Examining Treatment Strategies for Cholera Incorporating Spatial Dynamics

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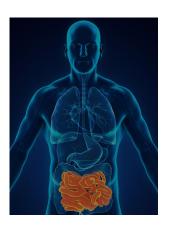
Introduction

• Treatments have not always gone as planned in history

Cholera

Some Biology on Cholera

- Vibrio cholerae
- Colonize small intestines
- 10 percent of infected develop symptoms
- Causes dehydration



Outbreaks in London (19^{th} Century)

- 1832, 1849, 1854, 1866
- Miasma Theory
- John Snow



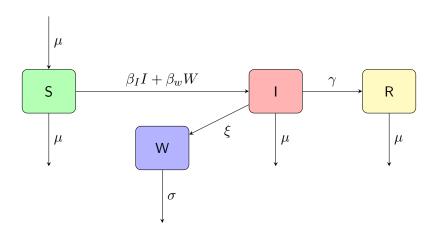
Developing a Single-Patch Model

- Entire population (N) included
- 3 Compartments : S, I, R
- Compartment values are proportional
- Environment (Water)

SIRW Model Assumptions

- Birth Rate = Natural Death Rate and is constant
- Homogenous susceptibility to cholera across population
- No waning immunity
- No latency period
- Only infected individuals can infect the water sources
- Water source is still

SIRW Model



R_0 Calculation

 Using the method of Next Generation Matrix (van den Driessche and Watmough, 2002)

$$F = \begin{pmatrix} \beta_i & \beta_w \\ 0 & 0 \end{pmatrix}$$
$$V = \begin{pmatrix} \frac{1}{\gamma + \mu} & 0 \\ \frac{1}{\gamma + \mu} & \frac{1}{\sigma} \end{pmatrix}$$

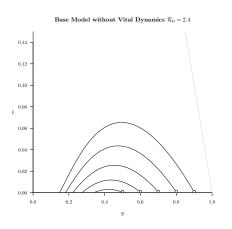
• R_0 is computed as the spectral radius of FV^{-1} :

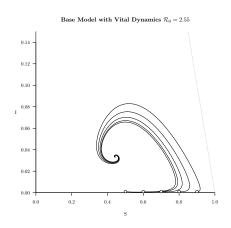
$$\mathcal{R}_0 = \rho(FV^{-1})$$
$$= \frac{\beta_i + \beta_w}{\gamma + \mu}$$

Equilibria and Stability

- Two equilibria:
 - **①** DFE: (S, I, R) = (1, 0, 0)
 - **2** EE: $(s^*, i^*, r^*) = (\frac{1}{R_0}, \frac{\mu}{\gamma + \mu}(1 s^*), i^*)$
- ullet The DFE is stable when $\mathcal{R}_0 < 1$
- The EE is stable when $\mathcal{R}_0 > 1$

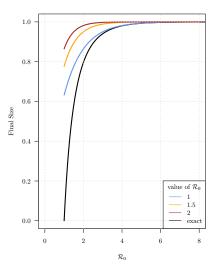
SIWR Model Phase Portrait





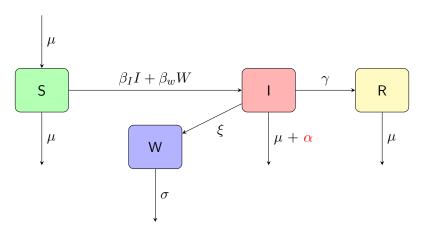
Final Size

- Assuming $\mu = 0$ and $\mathcal{R}_0 > 1$, final size formula still holds:
- $Z = 1 e^{-\mathcal{R}_0 Z}$

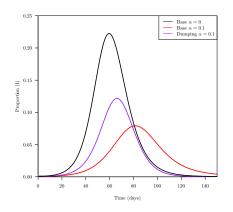


Effects of the 19th Century Treatments

• Added parameter death caused by cholera (α)



Effects of the 19th Century Treatments



- Estimated death rate of cholera in the 19th century ranges from a small percentage up to fifty percent
- Including disease induced death is "beneficial" if death rate by cholera is high (Why?)
- Improper sanitation increases peak prevalence

Multi-Patch Model

$$\frac{dS_i}{dt} = \mu N - \mu S_i - \beta_i S_i I_i - \phi \beta_i S_i \sum_{j=1}^{n} I_j - \beta_w S_i W_i - \psi \beta_w S_i \sum_{j=1}^{n} W_j$$

$$\frac{dI_i}{dt} = \beta_i S_i I_i + \beta_i \phi S_i \sum_{j=1}^n I_j + \beta_w S_i W_i + \beta_i \psi S_i \sum_{j=1}^n W_j - I_i (\gamma + \mu + \alpha)$$

$$\frac{dR_i}{dt} = \gamma I_i - \mu R_i$$

$$\frac{dW_i}{dt} = \xi I_i + \beta_i \psi I_i \sum_{j=1}^{n} W_j - \sigma W_i$$



Multi-Patch Model Assumptions

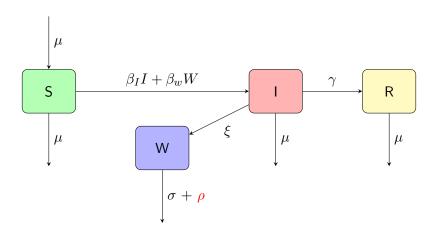
- No dispersal of individuals
- Infected individuals can infect the susceptible in neighboring patches
- All patches neighbouring i have the same transmission rate to patch i

Multi-Patch Model Simulation

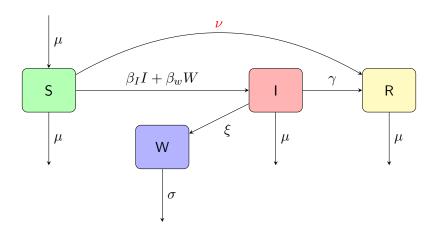
Treatment Strategies For Cholera

- Sanitation of Water
- Vaccinations
- Antibiotics

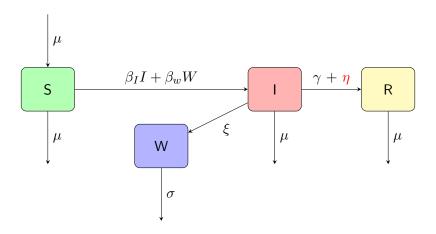
Sanitation of Water



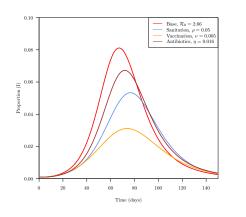
Vaccinations



Antibiotics



Comparing the Treatment Strategies









Comparing the Treatment Strategies

Conclusions and Further Research

- 19th century outbreaks
- Significance of the using multi-patch model
- Our treatment simulations suggest. . .
- Further research on the spread of water borne diseases like cholera can be done in areas like. . .

Thank you!

References I

Paneth N, Vinten-Johansen P, Brody H, Rip M.

A rivalry of foulness: official and unofficial investigations of the London cholera epidemic of 1854.

Am J Public Health. 1998;88(10):1545–1553.

Chao DL, Longini IM, Morris JG.

Modeling cholera outbreaks.

Curr Top Microbiol Immunol. 2014;379:195–209.

Tien JH, Poinar HN, Fisman DN, Earn DJ.

Herald waves of cholera in nineteenth century London.

J R Soc Interface. 2011;8(58):756-760.

Tuite AR, Tien J, Eisenberg M, Earn DJ, Ma J, Fisman DN.

Cholera epidemic in Haiti, 2010: using a transmission model to explain spatial spread of disease and identify optimal control interventions.

Ann Intern Med. 2011;154(9):593-601.

References II

Grad YH, Miller JC, Lipsitch M.

Cholera modeling: challenges to quantitative analysis and predicting the impact of interventions.

Epidemiology. 2012;23(4):523-530.

Wilford JN.

How epidemics helped shape the modern metropolis.

Epidemiology. 2008;.

Sciarra C, Rinaldo A, Laio F, Pasetto D.

Mathematical modeling of cholera epidemics in South Sudan.

arXiv e-prints. 2018;.

Codeco CT.

Endemic and epidemic dynamics of cholera: the role of the aquatic reservoir.

BMC Infect Dis. 2001;1:1.

References III

Tien JH, Earn DJ.

Multiple transmission pathways and disease dynamics in a waterborne pathogen model.

Bull Math Biol. 2010;72(6):1506-1533.

van den Driessche P.

In: Brauer F, van den Driessche P, Wu J, editors. Spatial Structure: Patch Models. Berlin, Heidelberg: Springer Berlin Heidelberg; 2008. p. 179–189.

Kaper JB, Morris JG, Levine MM.

Cholera.

Clinical Microbiology Reviews. 1995;8(1):48–86.

Li P. cholera: Amend, Augment and Aid Analysis of John Snow's Cholera Map; 2019.

References IV

Lee EC, Kelly MR, Ochocki BM, Akinwumi SM, Hamre KES, Tien JH, et al.

Model distinguishability and inference robustness in mechanisms of cholera transmission and loss of immunity.

J Theor Biol. 2017;420:68-81.

Azman AS, Rudolph KE, Cummings DA, Lessler J.

The incubation period of cholera: a systematic review.

J Infect. 2013;66(5):432-438.

Kong JD, Davis W, Wang H.

Dynamics of a cholera transmission model with immunological threshold and natural phage control in reservoir.

Bull Math Biol. 2014;76(8):2025-2051.

References V

Luo J, Wang J, Wang H.

Seasonal forcing and exponential threshold incidence in cholera dynamics.

Discrete and Continuous Dynamical Systems. 2017;22(6):2261–2290.

Riley S, Eames K, Isham V, Mollison D, Trapman P.

Five challenges for spatial epidemic models.

Epidemics. 2015;10:68-71.

WHO. Cholera; 2019.

Available from:

https://www.who.int/news-room/fact-sheets/detail/cholera.

Moe CL, Rheingans RD.

Global challenges in water, sanitation and health.

J Water Health. 2006;4 Suppl 1:41-57.

References VI

Earn DJ, Andrews PW, Bolker BM.

Population-level effects of suppressing fever.

Proc Biol Sci. 2014 Mar;281(1778):20132570.

Mukerjee S.

Preliminary studies on the development of a live oral vaccine for anti-cholera immunization.

Bull World Health Organ. 1963;29(6):753-766.

Graves PM, Deeks JJ, Demicheli V, Jefferson T.

Vaccines for preventing cholera: killed whole cell or other subunit vaccines (injected).

Chochrane Database Syst Rev. 2010;.

Nelson EJ, Nelson DS, Salam MA, Sack DA.

Antibiotics for both moderate and severe cholera.

N Engl J Med. 2011;364:5-7.

References VII

Saha D, Karim MM, Khan WA, Ahmed S.

Single-dose azithromycin for the treatment of cholera in adults.

N Engl J Med. 2006;364:2452-2462.

Fung IC, Fitter DL, Borse RH, Meltzer MI, Tappero JW.

Modelling the effect of water, sanitation, and hygiene and oral cholera vaccine implementation in Haiti.

Am J Trop Med Hyg. 2013;89(4):633-640.

Taylor DL, Kahawita TM, Cairncross S, Ensink JHJ.

The Impact of Water, Sanitation and Hygiene Interventions to Control Cholera: A Systematic Review.

PLoS ONE. 2015;10(8).