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POLIOMYELITIS

1. Introduction

The word poliomyelitis originates from the Greek word *'polio'* meaning *'grey'* and *'myelon'* meaning *'marrow.'* Polio, or poliomyelitis, is a crippling and life-threatening disease that results from infection with the poliovirus. The virus spreads from person to person and may infect a person's spinal cord causing paralysis.

1.1 Mode of Transmission

Poliomyelitis or the poliovirus spreads from person to person through:

- Coming in contact with the defecation of an infected person.
- By inhaling the droplets from a sneeze of an infected person.

1.2 Types

- The poliovirus consists of an RNA genome encased in a protein shell called a capsid.
- There are *three serotypes of wild poliovirus referred to as type 1, type 2, and type 3* each with a marginally diverse capsid protein.
- Immunity to one serotype doesn't prevent invulnerability to the next two.

1.3 Symptoms

About 25% of individuals have minor flu-like symptoms like:

- Sore throat
- Fever
- Tiredness
- Nausea
- Headache
- Stomach pain

These symptoms generally last 2 to 5 days, then disappear on their own.

A smaller proportion of people have more serious symptoms that affect the brain and spinal cord:

- Paraesthesia (feeling of pins and needles within the legs)
- Meningitis (infection of the covering of the medulla spinalis and/or brain)
- Paralysis or fragility in the arms or legs.

1.4 Diagnosis

Diagnosis of polio is mainly done symptomatically. Patients suffering from polio show symptoms like abnormal reflexes, stiffness in the back and neck region and difficulty in swallowing. To additionally affirm the illness a throat swab or a sample of stool is taken.

1.5 Treatment

There is no known treatment for polio; hence the only substitute is to give solace to the patients through:

- Pain mitigating drug.
- Physical therapy (which provides steadiness and strength to body muscles)
- In specific cases, ventilators are needed as the patient faces trouble in breathing.

1.6 Prevention

1.6.1 Passive Immunization

In 1950, *William Hammon* (University of Pittsburgh) decontaminated *gamma globulin*(component of the *blood plasma* of polio survivors), which contained antibodies to poliovirus, which could be used to stop the progress of poliovirus infection and lessen the harshness of disease in other patients. It was about 80 percent efficient in forestalling the advancement of paralytic poliomyelitis.

1.6.2 Vaccination

IPV and *OPV* are the two types of vaccine that can prevent polio. The difference between the two is the manner in which they operate:

- *Inactivated poliovirus vaccine (IPV)* involves inactivated poliovirus administered via injection in the leg or arm, depending on the patient's age.
- *Oral poliovirus vaccine (OPV)* involves a weakened poliovirus which is orally administered. There are two forms: *trivalent (tOPV)* which targets all the three types of wild virus and *bivalent (bOPV)* which targets type 1 and 2.

1.7 Anecdote

On 10th August 1921, A famous politician at the age of 39 was diagnosed with poliomyelitis leaving him paralyzed from the waist down. He came close to demise from the sickness. He abstained being seen utilizing his wheelchair in public and was towards the finish of his political career. After almost seven years of clinical treatment and daily exercise, he could stand on his legs. Later in 1933, he took the oath as 32nd president of the United States. He was none other than *Franklin D. Roosevelt*. In 1938, he established the National Foundation for Infantile Paralysis, prompting the advancement of polio vaccines.

1.7.1 The Cutter Incident

In the Cutter incident, a few lots of the Cutter vaccine—despite passing required safety tests— was found to contain live polio virus in what was assumed to be an inactivated-polio virus vaccine. Following this on April 27, Cutter Laboratories pulled back its vaccine from the market after vaccine-associated cases were reported.

One hundred and twenty thousand doses of polio vaccine were made with live polio virus. Forty-five percent of infants who received the vaccine suffered abortive poliomyelitis (a kind of poliomyelitis that does not affect the central nervous system) and 56 developed paralytic poliomyelitis—five of whom died from polio. There were 113 persons crippled and five people died as a direct result of the exposures.

POLIO TIMELINE

1804 FIRST OUTBREAK OF POLIO IN US

1908 DISCOVERY OF POLIOVIRUS

1916 POLIO EPIDEMIC IN US

1931 NEW STRAINS OF POLIOVIRUS FOUND

1935 EARLY POLIO VACCINE TRIALS

1952 POLIO CASES SURGE

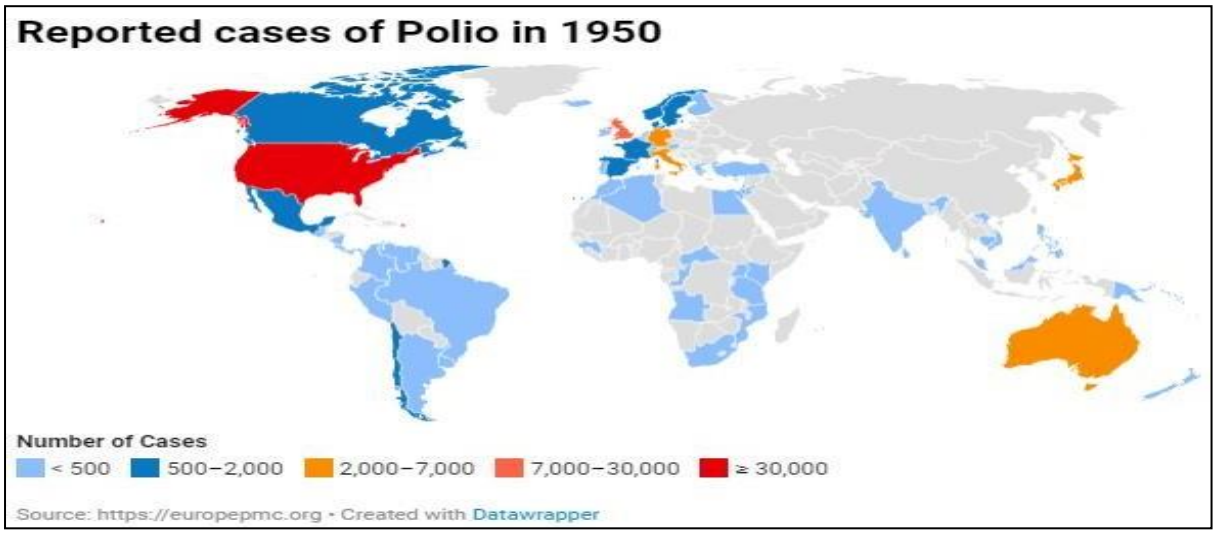
1955 THE CUTTER INCIDENT

1955 POLIO VACCINATION SUSPENDED

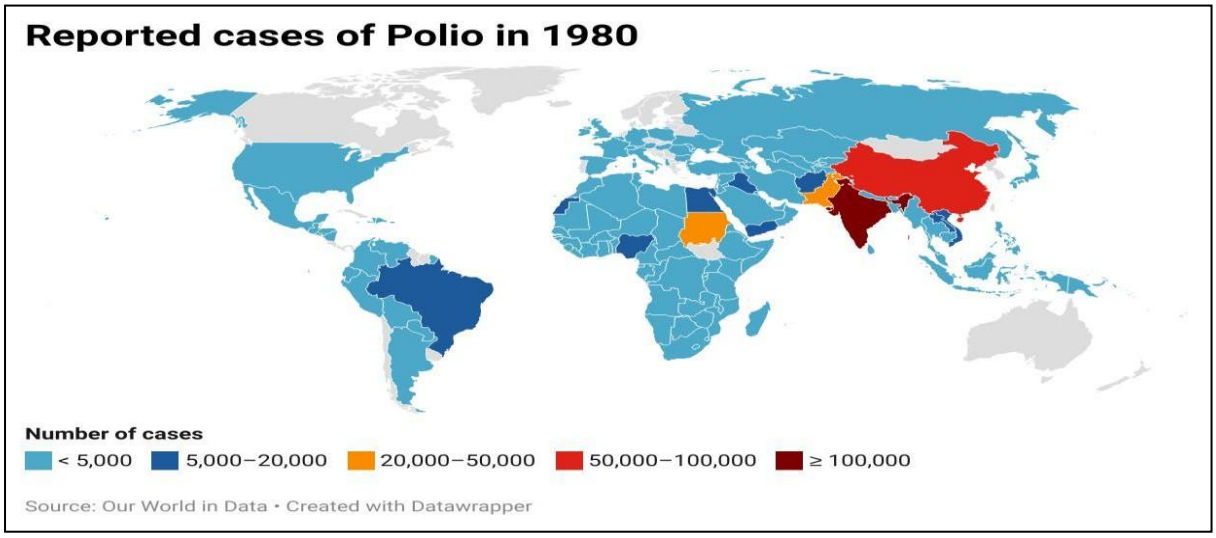
1988 GLOBAL POLIO ERADICATION INITIATIVE

2000 99% REDUCTION IN POLIO CASES

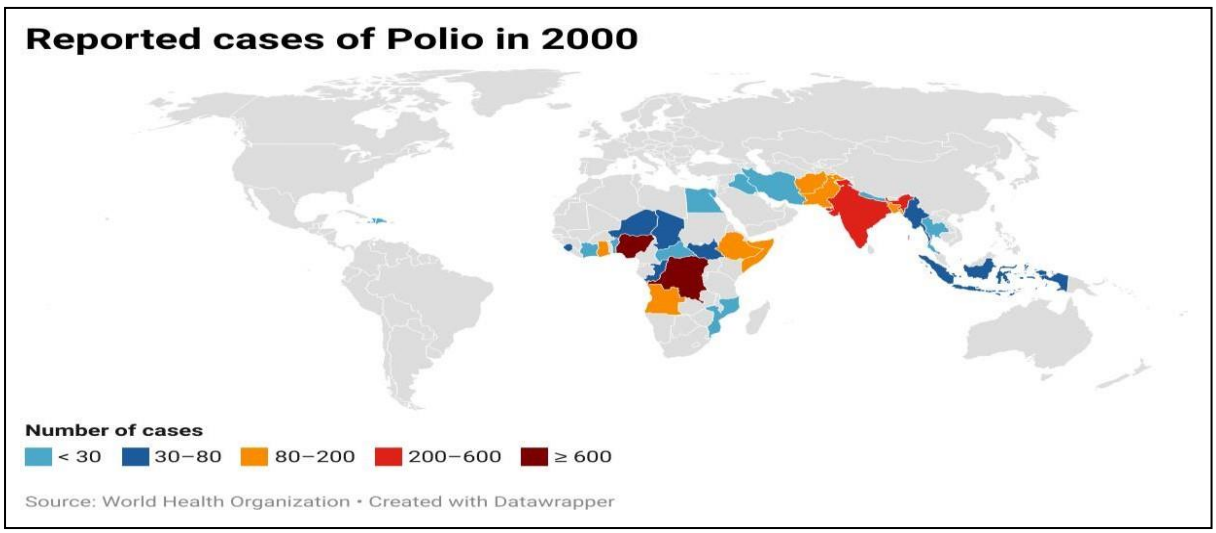
Map 1 -- 1950 when Polio cases emerged



Map 2 – 1980 when Polio cases surged



Map 3 – 2000 after Global Polio Eradication Initiative



SECONDARY ANALYSIS

Appendix

1. **Immunization Rate:** Percentage of infants who have received three doses of polio vaccine at one year of age.
2. **Health Expenditure per Capita (HPC):** A country's financial resources allocated to health care per person.
3. **Infant Mortality Rate (IMR):** Number of infant deaths per 1,000 live births in a particular geographic area.
4. **Polio Rate**: The number of Polio affected people per million people over a particular region.
5. **Fragile states index (SFI)**: Tool used to measure the overall fragility or pressure (political, economic, social, etc.) by a country
6. **Political stability index (PSI):** Indicators of political, governmental and economic stability are compiled in the Political Stability Index (PSI).
7. **Case Fatality Ratio (CFR):** The Case Fatality Ratio (CFR) indicates the number of people who died from a particular disease relative to those who were diagnosed with it.

2.1 Multiple Regression Model

Poliovirus eradication has been technically feasible since the introduction of polio vaccines in the 1950's and 60's. The implementation of robust immunization programs, however, has been hampered by social, political, and economic factors. Using the Multiple regression model, we evaluate the relationship between:

1. **Measures of infrastructure (Immunization rate and Health expenditure per capita) and Infant Mortality Rate [Economical Aspect]**

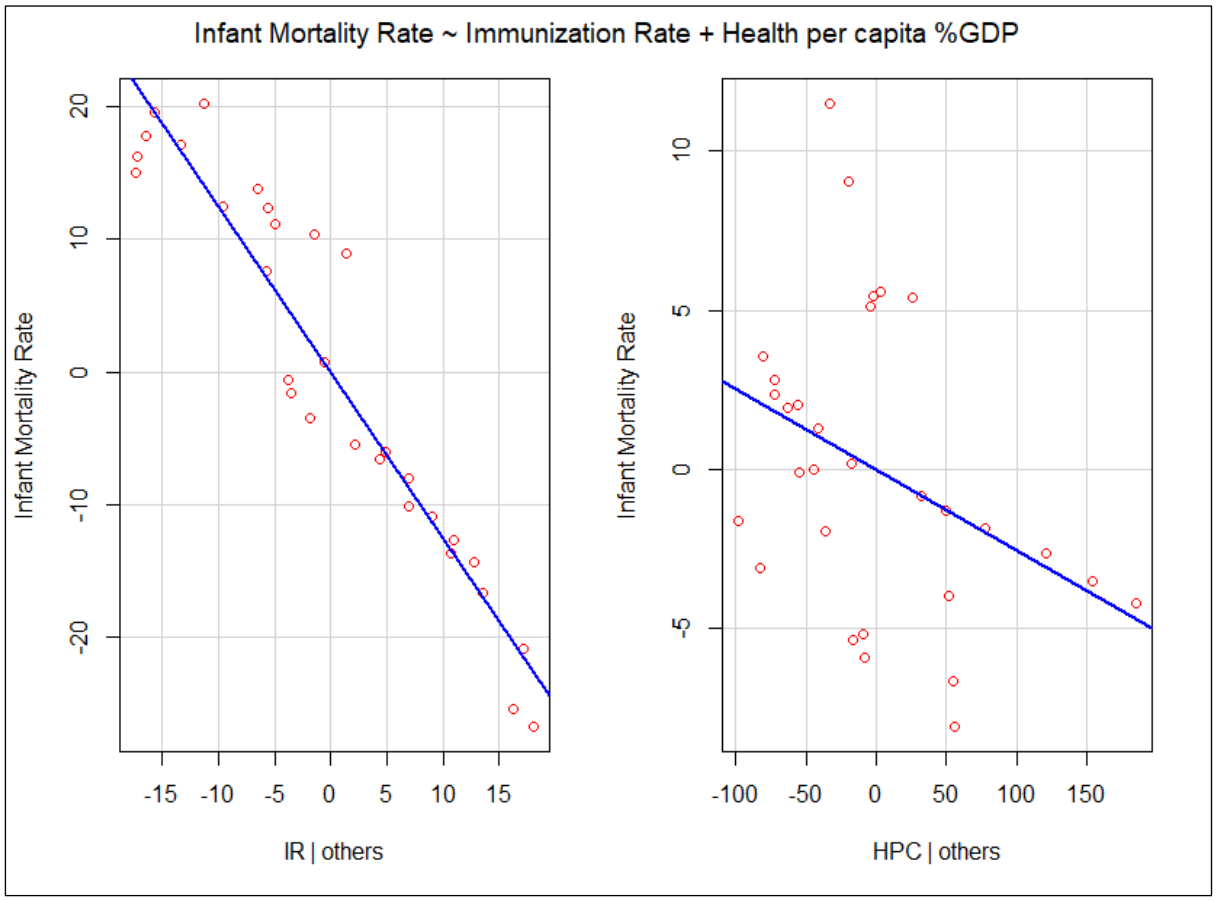
2. **Measures of instability (Fragile States Index and Political Stability Index) and polio rates. [Political Aspect]**

First regression model: Infant mortality ~ Immunization rate and Health per capita.

$\boldsymbol{H_0}$**:** There is no dependence of Infant mortality on immunization rate and health per capita
$\boldsymbol{H_1}$**:** There is dependence of Infant mortality on immunization rate and health per capita

Regression line: $\boldsymbol{Y = b_0 + b_1X_1 + b_1X_2}$

where **Y :** Polio rate is the dependent variable
$\mathbf{X_1}$**:** Immunization Rate
$\mathbf{X_2}$ **:** Health per capita % GDP are the independent variables.




```
Call:
lm(formula = IFR ~ IR + HPC, data = Multiple_Autosaved_)

Residuals:
    Min      1Q  Median      3Q     Max
-6.6398 -2.8076  0.1687  0.8874 10.6397

Coefficients:
             Estimate Std. Error t value Pr(>|t|)
(Intercept) 142.40009    5.28513  26.944  < 2e-16 ***
IR           -1.25039    0.07783 -16.065 2.42e-15 ***
HPC          -0.02535    0.01193  -2.125   0.0429 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 4.51 on 27 degrees of freedom
Multiple R-squared:  0.9661,    Adjusted R-squared:  0.9636
F-statistic: 384.4 on 2 and 27 DF,  p-value: < 2.2e-16
```

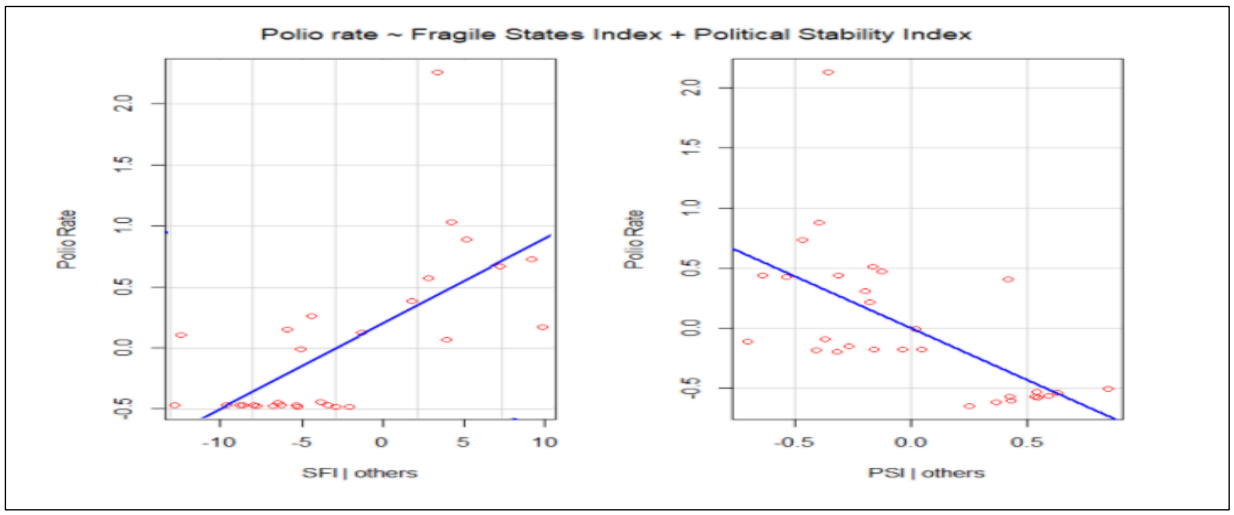
A small $P_r(>|t|)(\leq 5\%)$ for IR ($(2.42e-15 ***$) and HPC (0.0429*) indicates that there exists a relationship between the Polio rate (dependent) and the independent variables.
The small $p-value$ for the intercept ($<2e-16$) and large $F-statistic$ (38.4) indicates that we can reject the null hypothesis i.e., we conclude that there is a dependency of Infant mortality on immunization rate and health per capita and from the graphs we can conclude that there is a negative relationship between polio rates and infant mortality rate and health per capita respectively.

Second regression model: Polio rates ~ Fragile States Index and Political Stability Index

$\boldsymbol{H_0}$ **:** There is no dependence of Polio rates on Fragile States Index and Political Stability Index
$\boldsymbol{H_1}$ **:** There is dependence of Polio rates on Fragile States Index and Political Stability.

Regression line: $\boldsymbol{Y = b_0 + b_1X_1 + b_1X_2}$

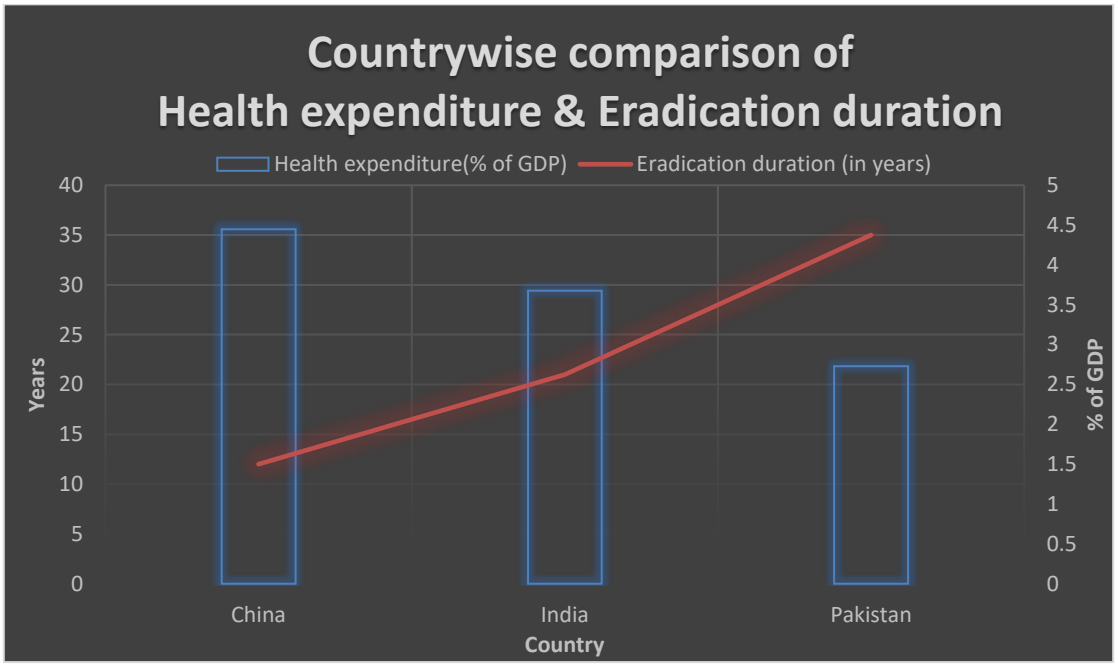
where **Y :** Polio rate is the dependent variable
X_1: Fragile States Index and
X_2: Political Stability Index are the independent variables.




```
Call:
lm(formula = PR ~ SFI + PSI, data = Multiple)

Residuals:
     Min       1Q   Median       3Q      Max
-0.71828 -0.27823 -0.08596  0.16387  1.82132

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)  5.42165    1.06781   5.077 2.47e-05 ***
SFI          0.07142    0.01516  -4.711 6.62e-05 ***
PSI         -0.86272    0.21065  -4.096 0.000344 ***
---
Signif. codes:
0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 0.4945 on 27 degrees of freedom
Multiple R-squared:  0.4512,    Adjusted R-squared:  0.4105
F-statistic:  11.1 on 2 and 27 DF,  p-value: 0.0003036
```

A small $P_r(>|t|)(5\%)$ for SFI $((6.62e-05***)$ and PSI (0.000344***) indicates that there exists a relationship between the Polio rate (dependent) and Fragile States Index, Political Stability Index (the independent variables).
The small p-value for the intercept (2.47e-05) and F-statistic (11.1) indicates that we can reject the null hypothesis i.e., we conclude that there is a dependency of Polio Rate on Fragile States Index and Political Stability Index.

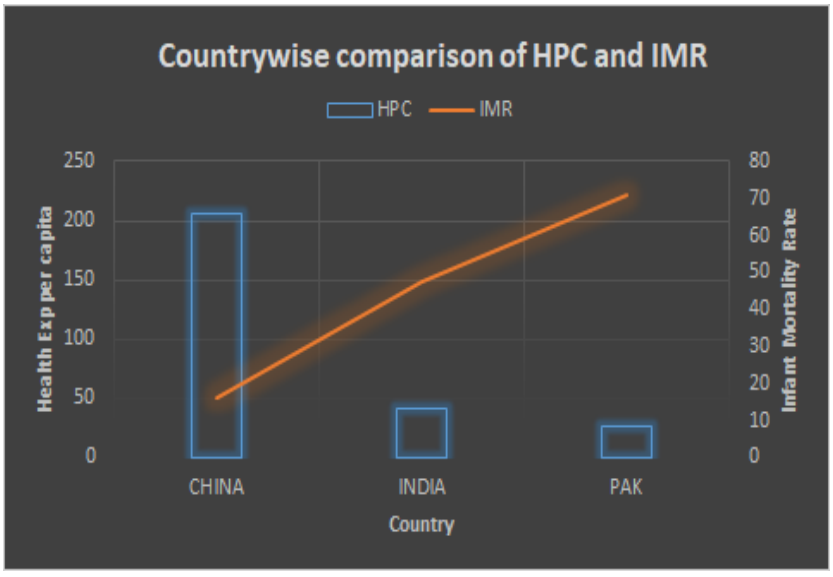
2.2 Comparison between Health Expenditure (% of GDP) and Eradication Duration



Countries that invest more in their health infrastructure as a percentage of GDP(Gross Domestic Product) are reported to be faster at eradicating polio, resulting in shorter eradication times.

China had the highest health expenditure (as a percentage of GDP) (4.49%) and the shortest eradication period (12 years), followed by India, whereas countries that invested less in their health infrastructure (as % of GDP) took much longer to eradicate polio, resulting in a long eradication period. Here, Pakistan has the lowest health expenditure (% of GDP) (2.73%) and is expected to have the longest eradication duration (35 years).

2.3 Study of Health Expenditure per Capita (HPC) and Infant Mortality Rate (IMR)

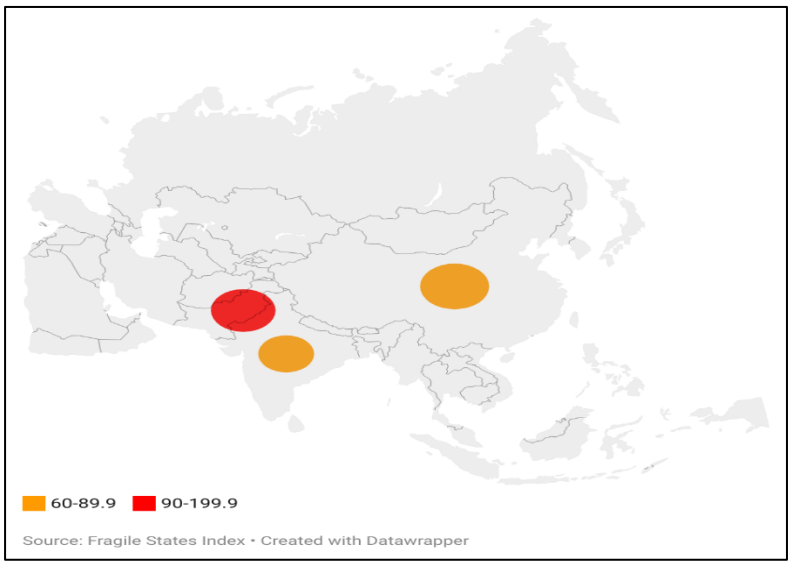


This graph compares Health Expenditure per capita and Infant Mortality Rate by country. The three countries under examination, China, India, and Pakistan, have very varied HPC and IMR values. According to the graph, China has the highest HPC (205.9043) among the three countries, while India has a marginally higher HPC (41.70609) when compared to Pakistan (26.40035).

Now, when we look at the IMR values shown in the graph an entirely different trend can be noticed. China has the lowest IMR (16.25263) among all the three nations. India's IMR value (47.50526) falls fairly below Pakistan's high IMR value (70.96316)

2.4 Impact of different economic and political factors on the epidemic

Fragile States Index: The index's ranks are based on twelve indicators of state vulnerability, grouped by category: Cohesion, Economic, Political, Social.



Pakistan with FSI score between 90-120 comes under the Alert category which indicates that it is highly vulnerable to failure whereas China and India with FSI Score between 60-89.9 come under warning category indicating that it has moderate or less amount of vulnerability to failure. Taking into consideration above information we can see that Pakistan had hard time dealing with polio than China and India.

Country	Political Stability Index
China	-0.55144
India	-1.2049
Pakistan	-2.61286

China's low negative number (-0.55144) indicates that the country is more politically stable than India and Pakistan. Pakistan has the highest negative PSI value (-1.2049), which explains why it has the least stable government, whilst India's PSI value (-2.61286) is in the middle, affecting its ability to combat polio.

2.5 Global Polio Eradication Initiative (GPEI) Surveillance

During the years 1988 to 1998, the annual number of Polio cases recorded worldwide declined as a result of the Global Polio Eradication Initiative (GPEI). For the entire polio eradication program, polio surveillance is essential in order to determine where and how poliovirus is still circulating:

1. Acute Flaccid Paralysis (AFP) is an irreversible paralytic condition that occurs in 1 in 1000 to 1 in 200 instances, with a Case Fatality Rate (CFR) of 5 to 10%

2. The term "Acute Flaccid Paralysis" (AFP) refers to a sudden start of flaccid paralysis in a child younger than 15 years of age without a clear cause (such as severe trauma or electrolyte imbalance) or to a paralytic sickness in which polio is suspected in any age group.

3. A country's ability to identify polio is measured by the number of AFP cases reported each year, even in nations where polio no longer exists.

4. WHO-accredited laboratories isolate Poliovirus using stool samples from AFP patients.

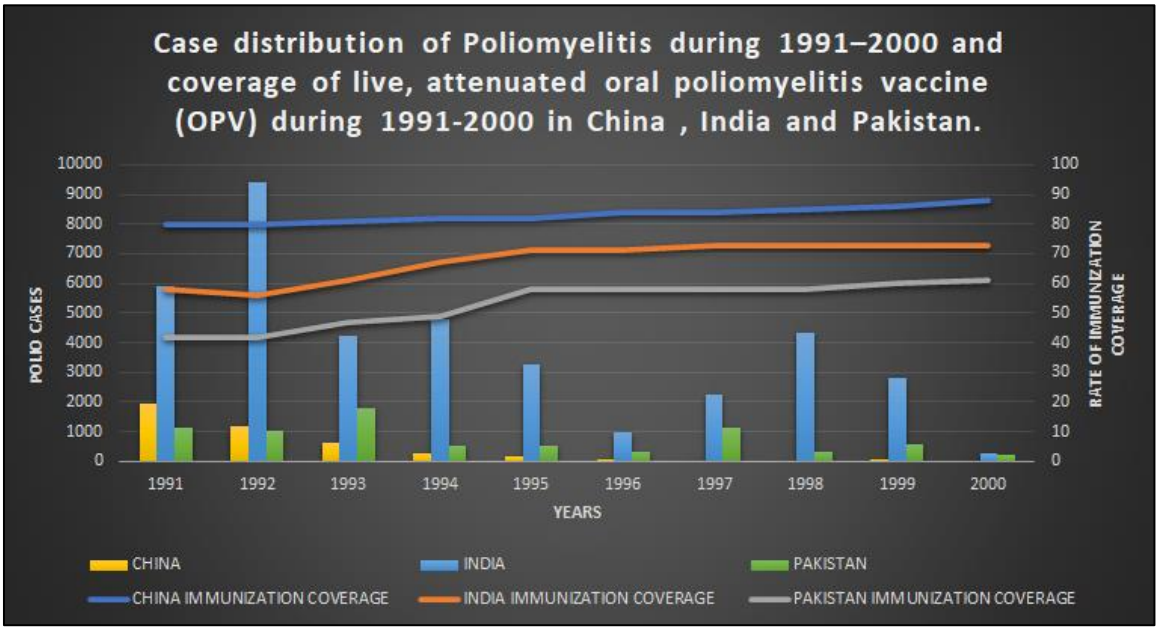
5. An AFP case is confirmed as being of Polio if
    - In the stool sample, wild Poliovirus has been isolated.
    - As long as there isn't a sufficient stool sample, the patient's residual weakness will last for 60 days or until they pass away.

6. Although there may be residual weakness 60 days after start of paralysis in AFP cases for which appropriate stool samples have tested negative for Wild Poliovirus and AFP cases without adequate stool samples are categorized as non-polio.

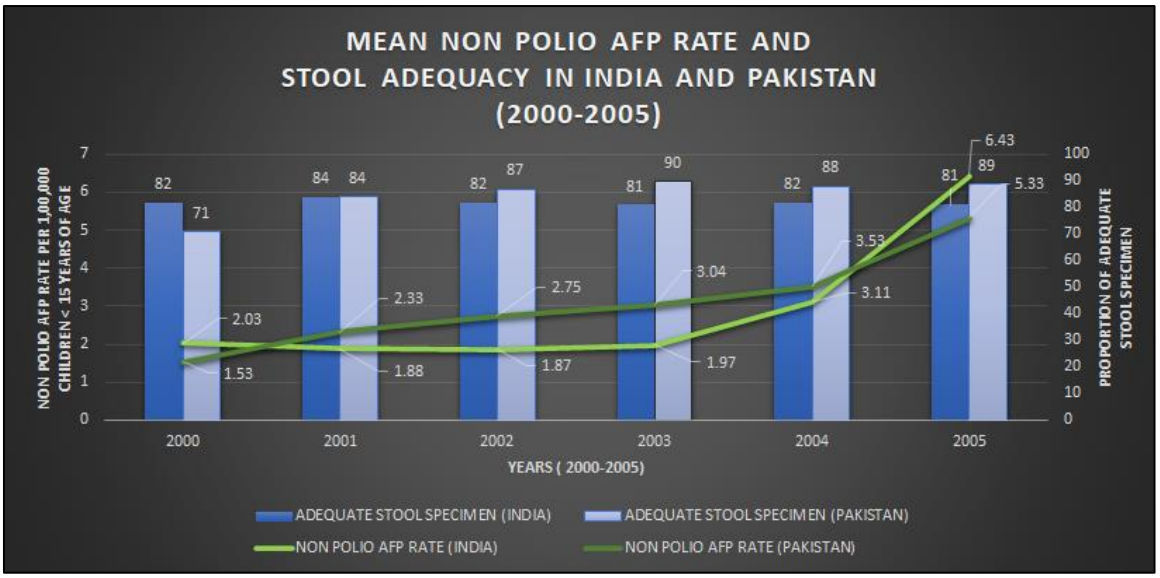
7. Polio Surveillance (certified by WHO) has the following main indicators:
    - > 1 per 100,000 children under 15 years old with non-polio AFP.
    - > 80% of AFP cases with adequate stool specimen

⇒ Poliomyelitis cases in India, the world's most populous country with endemic polio, made up more than 60% of all cases reported worldwide. GPEI's success hinged on India's progress.

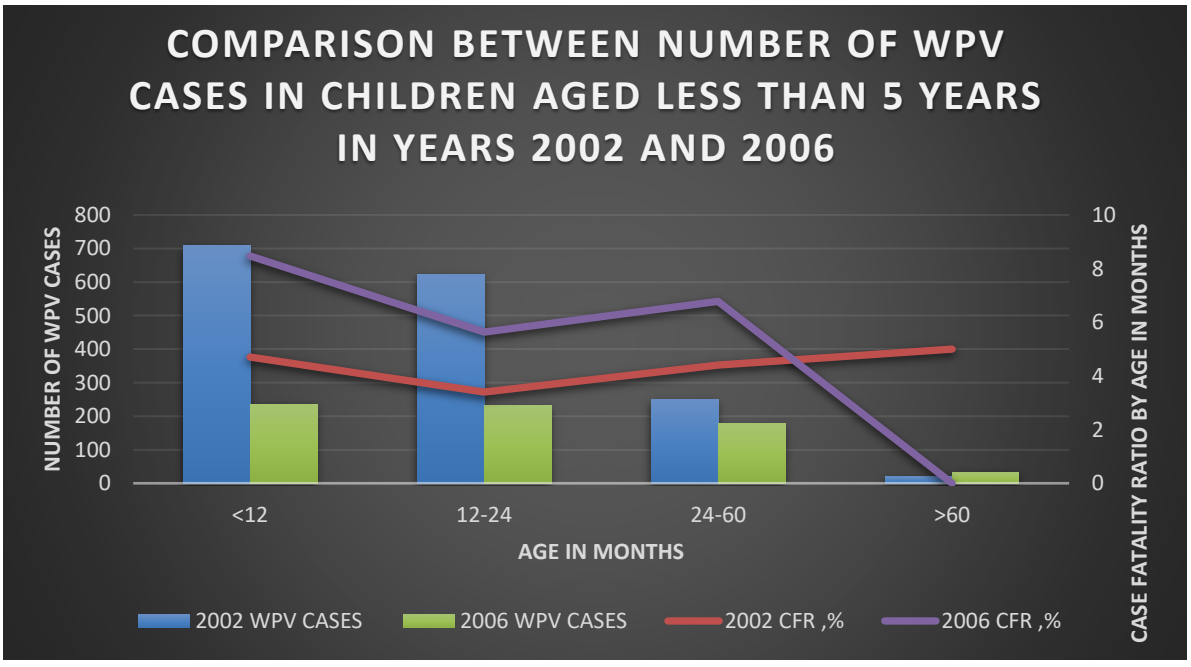
As of 1994, China had reached its childhood immunization objective of >85% coverage. Over the years, OPV (Oral Polio Vaccine) immunization coverage increased steadily, reaching >90% in 1998.



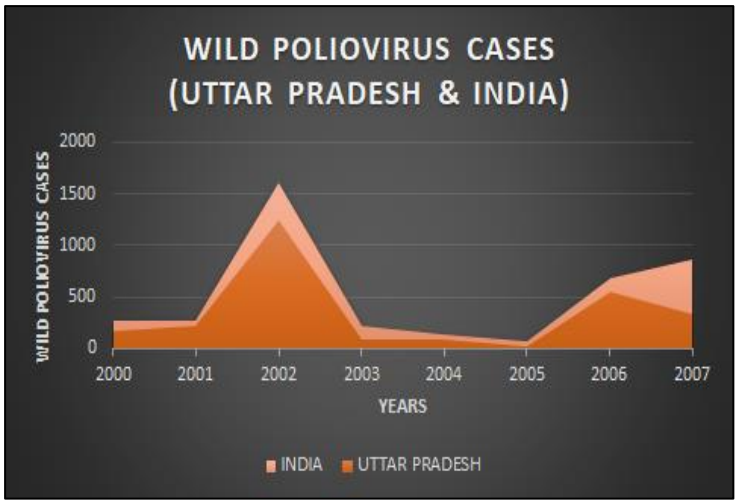
⇒ India and Pakistan's AFP cases with acceptable stool specimens were consistently over the minimal threshold of 80 percent (except for Pakistan in 2000) and the mean NP-AFP (Non Polio AFP) rate during the study period was > 1 per 100,000 children under 15 years of age, as shown in the graph below.



⇒ According to clinical follow-up data from the 2002 Indian outbreak, there were 1584 WPV cases out of a total 1600, and the CFR was 4.1 percent. Clinical follow-up data for 673 of the 676 total cases during the 2006 outbreak showed a CFR of 6.7%. From January to July 2002, the CFR averaged 3.9, while from January to July 2006, it averaged 9.6.

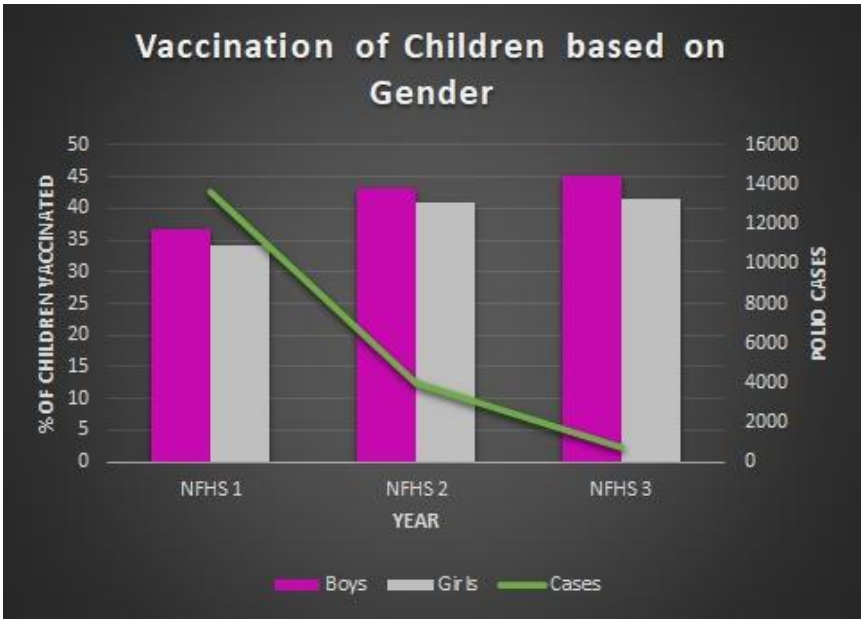


WPV-related mortality in children under the age of five accounted for 65 (98 percent) of the 66 deaths in the 2002 outbreak, and for all 45 deaths in the 2006 outbreak. All age groups of children aged 5 years in 2006 had higher CFRs than in 2002, but only those aged less than 12 months had statistically significant differences.



Uttar Pradesh, India's most populous state, was plagued by a poliomyelitis epidemic, which substantially hampered efforts to contain the disease. According to the Indian government, Uttar Pradesh was responsible for 81% of all cases of polio documented in 2002. The increase in non-polio AFP rate is mainly limited to the two polio hyperendemic states of Uttar Pradesh and Bihar. A considerable increase in booth coverage between 50 and 57 percent was observed in four high-risk districts in Uttar Pradesh where social mobilization operations were implemented.

2.6 Vaccination and Gender Disparity

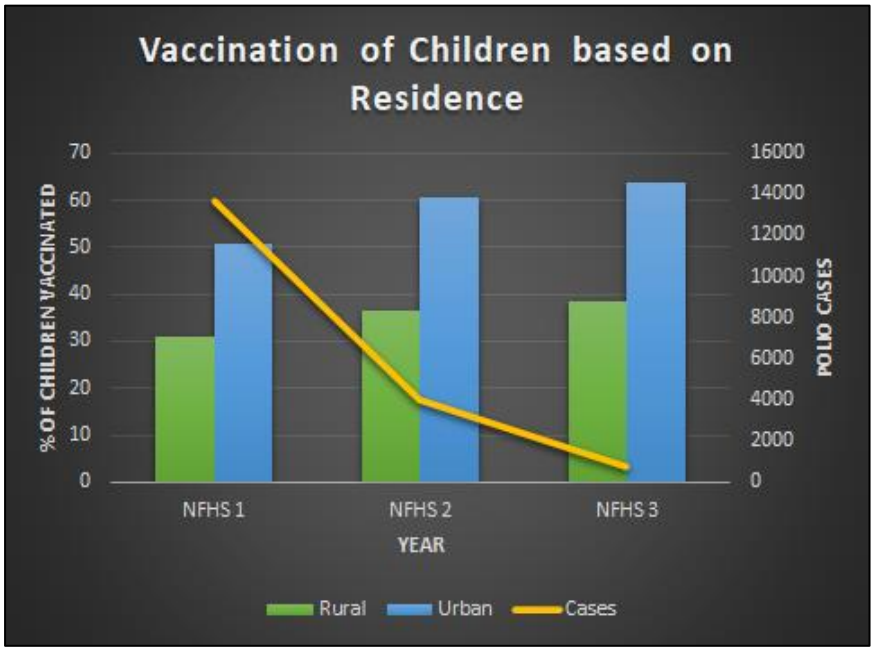


Males outnumbered females in the **National Family Health Survey-1,2,3 (NFHS)**. The complete vaccination rate varied between boys and girls in all the three surveys and it was seen that a greater number of boys received vaccinations than girls.

This gender disparity existed regardless of how vaccination status was determined. The gap between the genders is seen to be decreasing over the years, but it hasn't yet diminished completely. The percentage of boys and girls who did not receive any vaccine was 4.3 percent and 6.0 percent respectively in NFHS 3. As a result of the **Pulse Polio Drive**, the gender difference was significantly smaller for the three doses of OPV (around 2 percent).

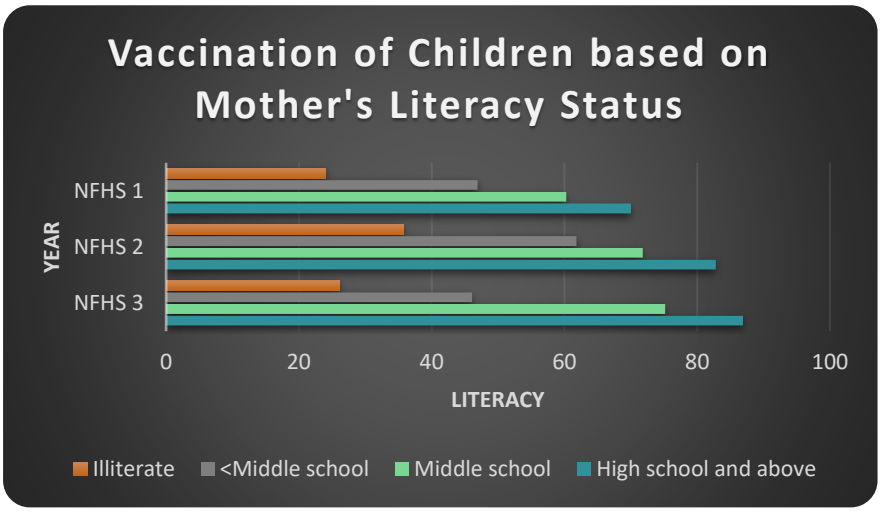
We can thus conclude that the Pulse Polio drive did not fail to reduce the gender gap, but could not diminish it completely.

2.7 Vaccination and Residence



In urban regions, vaccination coverage was substantially higher than in rural areas. By the time of the NFHS-3 survey, 58 percent of urban children aged 12-23 months had received all of the recommended vaccines, compared to only 39 percent of rural children. Urban areas also have lower (OPV) Polio Vaccine dropout rates than rural ones.

2.8 Vaccination and Mother's Literacy



In the NFHS-1,2,3 Surveys, the mother's education status was assessed. It was seen that there was greater complete immunization of infants among mothers with higher levels of education as compared to mothers who weren't educated or had just primary school education.

In the UNICEF 2009-10 survey, significant relation between education and complete immunization was seen. 45.3 percent of mothers had no education, 55.4 percent had fewer than 5 years of school, 64.9 percent had 5-7 years of education, 64.9 percent had 8-9 years of education, 74.1 percent had 10-11 years of education, and 76.6 percent had more than 12 years. Respective unvaccinated infants accounted for 14.3 percent, 9.0 percent, 5.1 percent, 3.8 percent, 2.1 percent, and 2.0 percent of the total number of babies.

According to the odds ratios for literate versus illiterate mothers and fathers in Delhi, maternal literacy was found to be a more relevant factor in childhood vaccination rates than father literacy.

2.9 Comparison between Polio cases and Gender

Numerous studies predict that there is dependency in between Polio cases and Gender. We consider data from the year 2000 in India to test this claim at a 99% confidence interval using a **CHI-SQUARE TEST.**

Level of Significance $= \boldsymbol{\alpha = 0.10}$

$\boldsymbol{H_0}$: The number of Polio cases are independent of gender
$\boldsymbol{H_1}$: The number of Polio cases is dependent on gender

Observed	Affected With Polio	Not Affected	Total
Males	2032	531277968	531280000
Females	1619	495738381	495740000
Total	3651	1027016349	1027020000

Expected	Affected With Polio	Not Affected	Total
Males	1888.671379	531278111.3	531280000
Females	1762.328621	495738237.7	495740000
Total	3651	1027016349	1027020000

Chi Square	Affected With Polio	Not Affected	Total
Males	10.87700789	0.00003866730	10.87704656
Females	11.65678935	0.00004143939	11.65683079
Total	22.53379725	0.00008010670	22.53387735

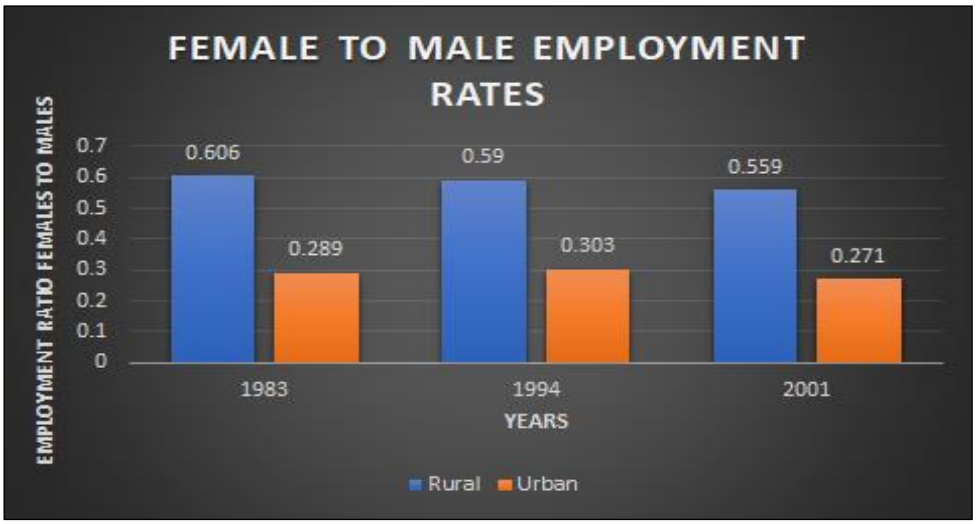
Thus, Chi square calculated = 22.5338773

$r - 1 = 1$	**critical value**	3.841458821
$c - 1 = 1$	**p value**	0.00000206470

- $\boldsymbol{P\,value \ll \alpha \;\; i.e \;\; 0.0000020647 \ll 0.01}$

Hence, we reject the null hypothesis.
Thus, there is dependency between the number of Polio cases and gender.

This dependency can be accounted for by the difference in exposure to communicable diseases amongst both the genders



The female to male exposure ratio throughout time can be explained by the female to male employment ratio. Because men work harder to earn a living in Indian communities, they spend more time away from home than their female counterparts. As a result, males are more likely to be exposed to infectious agents that cause Polio than females. As we can see from the given graph, the female to male ratio in India never exceeded above 60% till 2001 in urban areas. The same quantity reached an all-time high around 1994 in rural areas, wherein the ratio was 30%.

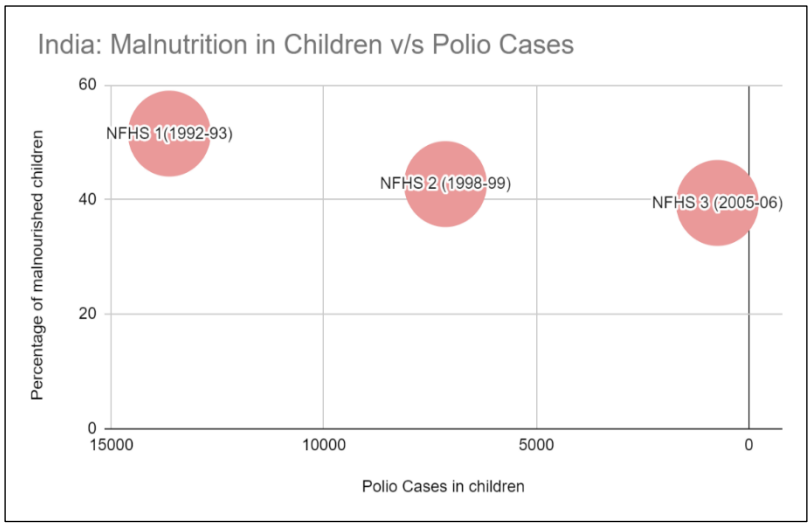
2.10 Polio and Malnutrition in India

Research predicts that Polio cases are related to malnutrition in children. Based on NFHS-1,2,3 data, we may deduce that as the percentage of malnourished children decreased, the number of polio cases decreased as well over time.

We find the **correlation** between malnutrition and the number of polio cases and percentage of malnourished children in the country.

YEAR	POLIO CASES	PERCENTAGE OF MALNOURISHED CHILDREN
1993	13632	51.5
1997	2275	41
1999	7139	42.7
2006	742	39.4

- The Pearson Product Moment Correlation coefficient for Polio Cases and % of Malnourished Children is **0.9676268708.** This shows that there is very high correlation between the two and hence, we can conclude that Polio cases in India are strongly correlated to the percentage of malnourished children.



A 12-month-old kid should receive all basic immunizations, including Polio, according to the immunization schedule recommended by the Indian government and the World Health Organization (WHO). Immunization rates have improved significantly since the National Family Health Survey (NFHS-1) in India, which found that just 36% had been fully immunized, while 30% had not been vaccinated. Since NFHS-1, the coverage of each single immunization has risen significantly, but India is yet to achieve complete vaccination status and still has a long way to go.

Poliomyelitis: Model and Assumptions

Poliomyelitis and the Carrier Model:

The majority of exposed patients (around 95%) and up to 72% of all polio infections in children are asymptomatic. Infected persons without symptoms shed virus within the stool and are capable of transmitting the virus to others.

Approximately 24% of polio infections in children contains a minor, nonspecific illness without clinical or laboratory evidence of central nervous system invasion.

Susceptible individuals usually excrete polioviruses for two to six weeks, and infrequently for up to 137 days after they have been immunized with oral poliovirus vaccine (OPV). All non-immune people are susceptible to infection.

After both clinically recognisable and in apparent infections, type-specific lifelong immunity occurs. Reinfection is rare but can occur if the person is infected with poliovirus of a different type.

Since, majority of patients are asymptomatic but spread the disease in close contact points to the fact that the spread of polio virus is indeed through carriers. ***Hence, poliomyelitis follows the carrier model.***

3.1 Carrier model

A major obstacle of many diseases is the existence of so-called carriers, individuals who, although apparently healthy themselves, are already infected and are capable of transmitting the infection to others. Diseases such as *poliomyelitis* is a typical examples. Some carriers may continue to be infectious for a very long time. Others may become clear of infection more quickly.
In either case the carriers are effectively removed from circulation, but as they are not ill and exhibit no normal symptoms of disease, they are not themselves usually recognized as actual cases.
On the other hand, carriers may be suspected because of the existence of an otherwise inexplicable occurrence of scattered cases. This may lead to a deliberate search for carriers, and some or all of them may be identified through the use of special tests.

3.2 Assumptions

The population under consideration is a closed population, which means that immigration and emigration does not take place in the population.

The removal rate (α) and infection rate (β) are constants.

We do not take birth and death rates into consideration.

We assume that the population is subject to homogeneous mixing, which is to say the individuals (susceptible and infected) of the population under study make contacts at random.

It is assumed that only carriers are responsible for the actual spread of infection. When a susceptible is infected, he is supposed to exhibit symptoms sufficiently quickly to be effectively recognized and removed from circulation before he can transmit the disease to others

The elimination of carriers proceeds at some finite rate, which may depend on both spontaneous recovery and public health detection.

The rate of spread of the poliovirus changes seasonally. It is observed that the spread of poliovirus in summer is far greater than in winter. But these seasonal factors don't affect the spread of the virus in tropical regions. Hence, for the convenience of this model we assume that the study takes place in a tropical region. (Hence, the rate of spread remains the same throughout the time period)

3.3 Deterministic model

Let us assume that initially we have ***'n'*** susceptible and ***'b'*** carriers.
Now, for time ***t=0*** and time ***t*** we have the following conditions.

Time (t)	Susceptible (x)	Carriers (y)
0	n	b
t	x	y

3.3.1 Equation for Susceptible

The change in the number of susceptible $\Delta \boldsymbol{x}$,in time $\Delta \boldsymbol{t}$ is taken to be $\boldsymbol{\beta \alpha \Delta t}$ where $\boldsymbol{\beta}$ is the *infection rate.*
Therefore we get,

$$\Delta \boldsymbol{x} = -\boldsymbol{\beta x y \Delta t}$$

(The negative sign in $-\boldsymbol{\beta x y \Delta t}$ implies that the number of susceptible keeps decreasing over time)

By differentiating the above equation, w.r.t to t we get

$$\frac{\boldsymbol{dx}}{\boldsymbol{dt}} = -\boldsymbol{\beta x y} \qquad (\mathbf{1})$$

3.3.2 Equation for Carriers

The change in the number of carriers is directly proportional to:
1. The total number of carriers in the population i.e., $\Delta \boldsymbol{y} \propto \boldsymbol{y}$
2. The change in time i.e., $\Delta \boldsymbol{y} \propto \Delta \boldsymbol{t}$

Therefore we have, $\Delta \boldsymbol{y} \propto \boldsymbol{y \Delta t}$

$\Delta \boldsymbol{y} = -\boldsymbol{\gamma y \Delta t}$, where γ is a constant

(The negative sign in $-\boldsymbol{\gamma y \Delta t}$ implies that the number of carriers keep decreasing over time)

Differentiating the above equation wrt to t we get,

$$\frac{\boldsymbol{dy}}{\boldsymbol{dt}} = -\boldsymbol{\gamma y} \qquad (\mathbf{2})$$

3.3.3 Equation to find the *x (susceptible)* and *y (carriers)* at *time t*

From equation (2) , we have

⇨ $\frac{dy}{dt} = -\gamma y$

⇨ $\frac{dy}{y} = -\gamma dt$

Integrating the above equation ,

⇨ $\int \frac{dy}{y} = \int -\gamma dt$

⇨ $log\ y\ = -\gamma t + c$ *(3)*

From the table we can see that, ***at t=0, x=n, y=b***

Substituting the values in equation (3), we get ,

⇨ $logb = c$

We substitute the value of c into equation (3), in order to get the value of y

⇨ $logy = -\gamma t + logb$

⇨ $log(\frac{y}{b}) = -\gamma t$

⇨ $\left(\frac{y}{b}\right) = e^{-\gamma t}$

⇨ $y = be^{-\gamma t}$ **(4)**

Frome equation (1) we have,

⇨ $\frac{dx}{dt} = -\beta xy$

Substituting the value of *y* from equation (4) we get

⇨ $\frac{dx}{dt} = -\beta x(be^{-\gamma t})$

⇨ $\frac{dx}{x} = -\beta(be^{-\gamma t})dt$ **(5)**

To find the value of *x* we integrate equation (5),

⇨ $\int \frac{dx}{x} = -\int \beta(be^{-\gamma t})dt$

⇨ $logx = \frac{-\beta be^{-\gamma t}}{-\gamma} + c$

⇨ $logx = \frac{\beta be^{-\gamma t}}{\gamma} + c$ **(6)**

From the table we know that **at *t=0, x=n, y=b***.
Substituting these values in equation (6) we get the following

$$\Rightarrow \quad \boldsymbol{\log n = \frac{\beta b e^{-\gamma t}}{\gamma} + c}$$

$$\Rightarrow \quad \boldsymbol{c = \log n - \frac{\beta b}{\gamma}}$$

Substituting value of c from the above equation in equation (6) we get,

$$\Rightarrow \quad \boldsymbol{\log x = \frac{\beta b e^{-\gamma t}}{\gamma} + \log n - \frac{\beta b}{\gamma}}$$

$$\Rightarrow \quad \boldsymbol{\log\left(\frac{x}{n}\right) = \beta b(e^{-\gamma t} - 1)}$$

$$\Rightarrow \quad \boldsymbol{x = n exp\left[\frac{\beta b(e^{-\gamma t} - 1)}{\gamma}\right]}$$

Value of *x* when the epidemic will end i.e., at time $\boldsymbol{t = \infty}$ will be

$$\Rightarrow \quad \boldsymbol{x^{\infty} = n e^{(\frac{-\beta b}{\gamma})}} \qquad \boldsymbol{\because e^{\infty} = 0}$$

Size of the epidemic (Total number of people who became carriers) is given by the difference between total population (n + b) at t=0 and number of susceptible at the end of the epidemic **(x^{∞})**

$$\therefore \textit{Size of the epidemic}(\boldsymbol{w}) = \boldsymbol{n + b - x^{\infty}}$$

$$\Rightarrow \quad \boldsymbol{w = n + b - n e^{(\frac{-\beta b}{\gamma})}}$$

Hence, the total size *w* of the observed epidemic is $\boldsymbol{n + b - n e^{(\frac{-\beta b}{\gamma})}}$

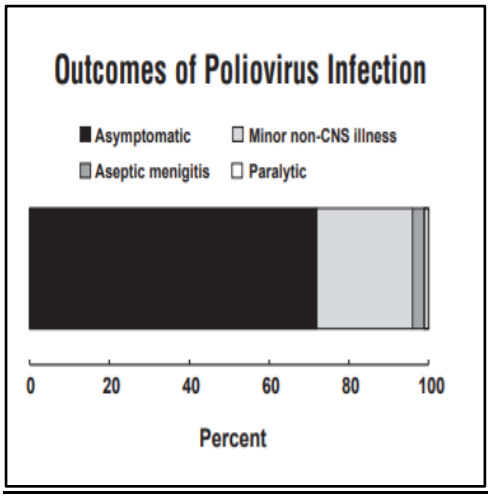
Clinical Trials of The Polio Vaccine

4.1 History of Vaccines

At the height of the Great Depression, Polio was the most feared disease in the world. Epidemics were reported every year, and in 1952, more than 21,000 cases were reported in the United States.
In the Roosevelt administration, the March of Dimes campaign was launched to develop a vaccine to combat Polio.
Three years later, Dr Jonas Salk developed an injectable, inactivated Polio vaccine, which would prove invaluable in the fight against polio. In 1955, Inactivated Poliovirus Vaccine (IPV) was licensed, which was used extensively until the early 1960s.
In 1961, Dr Albert Sabin developed an Oral Polio Vaccine (OPV) following which monovalent pneumococcal vaccine (MOPV) of types 1 and 2 was licensed, and then type 3 in 1962. Trivalent OPV became available in 1963 and was adopted by the majority of national immunization programs.

4.2 Clinical Features

4.2.1 Symptoms



- Children with polio infection are up to *72% asymptomatic.* Affected individuals shed virus in their stool, and they can therefore transmit it to others.

- In children, *24% of polio infections result in a mild, nonspecific illness* without clinical or laboratory evidence of central nervous system infection. This clinical presentation is known as abortive poliomyelitis, and results in complete recovery within a week. There are low grade fevers and sore throats.

- *1%–5%* of polio infections result in *nonparalytic aseptic meningitis* (symptoms of stiff neck, back, or legs)

- *Flaccid paralysis* occurs in fewer than *1%* of all polio infections in children.

4.2.2 Temporal Pattern

Tropical climatic conditions have no seasonally varying patterns of infection with the poliovirus. In temperate climates, infection peaks in summer.

4.2.3 Communicability

The virus is highly contagious; the seroconversion rate among susceptible household contacts of children is approximately 100%, and that of susceptible household contacts of adults is greater than 90%. The poliovirus is most infectious 7 to 10 days before and after the onset of symptoms, but the virus can remain present in the stool for 3 to 6 weeks after infection.

4.3 Laboratory Testing of the virus:

1. **Viral Isolation**
   Poliovirus can be found in stool, less likely in the pharynx, and rarely in the cerebrospinal fluid (CSF) or blood. To detect whether the virus is a wild type or a vaccine type, researchers should carry out reverse transcriptase - polymerase chain reaction (RT-PCR) or genomic sequencing on an isolate from a person with acute flaccid paralysis.

2. **Serology**
   An early serological diagnosis may be made if two specimens are obtained, one at the beginning of the illness and one three weeks afterward. A four-fold rise in the titer suggests infection with the poliovirus. In two specimens that have no antibodies detected, poliovirus can be ruled out. Titers have limitations too. patients with immunocompromised states may still be infected, despite having two specimens with no antibodies detected.

3. **Cerebrospinal Fluid (CSF)**
   In poliovirus infection, the CSF tends to contain higher levels of white blood cells (10-200 cells/mm3) and a mildly elevated protein level (40-50 mg/100 mL).

4.4 Characteristics of Polio Vaccines

1. **IPV (inactivated poliovirus vaccine)**
   In the vaccine, all three serotypes of polio virus are included. The cells are grown in Vero cells (monkey kidney tissue) and inactivated with formaldehyde. 2-phenoxyethanol is the principal preservative in the vaccine, along with trace amounts of neomycin, streptomycin, and polymyxin B. The vaccine comes in a syringe and should be administered subcutaneously or intramuscularly.

2. **OPV (oral polio vaccine)**
   The trivalent OPV vaccine is a 0.5-mL dose that contains strains of all three serotypes of the poliovirus in a 10:1:3 ratio. The vaccine virus strains are grown in Vero cells (monkey kidney tissue) and administered as a single dose in a plastic dispenser. OPV contains trace amounts of neomycin and streptomycin. However, OPV does not contain a preservative. Live attenuated polio viruses replicate in the intestinal mucosa, lymphocytes, and lymph nodes.
   The person who has been vaccinated excretes vaccine viruses for up to 6 weeks after a dose. The maximum amount of virus is shed in the first 1–2 weeks after vaccination, especially after the first dose. The vaccine virus may be transmitted to others if they come into contact with fecal material from vaccinated individuals.

4.5 Vaccine efficacy

1. IPV

IPV is exceedingly viable in creating resistance to poliovirus and protection from paralytic poliomyelitis. Ninety percent or more of vaccinated individuals develop antibodies to all three polioviruses after two dosages, and at least 99% are immune after taking three measurements.

Protection against paralytic malady relates with the nearness of antibody. As compared to OPV, IPV shows up to produce less local gastrointestinal immunity, so people who get IPV are more readily infected with wild poliovirus than OPV recipients. The duration of immunity with IPV isn't known with certainty, in spite of the fact that it likely gives long lasting immunity after a total series.

2. OPV

OPV is profoundly successful in creating insusceptibility to poliovirus. A single dosage of OPV produces resistance to all three vaccine viruses in around 50% of vaccinated individuals. Three doses produce resistance to all three types of polioviruses in more than 95% of recipients.

Considering cases of other live-virus vaccines, immunity from OPV is likely to be long lasting. It is responsible for producing great intestinal immunity, which aids in preventing infection with wild viruses.

Serologic studies have asserted that seroconversion following three doses of either IPV or OPV is approximately close to 100% to all three vaccine viruses. In any case, seroconversion rates after three doses of a combination of IPV and OPV are lower, especially for type 3 immunization virus (as low as 85% as seen in a study). A fourth dose (most studies used OPV as the fourth dose) usually produces seroconversion rates comparable to three doses of either IPV or OPV.

4.6 Vaccination Schedule and use.

The horde use of OPV since 1963, led to elimination of wild-type poliovirus in less than 20 years. However, one case of VAPP (Vaccine-associated paralytic polio) occurred for every 2 to 3 million doses of OPV administered i.e., 8 to 10 cases of VAPP each year. In the period of 1980 to 1999, VAPP accounted for 95% of all cases of paralytic poliomyelitis reported in the US. In 1996, ACIP recommended an increase in use of IPV through a sequential schedule of IPV followed by OPV.

There are 3 combination vaccines that contain inactivated polio vaccines.

Combination	Produced by	Contents	Licensed for:
Pediarix	GlaxoSmithKline	DTaP, hepatitis B and IPV	First three doses of DTaP
Kinrix	GlaxoSmithKline	DTaP and IPV	Only 5^{th} dose of DTaP and 4^{th} dose of IPV
Pentacel	Sanofi Pasteur	DTaP, Hib and IPV	First four doses of the component vaccine

4.7 Polio Vaccination Schedule of

1. Adults

For unvaccinated adults, primary immunization with IPV is recommended. The recommended schedule is two doses separated by 1 to 2 months, and a third dose given 6 to 12 months after the second dose (May separate first and second doses by 4 weeks if accelerated schedule is needed). The minimum interval between the second and third doses should be 6 months. For previously vaccinated adults, who are at increased risk of exposure to poliomyelitis should receive one dose of IPV given that they have completed the primary series of 3 doses. If one has not completed the first 3 doses, he/she should be given the remaining doses of IPV, regardless of the interval.

2. Children

Only IPV is available for routine polio vaccination of children in India. A polio vaccination schedule begun with OPV has to be completed with IPV. If a child receives both types of vaccine, four doses of any combination of IPV or OPV by 4 to 6 years of age is considered a complete poliovirus vaccination series. A minimum interval of 4 weeks should separate all doses of the series.

Age	Vaccine	Minimum Interval
2 months	IPV	---
4 months	IPV	4 weeks
6-18 months	IPV	4 weeks
4-6 years	IPV	6 months

4.8 Contraindications and Precautions to Vaccination

Immunization is permitted for individuals with skin allergies not considered anaphylactic - such as skin contact sensitivity, or until their symptoms subside - as opposed to those with severe or moderate acute illnesses.

4.9 Adverse Reactions Following Vaccination

IPV is commonly associated with local reactions (pain, redness) due to trace amounts of streptomycin, polymyxin B, and neomycin. People allergic to these antibiotics may experience allergic reactions to IPV.

4.10 Vaccine Storage and Handling

Manufacturers offer additional information on certain vaccine packaging inserts. Vaccines should be stored between 35°F and 46°F (2°C and 8°C) in the refrigerator.

5. References

- https://europepmc.org/backend/ptpmcrender.fcgi?accid=PMC2542300&blobtype=pdf
- https://rchiips.org/nfhs/
- https://who.int/data/gho/
- https://academic.oup.com/aje/article/162/4/358/105064
- https://data.worldbank.org/
- https://en.wikipedia.org/wiki/Polio
- https://knoema.com/
- https://ourworldindata.org/polio
- https://polioeradication.org/
- https://www.bbc.com/news/health-17072769
- https://www.cdc.gov/polio/what-is-polio/index.htm
- https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/polio.pdf
- https://www.historyofvaccines.org/timeline#EVT_100316
- https://www.pvamu.edu/aam/wp-content/uploads/sites/49/11_-agarwal-aam-r301-ma-082610.pdf
- Poliomyelitis surveillance: the model used in India for Polio Eradication
  Kaushik Banerjee , W.Gary Haldy , Jon. K. Andrus.
- Poliomyelitis relate case-fatality ratio in India, 2002-2006
  Hardeep S.Sandhu , Karen J Hymbaugh , Sunil B