher uptake. The values represent the increased probability of vaccination due to the intervention per week and was only applied to the intervention scenario.

[24] Averaged values from 6-23 months and 2-4 years and 5-11 years and 12-17 years to calculate estimates for 6 month – 4 years and 5 – 17 years, respectively.

**Table 3.7.** Utility Decrements

| Utility Decrement | Base Case | Range for Sensitivity Analysis | Type of Distribution | Standard Error | Source |
|---|---|---|---|---|---|
| **INFLUENZA ILLNESS** | | | | | |
| 6 months-4 years | 0.039 | 0.035 – 0.042 | Normal | 0.002 | DeLuca, 2023 |
| 5-17 years | 0.024 | 0.022 – 0.027 | Normal | 0.001 | |
| 18-49 years | 0.008 | 0.008 – 0.009 | Normal | 0.000 | |
| 50-64 years | 0.007 | 0.007 – 0.008 | Normal | 0.000 | |
| ≥65 years | 0.021 | 0.02 – 0.023 | Normal | 0.001 | |
| **HOSPITALIZATION** | | | | | |
| 6 months-4 years | 0.035 | 0.032 – 0.039 | Normal | 0.002 | DeLuca, 2023 |
| 5-17 years | 0.027 | 0.025 – 0.03 | Normal | 0.001 | |
| 18-49 years | 0.017 | 0.015 – 0.018 | Normal | 0.001 | |
| 50-64 years | 0.017 | 0.015 – 0.018 | Normal | 0.001 | |
| ≥65 years | 0.025 | 0.023 – 0.027 | Normal | 0.001 | |
| **SYSTEMIC REACTION** | | | | | |
| 6 months-4 years | 0.006 | 0.005 – 0.006 | Normal | 0.0002 | DeLuca, 2023 |
| 5-17 years | 0.004 | 0.003 – 0.004 | Normal | 0.0002 | |
| 18-49 years | 0.001 | 0.001 – 0.001 | Normal | 0.0001 | |
| 50-64 years | 0.001 | 0.001 – 0.001 | Normal | 0.0000 | |
| ≥65 years | 0.003 | 0.003 – 0.003 | Normal | 0.0001 | |
| **ANAPHYLAXIS**[25] | | | | | |
| All Ages | 0.014 | 0.014 – 0.014 | Normal | 0.0137 | DeLuca, 2023 |
| **GUILLAIN-BARRÉ SYNDROME** | | | | | |
| 6 months-4 years | 0.046 | 0.042 – 0.05 | Normal | 0.0021 | DeLuca, 2023 |
| 5-17 years | 0.044 | 0.04 – 0.048 | Normal | 0.0020 | |
| 18-49 years | 0.020 | 0.018 – 0.022 | Normal | 0.0009 | |
| 50-64 years | 0.022 | 0.02 – 0.024 | Normal | 0.0010 | |
| ≥65 years | 0.024 | 0.022 – 0.026 | Normal | 0.0011 | |

[25] Found no variation by age. Considered 1 day hospitalization and 1 week to return to usual health.

**Table 3.8.** Costs[26]

| Variable | Base Case | Range for Sensitivity Analysis | Type of Distribution | Distribution Parameter 1 | Distribution Parameter 2 | Source |
|---|---|---|---|---|---|---|
| **INFLUENZA-RELATED MEDICAL COSTS** | | | | | | |
| ***OTC medications for uncomplicated influenza***[27] | | | | | | |
| 6 months-4 years | $5.61 | | | | | DeLuca, 2023 |
| 5-17 years | $8.40 | | | | | |
| 18-64 years | $5.46 | | | | | |
| 50-64 years | $5.46 | | | | | |
| ≥65 years | $7.30 | | | | | |
| ***Outpatient visit for pneumonia and influenza***[28] | | | | | | |
| 6 months-4 years | $349.21 | $30.15 – 1,493.58 | Lognormal | 323 | 197 | DeLuca, 2023 |
| 5-17 years | $261.28 | $35.17 – 952.17 | Lognormal | 242 | 171 | |
| 18-49 years | $368.06 | $28.89 – 1,626.73 | Lognormal | 340 | 201 | |
| 50-64 years | $412.02 | $26.38 – 1,968.41 | Lognormal | 382 | 206 | |
| ≥65 years | $770.03 | $13.82 – 4,723.18 | Lognormal | 714 | 232 | |
| ***Hospitalization***[3] | | | | | | |
| 6 months-4 years | $20,170.24 | $1,943.29 – 83,577.66 | Lognormal | 18679 | 11798 | DeLuca, 2023 |
| 5-17 years | $20,907.61 | $2,281.2 – 82,918.18 | Lognormal | 19363 | 12730 | |
| 18-49 years | $31,546.06 | $2,872.85 – 133,262.74 | Lognormal | 29215 | 18109 | |
| 50-64 years | $36,687.55 | $3,147.95 – 158,050.64 | Lognormal | 33977 | 20646 | |
| ≥65 years | $28,702.11 | $2,585.19 – 121,374.4 | Lognormal | 26580 | 16414 | |
| ***Vaccination costs, 6 months-17 years*** | | | | | | |
| Per dose (IIV4) | $21.03 | | | | | CDC, 2023 |
| Physician office setting[29] | $23.35 | | | | | CMS, 2025 |
| Parent time (hours) | 2 | | | | | DeLuca, 2023 |
| Hourly earnings for parent/adult[30] | $36.44 | | | | | FRED, 2025 |
| ***Vaccination costs, ≥18 years***[31] | | | | | | |

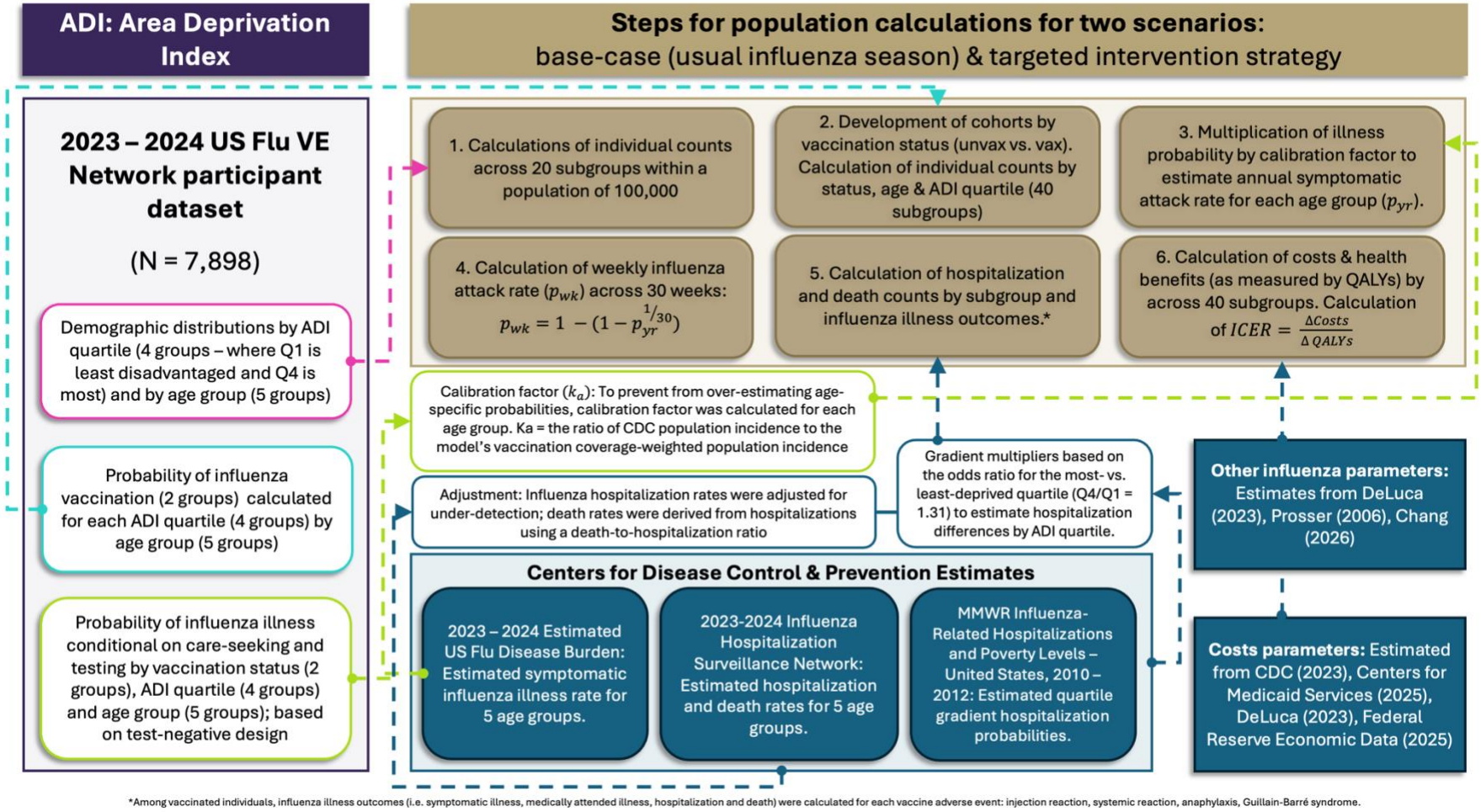
[26] Costs are reported in 2025 US dollar.
[27] Over the Counter (OTC) medication cost was calculated by costing out recommended dose of acetaminophen for average weight in each age group and are inflation-adjusted for 2025 using the U.S. Bureau of Labor Statistics.
[28] In this table parameter 1 refers to the mean. Lognormal distribution parameter 2 refers to median.
[29] CPT Code 90460: Immunization administration through 18 years of age via any route of administration, with counseling by physician or other qualified health care professional. Average of the national payment amounts for non-facility and non-facility limiting charges.
[30] 2025 Average Hourly Earnings of All Employees, dollars per hour, seasonally adjusted.
[31] Vaccination costs were calculated based on available vaccines and recommendations from the CDC for the 2023 – 2024 influenza season. We calculated the weighted average of all available vaccines for each age group based on published data.

| | | | | | | |
|---|---|---|---|---|---|---|
| Per dose (IIV4) | $20.52 | | | | | CDC, 2023; Hsiao, 2023 |
| Per dose (aIIV4) | $83.79 | | | | | CMS, 2023 |
| Per dose (RIV4), ≥65 years | $79.51 | | | | | CMS, 2023; Lloyd, 2025; Hsiao, 2023 |
| Per dose (HD-IIV4), ≥65 years | $79.51 | | | | | CMS, 2023; Lloyd (2025) |
| Physician office setting[32] | $23.35 | | | | | CMS, 2025 |
| **VACCINATION-RELATED ADVERSE EVENTS** | | | | | | |
| ***Physician visit for injection site reaction*** | | | | | | |
| 6 months – 17 years | $364.00 | $54 – 1,230 | Lognormal | 254 | 77 | DeLuca, 2023 |
| ***Physician visit for systemic reaction*** | | | | | | |
| 6 months-4 years | $349.21 | $30.15 – 1,493.58 | Lognormal | 323 | 197 | DeLuca, 2023 |
| 5-17 years | $261.28 | $35.17 – 952.17 | Lognormal | 242 | 171 | |
| 18-49 years | $368.06 | $28.89 – 1,626.73 | Lognormal | 340 | 201 | |
| 50-64 years | $412.02 | $26.38 – 1,968.41 | Lognormal | 382 | 206 | |
| ≥65 years | $762.49 | $13.82 – 4,685.49 | Lognormal | 706 | 231 | |
| ***Anaphylaxis, medical costs*** | | | | | | |
| 6 months-17 years | $8,607.24 | $99.24 – 26152.09 | Lognormal | 5687 | 3390 | DeLuca, 2023 |
| 18-49 years | $788.87 | $717.27 – 870.52 | Lognormal | 5687 | 3390 | |
| 50-64 years | $845.40 | $733.6 – 979.81 | Lognormal | 543 | 541 | |
| ≥65 years | $836.61 | $618.03 – 1133.06 | Lognormal | 583 | 579 | |
| ***Guillain-Barré syndrome, medical costs*** | | | | | | |
| 6 months-17 years | $61,218 | $12,668.42 – 150,040.08 | Lognormal | 40443 | 29343 | DeLuca, 2023 |
| ≥18 years | $114,692 | $77,104.65 – 154,720.55 | Lognormal | 79018 | 77968 | |
| ***Influenza-related death, productivity loss cost*** | | | | | | |
| 18-49 years | $2,744,326.68 | | | | | |
| ***INTERVENTION COSTS[33]*** | | | | | | |
| Incentive | $20.00 | | | | | Chang, 2026 |
| Letters | $2.30 | | | | | Ley, 2023; USPS, 2024 |
| Design Fee | $500.00 | | | | | |
| Vaccine voucher | Varies | | | | | |

[32] CPT Code 90460: Immunization administration through 18 years of age via any route of administration, with counseling by physician or other qualified health care professional. Average of the national payment amounts for non-facility and non-facility limiting charges.

[33] Design fee is divided across Quartile 4 population. The vaccine voucher cost depends on the individual's age to subsidize the cost of the vaccine.

**Figure 3.2.** Visual summary of analytical steps and sources for the distributional cost-effectiveness analysis




*Among vaccinated individuals, influenza illness outcomes (i.e. symptomatic illness, medically attended illness, hospitalization and death) were calculated for each vaccine adverse event: injection reaction, systemic reaction, anaphylaxis, Guillain-Barré syndrome.

**Table 3.9.** Calculation of distributional cost effectiveness and inequality parameters

| Step | Formula | Definitions/ Notes |
|---|---|---|
| **1. Calculate Quartile 4's (most disadvantage) share of incremental QALY** | $Porportion\ QALY_{Q(4)} = \frac{Q4\ QALYs\ gained}{Total\ QALYs\ gained}$ | $Q(4)$ = Quartile 4 (most disadvantage) |
| **2. Calculate health distribution by scenario (base case & intervention) and quartile** | $h_{Q(i)} = \frac{\sum QALY_{Q(i)}}{n_{Q(i)}}$ | $Q(i)$ = Quartiles 1 – 4<br>$h$ = QALYs per person<br>$n$ = Quartile population size |
| **3. Determine values of inequality aversion parameter ($\varepsilon$)**<br>a. 0 = No aversion (typical CEA)<br>b. 0.5 = Low aversion<br>c. 1.0 = Moderate aversion<br>d. 12.12 = Median U.S. estimate<br>e. 30.0 = Extreme aversion | *Range:* $0\ to\ \infty$ (theoretically) | ($\varepsilon$) quantifies society's preference for a more equal distribution of outcomes and are often calculated by specific countries.[139]<br>At $\varepsilon = 0$, there is no preference on the distribution of outcomes (no aversion to inequality).<br>As $\varepsilon \rightarrow \infty$, society demonstrates a willingness to sacrifice any amount of total health in pursuit of a more equal distribution (extreme aversion to inequality). |
| **4. Calculate Equally Distributed Equivalent (EDE) health** | $EDE = \left(\frac{1}{N}\sum h_{Q(i)}^{1-\varepsilon}\right)^{\frac{1}{1-\varepsilon}}$ | The EDE collapses health and cost outcomes as they are distributed across population subgroups into a single number.[139] Typical decision is to select scenario with highest EDE.<br><br>$h_{Q(i)}$ = QALY by quartile<br>$N$ = Total population per scenario |
| **5. Calculate the Atkinson inequality index (A($\varepsilon$))**<br><br>*The measure is expressed as a number between 0 (perfect equality) and 1 (maximum inequality).* | $A(\varepsilon) = 1 - \frac{EDE}{\bar{h}}$ | The A($\varepsilon$) relative loss of mean health attributable to its uneven distribution.[140] It is used to calculate the change in equity impact of the interventions.<br><br>$\bar{h}$ = average QALY |

| | | |
|---|---|---|
| **6. DCEA (Distributional Cost Effectiveness Analysis) ICER Input: $\Delta Cost$ (Incremental cost)** | $\Delta Cost = total\ costs\ of\ intervention - total\ costs\ of\ base\ case$ | |
| **7. DCEA ICER Input: $\Delta EDE$ (Incremental EDE health gain)** | $\Delta EDE = EDE_{I(\varepsilon)} - EDE_{BC(\varepsilon)}$ | $I =$ EDE of intervention at inequality aversion parameter $(\varepsilon)$<br><br>$BC =$ EDE of base case at $(\varepsilon)$ |
| **8. Calculate DCEA ICER at varying inequality aversion parameter $(\varepsilon)$** | $DCEA\ ICER = \frac{\Delta\ Cost}{[\Delta\ EDE(\varepsilon) * N]}$ | The DCEA ICER is an equity-weighted relative cost comparing to the standard ICER to assess how equ<br><br>$\Delta\ Cost$ equals the cost of the intervention delivery & influenza illness costs in the intervention scenario minus influenza illness costs in the base case scenario.<br>$\Delta\ EDE$ equals the EDE across the intervention scenario minus the EDE across the base case scenario for $(\varepsilon)$<br>$N =$ Total population across all quartiles |

**Table 3.10.** Medically attended infection (MAI), hospitalizations and deaths averted per season among Quartile 4 following a targeted vaccination intervention versus base case scenario

| Absolute Counts[34] | MAI | | Hospitalization | | Deaths | |
|---|---|---|---|---|---|---|
| **Age Groups** | **Average** | **95% CI** | **Average** | **95% CI** | **Average** | **95% CI** |
| 6 months-4 years | 221.56 | (163.91, 278.96) | 3.56 | (2.63, 4.48) | 0.02 | (0.017, 0.029) |
| 5-17 years | 109.18 | (68.59, 149.47) | 1.65 | (1.04, 2.26) | 0.01 | (0.004, 0.012) |
| 18-49 years | 70.64 | (42.34, 99.52) | 2.47 | (1.48, 3.48) | 0.04 | (0.021, 0.050) |
| 50-64 years | 89.27 | (6.71, 166.28) | 2.97 | (0.22, 5.54) | 0.08 | (0.006, 0.152) |
| ≥65 years | 15.89 | (2.84, 28.46) | 6.81 | (1.22, 12.20) | 0.32 | (0.056, 0.565) |
| Overall | 506.54 | (406.25, 613.34) | 17.47 | (11.38, 23.21) | 0.46 | (0.202, 0.718) |

| Rates (per 100K)[35] | MAI Rate | | Hospitalization Rate | | Death Rate | |
|---|---|---|---|---|---|---|
| **Age Groups** | **Estimate** | **95% CI** | **Estimate** | **95% CI** | **Estimate** | **95% CI** |
| 6 months-4 years | 5086.96 | (3763, 6405) | 81.70 | (60, 103) | 0.52 | (0.4, 0.7) |
| 5-17 years | 2293.46 | (1441, 3140) | 34.74 | (22, 48) | 0.17 | (0.1, 0.3) |
| 18-49 years | 802.72 | (481, 1131) | 28.05 | (17, 40) | 0.40 | (0.2, 0.6) |
| 50-64 years | 2117.36 | (159, 3944) | 70.53 | (5, 131) | 1.94 | (0.1, 3.6) |
| ≥65 years | 618.03 | (111, 1107) | 265.00 | (47, 475) | 12.26 | (2.2, 22.0) |
| Overall | 2050.58 | (1645, 2483) | 70.70 | (46, 94) | 1.87 | (0.8, 2.9) |

[34] Averages and 95% confidence intervals calculated with probabilistic sensitivity analysis.
[35] Rate = expected number of events per 100,000 individuals in Quartile 4 over one influenza season.

**Table 3.11.** Projected incremental costs, quality-adjusted life years (QALYs), and cost-effectiveness ratios by age of a targeted Quartile 4 vaccination intervention compared to a base case scenario over an influenza season

| | **Incremental Cost** *(2025 USD)* | | **QALYs** *(QALYs Gained)* | | **ICER** *(cost/ QALY gained)* |
|---|---|---|---|---|---|
| **Age Group** | **Output** | **95% CI** | **Output** | **95% CI** | **Output** |
| 6 months-4 years | $4.51 | ($3.09, $5.84) | 0.02352 | (0.01848, 0.02837) | $191.84 |
| 5-17 years | $5.52 | ($4.70, $7.93) | 0.01994 | (0.01583, 0.02397) | $276.75 |
| 18-49 years | $3.88 | ($2.26, $4.91) | 0.01491 | (0.01192, 0.01778) | $259.92 |
| 50-64 years | $3.93 | (-$0.54, $5.96) | 0.01540 | (0.01222, 0.01864) | $255.08 |
| ≥65 years | $3.77 | ($0.57, $5.84) | 0.01018 | (0.00802, 0.01233) | $370.60 |
| Overall | $4.20 | ($3.00, $5.12) | 0.01604 | (0.01285, 0.01904) | $261.85 |

**Table 3.12.** Average Net Monetary Benefit (NMB) and associated 95% confidence intervals (CI) for select cost-effectiveness thresholds based on probabilistic sensitivity analysis

| | ***$50,000 / QALY*** | | ***$100,000 / QALY*** | |
|---|---|---|---|---|
| Age Group | **Average** | **95% CI** | **Average** | **95% CI** |
| **6 months-4 years** | $1,157.03 | ($920, $1,413) | $2,318.74 | ($1,845, $2,832) |
| **5-17 years** | $978.58 | ($786, $1,192) | $1,963.18 | ($1,577, $2,391) |
| **18-49 years** | $732.86 | ($592, $885) | $1,469.71 | ($1,188, $1,774) |
| **50-64 years** | $758.46 | ($607, $927) | $1,521.01 | ($1,218, $1,859) |
| **≥65 years** | $497.39 | ($397, $615) | $998.68 | ($798, $1,232) |
| **Overall** | **$787.96** | **($638, $948)** | **$1,580.30** | **($1,281, $1,899)** |

**Figure 3.3.** Tornado diagram: one-way sensitivity analysis on the net monetary benefit of a targeted Quartile 4 vaccination intervention versus base case scenario over an influenza season

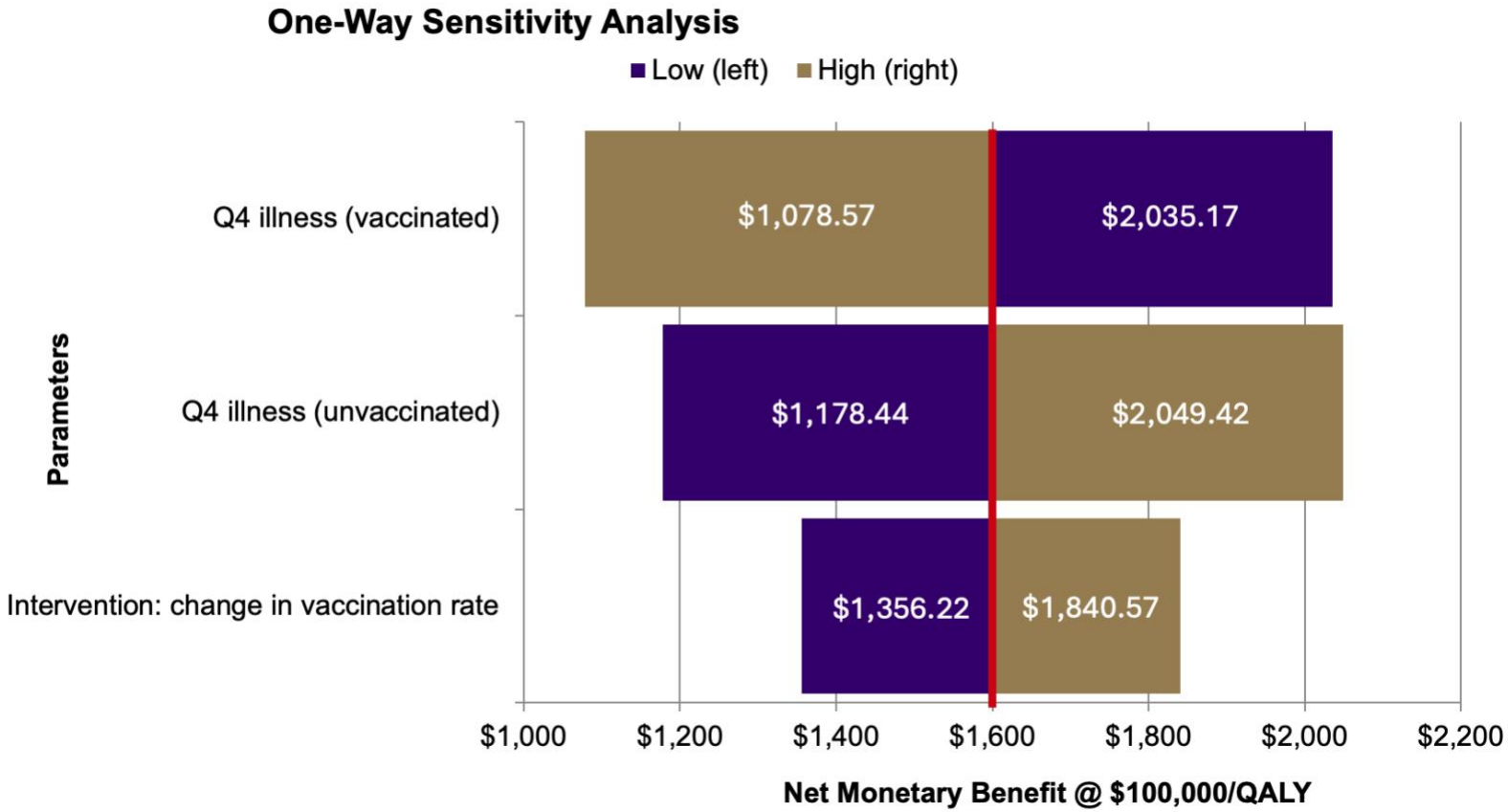


**Table 3.13.** One-way sensitivity analysis: Top 10 most influential parameters on the net monetary benefit (NMB) at willingness-to-pay threshold: $100,000/QALY[36]

| Parameter | NMB @ Low | NMB @ High | Swing |
|---|---|---|---|
| Q4 illness (vaccinated) | $2,035.17 | $1,078.57 | $956.61 |
| Q4 illness (unvaccinated) | $1,178.44 | $2,049.42 | $870.98 |
| Intervention: change in vaccination rate | $1,356.22 | $1,840.57 | $484.35 |
| Cost: Intervention (incentive+letters) | $1,599.86 | $1,593.05 | $6.81 |
| Death:hospitalization ratio | $1,600.13 | $1,605.19 | $5.05 |
| Cost: hospitalization | $1,599.05 | $1,601.84 | $2.78 |
| Prob: hospitalization | $1,599.14 | $1,601.76 | $2.62 |
| Cost: outpatient visit | $1,599.45 | $1,600.46 | $1.00 |
| Cost: Vaccine & administration | $1,600.12 | $1,599.32 | $0.81 |
| Quartile gradient steepness (Q4/Q1 OR) | $1,599.49 | $1,599.83 | $0.34 |

[36] The deterministic NMB is $1,599.66.

**Figure 3.4.** Incremental cost-effectiveness plane (willingness-to-pay threshold: $100,000/ QALY)

**Table 3.14.** Equity Assessment

| ε (inequality aversion parameter) | EDE | | | (A(ε)) | | | DCEA ICER |
|---|---|---|---|---|---|---|---|
| | *Base Case* | *Intervention* | *Difference* | *Base Case* | *Intervention* | *Relative Difference* | |
| ε = 0.0 (Standard CEA) | 28.29 | 28.31 | 0.01604 | 0.00000 | 0.00000 | - | $261.85 |
| ε = 0.5 | 28.29 | 28.31 | 0.01617 | 0.00003 | 0.00003 | 15.0% | $259.66 |
| ε = 1.0 | 28.29 | 28.31 | 0.01631 | 0.00006 | 0.00005 | 15.0% | $257.51 |
| ε = 3.0 | 28.29 | 28.30 | 0.01686 | 0.00019 | 0.00016 | 15.1% | $249.14 |
| ε = 12.12 (US-estimate) | 28.27 | 28.29 | 0.01948 | 0.00079 | 0.00067 | 15.5% | $215.60 |
| ε = 30.0 (Extreme aversion) | 28.23 | 28.26 | 0.02510 | 0.00200 | 0.00168 | 16.1% | $167.34 |

**Figure 3.5.** The equity-weighted, population impact of the intervention against a range of inequality aversion parameter values

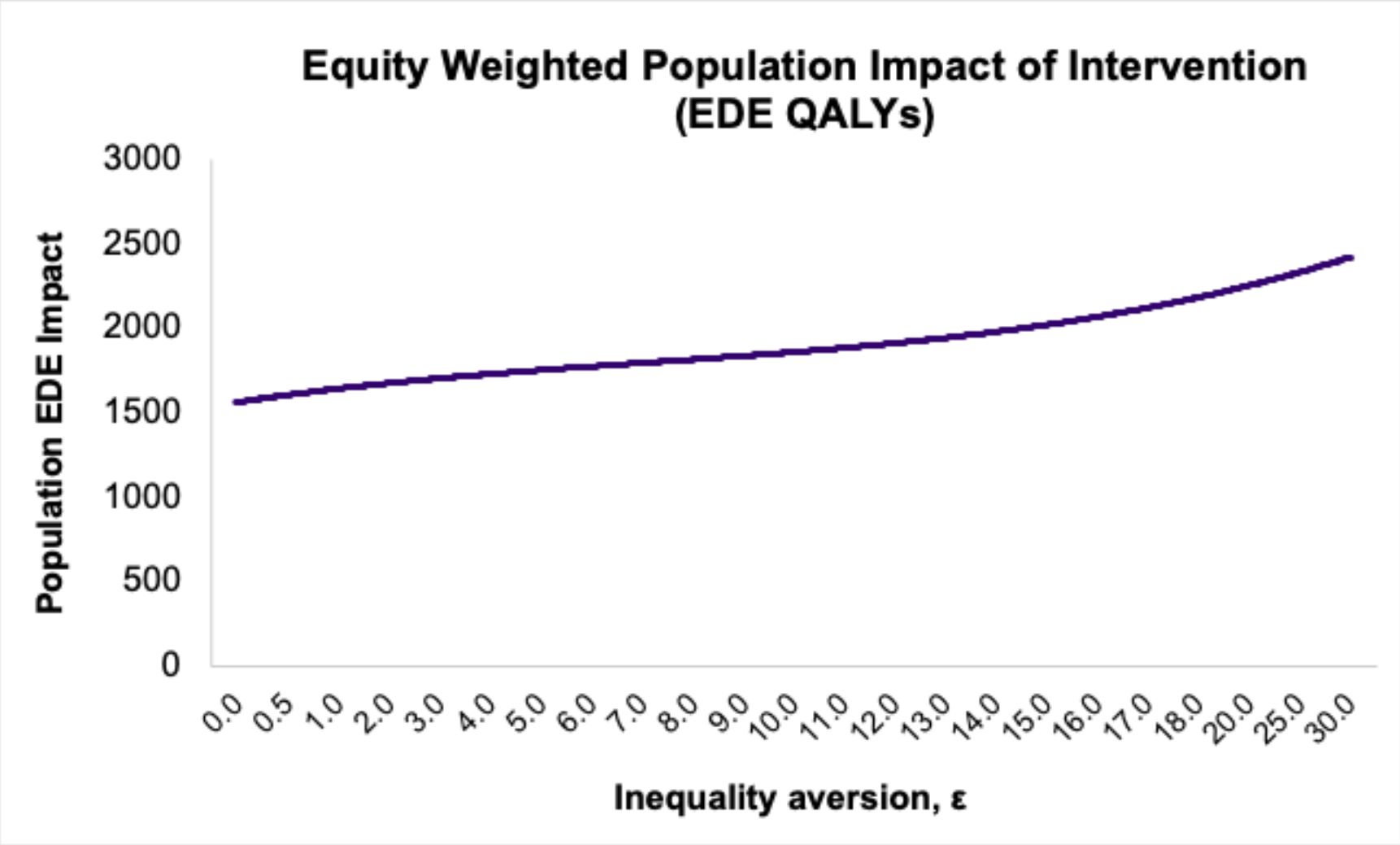
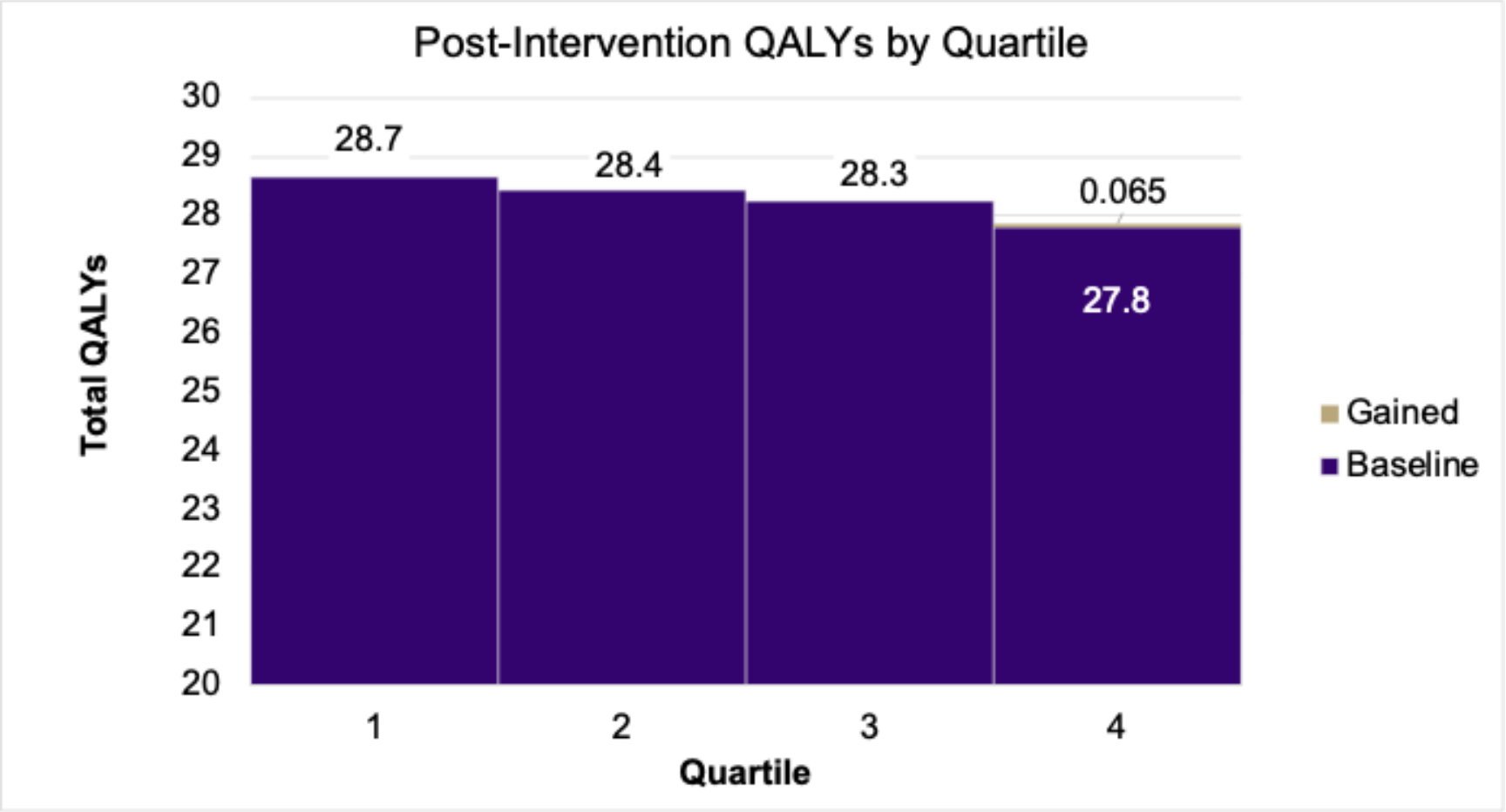


**Figure 3.6.** Comparison of the quality-adjusted life years (QALYs) gained following implementation of the targeted intervention



## SUMMARY OF FINDINGS

This dissertation applied the Area Deprivation Index (ADI) to the 2023–2024 US Flu Vaccine Effectiveness (Flu VE) Network to establish how neighborhood disadvantage should be measured in this population, how it relates to influenza outcomes (laboratory-confirmed influenza and receipt of seasonal influenza vaccination), and whether targeting disadvantaged communities for vaccination is cost-effective and equitable. The three chapters build on one another, moving from a methodological foundation to an epidemiologic analysis, closing with an economic and equity evaluation.

### Key Findings

- **Methodological Foundation (Chapter 1):** Across 7,898 participants in seven sites, ADI scores and population characteristics varied substantially by site. Relative quartile categorization kept the disadvantage gradient that a binary split would flatten while keeping cell sizes large enough for stable estimation. Whether to adjust for study site depended on the outcome: because site and ADI are both geographically defined and overlap considerably, adjusting for site attenuated the association between ADI and test-positivity, but site remained an appropriate covariate for vaccine uptake, where post-COVID-19 pandemic regional differences in policy and behavior are real confounders rather than proxies for disadvantage.
- **Disparities in Outcomes (Chapter 2):** Using ADI quartiles with full covariate adjustment, participants in the most disadvantaged neighborhoods were both the least likely to be vaccinated and the most likely to test positive for influenza—a compounding of risk and under-protection. Age and race were also associated with outcomes: adults over 65 had the highest vaccination likelihood while children under 18 were more likely to test positive, and Black participants were less likely to be vaccinated, with Asian and Black participants more likely to test positive. Notably, vaccine effectiveness itself did not differ significantly

across ADI quartiles, indicating that the vaccine works comparably well across the deprivation gradient and that the disparity lies in access and uptake rather than in biological response.

- **Cost-Effectiveness and Equity of Targeted Intervention Strategy (Chapter 3):** A distributional cost-effectiveness analysis of a targeted intervention (vaccine voucher, financial incentive, and mailed reminders for the most disadvantaged quartile) found it cost-effective under the standard framework, with an ICER of $262/QALY against a $100,000/QALY threshold, and an incremental net monetary benefit of roughly $160 million per 100,000 people. Incorporating equity weighting strengthened the case: the equity-weighted ICER fell to $216/QALY at the estimated inequality-aversion parameter, the Atkinson inequality index dropped about 15%, and all incremental health benefits were concentrated among the most disadvantaged quartile.

Altogether, the chapters reveal that disadvantaged neighborhoods carry a higher influenza burden alongside lower vaccination rates, that the vaccine itself is equally effective across the socioeconomic gradient, and that an intervention directed at the most disadvantaged neighborhoods is both efficient and equity-improving.

**Policy Recommendations**

Influenza prevention programs should explicitly incorporate neighborhood disadvantage, operationalized via ADI, when prioritizing populations and allocating resources during influenza seasons. Since the most disadvantaged quartile bears the dual burden of higher positivity and lower uptake, this group is the clearest target for interventions and directed resources. Targeted strategies combining vaccine vouchers, financial incentives, and mailed reminders for the most disadvantaged communities are a cost-effective use of resources and reduce health inequality, with the justification strengthening as greater weight is placed on equity.

For future analyses with Network data, we recommend that ADI should be categorized into relative quartiles for interpretability and stability, and study-site adjustment should be applied selectively. Site should be included when modeling vaccine uptake but excluded when estimating the overall effect of neighborhood disadvantage on influenza illness, to avoid over-adjustment and thereby masking socioeconomic associations.

**Future Research**

Future analyses should incorporate a measure of state-level vaccination policy to better capture geographic variation and reduce the residual confounding that study site only partially addresses. Further work could extend this framework beyond a single season to test whether the ADI categorization recommendations and the site-adjustment logic hold across seasons of differing severity and circulating strains and could examine the persistence of the observed racial and age disparities once neighborhood disadvantage is accounted for. Finally, the distributional cost-effectiveness findings suggest the need for real-world testing and expansion: a local health department could implement the modeled intervention strategy as a pilot project to determine whether the expected improvements in health, costs, and equity occur in practice. This process could also refine the parameters and inequality-aversion assumptions in the distributional model. Future analyses could extend the model to a transmission model to better understand how flu spreads by disadvantage category and how public health interventions can disrupt these pathways.

## REFERENCES


1. A retrospective on fundamental cause theory: State of the literature, and goals for the future - PMC. Accessed January 24, 2025. https://pmc.ncbi.nlm.nih.gov/articles/PMC8691558/

2. Phelan JC, Link BG. Is Racism a Fundamental Cause of Inequalities in Health? *Annu Rev Sociol*. 2015;41(Volume 41, 2015):311-330. doi:10.1146/annurev-soc-073014-112305

3. Noppert GA, Hegde ST, Kubale JT. Exposure, Susceptibility, and Recovery: A Framework for Examining the Intersection of the Social and Physical Environments and Infectious Disease Risk. *Am J Epidemiol*. 2022;192(3):475-482. doi:10.1093/aje/kwac186

4. Zelner J, Stone D, Eisenberg M, Brouwer A, Sakrejda K. Capturing the implications of residential segregation for the dynamics of infectious disease transmission. *Infectious Diseases (except HIV/AIDS)*. Preprint posted online June 26, 2024. doi:10.1101/2024.06.26.24309541

5. Mody A, Bradley C, Redkar S, et al. Quantifying inequities in COVID-19 vaccine distribution over time by social vulnerability, race and ethnicity, and location: A population-level analysis in St. Louis and Kansas City, Missouri. *PLOS Med*. 2022;19(8):e1004048. doi:10.1371/journal.pmed.1004048

6. Laster Pirtle WN. Racial Capitalism: A Fundamental Cause of Novel Coronavirus (COVID-19) Pandemic Inequities in the United States. *Health Educ Behav*. 2020;47(4):504-508. doi:10.1177/1090198120922942

7. Williams DR, Cooper LA. COVID-19 and Health Equity—A New Kind of "Herd Immunity." *JAMA*. 2020;323(24):2478-2480. doi:10.1001/jama.2020.8051

8. Kind AJH, Buckingham WR. Making Neighborhood-Disadvantage Metrics Accessible — The Neighborhood Atlas. *N Engl J Med*. 2018;378(26):2456-2458. doi:10.1056/NEJMp1802313

9. U.S. Census Bureau. *Understanding and Using American Community Survey Data: What All Data Users Need to Know*. U.S. Government Publishing Office, Washington, DC; 2020. https://www.census.gov/content/dam/Census/library/publications/2020/acs/acs_general_handbook_2020.pdf

10. Flanagan, B.E., Gregory, E.W., Hallisey, E.J., Heitgerd, J.L., & Lewis, B. A Social Vulnerability Index for Disaster Management. *J Homel Secur Emerg Manag*. 2011;8(1).

11. CDC. 2023-2024 Influenza Season Summary: Influenza Severity Assessment, Burden and Burden Prevented. Influenza (Flu). November 21, 2024. Accessed March 11, 2026. https://www.cdc.gov/flu/whats-new/flu-summary-addendum-2023-2024.html

12. Treanor JJ, Talbot HK, Ohmit SE, et al. Effectiveness of Seasonal Influenza Vaccines in the United States During a Season With Circulation of All Three Vaccine Strains. *Clin Infect Dis*. 2012;55(7):951-959. doi:10.1093/cid/cis574

13. Zipfel CM, Colizza V, Bansal S. Health inequities in influenza transmission and surveillance. *PLOS Comput Biol*. 2021;17(3):e1008642. doi:10.1371/journal.pcbi.1008642

14. Linn ST, Guralnik JM, Patel KV. Disparities in Influenza Vaccine Coverage in the United States, 2008. *J Am Geriatr Soc*. 2010;58(7):1333-1340. doi:10.1111/j.1532-5415.2010.02904.x

15. Breaux RD, Rooks RN. The intersectional importance of race/ethnicity, disability, and age in flu vaccine uptake for U.S. adults. *SSM - Popul Health*. 2022;19:101211. doi:10.1016/j.ssmph.2022.101211

16. Rollings KA, Noppert GA, Griggs JJ, Melendez RA, Clarke PJ. Comparison of two area-level socioeconomic deprivation indices: Implications for public health research, practice, and policy. *PLOS ONE*. 2023;18(10):e0292281. doi:10.1371/journal.pone.0292281

17. Thakore N, Khazanchi R, Orav EJ, Ganguli I. Association of Social Vulnerability, COVID-19 vaccine site density, and vaccination rates in the United States. *Healthcare*. 2021;9(4):100583. doi:10.1016/j.hjdsi.2021.100583

18. Vukovic V, Lillini R, Lupi S, et al. Identifying people at risk for influenza with low vaccine uptake based on deprivation status: a systematic review. *Eur J Public Health*. 2020;30(1):132-141. doi:10.1093/eurpub/cky264

19. Morenz AM, Liao JM, Au DH, Hayes SA. Area-Level Socioeconomic Disadvantage and Health Care Spending: A Systematic Review. *JAMA Netw Open*. 2024;7(2):e2356121. doi:10.1001/jamanetworkopen.2023.56121

20. Chung JR, Price AM, Zimmerman RK, et al. Influenza Vaccine Effectiveness Against Medically Attended Outpatients Illness, United States, 2023–2024 Season. *Clin Infect Dis*. Published online January 6, 2025:ciae658. doi:10.1093/cid/ciae658

21. Kirzinger A, Kearney A, Hamel L, Published MB. KFF COVID-19 Vaccine Monitor: The Increasing Importance of Partisanship in Predicting COVID-19 Vaccination Status. KFF. November 16, 2021. Accessed February 3, 2025. https://www.kff.org/coronavirus-covid-19/poll-finding/importance-of-partisanship-predicting-vaccination-status/

22. Zhang V, Zhu P, Wagner AL. Spillover of Vaccine Hesitancy into Adult COVID-19 and Influenza: The Role of Race, Religion, and Political Affiliation in the United States. *Int J Environ Res Public Health*. 2023;20(4):4. doi:10.3390/ijerph20043376

23. Diaz A, O'Reggio R, Norman M, Thumma JR, Dimick JB, Ibrahim AM. Association of Historic Housing Policy, Modern Day Neighborhood Deprivation and Outcomes After Inpatient Hospitalization. *Ann Surg*. 2021;274(6):985. doi:10.1097/SLA.0000000000005195

24. Walker RE, Schulte R, Pallotta AM, Wang M, Deshpande A, Rothberg M. Racial disparities in antibiotic selection for community-acquired pneumonia in hospitalized patients. *Infect Control Hosp Epidemiol*. Published online December 9, 2025:1-6. doi:10.1017/ice.2025.10371

25. Fitzgerald B, Steinbach TC, Sippel J, Griffith M. THE ASSOCIATION OF VULNERABILITY INDICES WITH INFLUENZA, PNEUMOCOCCAL, AND COVID VACCINATION RATES IN HIGH-RISK PULMONARY PATIENTS. *CHEST*. 2024;166(4):A3902. doi:10.1016/j.chest.2024.06.2356

26. Patel OP, Lawrence KG, Parks CG, et al. Neighborhood disadvantage and immune-related illnesses among residents living in the US Gulf States. *Ann Epidemiol*. 2023;78:44-46. doi:10.1016/j.annepidem.2022.12.012

27. Zhao X, Schmidt CJ, Zelner J, et al. Associations Between Community Social Vulnerability or Socioeconomic Deprivation and Respiratory Virus Infection in Decedents in a Large, Urban Medical Examiner's Office. *J Racial Ethn Health Disparities*. Published online May 20, 2025. doi:10.1007/s40615-025-02482-x

28. CDC. 2023-2024 Flu Season. Influenza (Flu). September 30, 2024. Accessed January 19, 2026. https://www.cdc.gov/flu/season/2023-2024.html

29. Zhu S, Quint J, León TM, et al. Estimating Influenza Vaccine Effectiveness Against Laboratory-Confirmed Influenza Using Linked Public Health Information Systems, California, 2023–2024 Season. *J Infect Dis*. 2025;232(5):1249-1257. doi:10.1093/infdis/jiaf248

30. CDC. Child and Adolescent Immunization Schedule by Age (Addendum updated August 7, 2025). Vaccines & Immunizations. October 29, 2025. Accessed January 19, 2026. https://www.cdc.gov/vaccines/hcp/imz-schedules/child-adolescent-age.html

31. Pearson WS, Dube SR, Ford ES, Mokdad AH. Influenza and pneumococcal vaccination rates among smokers: Data from the 2006 Behavioral Risk Factor Surveillance System. *Prev Med*. 2009;48(2):180-183. doi:10.1016/j.ypmed.2008.11.001

32. Han L, Ran J, Mak YW, et al. Smoking and Influenza-associated Morbidity and Mortality: A Systematic Review and Meta-analysis. *Epidemiology*. 2019;30(3):405. doi:10.1097/EDE.0000000000000984

33. Ferguson L, Taylor J, Davies M, Shrubsole C, Symonds P, Dimitroulopoulou S. Exposure to indoor air pollution across socio-economic groups in high-income countries: A scoping review of the literature and a modelling methodology. *Environ Int*. 2020;143:105748. doi:10.1016/j.envint.2020.105748

34. Phelan JC, Link BG, Tehranifar P. Social Conditions as Fundamental Causes of Health Inequalities: Theory, Evidence, and Policy Implications. *J Health Soc Behav*. 2010;51(1_suppl):S28-S40. doi:10.1177/0022146510383498

35. CDC. Influenza Activity in the United States during the 2023–2024 Season and Composition of the 2024–2025 Influenza Vaccine. Influenza (Flu). October 3, 2024. Accessed December 30, 2024. https://www.cdc.gov/flu/whats-new/flu-summary-2023-2024.html

36. LEARN MORE. 317 Coalition. Accessed March 13, 2026. https://www.317coalition.org/learn-more

37. WHO Essential Programme on Immunization: Confidence and Demand. Accessed May 31, 2024. https://www.who.int/teams/immunization-vaccines-and-biologicals/essential-programme-on-immunization/demand

38. CDC. People at Increased Risk for Flu Complications. Influenza (Flu). August 14, 2025. Accessed March 15, 2026. https://www.cdc.gov/flu/highrisk/index.htm

39. Parekh T. Disparities in Influenza Vaccination Coverage and Associated Factors Among Adults with Cardiovascular Disease, United States, 2011–2020. *Prev Chronic Dis*. 2022;19. doi:10.5888/pcd19.220154

40. Andrew MK, Pott H, Staadegaard L, et al. Age Differences in Comorbidities, Presenting Symptoms, and Outcomes of Influenza Illness Requiring Hospitalization: A Worldwide Perspective From the Global Influenza Hospital Surveillance Network. *Open Forum Infect Dis*. 2023;10(6):ofad244. doi:10.1093/ofid/ofad244

41. Hitchens A, Candrilli SD, Carrico J, et al. Prevalence of health conditions associated with higher risk for severe respiratory syncytial virus, influenza, or COVID-19. *Curr Med Res Opin*. 2025;41(7):1353-1361. doi:10.1080/03007995.2025.2535456

42. Jackson ML, Phillips CH, Benoit J, et al. The impact of selection bias on vaccine effectiveness estimates from test-negative studies. *Vaccine*. 2018;36(5):751-757. doi:10.1016/j.vaccine.2017.12.022

43. kffjenk. ACIP, CDC, and Insurance Coverage of Vaccines in the United States. KFF. June 13, 2025. Accessed May 4, 2026. https://www.kff.org/other-health/acip-cdc-and-insurance-coverage-of-vaccines-in-the-united-states/

44. kfflizw. Tracking State Actions on Vaccine Policy and Access. KFF. September 24, 2025. Accessed May 4, 2026. https://www.kff.org/state-health-policy-data/tracking-state-actions-on-vaccine-policy-and-access/

45. Staloff JA, Morenz AM, Hayes SA, Bhatia-Lin AL, Liao JM. Area-Level socioeconomic disadvantage and access to primary care: A rapid review. *Health Aff Sch*. 2025;3(4):qxaf066. doi:10.1093/haschl/qxaf066

46. Key Facts about the Uninsured Population | KFF. Accessed May 4, 2026. https://www.kff.org/uninsured/key-facts-about-the-uninsured-population/

47. Blumenshine P, Reingold A, Egerter S, Mockenhaupt R, Braveman P, Marks J. Pandemic Influenza Planning in the United States from a Health Disparities Perspective. *Emerg Infect Dis*. 2008;14(5):709-715. doi:10.3201/eid1405.071301

48. Schnake-Mahl A, Rollins H, Goldstein ND, Bilal U, Diez Roux AV. Neighborhood Disparities in Influenza and Influenza like Illness Hospitalization During Seasonal and Pandemic Influenza. *Open Forum Infect Dis*. 2025;12(8):ofaf468. doi:10.1093/ofid/ofaf468

49. Understanding the behavioural and social drivers of vaccine uptake WHO position paper – May 2022. Accessed February 3, 2025. https://www.who.int/publications/i/item/who-wer9720-209-224

50. CDC. 2024–2025 Influenza Season Summary: Severity, Disease Burden, and Burden Prevented. Flu Burden. May 5, 2026. Accessed May 6, 2026. https://www.cdc.gov/flu-burden/php/data-vis-vac/2024-2025-prevented.html

51. CDC. 2025-2026 United States Flu Season: Preliminary In-Season Severity Assessment. Flu Burden. May 1, 2026. Accessed May 6, 2026. https://www.cdc.gov/flu-burden/php/surveillance/in-season-severity.html

52. Breslau J, Martin L, Timbie J, Qureshi N, Zajdman D. *Landscape of Area-Level Deprivation Measures and Other Approaches to Account for Social Risk and Social Determinants of Health in Health Care Payments*. Office of the Assistant Secretary for Planning and Evaluation (ASPE) at the U.S. Department of Health & Human Services; 2022. doi:10.1377/forefront.20191025.776011

53. CDC. U.S. Influenza Surveillance: Purpose and Methods. FluView. December 2, 2025. Accessed May 6, 2026. https://www.cdc.gov/fluview/overview/index.html

54. Shaw-Saliba K, Hansoti B, Burkom H, et al. Cloud-Based Influenza Surveillance System in Emergency Departments Using Molecular-Based Testing: Advances and Challenges. *West J Emerg Med*. 2022;23(2):115-123. doi:10.5811/westjem.2021.9.52741

55. CDC. Information on Rapid Molecular Assays, RT-PCR, and other Molecular Assays for Diagnosis of Influenza Virus Infection. Influenza (Flu). May 1, 2026. Accessed May 6, 2026. https://www.cdc.gov/flu/hcp/testing-methods/molecular-assays.html

56. CDC. Grading of Recommendations, Assessment, Development, and Evaluation (GRADE): Updated COVID-19 vaccine (2023-2024 Formulation). Advisory Committee on Immunization Practices (ACIP). February 6, 2025. Accessed September 4, 2025. https://www.cdc.gov/acip/grade/covid-19-2023-2024-Monovalent.html

57. Increase the proportion of people who get the flu vaccine every year — IID-09 - Healthy People 2030 | health.gov. Accessed November 30, 2023. https://health.gov/healthypeople/objectives-and-data/browse-objectives/vaccination/increase-proportion-people-who-get-flu-vaccine-every-year-iid-09

58. Aguolu OG, Willebrand K, Elharake JA, et al. Factors influencing the decision to receive seasonal influenza vaccination among US corporate non-healthcare workers. *Hum Vaccines Immunother*. 18(6):2122379. doi:10.1080/21645515.2022.2122379

59. Woolfork MN, Haire K, Farinu O, et al. A health equity science approach to assessing drivers of COVID-19 vaccination coverage disparities over the course of the COVID-19 pandemic, United States, December 2020–December 2022. *Vaccine*. 2024;42:126158. doi:10.1016/j.vaccine.2024.126158

60. Oluyomi AO, Gunter SM, Leining LM, Murray KO, Amos C. COVID-19 Community Incidence and Associated Neighborhood-Level Characteristics in Houston, Texas, USA. *Int J Environ Res Public Health*. 2021;18(4):1495. doi:10.3390/ijerph18041495

61. Srivastava T, Schmidt H, Sadecki E, Kornides ML. Disadvantage Indices Deployed to Promote Equitable Allocation of COVID-19 Vaccines in the US. *JAMA Health Forum*. 2022;3(1):e214501. doi:10.1001/jamahealthforum.2021.4501

62. Tools That Measure Disadvantage Can Improve Health and Policymaking. Penn LDI. March 7, 2024. Accessed May 29, 2024. https://ldi.upenn.edu/our-work/research-updates/how-tools-that-measure-peoples-disadvantage-can-improve-health-and-policymaking/

63. Trinidad S, Brokamp C, Mor Huertas A, et al. Use Of Area-Based Socioeconomic Deprivation Indices: A Scoping Review And Qualitative Analysis. *Health Aff (Millwood)*. 2022;41(12):1804-1811. doi:10.1377/hlthaff.2022.00482

64. Manns BJ, Thomas S, Farinu O, Woolfork M, Walker CL. Hyperlocal lessons from the COVID-19 pandemic: Toward an equity-centered implementation science approach. *Soc Sci Humanit Open*. 2024;9:100844. doi:10.1016/j.ssaho.2024.100844

65. McConnell KH, Hajat A, Sack C, Mooney SJ, Khosropour CM. Associations Between Insurance, Race and Ethnicity, and COVID-19 Hospitalization Beyond Underlying Health Conditions: A Retrospective Cohort Study. *AJPM Focus*. 2023;2(3):100120. doi:10.1016/j.focus.2023.100120

66. CDC. US Flu VE Network. Centers for Disease Control and Prevention. October 18, 2022. Accessed February 27, 2023. https://www.cdc.gov/flu/vaccines-work/us-flu-ve-network.htm

67. Frutos AM. Interim Estimates of 2023–24 Seasonal Influenza Vaccine Effectiveness — United States. *MMWR Morb Mortal Wkly Rep*. 2024;73. doi:10.15585/mmwr.mm7308a3

68. Kind AJH, Buckingham WR. Making Neighborhood-Disadvantage Metrics Accessible — The Neighborhood Atlas. *N Engl J Med*. 2018;378(26):2456-2458. doi:10.1056/NEJMp1802313

69. Neighborhood Atlas - Mapping. Accessed June 5, 2023. https://www.neighborhoodatlas.medicine.wisc.edu/mapping

70. Belongia EA, Kieke BA, Donahue JG, et al. Effectiveness of Inactivated Influenza Vaccines Varied Substantially with Antigenic Match from the 2004–2005 Season to the 2006–2007 Season. *J Infect Dis*. 2009;199(2):159-167. doi:10.1086/595861

71. Frutos AM. Interim Estimates of 2023–24 Seasonal Influenza Vaccine Effectiveness — United States. *MMWR Morb Mortal Wkly Rep*. 2024;73. doi:10.15585/mmwr.mm7308a3

72. Why the Test-Negative Design Is Used for Routine Vaccine Monitoring | Infectious Diseases | JAMA Network Open | JAMA Network. Accessed June 29, 2026. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2850669?__cf_chl_f_tk=.2bqeL6CDmttoai2nG2cS7tZlUJvxJWW.kDs5fJGCd8-1782767912-1.0.1.1-rcXec1vHfq7kBr5DJLKBpt8pI7M91wwagsY6sc6fBtw

73. Bailey ZD, Feldman JM, Bassett MT. How Structural Racism Works — Racist Policies as a Root Cause of U.S. Racial Health Inequities. *N Engl J Med*. 2021;384(8):768-773. doi:10.1056/NEJMms2025396

74. Adkins-Jackson PB, Chantarat T, Bailey ZD, Ponce NA. Measuring Structural Racism: A Guide for Epidemiologists and Other Health Researchers. *Am J Epidemiol*. 2021;191(4):539-547. doi:10.1093/aje/kwab239

75. Smedley A, Smedley BD. Race as biology is fiction, racism as a social problem is real: Anthropological and historical perspectives on the social construction of race. *Am Psychol*. 2005;60(1):16-26. doi:10.1037/0003-066X.60.1.16

76. McDermott R. Ethics, epidemiology and the thrifty gene: biological determinism as a health hazard. *Soc Sci Med*. 1998;47(9):1189-1195. doi:10.1016/S0277-9536(98)00191-9

77. Mays VM, Ponce NA, Washington DL, Cochran SD. Classification of Race and Ethnicity: Implications for Public Health. *Annu Rev Public Health*. 2003;24:83-110. doi:10.1146/annurev.publhealth.24.100901.140927

78. O&rsquo A, Halloran M, Jennifer Whitmill Habeck MPH, et al. Influenza-Associated Hospitalizations During a High Severity Season — Influenza Hospitalization Surveillance Network, United States, 2024–25 Influenza Season. *MMWR Morb Mortal Wkly Rep*. 2025;74. doi:10.15585/mmwr.mm7434a1

79. Quinn SC, Kumar S, Freimuth VS, Musa D, Casteneda-Angarita N, Kidwell K. Racial Disparities in Exposure, Susceptibility, and Access to Health Care in the US H1N1 Influenza Pandemic. *Am J Public Health*. 2011;101(2):285-293. doi:10.2105/AJPH.2009.188029

80. Grantz KH, Rane MS, Salje H, Glass GE, Schachterle SE, Cummings DAT. Disparities in influenza mortality and transmission related to sociodemographic factors within Chicago in the pandemic of 1918. *Proc Natl Acad Sci*. 2016;113(48):13839-13844. doi:10.1073/pnas.1612838113

81. Dee DL, Bensyl DM, Gindler J, et al. Racial and Ethnic Disparities in Hospitalizations and Deaths Associated with 2009 Pandemic Influenza A (H1N1) Virus Infections in the United States. *Ann Epidemiol*. 2011;21(8):623-630. doi:10.1016/j.annepidem.2011.03.002

82. Stafford E, Dimitrov D, Trinidad SB, Matrajt L. Closing the Gap in Race-based Inequities for Seasonal Influenza Hospitalizations: A Modeling Study. Accessed February 6, 2026. https://dx.doi.org/10.1093/cid/ciae564

83. Zelner J, Masters NB, Naraharisetti R, Mojola SA, Chowkwanyun M, Malosh R. There are no equal opportunity infectors: Epidemiological modelers must rethink our approach to inequality in infection risk. *PLOS Comput Biol*. 2022;18(2):e1009795. doi:10.1371/journal.pcbi.1009795

84. Vaccination Programs: Community-Based Interventions Implemented in Combination | The Community Guide. January 28, 2026. Accessed February 18, 2026. https://www.thecommunityguide.org/findings/vaccination-programs-community-based-interventions-implemented-combination.html

85. Macias-Konstantopoulos WL, Collins KA, Diaz R, et al. Race, Healthcare, and Health Disparities: A Critical Review and Recommendations for Advancing Health Equity. *West J Emerg Med*. 2023;24(5):906-918. doi:10.5811/westjem.58408

86. Kim DeLuca E, Gebremariam A, Rose A, Biggerstaff M, Meltzer MI, Prosser LA. Cost-effectiveness of routine annual influenza vaccination by age and risk status. *Vaccine*. 2023;41(29):4239-4248. doi:10.1016/j.vaccine.2023.04.069

87. Gidengil C, Haviland A, Hambarsoomian K, Martino S, Dembosky JW, Elliott MN. Influenza Vaccination Among People With Medicare by Race and Ethnicity, Education, and Rurality. *JAMA Netw Open*. 2025;8(4):e254462. doi:10.1001/jamanetworkopen.2025.4462

88. Lippert JF, Buscemi J, Saiyed N, Silva A, Benjamins MR. Influenza and Pneumonia Mortality Across the 30 Biggest U.S. Cities: Assessment of Overall Trends and Racial Inequities. *J Racial Ethn Health Disparities*. 2022;9(4):1152-1160. doi:10.1007/s40615-021-01056-x

89. Lind ML, Goldmann E, Lalonde GS. Trends in influenza vaccine disparities in the U.S. following the introduction of COVID-19: Insights from the national health interview survey. *Prev Med Rep*. 2025;60:103288. doi:10.1016/j.pmedr.2025.103288

90. Popovian R, Winegarden W. Influenza's Economic Burden and the Impact of Adult Vaccination. *Health Economics*. Preprint posted online December 30, 2025. doi:10.64898/2025.12.23.25342685

91. Influenza Vaccination: A Summary for Clinicians | CDC. March 22, 2024. Accessed June 27, 2024. https://www.cdc.gov/flu/professionals/vaccination/vax-summary.htm

92. Anderson LJ, Shekelle P, Keeler E, et al. The Cost of Interventions to Increase Influenza Vaccination: A Systematic Review. *Am J Prev Med*. 2018;54(2):299-315. doi:10.1016/j.amepre.2017.11.010

93. CDC. Flu Vaccination Coverage, United States, 2023–24 Influenza Season. FluVaxView. December 18, 2025. Accessed April 13, 2026. https://www.cdc.gov/fluvaxview/coverage-by-season/2023-2024.html

94. Sibson K, Shrontz A, Jones J, et al. Successful Interventions to Improve Pediatric Vaccine Uptake in Hesitant Cohorts: A Scoping Review. *Cureus*. 17(5):e84399. doi:10.7759/cureus.84399

95. CDC. Influenza Vaccination Coverage and Intent for Vaccination, Adults 18 Years and Older, United States. FluVaxView. March 3, 2026. Accessed March 24, 2026. https://www.cdc.gov/fluvaxview/dashboard/adult-coverage.html

96. Hadler JL. Influenza-Related Hospitalizations and Poverty Levels — United States, 2010–2012. *MMWR Morb Mortal Wkly Rep*. 2016;65. doi:10.15585/mmwr.mm6505a1

97. Tools That Measure Disadvantage Can Improve Health and Policymaking. Penn LDI. March 7, 2024. Accessed May 29, 2024. https://ldi.upenn.edu/our-work/research-updates/how-tools-that-measure-peoples-disadvantage-can-improve-health-and-policymaking/

98. Rollings KA, Noppert GA, Griggs JJ, Melendez RA, Clarke PJ. Comparison of two area-level socioeconomic deprivation indices: Implications for public health research, practice, and policy. *PLOS ONE*. 2023;18(10):e0292281. doi:10.1371/journal.pone.0292281

99. Manns BJ, Thomas S, Farinu O, Woolfork M, Walker CL. Hyperlocal lessons from the COVID-19 pandemic: Toward an equity-centered implementation science approach. *Soc Sci Humanit Open*. 2024;9:100844. doi:10.1016/j.ssaho.2024.100844

100. Adkins-Jackson PB, Vázquez E, Henry-Ala FK, et al. The Role of Anti-Racist Community-Partnered Praxis in Implementing Restorative Circles Within Marginalized Communities in Southern California During the COVID-19 Pandemic. *Health Promot Pract*. 2023;24(2):232-243. doi:10.1177/15248399221132581

101. Mays VM, Ponce NA, Washington DL, Cochran SD. Classification of Race and Ethnicity: Implications for Public Health. *Annu Rev Public Health*. 2003;24:83-110. doi:10.1146/annurev.publhealth.24.100901.140927

102. Leidner AJ, Murthy N, Chesson HW, et al. Cost-effectiveness of adult vaccinations: A systematic review. *Vaccine*. 2019;37(2):226-234. doi:10.1016/j.vaccine.2018.11.056

103. Dabestani NM, Leidner AJ, Seiber EE, et al. A review of the cost-effectiveness of adult influenza vaccination and other preventive services. *Prev Med*. 2019;126:105734. doi:10.1016/j.ypmed.2019.05.022

104. Gatwood J, Ramachandran S, Shuvo SA, et al. Social determinants of health and adult influenza vaccination: a nationwide claims analysis. *J Manag Care Spec Pharm*. 2022;28(2):196-205. doi:10.18553/jmcp.2022.28.2.196

105. Kumar S, Shah Z, Garfield S. Causes of Vaccine Hesitancy in Adults for the Influenza and COVID-19 Vaccines: A Systematic Literature Review. *Vaccines*. 2022;10(9):9. doi:10.3390/vaccines10091518

106. Cookson R, Griffin S, Culyer AJ, Norheim OF. *Distributional Cost-Effectiveness Analysis: Quantifying Health Equity Impacts and Trade-Offs*. Oxford University Press; 2020.

107. Asaria M, Griffin S, Cookson R. Distributional Cost-Effectiveness Analysis. *Med Decis Making*. 2016;36(1):8-19. doi:10.1177/0272989X15583266

108. CDC. People at High Risk of Flu. Centers for Disease Control and Prevention. August 25, 2023. Accessed June 7, 2024. https://www.cdc.gov/flu/highrisk/index.htm

109. Liu J, Zhang Y, Zhang H, Tan H. Estimating the effects of interventions on increasing vaccination: systematic review and meta-analysis. *BMJ Glob Health*. 2025;10(4):e017142. doi:10.1136/bmjgh-2024-017142

110. Ley C, Duan H, Parsonnet J. Recruitment into antibody prevalence studies: a randomized trial of postcards vs. letters as invitations. *BMC Med Res Methodol*. 2023;23:170. doi:10.1186/s12874-023-01992-8

111. CDC. Estimated US Flu Disease Burden. Flu Burden. March 19, 2026. Accessed May 13, 2026. https://www.cdc.gov/flu-burden/php/data-vis/index.html

112. Prosser LA, Payne K, Rusinak D, Shi P, Uyeki T, Messonnier M. Valuing health across the lifespan: health state preferences for seasonal influenza illnesses in patients of different ages. *Value Health J Int Soc Pharmacoeconomics Outcomes Res*. 2011;14(1):135-143. doi:10.1016/j.jval.2010.10.026

113. Chang TY, Jacobson M, Shah M, Pramanik R, Shah SB. Impact of reminder messages, with and without financial incentives, on influenza vaccination: A randomized trial in a California health system. *Vaccine*. 2026;75:128263. doi:10.1016/j.vaccine.2026.128263

114. VFC | Current CDC Vaccine Price List | CDC. November 13, 2023. Accessed December 13, 2023. https://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/index.html

115. Medicare COVID-19 Vaccine Shot Payment | CMS. Accessed December 13, 2023. https://www.cms.gov/medicare/payment/covid-19/medicare-covid-19-vaccine-shot-payment

116. U.S. Bureau of Labor Statistics, Average Hourly Earnings of All Employees, Total Private. June 5, 2026. Accessed June 22, 2026. https://fred.stlouisfed.org/series/CES0500000003

117. CDC. How CDC Estimates the Burden of Seasonal Flu in the United States. Flu Burden. May 4, 2026. Accessed June 12, 2026. https://www.cdc.gov/flu-burden/php/about/how-cdc-estimates.html

118. CDC. Influenza Hospitalization Surveillance Network (FluSurv-NET). FluView. March 24, 2026. Accessed June 22, 2026. https://www.cdc.gov/fluview/overview/influenza-hospitalization-surveillance.html

119. Grohskopf LA. Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023–24 Influenza Season. *MMWR Recomm Rep*. 2023;72. doi:10.15585/mmwr.rr7202a1

120. Recombinant or Standard-Dose Influenza Vaccine in Adults under 65 Years of Age | New England Journal of Medicine. Accessed June 24, 2026. https://www.nejm.org/doi/full/10.1056/NEJMoa2302099

121. Lloyd PC, Acharya G, Zhao H, et al. Safety monitoring of health outcomes following influenza vaccination during the 2023–2024 season among U.S. Medicare beneficiaries aged 65 years and older. *Vaccine*. 2025;53:127069. doi:10.1016/j.vaccine.2025.127069

122. Izurieta HS, Lu M, Kelman J, et al. Comparative Effectiveness of Influenza Vaccines Among US Medicare Beneficiaries Ages 65 Years and Older During the 2019–2020 Season. *Clin Infect Dis*. 2021;73(11):e4251-e4259. doi:10.1093/cid/ciaa1727

123. Consumer Price Index. Bureau of Labor Statistics. Accessed June 13, 2026. https://www.bls.gov/cpi/

124. Notice 123 | Postal Explorer. Accessed March 13, 2024. https://pe.usps.com/text/dmm300/Notice123.htm

125. Value Assessment Framework. ICER. Accessed June 12, 2026. https://icer.org/our-approach/methods-process/value-assessment-framework/

126. Slejko JF, Ricci S, dosReis S, Cookson R, Kowal S. Health Inequality Aversion in the United States. *Value Health*. 2026;29(1):129-138. doi:10.1016/j.jval.2025.08.015

127. Husereau D, Drummond M, Augustovski F, et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) statement: Updated reporting guidance for health economic evaluations. *Health Policy OPEN*. 2022;3:100063. doi:10.1016/j.hpopen.2021.100063

128. Sanders GD, Neumann PJ, Basu A, et al. Recommendations for Conduct, Methodological Practices, and Reporting of Cost-effectiveness Analyses: Second Panel on Cost-Effectiveness in Health and Medicine. *JAMA*. 2016;316(10):1093-1103. doi:10.1001/jama.2016.12195

129. CDC. Innovative Uses of SVI During COVID-19. Place and Health - Geospatial Research, Analysis, and Services Program (GRASP). September 12, 2024. Accessed May 14, 2026.

https://www.atsdr.cdc.gov/place-health/php/covid19response/innovative-uses-of-svi-during-covid-19.html

130. Khazanov GK, Stewart R, Pieri MF, et al. The effectiveness of financial incentives for COVID-19 vaccination: A systematic review. *Prev Med*. 2023;172:107538. doi:10.1016/j.ypmed.2023.107538

131. Bonner KE, Chyderiotis S, Sicsic J, et al. What motivates adults to accept influenza vaccine? An assessment of incentives, ease of access, messaging, and sources of information using a discrete choice experiment. *SSM - Popul Health*. 2023;22:101384. doi:10.1016/j.ssmph.2023.101384

132. CDC. Influenza Vaccinations Administered in Pharmacies and Physician Medical Offices*, Adults, United States. FluVaxView. March 23, 2026. Accessed April 13, 2026. https://www.cdc.gov/fluvaxview/dashboard/adult-vaccinations-administered.html

133. Izurieta HS, Lu M, Kelman J, et al. Comparative Effectiveness of Influenza Vaccines Among US Medicare Beneficiaries Ages 65 Years and Older During the 2019–2020 Season. *Clin Infect Dis*. 2021;73(11):e4251-e4259. doi:10.1093/cid/ciaa1727

134. Vuong T, Sirajuddin S, Baker I. What is the indirect economic impact of influenza? *Evid-Based Pract*. 2020;23(5):39. doi:10.1097/EBP.0000000000000627

135. Rosenthal J. States no longer have to report Medicaid, CHIP vaccination rates to CMS, further undermining immunization. STAT. January 14, 2026. Accessed June 13, 2026. https://www.statnews.com/2026/01/14/childhood-vaccine-policy-data-reporting-rollback-cms/

136. Raney V. 2027 Updates to the Child and Adult Core Health Care Quality Measurement Sets and Mandatory Reporting Guidance.

137. Adler NE, Newman K. Socioeconomic Disparities In Health: Pathways And Policies. *Health Aff (Millwood)*. 2002;21(2):60-76. doi:10.1377/hlthaff.21.2.60

138. Jarris P, Dolen V. Section 317 Immunization Program: Protecting a National Asset. *Public Health Rep*. 2013;128(2):96-98.

139. Pandya A, Zhu J, Luviano A, James LP, Goshua G. A Threshold Inequality Aversion Parameter Approach to Interpret Distributional Cost-Effectiveness Analysis Results. *Value Health*. 2026;29(6):946-952. doi:10.1016/j.jval.2025.09.3064

140. Atkinson AB. On the measurement of inequality. *J Econ Theory*. 1970;2(3):244-263. doi:10.1016/0022-0531(70)90039-6