Methods

Study Objective

We estimated the projected additional health and economic burden attributable to declines in childhood vaccination coverage across U.S. states. Using deterministic equilibrium transmission models with demography, we estimated incremental cases, hospitalizations, deaths, workdays lost, and costs relative to baseline vaccination coverage.

Key Question

What is the incremental impact of disease burden if vaccination coverage declines among newborns, given current population immunity and state-specific demographic structure?

Model Overview

We developed state-level, disease-specific transmission models for three vaccine-preventable disease – rotavirus, pertussis, and measles - to estimate projected additional health and economic burden under vaccination coverage declines. Each disease and state was simulated independently using a deterministic endemic equilibrium framework with demographic turnover. This approach estimates the long-run annual burden under stable transmission conditions for each pathogen across the 50 U.S. states and the District of Columbia.

Modeling Framework

Diseases and Age Groups Modeled

The modeling framework includes rotavirus, measles, and pertussis (Table 1). Rotavirus and measles were modeled in children aged 0-4 years and 0-14 years, respectively using a Susceptible-Infectious-Recovered (SIR) structure, while pertussis was modeled in children 0-14 years using a Susceptible-Infectious-Recovered- Susceptible (SIRS) structure to account for waning immunity. [1] These age bands reflect differences in disease epidemiology, vaccination schedules, and concentration of disease burden. These diseases generally exhibit endemic transmission patterns, making them suitable for deterministic equilibrium modeling. However, measles dynamics are highly outbreak driven and non-linear, which are not well captured by equilibrium approximations; therefore, measles results are treated as sensitivity analysis rather than the primary focus of the burden projections.[2]

Table 1: Diseases and age group modeled

Disease	Model	Age band	Rationale
Rotavirus	SIR	0-4	Burden concentrated in young children, short immunity duration
Pertussis	SIRS	0-14 years	Waning immunity requires reinfection pathway
Measles	SIR	0-14 years	High R0 and strong herd immunity threshold effects

Equilibrium Incidence Framework

Annual per-capita incidence under varying vaccination coverage scenarios was estimated using deterministic equilibrium approximations of compartmental transmission models with demography. For each disease, state, and vaccine coverage decline j (0,0.20 in 0.01 increments), the models incorporated demographic turnover, disease-specific natural history parameters, state-specific age-band population sizes, and age-and state-specific vaccination coverage. The model was simulated per age group as defined by disease and a state of residence along with disease-specific parameters and age-band immunity status determined by age, state of residence and vaccination coverage. Each disease and state was modeled independently with disease-specific parameters, state age-band population, and disease epidemiology profile (Table 2).

Key model inputs were the basic reproduction number R_0 for each disease, the effective reproduction number, R_{eff}, and state-level age-band population and demographic turnover.

Model Parameterization

Disease-specific parameters are described in Table 2. All natural history parameters were fixed at values informed by the literature.

Table 2: Descriptions, values, and references for model parameters.

Parameter description	Symbol	Rotavirus values	Pertussis values	Sources
Model structure		SIR	SIRS	[1]Hethcote (2000)
Modeled age band		0-4y	0-14 years	
Basic reproduction number	R0	30	15	[3]Asare et al. 2020 (Rota)
Vaccine efficacy	VE	0.915	0.85	[4]Prunas et al. 2025 (Rota) [5]Cellès et al. 2019 (pertussis)
Vaccination coverage		State-specific	State-specific	[6,7]CDC SchoolVaxView & ChildVacView
Waning immunity rate	ω	0.005	0.011	[8]Cellès et al. 2019
Crude birth rate	μ	State-specific	State-specific	[9]NVSS
Hospitalization rate		0.015	0.05	[10]CDC Pink Book, CDC
Death rate		0.0001	0.0005	[9]NVSS
Average illness duration		5 days	14 days	[10]CDC Pink Book
Average hospitalization duration		3 days	7 days	[10]CDC Pink Book
Average daily wage		$ 200	$ 200	[11]US BLS

Model Structure and Equations

For each disease, state, and assumed coverage decline j (0.00, ….,0.20 in 0.01 steps), we computed the per capita annual incidence at endemic equilibrium. Table 3 summarizes model specifications and equations.

Parameter Estimation

Let R_0 denote the basic reproduction number (disease-specific), v the effective protection due to vaccination, μ the per-capita birth rate scaled to modeled age band, γ the recovery rate, ω waning immunity rate.

Vaccination reduces susceptibility by an effective protection level $v = VE\ x\ v_{struct}$, where v_{struct} is the structural age-band coverage, yielding an effective reproduction number defined[12] as:

$$R_{eff} = R_0(1 - v)$$

Equilibrium Susceptible and Infectious Fractions

At endemic equilibrium, the susceptible fraction[1] is:

$$s^* = \frac{1}{R_{eff}} = \frac{1}{R_0(1-v)}.$$

and the infectious proportion I^*, representing the long-run prevalence of infection is defined as:

$$i\ = (\gamma + \mu)I^*$$

$$where\ I^* = 1 - \ s^* = \ \left(1 - \frac{1}{R_0(1-v)}\right)$$

Disease-specific Incidence Definition

We defined the per-capita incidence i as the product of the equilibrium incidence scaling factor (prefactor) and the deficit from the herd immunity threshold[13]:

$$i = \underbrace{prefactor}_{per\ year}\ x\ \left(1 - \frac{1}{R_0(1 - v)}\right)$$

Disease-specific Incidence

For SIR diseases (rotavirus), equilibrium incidence is governed by the demographic turnover, so the prefactor equals the per-capita birth (and death) rate μ (per year) and the incidence[1,13] was defined as:

$$i_{SIR} = \ \mu\left(1 - \frac{1}{R_0(1 - v)}\right)$$

For SIRS disease (pertussis) with waning at rate ω and recovery at rate Y, both in per-year units, the per-capita annual incidence[1,13] (Clancy, 2015) was defined as:

$$i_{SIRS} = \frac{(\gamma + \mu)(\mu + \omega)}{\gamma + \mu + \omega}\left(1 - \frac{1}{R_0(1-v)}\right)$$

Annual age-band case counts were computed as: $I_{annual} = i\, N_{age-band}$, where $N_{age-band}$ is the relevant state-specific population in the modeled age group. Incidence is truncated at zero when $R_0(1-v) \leq 1$.

Table 3: Summary of model components and equations.

Component	Definition	Formula
Model type	Compartmental model models	SIR (rotavirus), SIRS (pertussis)
Basic reproduction number	Expected secondary cases in fully susceptible population	R_0
Effective reproduction number	Reproduction number under vaccination	$R_{eff} = R_0(1-v)$
Structural age-band coverage	Average across modeled age band	$v_{struct} = \left[\left(\frac{R-1}{R}\right)X + \frac{1}{R}(X-J) = X - \frac{j}{R}\right]$
Effective protection	Vaccine-derived reduction in susceptibility	$v = VE\ x\ \left(X - \frac{j}{R}\right)$
Susceptible fraction at equilibrium	Proportion susceptible at endemic steady state	$s^* = \frac{1}{R_{eff}} = \frac{1}{R_0(1-v)}.$
Infectious fraction at equilibrium	Long-run prevalence	$I^* = 1 - s^* = \left(1 - \frac{1}{R_0(1-v)}\right)$
Per-capita birth rate	Demographic inflow scaled to age band	$\mu = \frac{New\ births}{N_{age-band}}$
General per-capita incident	Incidence at equilibrium	$i = \underbrace{prefactor}_{per\ year}\ x\ \left(1 - \frac{1}{R_0(1-v)}\right) = (\gamma + \mu)I^*$
SIR prefactor	Scaling factor	μ
SIRS prefactor	Scaling factor	$\frac{(\gamma + \mu)(\mu + \omega)}{\gamma + \mu + \omega}$
SIR Incidence (i_{SIR})	Rotavirus equilibrium incidence	$i_{SIR}) = \mu\left(1 - \frac{1}{R_0(1-v)}\right)$
SIRS Incidence ()	Pertussis equilibrium incidence	$i_{SIRS} = \frac{(\gamma + \mu)(\mu + \omega)}{\gamma + \mu + \omega}\left(1 - \frac{1}{R_0(1-v)}\right)$
Annual incident cases	Age-specific annual cases	$I_{annual} = i * N$
Additional burden	Difference vs baseline	$\Delta = Outcome_{decline} - Outcome_{baseline}$

Vaccination Coverage Declines Assumptions

Birth-only Coverage Decline

Coverage declines were applied exclusively to newborn cohorts and average across the age band, so the effective coverage (structural age-band coverage) entering transmission was defined (Bauch & Earn, 2004) as:

$$v_{struct(j)} = X - \frac{j}{R} \text{ derived from } \left[\left(\frac{R-1}{R}\right)X + \frac{1}{R}(X-J)\right] \text{ for all diseases.}$$

Where X is the baseline coverage, j is the proportional reduction newborn-specific coverage (0-20%) and R is the width of the modeled age band in years (5 for rotavirus and 15 for pertussis). Under this framework, a 20% newborn coverage decline corresponds to a 4 percentage-point reduction structural coverage for children aged 0-4 years coverage for rotavirus and a 1.33 percentage-point reduction for children aged 0-14 years for pertussis. So, the effective protection entering transmission was $v = VE\ x\ v_{struct(j)}$.

Population and Demographic Inputs

State-level population estimates (total and age-specific) were obtained from the U.S Census Bureau American Community Survey (ACS) 2023, five-years estimates, accessed through the tidcensus R package. For each U.S. state s, we extracted the total population (all ages), $N_{s,\ all\ ages}$, and the age-specific populations for 0-4 years and 0-14 years[14]. Age- and state-specific vaccination coverage was extracted from the CDC's SchoolVaxView[6] and ChildVaxView[7] among kindergartners and young children aged 0-35 months, respectively.

State-specific crude birth rates (births per 1,000 population per year) obtained from the National Vital Statistics (NVSS)[9] were used to compute the annual births defined as:

$$New\ births_s = \frac{Birth\ rate}{1000}\ x\ N_{s,\ all\ ages}$$

To parameterize demographic turnover in the equilibrium transmission model, the per-capita birth rate, μ_s applied within the modeled age-band was defined as:

$$\mu_s = \frac{New\ births}{N_{s,\ age-band}}$$

Where $N_{s,\ age-band}$ is the state-specific population of the modeled child age group. This ensures that incidence reflects the inflow of new susceptibles into the modeled age group.

Outcome Estimation

For each state, disease, and coverage decline scenarios, we estimated annual incidence rate, annual incident cases, hospitalizations, deaths, workdays lost and direct medical costs and productivity costs. Annual outcome counts are defined as $count = i * N_{s,\ age-band}$, where

$N_{s,\ age-band}$ is the state-age-band population. Outcomes were reported as absolute counts and rates per 100,000 age-band population.

Additional Burden

The primary outcomes of interest were additional (incremental) burden attributable to coverage declines, defined as differences relative to baseline coverage:

$$\Delta_{Outcome} = Outcome_{decline} - Outcome_{baseline}$$

Cost estimation

Direct medical and productivity costs were estimated using disease-specific inputs for hospitalization rates and duration, cost per hospital day, days of illness, and daily wage loss. Productivity costs were estimated using a fixed national daily average derived from the U.S. Bureau of Labor Statistics (BLS) data on average weekly earnings for private-sector employees[11]. The expected total cost per infection was defined as:

$$Cost_{per\ infection} = \left(Hosp\ rate\ x\ Days\ Hosp\ x \frac{Cost}{Days\ Hosp}\right) + (Days\ Sick\ x\ Daily\ Wage)$$

Total and incremental costs were calculated by multiplying the per-infection costs by the corresponding annual incidence.

Software and Reproducibility

All analysis was conducted in R using reproducible project structure. Package versions were managed using renv. All parameters were externalized in configuration files to enable transparency and replication.

Assumptions

- Consistent with prior equilibrium transmission analyses, we assumed:
- Vaccination coverage declines affect newborns only
- Homogeneous mixing within state and age band
- No transmission coupling between states
- No age-specific heterogeneity within the modeled age band (e.g. <5-year-olds and 10-year-olds assumed identical for pertussis).
- Cross-age transmission is averaged across the modeled age group.
- Natural history parameters do not vary by state
- Endemic equilibrium represents long-run average annual burden

Summary of Data Sources:

1. State population (all ages): https://data.census.gov/table/ACSDT1Y2022.B01001
2. Birth rate: chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://www.cdc.gov/nchs/data/nvsr/nvsr74/nvsr74-1.pdf
3. State vaccine coverage:
    1. Rotavirus: 2021 - https://www.cdc.gov/childvaxview/about/interactive-reports.html
    2. Pertussis: 2024-2025 - https://www.cdc.gov/schoolvaxview/data/index.html#cdc_data_surveillance_section_1-schoolvaxview-interactive
4. Average daily cost: https://www.bls.gov/charts/state-employment-and-unemployment/average-hourly-earnings-and-weekly-hours-and-earnings-by-state.htm
5. Other parameters – see references

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