Mathematical Modelling of 2000/1 Cholera Transmission Dynamics in South Africa

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1. Abstract

This project focuses on understanding the spread of cholera through a mathematical model that captures both symptomatic and asymptomatic infections. The model also captures bacteria concentration as a major component for transmission due to spread of bacteria and evaluates the effectiveness of various control measures proposed by the WHO. Numerical simulations were used to analyze the progression of the disease, highlighting the impacts on symptomatic and asymptomatic infectious cases, recovery, deaths, and bacteria concentration in the environment. Residual analysis compared the model's predictions to observed data, showing good fit for the data for further analysis. Sensitivity analysis identified the most influential parameters, providing insights into which control measures can have the greatest impact. Results show that vaccination strategies, for further developments can significantly reduce infection peaks and help control the disease to reach an endemic state. This project demonstrates how mathematical modeling can guide effective public health interventions and resource allocation to combat cholera outbreaks.

2. Introduction

Cholera is an acute diarrheal infection caused by the bacterium Vibrio cholerae which is primarily transmitted through the ingestion of food or contaminated water. Most people infected with V. cholerae do not show symptoms, although the bacteria present in their feces lasts unto 1 to 10 days after infection, potentially spreading the disease. In symptomatic cases, infected individuals show symptoms like severe dehydration, diarrhea, and vomiting, which can lead to death if not treated promptly.

The disease is most prevalent in areas with poor sanitation, unsafe drinking water, and inadequate hygiene, placing vulnerable populations at significant risk. Globally, cholera affects 1.3 to 4 million people annually, resulting in 21,000 to 143,000 deaths.
Cholera spreads rapidly in places with untreated sewage and drinking water and is closely linked to poverty and inadequate public infrastructure.

In 2000–2001 South Africa witnessed a huge surge in cholera related cases and recorded over 86,000 cases and 181 deaths. To control this situation the WHO along with the govt authorities of South Africa suggested the people to effectively implement several control measures like adequate supply of safe drinking water, washing hands frequently, hygienic disposal of human faces and well-cooked and hygienic food to reduce the cases and deaths.
Mathematical modeling approach in this scenario is an important part in analyzing and capturing the whole scenario and evaluating the control measures proposed by the WHO suggesting how further enhancement can improve the situation and eliminate cholera cases from South Africa.

3. Problem Description

The main causes of the cholera outbreak in South Africa in 2000–2001 were lack of access to clean water and inadequate sanitation facilities. Vibrio cholerae was mostly distributed by contaminated water supplies, and the germs spread swiftly in areas where people did not practice good hygiene. During 2000/1 Cholera outbreak in South Africa, over 86,000 cases and 181 deaths were recorded by the end of April 2001, situation being made worse by the densely populated areas, inadequate healthcare, and a lack of public health education. Table 1 shows the recorded cases and deaths from October 2000 – April 2001 which was retrieved from the WHO archives.

Date	cases (total)	deaths (total)
Oct 13,2000	2175	22
Oct 18,2000	3075	26
Oct 19, 2000	3279	27
Oct 26, 2000	3806	33*
Nov 02, 2000	4270	32
Nov 09,2000	4583	33
Nov 19,2000	5285	35
Nov 27, 2000	5876	35
Dec 05, 2000	6548	35
Dec 19,2000	8137	41
Dec 29,2000	11183	51
Jan 09, 2001	15983	60
Jan 14, 2001	19499	66
Jan 25, 2001	27431	74
Feb 04, 2001	37204	85
Feb 14, 2001	48647	108
Feb 22, 2001	56092	120
Mar 03, 2001	62607	131
Mar 14, 2001	69761	139
Mar 28, 2001	78140	163
Apr 16, 2001	86107	181

Table 1. Cholera outbreak in South Africa 2000/1 (Data from the WHO archives).

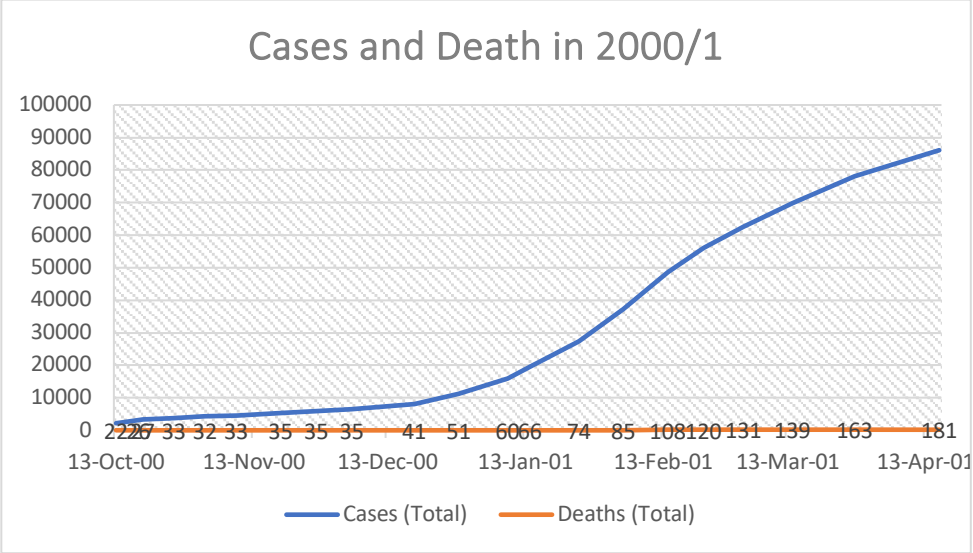


Figure 1. Cases and deaths from 2000 Oct – April 16.

Figure 1 shows that the number of cases has spiked high over time and immediate control of the disease is required to reduce the cases. To control the scenario in South Africa the WHO recommends four key control mechanisms to mitigate the outbreak:

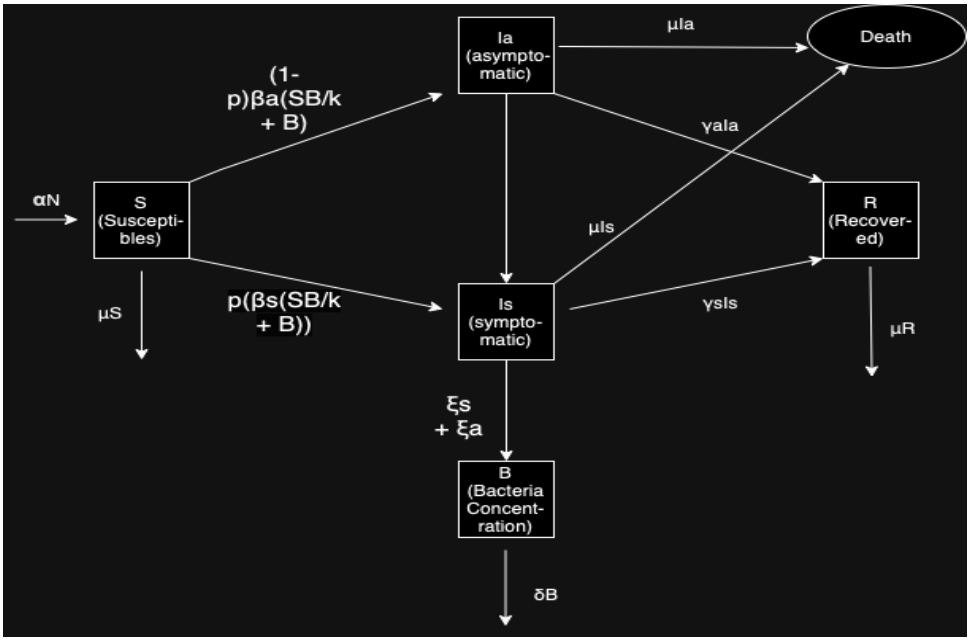
- Hygienic disposal of human feces
- Adequate supply of safe drinking water
- Good food hygiene and cooking practices
- Handwashing after defecation and before meals

To understand the effectiveness of these interventions, we analyze the outbreak data provided in Table 1 which records the cumulative cases and deaths over time.

The impact of the WHO's suggested control measures is evaluated using a mathematical model that captures the cholera dynamics. The dynamics of cholera transmission are simulated by this model in various scenarios:

1. Baseline Scenario (Without any control mechanism)
2. Intervention scenario (With the control mechanism)
    - hygienic disposal of human feces,
    - adequate supply of safe drinking water
    - good food hygiene, cooking.
    - washing hands after defecation and before meals.

4. Formulation of the Mathematical Model



1. S (Susceptible):

   Represents individuals who are not yet infected but are at high risk of developing cholera. They enter this group at a rate αN (population growth) and leave either through natural death at a rate μS or infection, where they transition to the infected groups I_s and I_a.

2. I_s (Symptomatic Infectious):

   Represents individuals who are infected and show symptoms like diarrhea and severe dehydration. The probability of becoming symptomatic is p, and the transmission of the disease depends on the bacteria concentration (B) and the transmission rate βs. The term $\frac{\beta sSB}{k+B}$ represents the transmission of cholera from the environment to the susceptible population.

3. I_a (Asymptomatic Infectious):

   Represents individuals who get infected but do not show symptoms. The fraction of people who become asymptomatic is 1 − p, where p is the fraction of symptomatic cases. The infection depends on the bacteria concentration (B) in the environment, as well as the

transmission rate βa , which reflects how the bacteria spread.

4. B (Bacteria Concentration):

   Represents the level of V. Cholera bacteria present in the environment mostly through contaminated water of human feces. Both symptomatic $I_s$and asymptomatic I_a individuals contribute to the spread of bacteria in the environment at rates $\xi_s I_s$ and $\xi_a I_a$, respectively. The bacteria naturally die or are removed from the environment at a decay rate δB.

5. R (Recovered):

   Represents individuals who have recovered from cholera and are no longer infectious. Recovery rates depend on the number of symptomatic and asymptomatic individuals, with the recovery rates $\gamma_s\ I_s$ for symptomatic cases and $\gamma_a I_a$ for asymptomatic cases. Recovered individuals may also die naturally at rate μ, and they do not contribute to transmission.

4.1 Model Equations:

$$\frac{dS}{dt} = \alpha\text{N} - \text{p} * \frac{\beta\text{sSB}}{k+B} - (1\text{-p})\frac{\beta\text{aSB}}{k+B} - \mu\text{S}$$

$$\frac{dI_s}{dt} = \text{p} * \frac{\beta\text{sSB}}{k+B} - (\gamma_s + \mu)\ I_s$$

$$\frac{dI_a}{dt} = (1\text{-p})\frac{\beta\text{aSB}}{k+B} - (\gamma_a + \mu)\ I_a$$

$$\frac{dR}{dt} = \gamma_s\ I_s + \gamma_a I_a - \mu R$$

$$\frac{dB}{dt} = \xi_s I_s + \xi_a I_a - \delta B$$

$$\frac{dD}{dt} = \mu_s I_s - \mu_a I_a$$

4.2 Assumptions:

1. The model implicitly assumes a well-mixed population where all individuals interact uniformly. The population is treated as a single homogeneous group without considering age, gender, or other demographic differences.
2. New individuals enter the susceptible population at a constant rate αN.
3. Individuals can exit the system through natural deaths at rates μS and μR, or through cholera-related deaths for symptomatic individuals and asymptomatic cases at the rates $\mu_s I_s$ and $\mu_a I_a$.
4. Cholera transmission occurs through environmental contamination, specifically via bacterial concentration in water and human feces (B). The probability of infection for symptomatic individuals p and asymptomatic individuals 1−p depends on the bacterial concentration relative to a "half-saturation constant" k, which determines the point at which the transmission rate is half of its maximum.
5. Infected individuals recover and move into the recovered compartment R or die due to infection and move to the death compartment D.
6. The bacterial concentration (B) increases through shedding by both symptomatic ($\xi_s I_s$) and asymptomatic ($\xi_a I_a$) individuals. The bacteria decay naturally at the rate δB.
7. All the parameters are constant over time and do not vary with environmental or seasonal factors.
8. Recovered individuals do not return to the susceptible.
9. The model does not account for seasonal or temporal variations in parameters like bacterial growth or decay rates.

4.2 Parameter Estimation:

The parameter values used for the simulations of the model were assumed by a careful review on several articles based on mathematical modeling for cholera transmission that provided a realistic approach for the simulations. Transmission rates β_s and β_a were selected based on the higher infectiousness of symptomatic individuals compared to asymptomatic ones. The recovery rates γ_s and γ_a reflect the cholera recovery periods, with symptomatic individuals recovering faster as they get diagnosed and treated early. Bacterial shedding rates ξ_s and ξ_a were set since symptomatic individuals shed significantly more bacteria into the environment than asymptomatic ones. The half-saturation constant (k) was selected to model the saturation effect in transmission as bacterial concentration increases. These parameter values were carefully selected to closely replicate the dynamics of cholera outbreaks, ensuring realistic and grounded simulation results.

Parameter	Description	Value
α	Natural death	9.1×10^{-3}
β_s	Transmission rate for Symptomatic individuals (per day)	2×10^{-2}
β_a	Transmission rate for Asymptomatic individuals (per day)	5×10^{-3}
k	Half saturation constant	1×10^{3}
γ_s	Recovery rate for Symptomatic individuals (per day)	1/3
γ_a	Recovery rate for Asymptomatic individuals (per day)	1/4
μ_s	Cholera related deaths for symptomatic individuals. (Per day)	5.532×10^{-4}
μ_s	Cholera related deaths for symptomatic individuals. (Per day)	1.869×10^{-8}
p	Proportion of Symptomatic cases	0.2
ξ_s	Bacteria Shedding rate for Symptomatic individuals. (cells/ml/day)	1×10^{4}
ξ_a	Bacteria Shedding rate for Asymptomatic individuals. (cells/ml/day)	1×10^{3}
δ	Net decay rate of bacteria (per day)	0.4
N	Total population size	10^{5}

5. Model Simulations

The model was simulated over a time span of 200 days to understand the dynamics of cholera transmission. The analysis is divided into two main parts: time series analysis (without intervention and with intervention of the control measures).

The model's output dynamics, representing the cholera outbreak progression without any control measures, are shown below in figure 2.

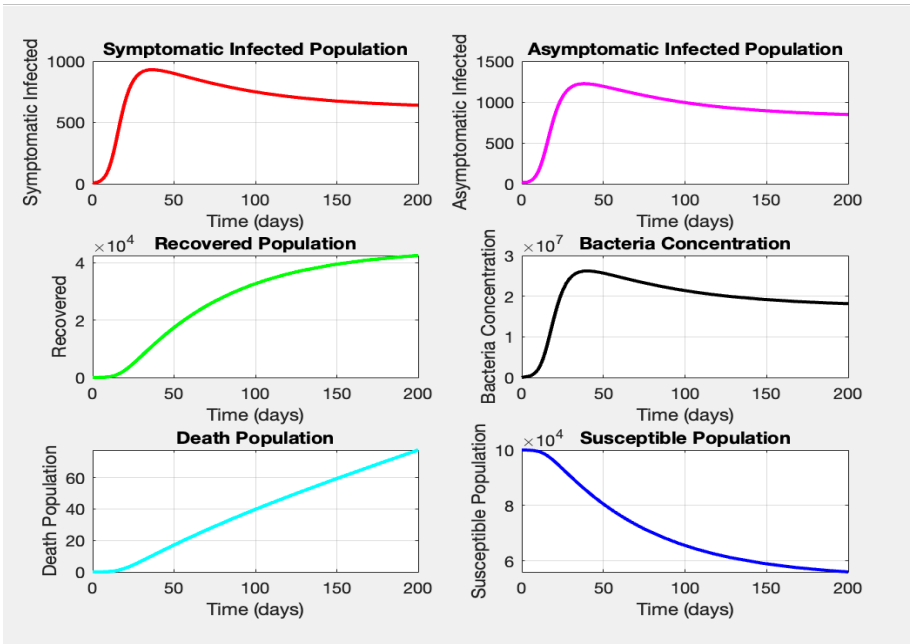


Figure 2. Simulations without control measures

The simulation reveals the following trends:

- **Symptomatic Infected Population**: Increases sharply during the initial phase, peaking around day 40. This indicates the rapid spread of cholera during the early stages.
- **Asymptomatic Infected Population**: Exhibits a similar rising trend but at a slower rate due to the lower transmission rate from asymptomatic individuals.
- **Bacteria Concentration**: Mirrors the infection trends, showing a rise and peak around day 50, emphasizing the critical role of bacterial load in driving transmission.
- **Susceptible Population**: Declines steadily as individuals either become infected or succumb to the disease.
- **Recovered Population**: Gradually increases as more individuals recover from both symptomatic and asymptomatic infections.
- **Deaths**: Shows a steady rise throughout the simulation period, reflecting the cumulative toll of cholera.

5.1 Residual Analysis:

Residual analysis is performed to assess the goodness-of-fit between the model's simulated outcomes and observed data focusing on symptomatic cases and deaths. **Figure 3** illustrates the residuals for symptomatic cases and deaths, providing insight into the model's performance:

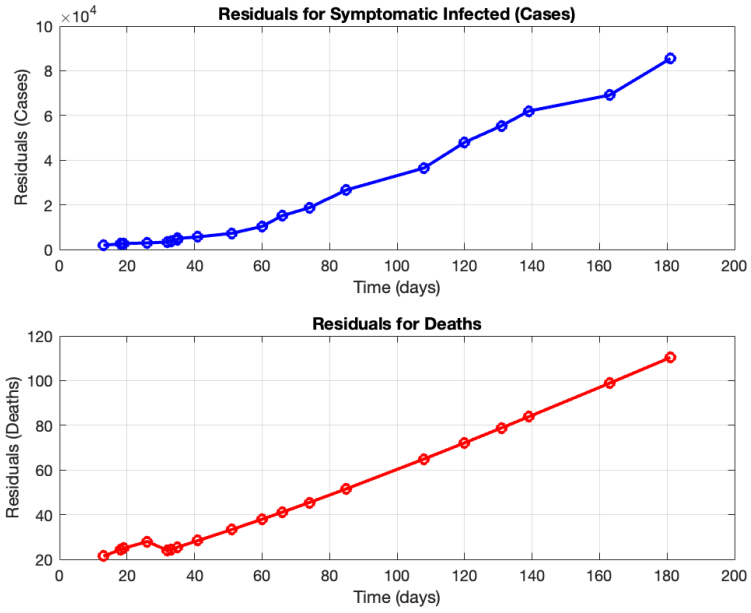


Figure 3. Residual Analysis for cases and deaths

Figure 3 shows the residual analysis for cases and deaths highlighting the discrepancies between the model's predictions and the actual outbreak data. The graph reveals:

- **Cases**: Residuals for symptomatic cases display a clear upward trend, indicating that the model tends to underestimate the number of cases as the outbreak progresses.
- **Deaths**: Similarly, residuals for deaths reveal a systematic underestimation, particularly in the later stages of the outbreak.

While the residual analysis shows that the model has limitations, it is still a robust framework for exploring different intervention strategies. It effectively captures the key dynamics of cholera transmission, such as environmental bacterial concentration, symptomatic and asymptomatic infections, recovery, and deaths. These features make it valuable for simulating and comparing control measures.

5.2 Sensitivity Analysis:

Sensitivity analysis is done to analyse how changes in the values of model parameters influence the model's output. It identifies which parameters have the most significant impact on the results and helps to understand the relationships between variables in a system. It is performed to understand the model parameters and how it effects the system's behaviour, also this analysis is helpful for robustness testing i.e., to determine whether the model's conclusions remain valid under varying assumptions or parameter changes.

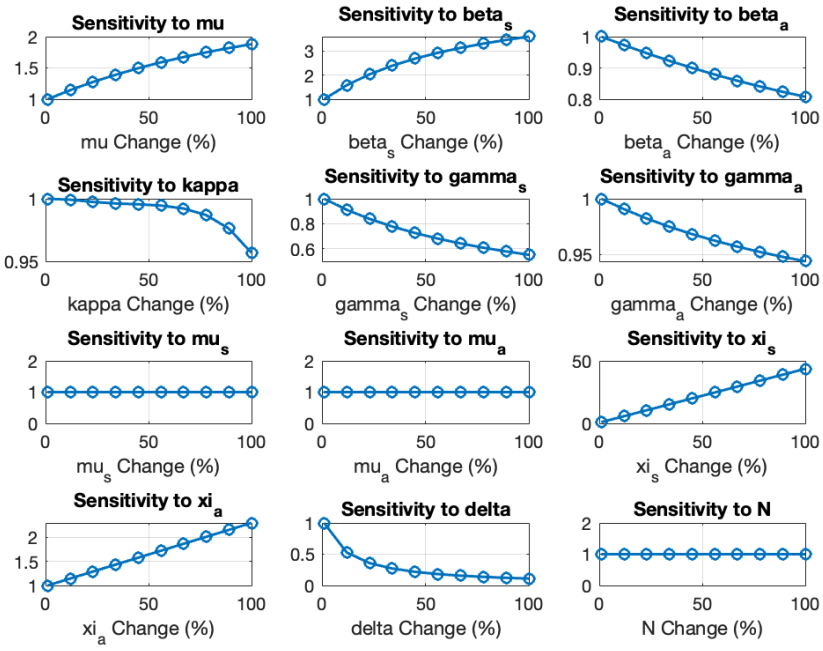


Figure 4. Sensitivity Analysis.

The sensitivity plots reveal that transmission rates and shedding rates ($\beta_s, \beta_a, \xi_s, \xi_a$) are the high sensitivity parameter indicating the importance of targeting these factors. Changes in these parameters may lead to substantial variations in the bacteria concentration, emphasizing their critical role in the system dynamics whereas parameters such as γ_s, γ_a and δ show moderate sensitivity highlighting their importance but to a lesser degree compared to highly sensitive parameters.

5.3 Control Measure 1: Hygienic disposal of human feces.

To evaluate the impact of improved hygienic practices on cholera transmission, I introduced a control mechanism aimed at reducing the bacterial shedding rates. This control measure simulates **hygienic disposal of human feces**, which directly limits the contamination of the environment and water sources by cholera bacteria.

In the model, the bacterial shedding rates for both symptomatic ξ_s and asymptomatic ξ_a individuals were modified to reflect the implementation of this control assuming that half of the population implemented this control measure effectively :

$$\Rightarrow \xi_s^{control} = \xi_s\,(1\text{-}u_1), \quad \xi_a^{control} = \xi_a(1\text{-}\,u_1)$$

Where u_1 = 0.5 represents a 50% reduction in bacterial shedding due to hygienic practices. This adjustment simulates a significant improvement in sanitation.

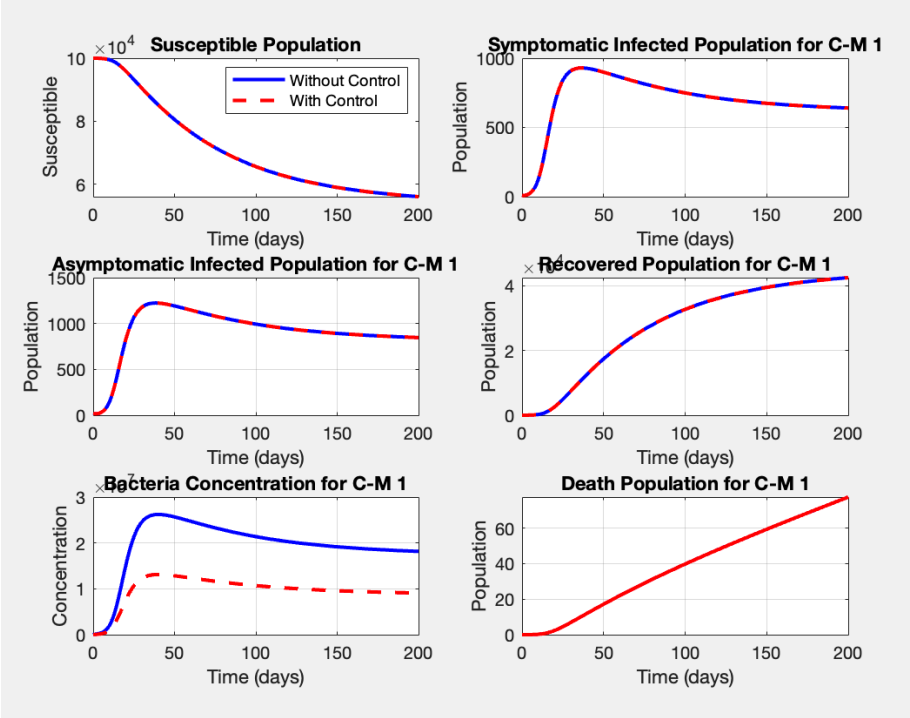


Figure 5. Simulations for control Measure 1

The simulation results in Figure 5 shows the dynamics of the cholera outbreak with and without the first proposed control measure.
This control mechanism effectively reduces bacterial concentration in the environment which may lead to low transmission rates in time. Hygienic disposal of feces not only decreases the bacterial concentration in the environment but also mitigates the disease's impact on public health by reducing the infection overall.

5.4 Control Measure 2: Adequate supply of safe drinking water.

This control measure focuses on reducing cholera transmission by ensuring the population has access to safe drinking water. Contaminated water is a primary aspect for the spread of cholera, so improving water quality directly impacts the transmission dynamics.
To simulate the effect of an improved water supply, I adjusted the transmission rates for both symptomatic and asymptomatic infections as follows:

$$\Rightarrow \beta_s^{control} = \beta_s \times (1-u_2), \quad \beta_a^{control} = \beta_s \times (1-u_2)$$

where β_s and β_a are the transmission rate for symptomatic and asymptotic individuals. u_2 =0.5 is the 50% reduction in transmission due to safe water supply, assuming that half of the population implemented this control measure effectively .

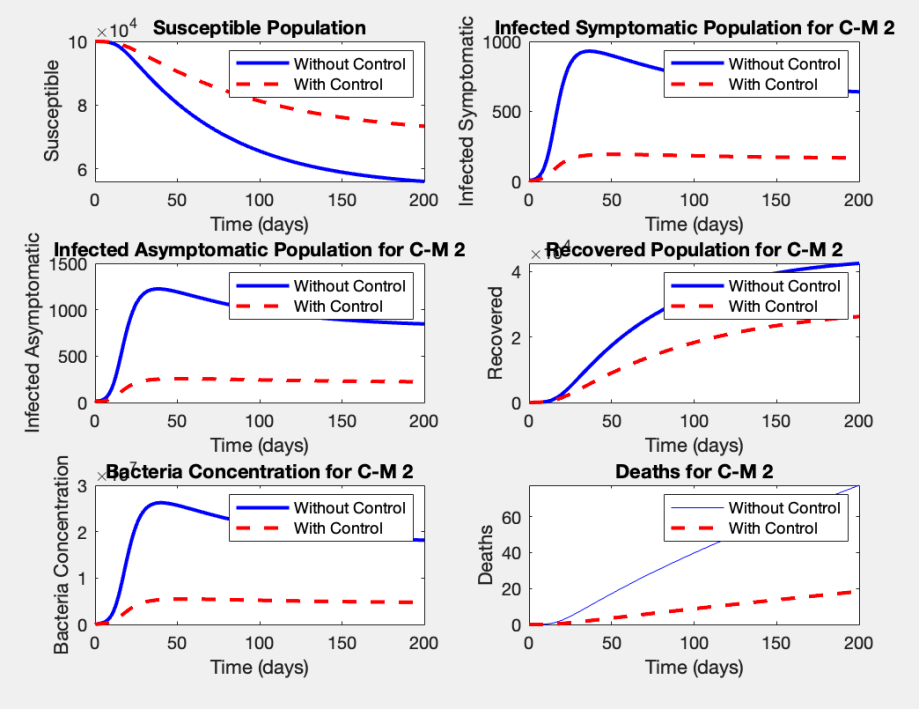


Figure 6. Simulations for Control Measure 2.

Figure 5 illustrating the simulations of with and without the control measure 2 shows a significant impact with the reduced peak for both symptomatic and asymptomatic cases. This indicates that improved water quality effectively limits the disease's transmission. The bacteria concentration in the environment also decreased sharply under this control, the deaths are also markedly reduced making this a strong and effective control measure.

5.4 Control Measure 3: Good food hygiene, Cooking.

This control mechanism focuses on reducing the disease by promoting good food hygiene practices and ensuring proper cooking of food. Contaminated food is a significant route for the spread of cholera, especially in areas where water and sanitation infrastructure are inadequate. To model the effects of this intervention, the transmission rates for both symptomatic and asymptomatic infections were adjusted to account for a reduction in transmission due to improved food hygiene. The modified transmission rates were calculated as:

$$\Rightarrow \beta_s^{control\_food} = \beta_s \times (1-u_2)\,(1-u_3), \quad \beta_a^{control\_food} = \beta_a \times (1-u_2)\,(1-u_3)$$

where u_3=0.5 represents a 50% reduction in transmission due to good food hygiene, building on the reduction already achieved by safe water supply (u_2).

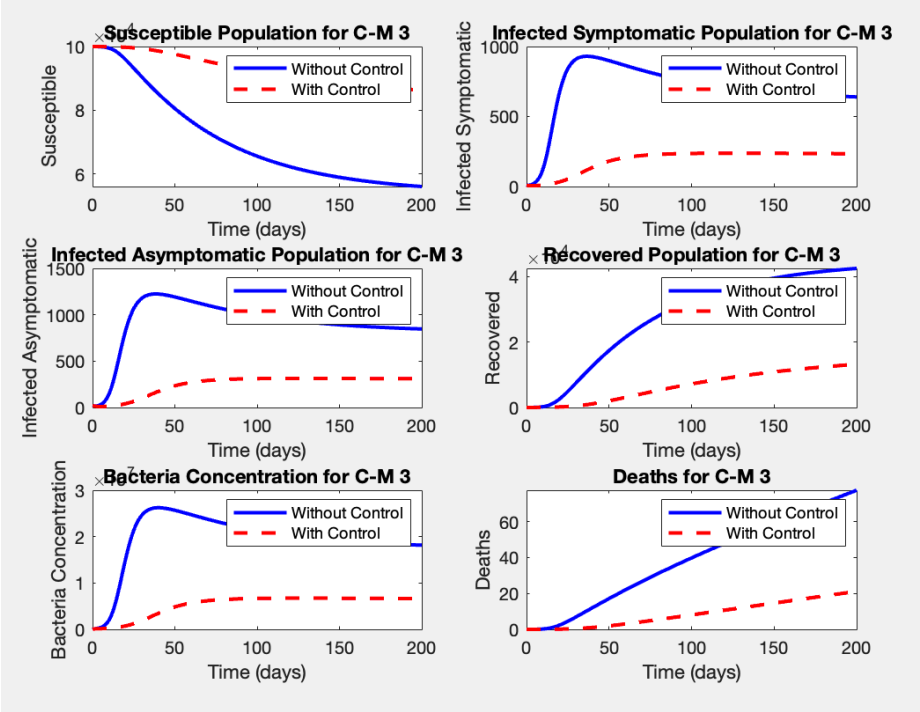


Figure 7. Simulations for Control Measure 3.

Control measure 3 shows similar results as the control measure 2, both are equally effective with a reduced peak for infectious individuals. The bacteria concentration also decreases substantially. Deaths with control also showed decrease emphasizing the effectiveness of this measure in preventing severe outcomes. These findings highlight the critical role of food hygiene in controlling cholera outbreaks.

5.5 Control Measure 4: Washing hands after defecation and after meals.

The control measure 4 emphasizes the role of personal hygiene, particularly handwashing after defecation and before meals, in reducing cholera transmission. Poor hand hygiene is a significant contributor to the spread of the disease as it facilitates the transfer of Vibrio cholerae bacteria from fecal matter to food and water sources.
To simulate the impact of improved hand hygiene, the following adjustments were made in the model:

$$\Rightarrow \beta_s^{hands} = \beta_s \times (1-u_4),\ \beta_a^{hands} = \beta_a \times (1-u_4)$$
$$\Rightarrow \gamma_s^{hands} = \gamma_s \times (1-u_5),\ \gamma_a^{hands} = \gamma_a \times (1-u_5)$$

where $u_4 = 0.5$ represents a 50% reduction in transmission due to improved hand hygiene, and $u_5 = 0.5$ represents a 50% improvement in recovery.

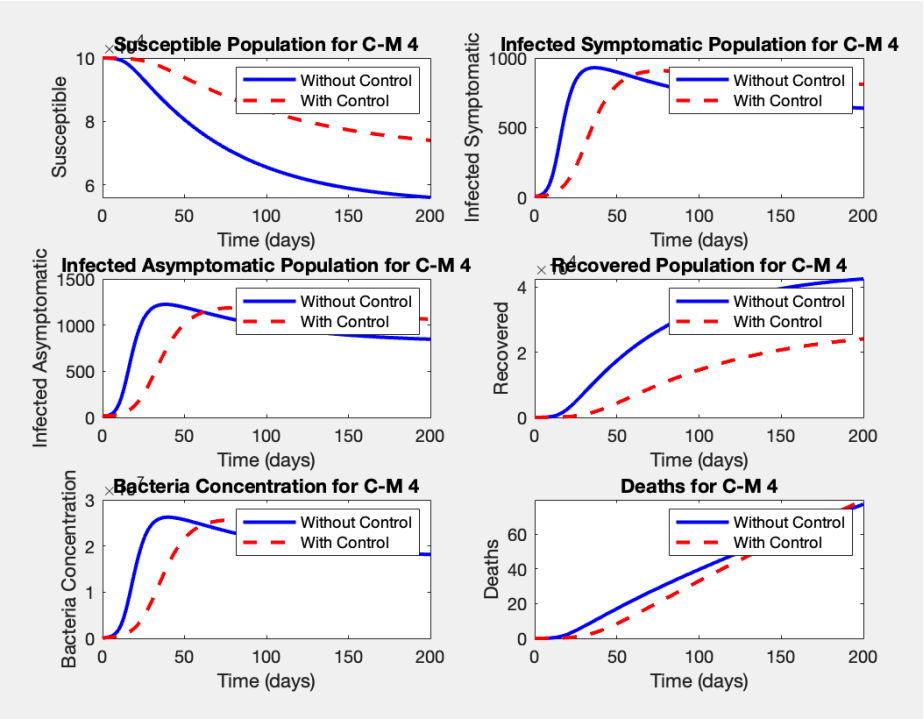


Figure 8. Simulations for Control Measure 4

Control Measure 4, which focuses on handwashing after defecation and meals, shows little to no impact on the cholera dynamics compared to the uncontrolled scenario. This suggests that while handwashing is an important general hygiene practice, its isolated implementation, without addressing other critical pathways like water and food contamination, may not be sufficient to significantly alter the course of the outbreak.

6. Results and Interpretations

The model simulations provided valuable insights into cholera transmission dynamics and the effectiveness of various control measures. Without the intervention of control mechanisms, the simulations revealed a rapid rise in infections, high bacterial concentration, and a steady increase in deaths during the 2000/1 period, emphasizing the need for effective control strategies. Residual analysis showed reasonable alignment between model predictions and observed data, despite some deviations indicating the model can further be enhanced using more detailed data. Sensitivity analysis highlighted that transmission rates and bacterial shedding rates had the most significant influence on disease progression.

Among the four control measures simulated, Control Measures 2 (safe drinking water) and 3 (food hygiene) showed the most significant reductions in infections. Control Measure 1 (hygienic feces disposal) also contributed to reducing bacterial concentration but with less impact on the infection cases peaks whereas Control Measure 4 (frequent handwashing) showed negligible impact when implemented, suggesting that it is insufficient without complementary measures.

These results underscore the importance of focusing on improving water quality and food hygiene to have a disease-free endemic state in South Africa.

7. Further Development

In contrast to the results obtained from the mathematical simulations, the implementation of vaccination strategies can be a major component in eradicating cholera from South Africa over time. Vaccines can significantly reduce infection peaks by increasing immunity within the population, preventing individuals from developing the disease even when exposed to the bacteria. As observed in the sensitivity analysis, transmission rates and bacterial shedding rates are among the most influential parameters for disease progression. Vaccination directly targets these parameters by reducing the number of infectious individuals and limiting bacterial contamination in the environment.

When combined with existing control measures—safe drinking water, improved food hygiene, and hygienic feces disposal—the addition of vaccination strategy can create a significant impact. While the current measures do not completely eliminate the disease; vaccines have the potential to reduce the susceptible population to a point where the disease can no longer sustain itself, driving the system toward a cholera-free endemic state. Over time, this integrated approach would lead to a decline in transmission and bacterial concentrations, eventually eradicating the disease and securing long-term public health benefits for South Africa.

8. References

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9. Appendices

9.1 MATLAB Code

```
% Assigning parameters
alpha = 0.0091;     % Natural birth rate (per day)
mu = 9.1e-3;        % Natural death rate (per day)
beta_s = 2e-2;      % Transmission rate for symptomatic individuals (per day)
beta_a = 5e-3;      % Transmission rate for asymptomatic individuals (per
day)
kappa = 1e3;        % Half-saturation constant
gamma_s = 1/3;      % Recovery rate for symptomatic
gamma_a = 1/4;      % Recovery rate for asymptomatic
mu_s = 5.5329e-4;   % Cholera-related death rate for symptomatic (per day)
mu_a = 1.8694e-8;   % Cholera-related death rate for asymptomatic (per day)
p = 0.2;            % Proportion of symptomatic cases
xi_s = 1e4;         % Shedding rate for symptomatic (cells/ml/day)
xi_a = 1e3;         % Shedding rate for asymptomatic (cells/ml/day)
delta = 0.4;        % Net decay rate of bacteria (per day)
N = 1e5;            % Total population size

% Initial conditions
S0 = N - 10;        % Initial susceptible individuals
I_s0 = 10;          % Initial symptomatic infected individuals
I_a0 = 20;          % Initial asymptomatic infected individuals
R0 = 0;             % Initial recovered individuals
B0 = 1;             % Initial bacterial concentration
D0 = 0;             % Initial deaths

% Time span
tspan = [0, 200];   % Simulation time for 200 days

ode = @(t, y) [
    alpha * N - p * (beta_s * y(1) * y(4)) / (kappa + y(4)) - (1-p) * (beta_a
* y(1) * y(4)) / (kappa + y(4)) - mu * y(1);  % dS/dt
    p * (beta_s * y(1) * y(4)) / (kappa + y(4)) - (gamma_s + mu) * y(2);
% dI_s/dt
    (1 - p) * (beta_a * y(1) * y(4)) / (kappa + y(4)) - (gamma_a + mu_a) *
y(3);                                       % dI_a/dt
    gamma_s * y(2) + gamma_a * y(3) - mu * y(4);
% dR/dt
    xi_s * y(2) + xi_a * y(3) - delta * y(5);
% dB/dt
    mu_s * y(2) + mu_a * y(3);
% dD/dt
];


% Initial conditions vector
y0 = [S0, I_s0, I_a0, R0, B0, D0];
```

```
% Solve the system using ode45
[t, y] = ode15s(ode, tspan, y0);

% Extract the results
S = y(:, 1);
I_s = y(:, 2);
I_a = y(:, 3);
R = y(:, 4);
B = y(:, 5);
D = y(:, 6);

% Initializing the plots
figure;

% Plot of Susceptible population
subplot(3, 2, 6);
plot(t, S, 'b-', 'LineWidth', 2, 'DisplayName', 'Susceptible (Model)');
xlabel('Time (days)');
ylabel('Susceptible Population');
title('Susceptible Population');
grid on;

% Plot for Symptomatic Infected population
subplot(3, 2, 1);
plot(t, I_s, 'r-', 'LineWidth', 2, 'DisplayName', 'Symptomatic Infected
(Model)');
xlabel('Time (days)');
ylabel('Symptomatic Infected');
title('Symptomatic Infected Population');
grid on;

% Plot for Asymptomatic Infected population
subplot(3, 2, 2);
plot(t, I_a, 'm-', 'LineWidth', 2, 'DisplayName', 'Asymptomatic Infected
(Model)');
xlabel('Time (days)');
ylabel('Asymptomatic Infected');
title('Asymptomatic Infected Population');
grid on;

% Plot for Recovered population
subplot(3, 2, 3);
plot(t, R, 'g-', 'LineWidth', 2, 'DisplayName', 'Recovered (Model)');
xlabel('Time (days)');
ylabel('Recovered');
title('Recovered Population');
grid on;

% Plot for Bacteria concentration
subplot(3, 2, 4);
plot(t, B, 'k-', 'LineWidth', 2, 'DisplayName', 'Bacteria (Model)');
xlabel('Time (days)');
ylabel('Bacteria Concentration');
title('Bacteria Concentration');
grid on;
```

```
% Plot for Deaths
subplot(3, 2, 5);
plot(t, D, 'c-', 'LineWidth', 2, 'DisplayName', 'Deaths (Model)');
xlabel('Time (days)');
ylabel('Death Population');
title('Death Population');
grid on;



% RESIDUAL ANALYSIS

% provided data
data_time = [13, 18, 19, 26, 32, 33, 35, 35, 41, 51, 60, 66, 74, 85, 108,
120, 131, 139, 163, 181];  % Time (in days)
data_cases = [2175, 3075, 3279, 3806, 4270, 4583, 5285, 5876, 6548, 8137,
11183, 15983, ...
              19499, 27431, 37204, 48647, 56092, 62607, 69761, 86107];  %
Total cases
data_deaths = [22, 26, 27, 33, 32, 33, 35, 35, 41, 51, 60, 66, 74, 85, 108,
120, 131, 139, 163, 181];  % Total deaths

% Interpolate model results to match the observed data time points
I_s_interpolated = interp1(t, I_s, data_time, 'linear');
D_interpolated = interp1(t, D, data_time, 'linear');

% Calculate residuals
residual_cases = data_cases - I_s_interpolated;
residual_deaths = data_deaths - D_interpolated;

% Plot the residuals
figure;
subplot(2, 1, 1);
plot(data_time, residual_cases, 'bo-', 'LineWidth', 2);
xlabel('Time (days)');
ylabel('Residuals (Cases)');
title('Residuals for Symptomatic Infected (Cases)');
grid on;

% Plot residuals for deaths
subplot(2, 1, 2);
plot(data_time, residual_deaths, 'ro-', 'LineWidth', 2);
xlabel('Time (days)');
ylabel('Residuals (Deaths)');
title('Residuals for Deaths');
grid on;




% Sensitivity Analysis
```

```
% Define the parameter ranges
param_ranges = {
    [1e-3, 1e-2],
    [1e-2, 1e-1],
    [1e-3, 1e-2],
    [1e2, 1e4],
    [1/4, 1/2],
    [1/5, 1/3],
    [1e-4, 1e-3],
    [1e-8, 1e-6],
    [1e3, 1e5],
    [1e2, 1e4],
    [0.1, 0.9],
    [1e4, 1e5]
};

param_names = {'mu', 'beta_s', 'beta_a', 'kappa', 'gamma_s',
'gamma_a','mu_s', 'mu_a', 'xi_s', 'xi_a', 'delta', 'N'};

% Initial conditions and time span
y0 = [S0, I_s0, I_a0, R0, B0, D0];
tspan = [0, 200];

% Number of parameter variations to test
n_points = 10;

% Initialize variables for storing normalized outputs
output_results = zeros(length(param_ranges), n_points);

% Perform sensitivity analysis: loop through each parameter
for i = 1:length(param_ranges)
    % Generate parameter values for this parameter
    param_range = param_ranges{i};
    param_values = linspace(param_range(1), param_range(2), n_points);

    % Store the output for each variation
    param_output = zeros(n_points, 1);

    for j = 1:n_points
        % Creating a copy of the parameters
        params = {mu, beta_s, beta_a, kappa, gamma_s, gamma_a, mu_s, mu_a,
xi_s, xi_a, delta, N};

        % Modifying the parameter of interest
        params{i} = param_values(j);  % Update the parameter being varied

        % Define the ODE system
        ode = @(t, y) [
            params{1} * N - p * (params{2} * y(1) * y(4)) / (params{4} +
y(4)) - (1 - p) * (params{3} * y(1) * y(4)) / (params{4} + y(4)) - params{1}
* y(1);  % dS/dt
            p * (params{2} * y(1) * y(4)) / (params{4} + y(4)) - (params{5} +
params{1}) * y(2);  % dI_s/dt
```

```
            (1 - p) * (params{3} * y(1) * y(4)) / (params{4} + y(4)) -
(params{6} + params{1}) * y(3);  % dI_a/dt
            params{5} * y(2) + params{6} * y(3) - params{1} * y(4);  % dR/dt
            params{9} * y(2) + params{10} * y(3) - params{11} * y(5);  %
dB/dt
            params{7} * y(2) + params{8} * y(3);  % dD/dt
        ];

        % Solve the ODE system
        [~, y] = ode15s(ode, tspan, y0);

        param_output(j) = y(end, 5);  % Get the final bacteria concentration
    end

    output_results(i, :) = param_output / param_output(1);  % Normalize by
the first output
end

% Plot the sensitivity analysis results
figure;
for i = 1:length(param_names)
    subplot(4, 3, i);  % Arrange subplots in a grid (4 rows, 3 columns)
    plot(linspace(1, 100, n_points), output_results(i, :), '-o', 'LineWidth',
1.5);
    title(['Sensitivity to ', param_names{i}]);
    xlabel([param_names{i}, ' Change (%)']);
    grid on;
end

% Highlight the most sensitive parameters
variances = var(output_results, 0, 2);  % Variance along the rows
(parameters)
[~, sorted_indices] = sort(variances, 'descend');

fprintf('Most Influential Parameters (by Variance):\n');
for i = 1:length(sorted_indices)
    fprintf('%s: Variance = %.4f\n', param_names{sorted_indices(i)},
variances(sorted_indices(i)));
end



% Hygienic disposal of human feces

% Applying control mechanism 1 (hygienic disposal of feces)
u1 = 0.5;  % Control mechanism effectiveness
xi_s_control = xi_s * (1 - u1);
xi_a_control = xi_a * (1 - u1);

% ODE function with control mechanism 1
ode_control_1 = @(t, y) [
    alpha * N - p * (beta_s * y(1) * y(4)) / (kappa + y(4)) - (1-p) * (beta_a
* y(1) * y(4)) / (kappa + y(4)) - mu * y(1);  % dS/dt
    p * (beta_s * y(1) * y(4)) / (kappa + y(4)) - (gamma_s + mu) * y(2);
% dI_s/dt
```

```
    (1 - p) * (beta_a * y(1) * y(4)) / (kappa + y(4)) - (gamma_a + mu) *
y(3);                                                   % dI_a/dt
    gamma_s * y(2) + gamma_a * y(3) - mu * y(4);
% dR/dt
    xi_s_control * y(2) + xi_a_control * y(3) - delta * y(5);
% dB/dt
    mu_s * y(2) + mu_a * y(3);
% dD/dt
];

% Solve the system using ode15s with control mechanism
[t_original, y_original] = ode15s(ode, tspan, y0);
[t_control, y_control] = ode15s(ode_control_1, tspan, y0);

% Extract the results
S_original = y_original(:, 1);
I_s_original = y_original(:, 2);
I_a_original = y_original(:, 3);
R_original = y_original(:, 4);
B_original = y_original(:, 5);
D_original = y_original(:, 6);

S_control = y_control(:, 1);
I_s_control = y_control(:, 2);
I_a_control = y_control(:, 3);
R_control = y_control(:, 4);
B_control = y_control(:, 5);
D_control = y_control(:, 6);

figure; % Plot Susceptible population
% Plot Susceptible population (S)
subplot(3, 2, 1);
plot(t_original, S_original(:, 1), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on;
plot(t_control, y_control(:, 1), 'r--','LineWidth', 2, 'DisplayName', 'With
Control');
xlabel('Time (days)');
ylabel('Susceptible');
title('Susceptible Population');
legend;

% Plot for Symptomatic Infected population
subplot(3, 2, 2);
plot(t_original, y_original(:, 2), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on;
plot(t_control, y_control(:, 2), 'r--','LineWidth', 2, 'DisplayName', 'With
Control');
xlabel('Time (days)');
ylabel('Population');
title('Symptomatic Infected Population for C-M 1');
grid on;

% Plot for Asymptomatic Infected population
```

```
subplot(3, 2, 3);
plot(t_original, y_original(:, 3), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on;
plot(t_control, y_control(:, 3), 'r--','LineWidth', 2, 'DisplayName',
'Without Control');
xlabel('Time (days)');
ylabel('Population');
title('Asymptomatic Infected Population for C-M 1');
grid on;
% Plot for Recovered population
subplot(3, 2, 4);
plot(t_original, y_original(:, 4), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on;
plot(t_control, y_control(:, 4), 'r--','LineWidth', 2, 'DisplayName',
'Without Control');
xlabel('Time (days)');
ylabel('Population');
title('Recovered Population for C-M 1');
grid on;
% Plot Bacteria concentration
subplot(3, 2, 5);
plot(t_original, y_original(:, 5), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on;
plot(t_control, y_control(:, 5), 'r--','LineWidth', 2, 'DisplayName',
'Without Control');
xlabel('Time (days)');
ylabel('Concentration');
title('Bacteria Concentration for C-M 1');
grid on;
% Plot Deaths
subplot(3, 2, 6);
plot(t_original, y_original(:, 6), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on; plot(t_control, y_control(:, 6), 'r-','LineWidth', 2, 'DisplayName',
'Without Control');
xlabel('Time (days)');
ylabel('Population');
title('Death Population for C-M 1');
grid on;



% control mechanism 2 adequate supply of safe drinking water;

u2 = 0.5;  % Control mechanism effectiveness
beta_s_control = beta_s * (1 - u2);
beta_a_control = beta_a * (1 - u2);

% ODE system for model with second control mechanism (safe drinking water)
ode_with_control_2 = @(t, y) [
    alpha * N - p * (beta_s_control * y(1) * y(4)) / (kappa + y(4)) - (1-p) *
(beta_a_control * y(1) * y(4)) / (kappa + y(4)) - mu * y(1);  % dS/dt
```

```
    p * (beta_s_control * y(1) * y(4)) / (kappa + y(4)) - (gamma_s_control +
mu) * y(2);                                                    % dI_s/dt
    (1 - p) * (beta_a_control * y(1) * y(4)) / (kappa + y(4)) -
(gamma_a_control + mu) * y(3);                                          %
dI_a/dt
    gamma_s_control * y(2) + gamma_a_control * y(3) - mu * y(4);
% dR/dt
    xi_s * y(2) + xi_a * y(3) - delta * y(5);
% dB/dt
    mu_s * y(2) + mu_a * y(3);
% dD/dt
];


% Solve ODEs for both cases
[t_without_2, y_without_2] = ode15s(ode, tspan, y0); % Without control
[t_with, y_with] = ode15s(ode_with_control_2, tspan, y0);      % With control
(safe drinking water)

figure;

% Plot for Susceptible population (S)
subplot(3, 2, 1);
plot(t_without_2, y_without_2(:, 1), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on;
plot(t_with, y_with(:, 1), 'r--','LineWidth', 2, 'DisplayName', 'With
Control');
xlabel('Time (days)');
ylabel('Susceptible');
title('Susceptible Population');
legend;

% Plot for Infected Symptomatic population (I)
subplot(3, 2, 2);
plot(t_without_2, y_without_2(:, 2), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on;
plot(t_with, y_with(:, 2), 'r--','LineWidth', 2, 'DisplayName', 'With
Control');
xlabel('Time (days)');
ylabel('Infected Symptomatic');
title('Infected Symptomatic Population for C-M 2');
legend;

% Plot for Infected Asymptomatic population (A)
subplot(3, 2, 3);
plot(t_without_2, y_without_2(:, 3), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on;
plot(t_with, y_with(:, 3), 'r--','LineWidth', 2, 'DisplayName', 'With
Control');
xlabel('Time (days)');
ylabel('Infected Asymptomatic');
title('Infected Asymptomatic Population for C-M 2');
```

```
legend;

% Plot for Recovered population (R)
subplot(3, 2, 4);
plot(t_without_2, y_without_2(:, 4), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on;
plot(t_with, y_with(:, 4), 'r--','LineWidth', 2, 'DisplayName', 'With
Control');
xlabel('Time (days)');
ylabel('Recovered');
title('Recovered Population for C-M 2');
legend;

% Plot for Bacteria concentration (B)
subplot(3, 2, 5);
plot(t_without_2, y_without_2(:, 5), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on;
plot(t_with, y_with(:, 5), 'r--','LineWidth', 2, 'DisplayName', 'With
Control');
xlabel('Time (days)');
ylabel('Bacteria Concentration');
title('Bacteria Concentration for C-M 2');
legend;

% Plot for Deaths (D)
subplot(3, 2, 6);
plot(t_without_2, y_without_2(:, 6), 'b-', 'DisplayName', 'Without Control');
hold on;
plot(t_with, y_with(:, 6), 'r--','LineWidth', 2, 'DisplayName', 'With
Control');
xlabel('Time (days)');
ylabel('Deaths');
title('Deaths for C-M 2');
legend;


% Control mechanism 3; good food hygiene, cooking.

u3 = 0.5;  % Control mechanism effectiveness
beta_s_control_food = beta_s * (1 - u2) * (1-u3);
beta_a_control_food = beta_a * (1 - u2) * (1-u3);

% ODE system for model with second control mechanism
ode_with_control_3 = @(t, y) [
    alpha * N - p * (beta_s_control_food * y(1) * y(4)) / (kappa + y(4)) -
(1-p) * (beta_a_control_food * y(1) * y(4)) / (kappa + y(4)) - mu * y(1);  %
dS/dt
    p * (beta_s_control_food * y(1) * y(4)) / (kappa + y(4)) - (gamma_s + mu)
* y(2);                                          % dI_s/dt
    (1 - p) * (beta_a_control_food * y(1) * y(4)) / (kappa + y(4)) - (gamma_a
+ mu) * y(3);                                    % dI_a/dt
    gamma_s * y(2) + gamma_a * y(3) - mu * y(4);
% dR/dt
```

```
    xi_s * y(2) + xi_a * y(3) - delta * y(5);
% dB/dt
    mu_s * y(2) + mu_a * y(3);
% dD/dt
];


% Solve ODEs for both cases
[t_without_3, y_without_3] = ode15s(ode, tspan, y0); % Without control
[t_with_3, y_with_3] = ode15s(ode_with_control_3, tspan, y0);      % With
control (food hygiene)

figure;

% Plot for Susceptible population (S)
subplot(3, 2, 1);
plot(t_without_3, y_without_3(:, 1), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on;
plot(t_with_3, y_with_3(:, 1), 'r--','LineWidth', 2, 'DisplayName', 'With
Control');
xlabel('Time (days)');
ylabel('Susceptible');
title('Susceptible Population for C-M 3');
legend;

% Plot for Infected Symptomatic population (I)
subplot(3, 2, 2);
plot(t_without_3, y_without_3(:, 2), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on;
plot(t_with_3, y_with_3(:, 2), 'r--','LineWidth', 2, 'DisplayName', 'With
Control');
xlabel('Time (days)');
ylabel('Infected Symptomatic');
title('Infected Symptomatic Population for C-M 3');
legend;

% Plot for Infected Asymptomatic population (A)
subplot(3, 2, 3);
plot(t_without_3, y_without_3(:, 3), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on;
plot(t_with_3, y_with_3(:, 3), 'r--','LineWidth', 2, 'DisplayName', 'With
Control');
xlabel('Time (days)');
ylabel('Infected Asymptomatic');
title('Infected Asymptomatic Population for C-M 3');
legend;

% Plot for Recovered population (R)
subplot(3, 2, 4);
plot(t_without_3, y_without_3(:, 4), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on;
```

```
plot(t_with_3, y_with_3(:, 4), 'r--','LineWidth', 2, 'DisplayName', 'With
Control');
xlabel('Time (days)');
ylabel('Recovered');
title('Recovered Population for C-M 3');
legend;

% Plot for Bacteria concentration (B)
subplot(3, 2, 5);
plot(t_without_3, y_without_3(:, 5), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on;
plot(t_with_3, y_with_3(:, 5), 'r--','LineWidth', 2, 'DisplayName', 'With
Control');
xlabel('Time (days)');
ylabel('Bacteria Concentration');
title('Bacteria Concentration for C-M 3');
legend;

% Plot for Deaths (D)
subplot(3, 2, 6);
plot(t_without_3, y_without_3(:, 6), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on;
plot(t_with_3, y_with_3(:, 6), 'r--','LineWidth', 2, 'DisplayName', 'With
Control');
xlabel('Time (days)');
ylabel('Deaths');
title('Deaths for C-M 3');
legend;


% Control Mechanism 4; washing hands after defecation and after meals.
u4 = 0.5;% Control mechanism effectiveness
u5 = 0.5;
beta_s_hands = beta_s * (1 - u4);
beta_a_hands = beta_a * (1 - u4);
gamma_a_hands = gamma_a * (1 - u5);
gamma_s_hands = gamma_s * (1 - u5);

% ODE system for model with second control mechanism
ode_with_control_4 = @(t, y) [
    alpha * N - p * (beta_s_hands * y(1) * y(4)) / (kappa + y(4)) - (1-p) *
(beta_a_hands * y(1) * y(4)) / (kappa + y(4)) - mu * y(1);  % dS/dt
    p * (beta_s_hands * y(1) * y(4)) / (kappa + y(4)) - (gamma_s_hands + mu)
* y(2);                                                  % dI_s/dt
    (1 - p) * (beta_a_hands * y(1) * y(4)) / (kappa + y(4)) - (gamma_a_hands
+ mu) * y(3);                                             % dI_a/dt
    gamma_s_hands * y(2) + gamma_a_hands * y(3) - mu * y(4);
% dR/dt
    xi_s * y(2) + xi_a * y(3) - delta * y(5);
% dB/dt
    mu_s * y(2) + mu_a * y(3);
% dD/dt
];
```

```
% Solve ODEs for both cases
[t_without_4, y_without_4] = ode45(ode, tspan, y0); % Without control
[t_with_4, y_with_4] = ode45(ode_with_control_4, tspan, y0);      % With
control (food hygiene)

figure;
% Plot for Susceptible population (S)
subplot(3, 2, 1);
plot(t_without_4, y_without_4(:, 1), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on;
plot(t_with_4, y_with_4(:, 1), 'r--','LineWidth', 2, 'DisplayName', 'With
Control');
xlabel('Time (days)');
ylabel('Susceptible');
title('Susceptible Population for C-M 4');
legend;

% Plot for Infected Symptomatic population (I)
subplot(3, 2, 2);
plot(t_without_4, y_without_4(:, 2), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on;
plot(t_with_4, y_with_4(:, 2), 'r--','LineWidth', 2, 'DisplayName', 'With
Control');
xlabel('Time (days)');
ylabel('Infected Symptomatic');
title('Infected Symptomatic Population for C-M 4');
legend;

% Plot for Infected Asymptomatic population (A)
subplot(3, 2, 3);
plot(t_without_4, y_without_4(:, 3), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on;
plot(t_with_4, y_with_4(:, 3), 'r--','LineWidth', 2, 'DisplayName', 'With
Control');
xlabel('Time (days)');
ylabel('Infected Asymptomatic');
title('Infected Asymptomatic Population for C-M 4');
legend;

% Plot for Recovered population (R)
subplot(3, 2, 4);
plot(t_without_4, y_without_4(:, 4), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on;
plot(t_with_4, y_with_4(:, 4), 'r--','LineWidth', 2, 'DisplayName', 'With
Control');
xlabel('Time (days)');
ylabel('Recovered');
title('Recovered Population for C-M 4');
```

```
legend;

% Plot for Bacteria concentration (B)
subplot(3, 2, 5);
plot(t_without_4, y_without_4(:, 5), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on;
plot(t_with_4, y_with_4(:, 5), 'r--','LineWidth', 2, 'DisplayName', 'With
Control');
xlabel('Time (days)');
ylabel('Bacteria Concentration');
title('Bacteria Concentration for C-M 4');
legend;

% Plot for Deaths (D)
subplot(3, 2, 6);
plot(t_without_4, y_without_4(:, 6), 'b-','LineWidth', 2, 'DisplayName',
'Without Control');
hold on;
plot(t_with_4, y_with_4(:, 6), 'r--','LineWidth', 2, 'DisplayName', 'With
Control');
xlabel('Time (days)');
ylabel('Deaths');
title('Deaths for C-M 4');
legend;
```