Christine Gonzalez, 6/10/2025, Updated 8/7/2025
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Measles Outbreak 1928-2002 Methodology:

1. Conduct timeseries charting and analysis to identify patterns and trends overtime

2. Conduct regional comparisons
    a. Growth-rate patterns by region and/or state

3. Growth rate of measles outbreak before and after vaccination
    a. Annually, by region, and/or by season

4. Identify patterns such as delays in response to measles outbreak once vaccination was introduced
    a. Q: Which states received vaccinations first?
    b. Q: What was the scheduling?
    c. Q: Were vaccinations administered by groupings or segmentation of populations (i.e. gender, age, health status, states or regions most affected, or just by location)?
    d. Q: When did they decide to require two vaccinations?

5. Create predictive model or charting analysis to determine the ongoing growth-rate in the last 5-10 years
    a. Identify patterns that can accurately predict what the growth rate will be in the next 5-10 yrs
    b. Q: How will the current administration impact growth-rates or vaccination requirements given that this administration has officials who are anti-vaxxers

6. Conduct additional research to determine when vaccinations were introduced by state.

7. Create charts based on seasonal trends or by month.

If doing all three:

To demonstrate the effectiveness of vaccinations:

1. Trends in vaccine-preventable diseases in the US showing measles, hepatitis, and diphtheria
    a. Number of cases vs growth-rate(incidences)
    b. Split by pre – and post- vaccinations
2. Spot any trends in regions where spikes in outbreaks occur more often between all three (so better response protocol and allocation of resources for the specified areas due to X amount of factors – i.e. metropolitan area, population size, political affiliations, religious views)
3. Seasonal trends for all three diseases – may be able to show a pattern, but it depends on the disease and how transmission occurs
4. Measles, Polio, and Smallpox vaccines may have all been introduced around the same time…

DEFINE MEASLES

- Measles:
    - highly contagious viral infection
    - spread via respiratory droplets in air
    - symptoms produce coughing, sneezing, rash, high fever
- Can be serious and fatal for:
    - children < age 5
    - people who are immunocompromised
- Easily preventable through vaccination

US Census
Urban and rural areas of the US:

- Urban- Initial minimum threshold of 2,500 inhabitants: Territory, persons, housing units
- 1920 census – first time 50 percent of US population was defined as urban
- 1950 census – “urbanized area concept” – increased growth in suburban areas outside of urban areas of 50,000+
- 1960 census- Population density threshold of >=1000 per square mile

Outbreak Markers: Pre-Vaccination (urban/rural regional charts)

- Population increases
- Urbanization
- Industry:
    - Auto industry
- Jobs and Workers:
    - Factories
    - Child labor (poverty)

Post-Vaccination (70-80% reduction in measles cases)
(Bar chart and line chart comparisons)
*Requirements: good contextualization of the statistical analysis in the selected region

How does this compare to events today?

- Child labor in the US is on the rise:
    - [Name companies as examples]
- Politicians even considered a bill to push back on child labor laws
- Anti-vaxxers among certain communities:
    - Religious groups: [name some that are strict anti-vaxxers]
    - Republicans
    - Jewish communities
    - Autism advocates

Was poverty also a factor in the progression of measles outbreaks?

- Considerations:
    - Children and child labor
    - Disabilities at home
    - Unable to work or seek medical attention
    - The Great Depression

Statistical story outline:

Scientific Analysis of Measles Disease Progression Pre- and Post-Vaccine Era 1928-2002

1. In the absence of vaccination (pre-1963), was increased measles transmission driven by urban expansion and population mobility?
2. Did higher mean incidences of pre-vaccination measles cases correlate with states that experienced the largest mean cases?
3. What does autocorrelation tell us about the pattern of progression and regression of measles disease overtime?
4. What additional variable or derived feature can be introduced to further stratify the data based on observed autocorrelation patterns?
5. Did regional proximity lead to fewer measles cases or was this due to delays and limitations on data reporting?
6. To what extent did land area and population density influence the incidence rates of measles across U.S. states?
7. What indicators support measles vaccine sensitivity, specificity, and efficacy?
8. What predictive models can we create to determine the risk ratio of each state based on historical case data, incidences, and estimated population size?

A. Factor seasons as <u>outbreak indicators</u> – Seasons in US. Winter, Spring, Summer, Fall

B. Factor regions as <u>growth indicators</u> – number of incidences compared to more urbanized areas
    - Can this be an indicator of better resource allocation or better protocols in place if number of incidences or cases are lower?
    - Dispersion of measles outbreak – tight concentrations pre-vaccination, more outward dispersion post-vaccination
    - What regions had lower incidences post-vaccination?

C. Can you determine urbanization based on number of cases? Does an Increase in Disease Incidence Reflect Underlying Population Expansion or Mobility? Is the Increase in Reported Cases Attributable to Population Growth? Do Increases in Case Counts Reflect Larger Population Sizes?
    - is that number higher or lower? <u>population indicator</u> as well
    - (versus auto industry, mobilization, the great depression)
    - Density charts, geom_tile heatmap

D. Contextualization of both questions below can be used with density chart or tile heatmaps
   - "Does the rise in pre-vaccine measles incidence reflect patterns of urbanization and population mobility?"
   - "In the absence of vaccination (pre-1963), was increased measles transmission driven by urban expansion and population mobility?"

"Urbanization in the pre-vaccine era" (1963) contextualizes why incidence might have been affected by social/demographic change (and rather than medical intervention post- vaccine era).

E. What <u>indicators support measles vaccine sensitivity, specificity, and efficacy</u>?
   - charts with percentage decreases: pre- vs post-vaccine period
   - compare seasons pre- and post- vaccination

F. Predictive: Can you develop a risk assessment or risk ratio (probability scoring) based on number of incidences? What predictive models can we create to determine the risk ratio of each state based on the number of incidences and estimated population size?

G. Frequency table to highlight outbreaks in each state: Identify epi_weeks where the number of cases in each state exceeded that state's average weekly case count, count the spikes, maybe to plot frequency of outbreaks per state or over time.
   - Calculate the average cases and count the number of times it was above average across multiple weeks. Show in range of months to demonstrate high and low seasonal activity or patterns of occurrence.
   - Calculate percentage change for the same states post-vaccine era

H. Look at the few states with no cases along the timeseries, make population estimates, and look at regional proximity.

I. We can get population estimates and land area to compare population density and see if the states with the highest incidence spikes have smaller population estimates in comparison to states with higher case spikes (outbreaks) and lower incidences. * geom_density_2d_filled() looks interesting to explore for states that had high incidence or are smaller with higher density. https://www.census.gov/geographies/reference-files/2010/geo/state-area.html
   Source: U.S. Census Bureau, unpublished data from the MAF/TIGER database
J. A closer look at the year 1945
K. Create a linear regression model to predict incidences or measles cases if no vaccine were introduced. Have to decide which year to use. Use population as independent and measles cases as dependent variable.
L. Compare population growth, densities overtime against measles decline pre-vaccine era to establish urbanizations role in reducing measles transmission
   a. 1941-1962: determine rate of decline – percentage change
   b. Examine biggest decline years (1958-1962) against population growth. Count decline years and calculate percentage change.

Timeline

John Franklin Enders and his team tested their measles vaccine on small groups of children from 1958 to 1960, before beginning trials on thousands of children in New York City and Nigeria. In 1961 it was hailed as 100% effective and the first measles vaccine was licensed for public use in 1963.

Individual countries introduced mass vaccination programs against measles at the national level from the 1960s on, and the first internationally focused measles immunization programs took place in Africa from 1966.

By May 1967 The Gambia became the first country in the world in which transmission of the virus was interrupted. (this means that measles transmission was still possible prior to 1967)

An improved version of the measles vaccine was created in 1968 when Dr Maurice Hilleman, a pioneer in vaccine development, passed the virus through chick embryo cells 40 times to weaken it, producing a vaccine that did not cause such severe side effects.

This weaker version, known as the Edmonston-Enders strain, was developed into some of the strains still used in measles vaccines today.

In 1971 Hilleman combined the recently developed vaccines against measles, mumps and rubella into the MMR vaccine, administered as a single shot, with one booster dose following – and in 2005, the varicella vaccine was added, to make the combined MMRV vaccine.

OBSERVATIONS AND INSIGHTS FROM HEATMAP AND TABLES

Highest average incidences of measles cases pre-vaccination did not correlate with higher average case counts except in Wisconsin and New Jersey. Urbanization in the pre-vaccine era (< 1963) may point to lower incidences, rather than medical intervention post-vaccine era. Changes in socioeconomic status, social-demographics, including education, and resource allocation as defined by the “urbanized area concept” may account for lower incidence rates, despite having higher case counts due to population density. However, you cannot rule out population mobility as an underlying contributor of incidence in states like Wisconsin and Vermont because of proximity to areas with higher case counts. It’s more evident in states Alaska and Hawaii.

Both Wisconsin and Vermont experienced the highest mean incidences.

1. Which States had Higher Incidences of Measles Cases Pre-Vaccine Era?

	State	Average_Incidences
1	WI	17.37401484865791
2	VT	17.15307028360049
3	UT	14.51777645659929

4	AK	12.94591016548463
5	MT	12.72423668639053
6	HI	12.24715163934426
7	NJ	10.89280251141552
8	AZ	10.07527084601339
9	CO	10.04518775274408
10	CT	10.03849283667622

2. Which States had the Largest Average Number of Measles Cases Pre-Vaccination?

	State	Average_Cases
1	NY	959.358361774744
2	PA	804.8680115273776
3	CA	704.9591141396934
4	TX	599.7686093479515
5	WI	578.7881210736722
6	MI	541.3489167616875
7	NJ	510.0776255707763
8	OH	458.314497716895
9	IL	455.2682232346241
10	MA	441.3893956670468

Below is a frequency table accounting for the number of outbreaks in each state prior to vaccine availability. Outbreaks are represented as the total number of case counts above the state's average. Outbreaks occurred in all 50 states pre-vaccination (<1963), but went down significantly post-vaccination for half of the states with the largest outbreak occurrences. Gathering a count of outbreaks is helpful to determine a state's likelihood of experiencing a resurgence of cases and help guide for better response and resource allocation. While further study can help identify the main contributors to resurgences so those areas can be addressed accordingly.

Number of Measles Outbreaks Pre-Vaccine (counts above mean cases)

state	spike_count	
1	NY	628
2	MA	597
3	WA	584
4	OH	566
5	PA	564
6	NJ	560
7	WI	550
8	CA	543
9	WV	538
10	ME	535

Number of Measles Outbreaks Post-Vaccine

state spike_count

1	CA	329
2	NY	311
3	TX	287
4	PA	269
5	MI	254
6	WI	172

POPULATION DENSITIES AND MEASLES INCIDENCES

Density levels do not take cities or counties into account. So, while some states' populations are more concentrated in higher density areas, the data distributes these populations across the entire state. Nevada, for example, has most of its population distributed within higher density areas, but the data calculates its density levels at .71 people per square kilometers, which is low. Nevada also had a lower mean incidence of 6.5. It may be that the distribution of measles cases may either be low due to its restriction to denser areas with better interventions or more widely distributed to areas with lower densities.

POSITIVE OUTCOMES, METHODS, AND LIMITATIONS OF WORK

A heatmap was used to observe mean incidences across US states from the onset of the measles outbreak until 1963, the year the vaccine was introduced. The earliest highest incidences of measles cases were observed on the East coast, including in states South Carolina, North Carolina, Massachusetts, Maryland, and District of Columbia. A closer look at 1945 of the heatmap shows that rates of measles were on decline and perhaps stabilizing due to nationwide and global events, as well as advancements in medicine and healthcare. (need citation to back this up)

A frequency table was created to calculate national outbreak occurrences pre- and post-vaccination

1. Calculate mean cases per state
2. Join this mean back to original data
3. Filter rows where weekly cases exceed the state's mean
4. Count how often that happens, per state and per year

Autocorrelation (ACF) graph was used to determine the degree of similarity across all weeks pre- and post- vaccination with measles cases. Positive autocorrelation was observed with positive values remaining high every 52-week lag and low negative values in between peaks, suggesting annual seasonality and alternating cycles.

Clusters of measles cases follow a similar pattern to influenza, with cases increasing during seasons of lower temperatures and decreasing during higher seasonal temperatures. We can further segment the data to account for this seasonality, but must also consider segmenting for alignment with the school-year in the US. Other possible segments can include regions or states with hotter climates to further explore patterns of seasonality.

*Positive average values are of similar magnitude and gradually decrease, while negative average values are of similar magnitude that gradually decrease. Segment the data for seasonality and observations of waves and clusters.

Population estimates were aggregated from the data by taking the total number of cases multiplied by 100,000 and dividing by the incidence rate.

Fig. X: estimated_population = (cases * 100000) / incidence_rate

Aggregation for population density was achieved after calculating population estimates and dividing by land area. Land area data was collected from the US Census Bureau's 2010 State and Local Geography dataset. The area measurements, in square kilometers, were derived from their Master Address File/Topologically Integrated Geographic Encoding and Referencing (MAF/TIGER®) database.

Fig. X: population_density = population / land area (sq. km.)

Population density for each state needs to be segmented and categorized from high to low to display accurately on the geom_density_2d_filled plot. The challenge is determining which variables need to be represented in the plot:

a. Focus on highest and lowest incidences to correlate with density and land area
b. Consider what is dense relative to land area to categorize the data

Population density and average incidences were segmented for each state using quantiles, divided into three parts and categorized as "high," "medium," "low" for plotting into a density chart.

DATA LIMITATIONS:

Seasonality segmentation still demonstrates some limitations to the data because we would still need to confirm or rule out temperature as a variable. Measles is an airborne virus with similar flu-season patterns.

There is no available data on the number of vaccinations administered per state and within the vaccination timeline. This would have provided better evidence to support the measles vaccination's efficacy in reducing susceptibility and transmission of the disease. There is also no available demographic data or school season data to account for age groups and mobility.

Population density posed some challenges since distribution of people per square kilometer varies across states and the data does not account for incorporated versus unincorporated land area use. Examining incorporated against unincorporated areas would allow for better data accuracy and provide a more meaningful measure of density levels for settlements that exist. It is also much more useful for comparing settlement intensity across geographies of similar scale.[1]

*Subtracting unincorporated land area from incorporated land area would provide a better measurement for density. Only about 3-5% of land area is incorporated in the US.

Quartiles(.25 or .75) versus terciles(.33 each)

Compare population overtime to support:
A X% reduction in measles cases pre-vaccine era helps establish urbanization's role in minimizing infectious disease transmission; following vaccine introduction, measles cases declined by 49%

A X% reduction in measles cases pre-vaccine era and X% increase in mean population growth helps establish urbanization's role in minimizing infectious disease transmission; following vaccine introduction, measles cases declined by 49%

Evaluated incidence and population densities to support urbanization's role, resulting in X% reduction in cases between X and X periods

Urbanization contributed to a X% reduction in measles cases pre-vaccine era, while vaccine introduction led to a 49% decline

X% increase in population growth and X% reduction in measles cases supports urbanization's role in minimizing measles transmission pre-vaccine era; following vaccine introduction, measles cases declined by 49%

Factors including population growth, densities, and urbanization were all indicators leading to X% reductions in measles cases pre-vaccine, and a 49% reduction post-vaccine

Lower incidence trends in dense areas support urbanization's role in controlling measles transmission, and led to X% reductions pre- and 49% decline in measles cases post-vaccine era

Incidence and population densities as markers in reducing measles transmission, 49% decrease in outbreaks

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[1] Cohen, Darryl (2015), Understanding Population Density. https://www.census.gov/newsroom/blogs/random-samplings/2015/03/understanding-population-density.html. Accessed 17 June 2025.

Christine Gonzalez, 6/10/2025, Updated 8/7/2025
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Examining Spatial Patterns of Urbanization, Mobility, and Population Densities as Drivers of Measles Transmission

A Scientific Analysis of Measles Disease Progression Pre- and Post-Vaccine Era 1928-2002

PROBLEM STATEMENT AND OBJECTIVES

This project focuses on U.S. measles data obtained from the Project Tycho dataset. Data is divided and categorized by epi-week, location, number of cases, and incidence per 100,000. The project examines population growth, population densities, and patterns of measles incidence as indicators of urbanization throughout the U.S. between 1928 and 2002. It also explores advancements in public health interventions as an indicator of urbanization through further examination of measles incidences pre-vaccine era (before 1963) and post-vaccine era. Lastly, it determines how much of a role urbanization played in helping to reduce rates of transmission before measles vaccine was introduced.

QUESTIONS FOR ANALYSIS

* In the absence of vaccination (pre-1963), was increased measles transmission driven by urban expansion and population mobility?
* Did higher mean incidences of pre-vaccination measles cases correlate with states that experienced the largest mean cases?
* What does autocorrelation tell us about the pattern of progression and regression of measles disease overtime?
* What additional variable or derived feature can be introduced to further stratify the data based on observed autocorrelation patterns?
* Did regional proximity lead to fewer measles cases or was this due to delays and limitations on data reporting?
* To what extent did land area and population density influence the incidence rates of measles across U.S. states?
* What indicators support measles vaccine sensitivity, specificity, and efficacy?
* What predictive models can we create to determine the risk ratio of each state based on historical case data, incidences, and estimated population size?

MEASLES OVERVIEW AND VACCINE TIMELINE

Measles is a contagious virus with high human-to-human transmission through tiny respiratory droplets in the air. Susceptible groups include children age 5 years and under, as well as individuals with an underlying health condition or immunocompromised. The disease presents symptoms of coughing, sneezing, rash, and high fever and can be serious or fatal for those in the susceptible groups. While no antiviral treatments exist for measles, it can be easily prevented through MMR vaccination in the US.

The first live measles vaccine was licensed for public use in September 1963 and was initially administered to 25,000 people in the US. By mid-1966, the vaccine was administered to approximately 15 million children and reported incidences of measles fell by half. In 1965, reports of a strange measles-like illness in children appeared. These children were exposed to natural measles after receiving both the inactivated vaccine and live vaccine. By 1968, recommendations for the use of live vaccine alone showed strong support and the inactivated vaccine was withdrawn.¹ In the same year, an improved version was developed by Dr. Maurice Hilleman, a pioneer in vaccine development. This was a weaker version of the vaccine, known as the Edmonston-Ender strain, which was introduced with minimal side effects and is still used in measles vaccines today.²

TIMESERIES LINE CHART TRACKING TOTAL MEASLES CASES PRE- AND POST-VACCINE ERA

Pre-1963 Era: The line chart in Fig. 1 summarizes total measles cases from 1928 through 2002. Fluctuations were observed before and after 1940, which had several events occurring simultaneously including the stock market crash which led to The Great Depression, WWII, and the popularity of the automobile. Measles often exhibited in ordinal cycles, with one year representing significant spikes after a season of lower occurrences. The left side of the chart shows large recurring peaks in measles cases. These peaks occurred almost every year, reflecting the disease's seasonal epidemic pattern in the absence of widespread immunity. The highest peaks exceeded 60,000 cases per week, indicating severe outbreaks. The sharp, repeating peaks reflect the predictable annual epidemics characteristic of infectious diseases before vaccines were introduced.

A closer look at 1945 of the line chart shows that rates of measles were on decline and gradually stabilizing, possibly due to advancements in medicine and healthcare.

Post-1963 Era: The red vertical line signifies the first introduction of the measles vaccine in 1963. Immediately following this, there is a rapid decline in weekly cases, confirming the vaccine's dramatic impact on transmission. After the vaccine introduction, cases dropped significantly (recalculate), though occasional small spikes are visible. These could reflect localized outbreaks that coincided with measles recurrences that were associated with the inactivated vaccine.

HEATMAP DISPLAYING AVERAGE MEASLES INCIDENCES IN THE UNITED STATES

The heatmap in Fig. 2 was used to observe mean incidences across states from the onset of the measles outbreak until 2002. It also illustrates how widespread measles was across the U.S. prior to the introduction of the vaccine. Mean incidences are represented in coral gradients, with the brightest coral referencing the high values of between 60 and 70 incidences per 100,000, and the darkest gradient representing the lowest. The heatmap post 1963 shows that vaccine introduction was effective in reducing cases in all regions.

Earliest measles cases with the highest mean incidences were observed on the East coast, including in states South Carolina, North Carolina, Massachusetts, Maryland, and the District of Columbia. Cells in white either represent missing values or underreported measles incidence due to gaps in surveillance. Underreporting may have continued following the most successful vaccine interventions based on the belief that measles had been completely eradicated. This may explain the spread of missing values seen across most states after 1980.

FREQUENCY OF OUTBREAKS: PRE- VERSUS POST-VACCINE ERA

The frequency chart accounts for the top 10 states (NY, MA, WA, OH, PA, NJ, WI, CA, WV, ME) with the highest number of outbreaks prior to vaccine availability. Outbreaks are represented as the total number of case counts above the state’s mean. Top 10 states were selected based on their average weekly cases and counted when cases exceeded this average (spikes). They are plotted alongside their post-vaccine spike counts to demonstrate measles vaccine's effectiveness at achieving widespread immunity and reducing transmission.

Outbreaks occurred in all 50 states pre-vaccination, but went down significantly (49% nationwide and 57% in top 10 states) post-vaccination for all states with the largest outbreak occurrences. Higher mean case counts did not correlate with higher mean incidences of measles in the top 10, except in NJ and WI.

AUTOCORRELATION OF WEEKLY MEASLES CASES

An autocorrelation (ACF) graph was used to determine the degree of similarity across all weeks pre- and post- vaccination with measles cases. Positive autocorrelation was observed with positive values remaining high every 52-week lag with low negative values in between peaks, suggesting annual seasonality and alternating cycles.

SEASONALITY OF MEASLES IN THE UNITED STATES

Clusters of measles cases follow a similar pattern to influenza, with cases increasing during seasons of lower temperatures and decreasing during higher seasonal temperatures. Seasonal variations have most often been attributed to children in school, which correlates with the alternating cyclical pattern of annual measles cases. Earlier simulations indicate "that the persistence of the biennial pattern of measles outbreak implies that the vaccine was not being used uniformly throughout the population."³

Other possible segments can include regions or states with hotter climates to further explore patterns of seasonality and to confirm its correlation with the school year in the US.

POPULATION DENSITIES AND MEASLES INCIDENCES

Aggregations for density levels in Fig. 5 do not take US cities or counties into account. Instead, density levels distribute these populations across the entire state. This has no significant impact on the data except when aggregating totals over multiple years to analyze measles vaccine's effectiveness.

Alaska, Nevada, and Hawaii were represented as outliers in the group. Nevada, for example, had a lower mean incidence of 6.5, but measles cases remained about the same pre and post-vaccination. Although incidence of infectious disease usually occurs within densely populated urbanized areas, average density levels for Nevada were low. However, population density grew from .71 people per square kilometers to 3.1 people per square kilometers, which implies that changes in densities and population growth served as underlying factors in measles transmission. In this case, growth contributed to caseload. This further suggests that population growth and densities remain critical variables for controlling seasonal outbreaks of infectious disease.<sup>4<sup/>

Segmenting by years pre and post would explain the distribution of measles cases over time and determine if incidence was more uniformly or non-uniformly distributed over the years.

Climatic conditions also need to be considered across states to reflect regional differences.

MULTILINEAR REGRESSION ANALYSIS

The multilinear regression model below indicates strong correlation between population and measles cases. Therefore, as population grew post-vaccine era, cases of measles increased. Population densities, however, decreased as cases increased. This could have resulted in wider distributions of human settlements as more incorporated urban areas were established overtime.

To confirm this, we can use Chi-Square statistics, which gives us 47.575 on 2 degrees of freedom. This provides a p-value that is less than .05 level of significance. Therefore, we can reject the null hypothesis since the slope of the variables are useful in predicting the probability of the dependent variable. In this case, population estimates and population densities contribute significantly to caseload.

EXCERPTS & CITATIONS:

W. P. London, J. Yorke (1973), Recurrent outbreaks of measles, chickenpox and mumps. I. Seasonal variation in contact rates.
Published Dec 1, 1973 ·
American journal of epidemiology, DOI: 10.1093/oxfordjournals.aje.a121575

"seasonal variation is attributed primarily to the gathering of children in school... For populations in which most members are vaccinated, simulations show that the persistence of the biennial pattern of measles outbreaks implies that the vaccine is not being used uniformly throughout the population."

Am J Public Health. 2013 Aug;103(8):1393–1401. doi: 10.2105/AJPH.2012.301075

Measles Vaccination Before the Measles-Mumps-Rubella Vaccine
Jan Hendriks 1, Stuart Blume 1,

"In September 1963 the US Surgeon General Luther Terry published a statement on the status of measles vaccines. The live vaccine had by this time been given to some 25 000 people in the United States."

"Approximately 15 million children were given one of the new measles vaccines starting with their licensing in 1963 and continuing until mid-1966, and the reported incidence of the disease fell by half."

"Some 11.7 million doses of measles vaccine were distributed in 1967–1968, and the estimated number of cases of measles fell from 900 000 to 250 000. However, because budgetary politics subsequently led to fluctuating federal support for community-based immunization programs, the expectation that measles would soon be eradicated was to prove wildly overoptimistic."

"In 1965 the first reports of a strange measles-like illness in children exposed to natural measles after receiving the inactivated vaccine appeared in the United States, and it appeared that this could also occur when live vaccine was administered after inactivated vaccine. There was a growing sense, internationally, that the inactivated virus vaccine should be avoided."

"In May 1968 a second report of the MRC measles vaccine trial was published... The MRC concluded that "there is a strong case for the use of live measles vaccine alone... In 1968, by which time the inactivated vaccine had been withdrawn in the United States."

History of the Measles Vaccine. https://www.who.int/news-room/spotlight/history-of-vaccination/history-of-measles-vaccination#:~:text=One%20of%20the%20most%20contagious,%C2%A9. World Health Organization. Accessed June 29, 2025

Jamal, Yusuf (2022), Identification of Thresholds on Population Density for Understanding Transmission of COVID-19. National Library of Medicine. https://pmc.ncbi.nlm.nih.gov/articles/PMC9347488/

"Using logistic regression techniques, estimates of threshold levels of population density were computed corresponding to the incidence (case counts) in the human population. Regions with population densities greater than 3,000 person per square mile in the United States have about 95% likelihood to report 43,380 number of average cumulative cases of COVID-19. Since case numbers of COVID-19 dynamically changed each day until 30 November 2020, ca. 4% of US counties were at 50% or higher probability to 38,232 number of COVID-19 cases. While threshold on population density is not the sole indicator for predictability of coronavirus in human population, yet it is one of the key variables on understanding and rethinking human settlement in urban landscapes."

"However, thresholds of population density relative to the outbreak of the disease in humans remains unknown. The relative importance of knowledge of threshold on population density with reference to infectious disease such as COVID-19 is important for the future of modern cities and urban landscapes in the USA, given about 71% of the population reside in urbanized areas with an average density of 2,534 persons per square mile (https://www.census.gov/programs-surveys/geography/guidance/geo-areas/urban-rural/ua-facts.html)

Influenza transmission dynamics, which allow parallel comparison with COVID-19 transmission, depend on several socio-demographic factors (such as race, income level, education, and location), but population density remains a critical variable for controlling an outbreak of seasonal influenza (Atkinson & Wein, 2008; Merler & Ajelli, 2010)."

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