The Relationship Between Measles Cases and Vaccination Coverage

Research Question
What is the relationship between the global vaccination coverage of measles (measured by the number of first doses administered out of all eligible people) and the number of measles cases from 1980 to 2020?

Personal Engagement
I have always had a fear of needles and dreaded getting the flu shot and in-school vaccinations. I remember trying to negotiate with my parents about the necessity of getting them. While I knew that vaccines were important in virus resistance, I would still sometimes get the flu and found myself wondering if I had to get them and wondering how effective they were. With the recent pandemic and the creation of a new vaccine, I was able to see the cases slowly decrease on the news. Although I have learned the science behind vaccinations and immune response, I wanted to investigate how much of a difference vaccination coverage truly made. However, instead of researching into COVID-19, I decided to investigate the vaccine for measles, as it has been around much longer to see a more developed trend.

Background
Measles is a highly contagious respiratory illness caused by a virus that infects the respiratory tract before spreading to the rest of the body. It was first documented in the tenth century by a Persian physician, differentiating it from smallpox. The present virus is adapted to only infect humans (Berche, 2022). After global exploration, it became widespread with devastating consequences, as regions without previous exposure were extremely vulnerable. There were an estimated 30 million cases with 2 million deaths globally every year (*History of Measles Vaccination*, n.d.). The symptoms of this virus tend to be fever, a dry cough, runny nose, Koplik's spot and skin rash (Moss, 2017). However, measles frequently lead to complications, like diarrhea, pneumonia, and encephalitis (Berche, 2022).

John Franklin Enders created the first effective measles vaccine from the initial isolation of the virus in tissue cultures and became publicly distributed in 1963. The measles-mumps-rubella (MMR) vaccine combined the newly developed vaccines for all three viruses in 1971 and is still being distributed today (Katz, 2009.). The World Health Organization now recommends that the first dose be administered at 9 months in areas where measles is common, and 12–15 months in other areas. However, around 15% of children do not gain immunity after the first shot, so a second dose is highly recommended. The MMR is an attenuated live virus vaccine. The pathogen has been mutated and weakened so that no serious consequences will happen, but the immune system will be triggered, causing the production of memory B cells. Two doses are required, as some people have not developed enough antibodies after one (*History of Measles Vaccination*, n.d.). The estimated percentage of population vaccine coverage required for herd immunity to measles is around 95%. Herd immunity refers to the resistance to something infectious in a population, limiting the spread of the disease or virus (MacMillan, 2021).

Variables

Dependent: Global cases of measles, measured as cases per one million population every two years from 1980 to 2020.
Independent Variable: The percentage of MMR first doses administered to the target population (eligible people).
Controlled Variables: Source of data, processing software, type of vaccine monitored (the MMR)

Materials

- Microsoft Excel - calculation and data processing
- Word Health Organization (WHO) database - measle case and vaccination statistics
- MacroTrends database - total population

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Safety & Ethical Concerns

There are no safety or ethical concerns for this investigation. The data comes from the World Health Organization, which collects it through a Joint Reporting Form (JRF) from each member of the United Nations; the data is presumed to be ethically collected as there is as there are many policies and committees that promote and ensure the standards.

Hypothesis

It can be predicted that there is a negative correlation between the cases of measles and the number of first doses administered. As more of the population becomes immunized by the vaccine, the chance of getting measles decreases, as well as fewer people being susceptible to measles.
The hypotheses for statistical analysis are as follows:

Null Hypothesis (H_0): There is no relationship between global vaccination coverage and cases of measles.
Alternative Hypothesis (H_1): There is a relationship between global vaccination coverage and cases of measles.

Preliminary Study

The following trial investigation was done with a span of ten years, 1980-1990, which demonstrates the methodology that will be used and a sense of the relationship that exists between the variables.

Table 1: Raw data showing the global target population, first doses administered, cases and population every two years between 1980 and 1990

Year	Target Population (±2%)	First Dose (±100000)	Cases (±100000)	Population (±2%)
1980	118592384	18796051	3852242	4444007706
1982	124361787	24138552	3623758	4607984871
1984	125404912	50568981	3026973	4775836074
1986	130534072	60140380	2078696	4950063339
1988	132233941	82008081	1663940	5132293974
1990	134857363	98592614	1325074	5316175862

MacroTrends takes the data from the United Nations, and the UN states that there is a 1-2% margin of error in their population counts (Staughton, 2017)
However, first doses come from WHO, who have to estimate/interpolate data from certain countries or will compare reported data to survey data to accept it. Since there is a decent amount of estimation, the uncertainty of 100,000 doses is chosen.
Case data is also taken from WHO, who state that nations do not always follow their surveillance recommendations, leading to underreporting, so I decided on the same uncertainty as the first doses.

To calculate the vaccine coverage, the number of vaccination doses administered can be divided by the target population; it is then converted into a percentage to represent the number of eligible people who received the vaccine.

Sample: Global coverage in 1980

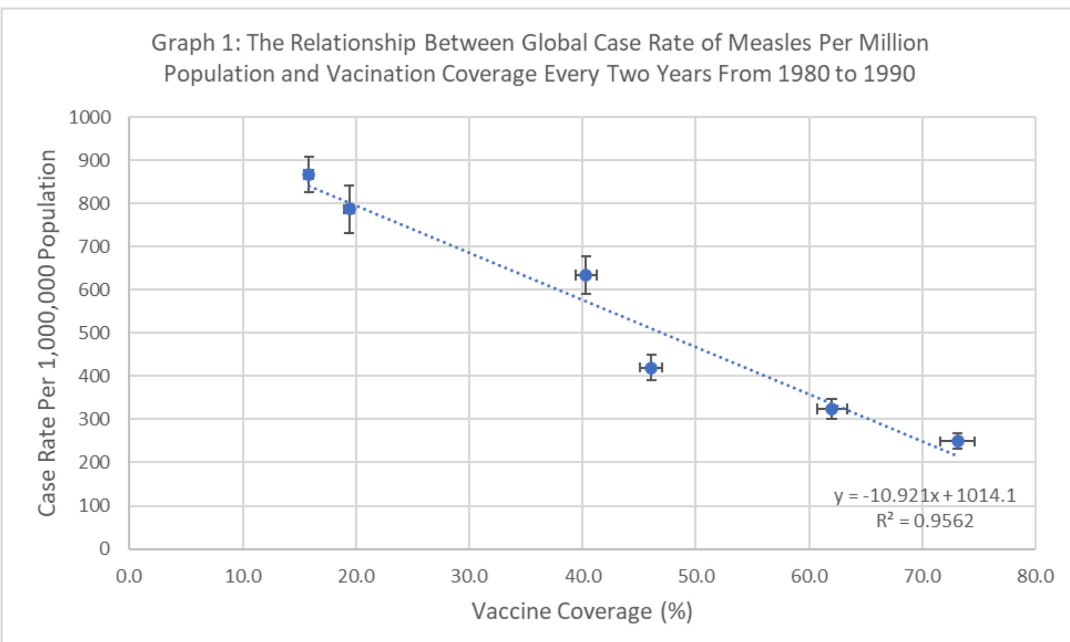
$$
\begin{aligned}
Coverage &= \frac{First\ Dose}{Target\ Population} \cdot 100\% \\
&= \frac{18796051 \pm (100000/18796051)}{118592384 \pm 2\%} \cdot 100\% \\
&= 15.8\% \pm 0.0253... \\
&= 15.8\% \pm 0.4\%
\end{aligned}
$$

To process the number of cases, it can be divided by the total population, resulting in number of cases per person. The cases of measles per one million population can be obtained by multiplying by 1,000,000.

$$case\ rate\ per\ 1,000,000\ population\ = \frac{cases}{population} \cdot\ 1,000,000$$
$$case\ rate\ per\ 1,000,000\ population\ = \frac{3852242 \pm (100000/3852242)}{4{,}458{,}003{,}514 \pm 2\%} \cdot\ 1,000,000$$
$$case\ rate\ per\ 1,000,000\ population\ = 867 \pm 0.0460...\%$$
$$case\ rate\ per\ 1,000,000\ population\ = 867 \pm 40$$

Table 2: The processed data of cases rate of measles per 1,000,000 population and vaccination coverage every two years from 1980 to 1990

Year	Coverage of Vaccine (%)	Cases/million
1980	15.8±0.4	867±40
1982	19.4±0.5	786±55
1984	40.3±0.9	634±44
1986	46.1±1.0	420±29
1988	62.0±1.3	324±23
1990	73.1±1.5	249±17



The R^2 value depicts a strong linear relationship between the variables. The investigation will follow the same methodology with a larger range of years.

Investigation

Table 3: Raw data showing the global target population, first dose administered, cases and population every two years between 1980 and 2020

Year	Target Population (±2%)	First Dose (±100000)	Cases (±100000)	Population (±2%)
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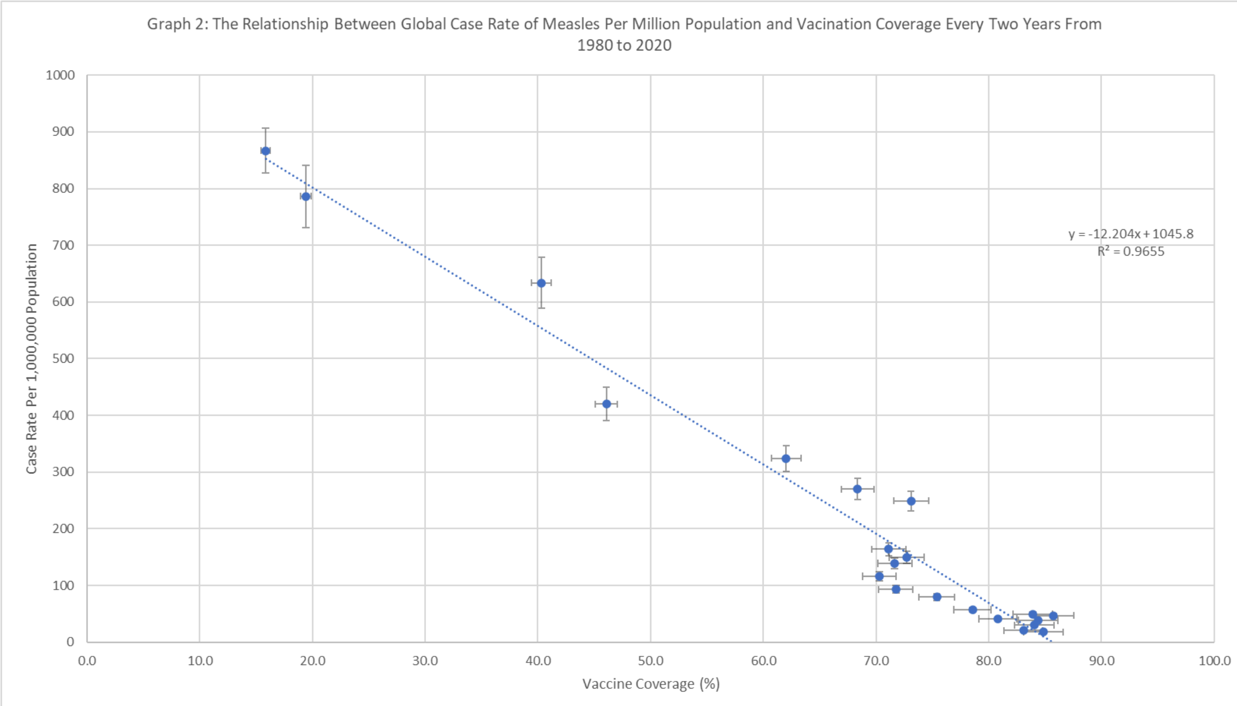
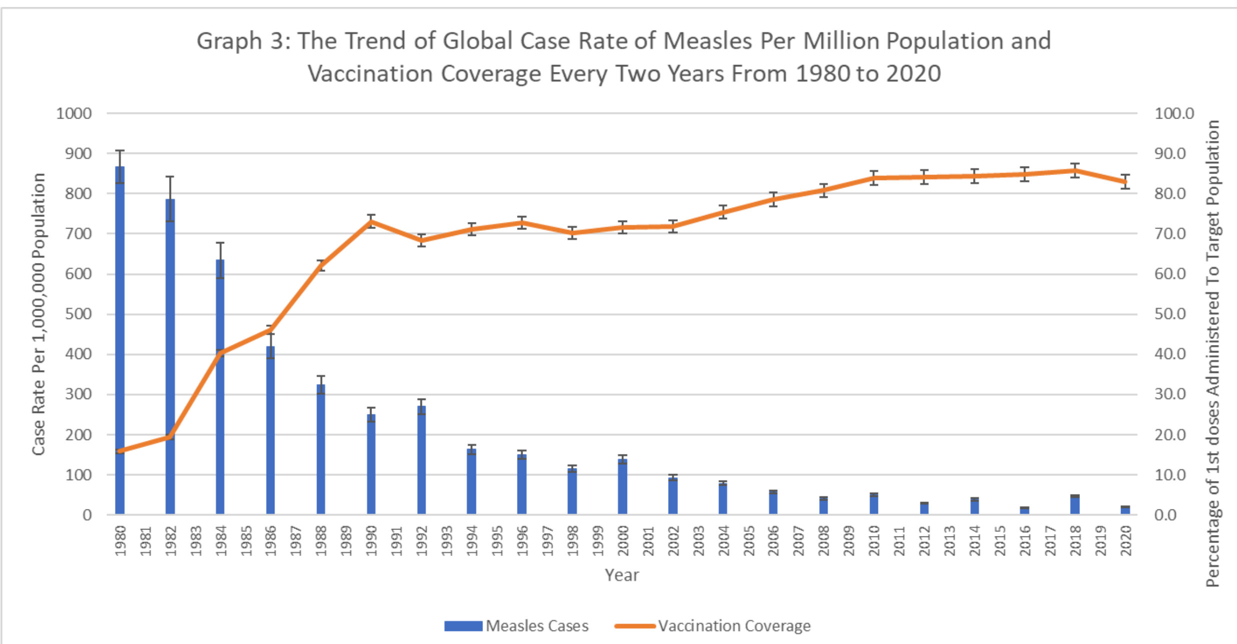
1988	132233941	82008081	1663940	5132293974
1990	134857363	98592614	1325074	5316175862
1992	128596356	87920206	1481192	5492686093
1994	127519232	90695406	926808	5660727993
1996	126653412	92103081	870218	5825145298
1998	126156896	88689654	694466	5987312480
2000	128143745	91812931	853479	6148898975
2002	128446154	92185234	586471	6312407360
2004	129937017	97964263	513406	6475751478
2006	131883147	103615553	377576	6641416218
2008	135336045	109324974	278751	6811597272
2010	137042460	114999257	343806	6985603105
2012	139756726	117481408	212376	7161697921
2014	139468173	117674294	282078	7339013419
2016	139246938	118148932	132490	7513474238
2018	135879534	116518393	360296	7683789828
2020	131592953	109320604	159067	7840952880

Table 4: The processed data of global cases rate of measles per 1,000,000 population and vaccination coverage every two years from 1980 to 2020

Year	Coverage of Vaccine (%)	Cases/million
1980	15.8±0.4	867±40
1982	19.4±0.5	786±55
1984	40.3±0.9	634±44
1986	46.1±1.0	420±29
1988	62.0±1.3	324±23
1990	73.1±1.5	249±17
1992	68.4±1.4	270±19
1994	71.1±1.5	164±11
1996	72.7±1.5	149±10
1998	70.3±1.5	116±8
2000	71.6±1.5	139±10
2002	71.8±1.5	93±7
2004	75.4±1.6	79±6
2006	78.6±1.6	57±4
2008	80.8±1.7	41±3
2010	83.9±1.8	49±3
2012	84.1±1.8	30±2
2014	84.4±1.8	38±3
2016	84.8±1.8	18±1
2018	85.8±1.8	47±3
2020	83.1±1.7	20±1





Statistical Analysis

Pearson's Product-Moment Correlation Coefficient determines the strength of association between two variables, but has 3 requirements; the data must have no outliers, the relationship is linear, and each variable is normally distributed. However, Graphs 3 and 4 are histograms, showing that neither of the variables is normally distributed. Instead, Spearman's Ranked Correlation Coefficient, denoted by r_s will be used. The strength and direction of association between ranked variables can be determined. The variable d and d^2 will represent the absolute difference between the ranks and the difference squared respectively. The sample size, n, is 21.

Table 5: Data Required For Spearman's Ranked Correlation Coefficient

Coverage of Vaccine (%)	Cases/million	Rank (Coverage of Vaccine (%)	Rank (Cases/million)	d	d^2
15.8	867	1	21	20	400
19.4	786	2	20	18	324
40.3	634	3	19	16	256
46.1	420	4	18	14	196
62.0	324	5	17	12	144
73.1	249	12	15	3	9
68.4	270	6	16	10	100
71.1	164	8	14	6	36
72.7	149	11	13	2	4
70.3	116	7	11	4	16
71.6	139	9	12	3	9
71.8	93	10	10	0	0
75.4	79	13	9	4	16
78.6	57	14	8	6	36
80.8	41	15	5	10	100
83.9	49	17	7	10	100
84.1	30	18	3	15	225
84.4	38	19	4	15	225
84.8	18	20	1	19	361
85.8	47	21	6	15	225
83.1	20	16	2	14	196

The data will be used in the Spearman's Rank Correlation Coefficient formula, which is stated below

$$r_s = 1 - \frac{6\Sigma d^2}{n(n^2-1)}$$

$$r_s = 1 - \frac{6(2978)}{21(21^2-1)}$$

$$r_s = -\ 0.9338$$

Figure 1: Interpreting the strength of association by r value (Adapted from "Correlation Coefficients: Appropriate Use and Interpretation)

Absolute Magnitude of the Observed Correlation Coefficient	Interpretation
0.00–0.10	Negligible correlation
0.10–0.39	Weak correlation
0.40–0.69	Moderate correlation
0.70–0.89	Strong correlation
0.90–1.00	Very strong correlation

Using Figure 1, the r value obtained suggests that there is a very strong correlation between the global vaccination coverage of measles and the number of measles cases

The significance of the Spearman's Rank Correlation Coefficient will be tested while referring back to the original hypotheses:
Null Hypothesis (H_0): There is no relationship between global vaccination coverage and cases of measles.
Alternative Hypothesis (H_1): There is a relationship between global vaccination coverage and cases of measles.

A two-tailed test is used, as the hypothesis tests any correlation. A sample size of 21 is used (as 21 years were used) and the level of significance tested is 0.05. The critical value from the critical value table is 0.435. The calculated Spearman's rho (r_s) magnitude was 0.9338. Because the obtained rho is greater than the critical value, the null hypothesis is rejected, and the alternative hypothesis is accepted.

Conclusion

The research question, "What is the relationship between the global vaccination coverage of measles (measured by the number of first doses administered out of all eligible people) and the number of measles cases from 1980 to 2020?", can be concluded that there is a very strong,

significant, negative linear relationship between global vaccination coverage and the number of measles cases.
As shown through the R^2 value in graph 2, there is little deviation from the trend line. There is high confidence in the data. Based on the Spearman's Rank Correlation Coefficient, it can be determined that there is a relationship between these two variables. When looking at the error bars, there is a greater variation of vaccination coverage as cases get lower. However, the overall negative trend is unaffected.

In graph 2 and 3, the trend shows that as the global vaccination coverage increases, the cases of measles also significantly decrease. Their relationship especially stands out in 1990, where the slight increase in measles vaccination coverage directly corresponds with a slight dip in global cases. The data shows the drastic decrease in measles cases near the introduction of the MMR vaccine and is now plateauing as we reach the herd immunity threshold, which is 95%. While globally, the vaccination coverage in different regions (like European Region, 94% in 2020, or the Western Pacific Region, 93% in 2020) has a much higher rate, which have gotten relatively close to herd immunity. The measles cases are mainly in the African region, where the vaccination coverage is not as high (68% in 2020). Unfortunately for less developed countries, COVID-19 placed huge strain on health systems and accessibility to other diseases, like measles. The WHO now has placed a plan for Measles outbreak prevention, preparedness, response and recovery.

The MMR is a live attenuated vaccine, which is a weakened version of measles. Because the vaccine is so similar to the actual measles virus, it helps create lasting immunity. The live attenuated vaccine stimulates the immune response of the body when it begins to replicate. As a result, viral proteins surround and digest the infected cells, leaving antigen-present cells to circulate the body. This eventually triggers T-helper lymphocytes. Helper T cell-regulated B-cell builds immunity, in which they will recognize the peptide complexes on activated antigen-presenting cells. However, this type of vaccine has to be kept cool, leading to distribution to countries without refrigeration difficult.

Evaluation

Table 6: Limitations/Sources of Errors and Improvements/Extensions of the Investigation

Limitations and Sources of Errors	Improvements and Extensions
Other factors that were not considered may have affected the case numbers (i.e. wars or economic situations). These factors may have altered the exposure or risks of infection, resulting in higher case numbers. Additionally, the large global population's vaccine coverage may have overshadowed a lower coverage in an area of an outbreak, skewing the trend.	Testing data from different regions (WHO has data further split into 6 regions) that had different variables and factors to see if the same relationship occurred despite changes. Following a single region also makes it easier to track any major events (like wars).
Every two years was tested, which increased possible random error. Any data that is an outlier has a more significant weighting due to fewer data points.	Data from before the introduction of the vaccine could be used to help determine the full trend and correlation between the vaccine and virus, however it is harder to find and most likely less precise. Additionally, testing data from every year will more accurately represent the relationship and decrease random error present in the data.
Only the first dose was taken into account, and not the children who have the first dose but may not have enough antibodies to actually gain immunity.	Only testing second dose would not account for those who did not have access or chose not to get a second dose. A comparison of first and second dose coverage, however, would show how effective receiving one or two doses is.
Data from less developed countries may not be as reliable due to less reliable/accessible healthcare or administrative systems.	This investigation could also be extended into different diseases or viruses, observing the trend when there is a different type of administration (flu vaccines can be delivered via the nose) or type of shot (there were 4 categories of COVID-19 vaccines: whole virus, protein subunit, viral vector and nucleic acid).

A strength of this investigation was investigating measles compared to other diseases, as the vaccine has been around for a while, allowing for a more developed trend. There is also only one vaccine for it (although there is a variation called the MMRV which includes chicken pox, but does not change the measles immunity and is also accounted for in the data); there is no need to account for more effective/accessible types of vaccines. Additionally, a strength was using the number of first doses administered instead of second doses. While having both doses significantly increases the effectiveness of the measles vaccine, some people who have the first dose do not have access or choose to get their second. By measuring second doses administered, the partial protection given by the first dose is discounted.

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