Research Proposal

Ziyabukwa Mthi (24863831@sun.ac.za)

July 19, 2022

Introduction

Measles is one of Vaccine-Preventable Diseases (VPDs) that can cause serious disease and complications of disease. Measles is a highly contagious aerial viral infection.Measles is an infection that causes fever, rash, cough, and redness of the eyes. It causes serious complications like encephalitis and can even lead to deafness[1]. Transmission occurs through direct contact with infectious droplets or by airborne spread when an infected person breathes, coughs, or sneezes[2]. About 90% of exposed susceptible individuals have measles. Clinically, the incubation period from exposure to an early symptom indicating the onset of a disease averages 10-12 and 14 days from exposure to the rash. The serious complications caused by measles can occur approximately 30% of measles cases, especially children under 5 years of age or adults [3].

Prior to the development of the measles vaccine in the 1960s, measles was a major cause of morbidity and mortality [4]. Childhood measles infections have become practically universal since the development of safe and effective vaccines in 1963, killing an estimated every year, 2.6 million people are affected. [5]. Despite the availability of vaccines, measles continues to be the leading cause of death in children under the age of five [6]. Measles outbreaks are still occurring in countries where vaccination coverage is low [7]. According to the WHO, global efforts to increase vaccination coverage lowered deaths by 73% in 2018, with Africa accounting for the majority of deaths saved. In 2012, WHO updated the Measles Eradication Initiative with the goal of eradicating measles in at least five of the six regions of the world by 2020 [8].Measles elimination is defined by the World Health Organization as the absence of indigenous measles cases in a certain area for up to 12 months in the presence of high-quality surveillance systems. WHO also requires a national measles vaccination rate of 95% in all districts with two vaccinations per child. Within a year, at least 80% of districts should examine at least one suspicious case and report a nationwide non-measles case rate of at least 2 cases per 100,000 people. [9].

Vaccination is the most effective way to avoid measles. Single-dose measles vaccine became available in South Africa in 1975 as part of the Expanded Programme on Immunization (EPI). Single dose vaccination against measles was started in South Africa in 1975 as part of the Expanded Program on Immunization (EPI). Then, in 1995, a two-dose strategy was introduced in 9 and 18 months, with additional vaccination campaigns every 3-4 years. The two vaccination schedules for measles were altered to 6 months and 12 months in 2016. The first dose at 6 months is intended to prevent the high morbidity and mortality associated with infant illness [10-12]. To prevent the outbreak of measles, the immunity rate of the population is estimated to be about 95% [13]. In 2016, the World Health Organization (WHO) found that only 85% of children worldwide received the first dose of measles vaccine through regular medical services by the first birthday, and 64% received the second dose [14]..

World Health Organization (WHO) strongly encouraged the usage of MMR vaccines to get rid of measles virus with inside the nations enforcing large-scale immunization program[15]. The National Institute Communicable Diseases recommends that all children be vaccinated twice with the MMR (Measles and Mumps Rubella) vaccine. The first vaccination is 12 to 15 months and the second vaccination is 4 to 6 years old. Children can receive a second dose earlier if at least 28 days have passed since the first dose [22].

One of the most important contributors to population heterogeneity is age distribution, which has a significant impact on the timing and outcome of infectious illness transmission and spread. Most crucially, there is a considerable degree of non-uniformity in transmission rates due to the patterns and frequency of individual encounters, which can range dramatically between age groups. Age-related differences in immunity to infections are another possibility. Age-specific mortality and infection-related recovery may be impacted by these variations. Understanding the complexity of disease dynamics and implementing effective disease control and prevention depend on modeling the effect of population age composition on the spread of infectious diseases.

The age structure of epidemiological models has been studied in the literature using both discrete and continuous approaches. Discrete age Ordinary Differential Equation (ODE) Model [23, 24, 25]. The mathematical frameworks of ODE models are relatively simple due to their finite dimensional involving properties unaltered space, but the challenge in their theoretical analysis lies in the high dimensionality and scale of the ODE system, which is not possible. Establishing global dynamics for trendy models of age structure.

Consider a linking system of nonlinear differential equations on a transmission network as a disease model with a discrete age structure. Each age group in this situation can be thought of as a node, and inter-group transfers determine the connections between the nodes and the aging process.

In this paper, we present discrete age structured SVEIR epidemic model with application to measles vaccination strategy. Vaccines are the most effective way to prevent infectious diseases. The measles vaccine, which is commonly administered to babies as part of the measles-mumps-rubella (MMR) vaccination, is one of the most widely used and effective vaccines. The effectiveness of a single dose of the measles vaccination administered to babies at 6 months of age ranges from 85% to 93% . And the second dose is administered at 12 months [16]. The effectiveness of two doses of measles vaccine is 93-99% . In addition to regular vaccinations, South Africa has supplementary vaccination activities every 3-4 years. These are usually vaccination campaigns for all children under the age of five. These objectives are to immunize children who may have missed the measles vaccine and increase the effectiveness of the vaccine [26].

The World Health Organization (WHO) estimates that millions of measles cases occur in developing countries each year, primarily due to measles, even with regular immune programs [27], mainly due to the vaccination rate is too low. A discrete age structure model was fitted to analyze measles data from South Africa. Investigating the impact of current vaccination programs in South Africa The incidence of measles is the highest in the world.

Mathematical Model

An application to vaccination strategies for measles

Measles is a disease that can be prevented with a vaccine. When given as part of the measles, mumps, rubella (MMR) vaccine, the measles vaccine usually needs to be given twice. The measles vaccine (MMR1) is normally administered to infants 12 to 15 months of age. It is effective for 85% to 93% of infants at this age. A second dose (MMR2) should be given before the child starts school. Efficacy with 2 doses can reach 97% of MMR [16,17]. World Health Organization recommends that children between 15 and 18 months of age or at admission receive MMR2 for high immunity, either to prevent measles or as a part of admission for better immunity. [18].

In this section, we develop a two-dose vaccination version with two age corporations to observe the vaccination strategies for measles epidemics.

Measles vaccination model

Measles can be prevented with the MMR vaccine. The CDC recommends that children receive the MMR vaccine twice. The first dose is 6 months old and the second dose is 12 months old [19]. One dose of MMR vaccine is 93% effective against measles while two doses of MMR vaccine are 97% effective against measles. A small number of vaccinated individuals can get measles, but the disease is milder than unvaccinated individuals [20].

Subdivide the host population into two age groups, taking into account age-specific differences in vaccination schedules, case fatality rates, and contact patterns.

The model structure is shown in the transmission diagram in Figure 1. Two doses of measles vaccine were incorporated: MMR1 for age group 1 (12-15 months), MMR2 for age group 2 (4-6 years). The model is described by the following system of differential equations.

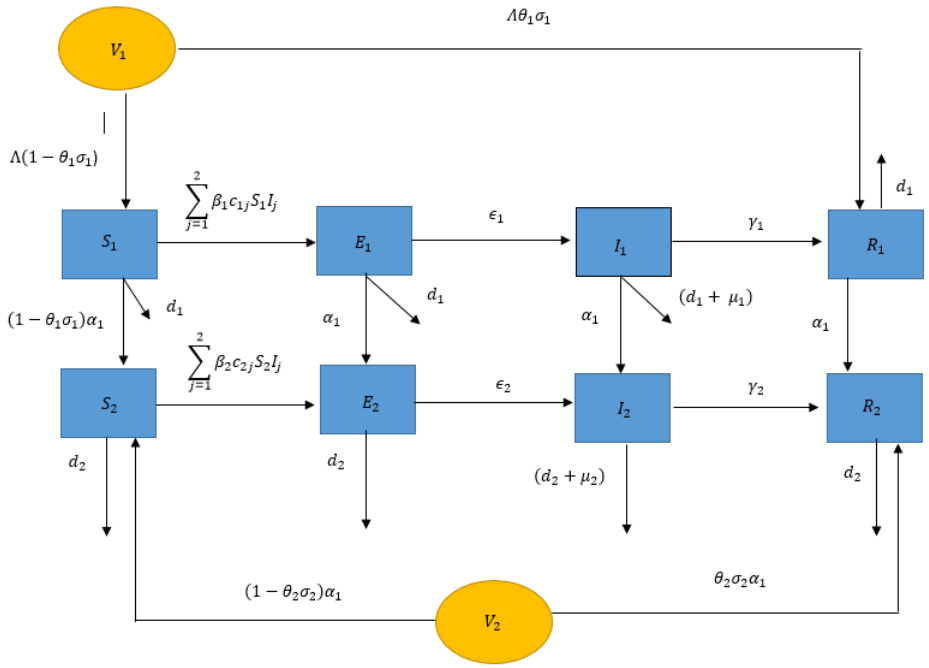

Figure 1: Transfer diagram for a vaccination model with two age groups.

Differential equations for age group 1:

$$\frac{dS_1}{dt} = \Lambda(1-\theta_1\sigma_1)V_1 - \sum_{j=1}^{2}\beta_1 c_{1J} S_1 I_J - (1-\theta_1\sigma_1)\alpha_1 S_1 - d_1 S_1$$
$$\frac{dV_1}{dt} = -(\Lambda(1-\theta_1\sigma_1) + \Lambda\theta_1\sigma_1)V_1$$
$$\frac{dE_1}{dt} = \sum_{j=1}^{2}\beta_1 c_{1J} S_1 I_J - (\alpha_1 + d_1 + \epsilon_1)E_1$$
$$\frac{dI_1}{dt} = \epsilon_1 E_1 - (\alpha_1 + \gamma_1)I_1 + (d_1 + \mu_1)I_1$$
$$\frac{dR_1}{dt} = \gamma_1 I_1 + \Lambda\theta_1\sigma_1 V_1 - d_1 R_1$$

Differential equations for age group 2:

$$\frac{dS_2}{dt} = (1-\theta_2\sigma_2)\alpha_1 V_2 + (1-\theta_1\sigma_1)\alpha_1 S_1 - \sum_{j=1}^{2}\beta_2 c_2 J S_2 I_J - d_2 S_2$$
$$\frac{dV_2}{dt} = -((1-\theta_2\sigma_2)\alpha_1 + \theta_2\sigma_2\alpha_1)V_2$$
$$\frac{dE_2}{dt} = \sum_{j=1}^{2}\beta_2 c_2 J S_2 I_J + \alpha_1 E_1 - (d_2 + \epsilon_2)E_2$$
$$\frac{dI_2}{dt} = \epsilon_1 E_2 + \alpha_1 I_1 - \gamma_2 I_2 + (d_2 + \mu_2)I_2$$
$$\frac{dR_2}{dt} = \gamma_2 I_2 + \theta_2\sigma_2\alpha_1 V_2 - \alpha_1 R_1 - d_2 R_2$$

The model parameters are shown in Table 1 along with their description and parameters. Specifically, θ_1 and θ_2 are the vaccination rates of MMR1 and MMR2, respectively, σ_1 and σ_2 are the effects of MMR1 and MMR2, respectively, and $\theta_1\sigma_1$ and $\theta_1\sigma_1$ are the effective ranges of MMR1 and MMR2, respectively.

The transmission coefficient β_{kj} between S_k and I_j is decomposed into two factors $\beta_{kj} = c_{kj}$ where β_k k is the probability of transmission for an average contact between a susceptible individual in age group k S_k, and c_{kj} is the mean. Number of contacts between people in age group and people in age group k.Note that c_{kj} and c_{jk} are not the same and the contact matrix (c_{jj}) may not be symmetric because of different ages.

Influx susceptible individuals are recruited by the rate of Λ_k. Exposed individuals move to the infectious class at a rate of a age group of ϵ_kİnfectious individuals move to the recovered compartment at a rate of a age group of γ_k. Individuals are aging at a rate α_k. Natural fatality rate of a age group is represented by $\dot{k}$, while case fatality of a age group is represented by a rate of μ_k.

Table 1: Parameters and their estimated values for model

Parameters	Values/Range	Unit	Description	Reference
Λ_k	650	10^3/week	Influx of susceptible	
d_k		week^{-1}	Natural mortality rate of age group k	
α_k		week^{-1}	Aging rate of age group k	
γ_k		week^{-1}	Recovery rate of age group k	
ϵ_k		week^{-1}	Exposed rate of age group	
μ_k			Case fatality rate of age group k	
θ_k			Immunization rate of Measles vaccine	
σ_1			Efficacy of MCV1	
σ_2			Efficacy of MCV2	
β_1			Probability of transmission per contact for age group 1	
β_2			Probability of transmission per contact for age group 2	
c_{kj}		week^{-1}	Average number of contacts from age group j to age group k	

Immune profile analysis

A scale model is used to build an immune profile of measles in the general population and of different age groups. It is based on South Africa current measles vaccination policy: single dose (MCV1) for children of the first age group (4 years and younger). Second dose (MCV2) for children (5-9 years) in the second age group (5-9 years) from 2000 to 2010 and after 2010.

Effect of increasing measles vaccination coverage

References

1. https://my.clevelandclinic.org/health/diseases/8584-measles
2. Battegay, R., Itin, C. and Itin, P., 2012. Dermatological signs and symptoms of measles: a prospective case series and comparison with the literature. Dermatology, 224(1), pp.1-4.
3. Centers for Disease Control and Prevention. Measles. Epidemiology and Prevention of Vaccine-Preventable Diseases. Hamborsky J, Kroger A, Wolfe S, eds. 13th ed. Washington D.C. Public Health Foundation, 2015.
4. Moss, W.J., Cutts, F. and Griffin, D.E., 1999. Implications of the human immunodeficiency virus epidemic for control and eradication of measles. Clinical Infectious Diseases, 29(1), pp.106-112.
5. WHO Measles: Fact sheet, Reviewed January 2018. Available from: http://www.who.int/mediacentre/factsheets/fs286/en/
6. Hayman, B. and Pagliusi, S., 2020. Emerging vaccine manufacturers are innovating for the next decade. Vaccine: X, 5, p.100066.
7. World Health Organization, 2019. More than 140,000 die from measles as cases surge worldwide. World Health Organization, Geneva, Switzerland.
8. World Health Organization, 2012. Global measles and rubella strategic plan: 2012.
9. Masresha, B., Luce, R., Shibeshi, M., Katsande, R., Fall, A., Okeibunor, J., Weldegebriel, G. and Mihigo, R., 2018. Status of measles elimination in eleven countries with high routine immunisation coverage in the WHO African region. Journal of immunological sciences, p.140.
10. Hong, H., Makhathini, L., Mashele, M., Malfeld, S., Motsamai, T., Sikhosana, L., Manamela, J., Ntshoe, G., Motaze, N.V., Smit, S. and Maseti, E., 2017. Annual measles and rubella surveillance review, South Africa, 2017. Natl Inst Commun Dis Public Heal Surveill Bull, 16(2), pp.64-77.
11. Panagiotopoulis T, Antoniadou I, Valassi-Adam E. Increase in congenital rubella occurrence after immunization in Greece: Retrospective survey and systematic review. BMJ 1999; 319:1462-1467
12. Boshoff L Tooke L. Congenital rubella - is it nearly time to take action? South African Journal of Child Health, 2012; 6: 106-108.
13. Moss WJ and Griffin DE. Measles. Lancet 2012; 379:153-164
14. Joint WHO/UNICEF 2016 Country and regional immunization coverage data. Available from: http://www.who.int/entity/immunization/monitoring_surveillance/data/en/index.html
15. World Health Organization, Weekly Epidemiological Record, (2007), 49 â 60.
16. U.S. CDC, Measles vaccination,https://www.cdc.gov/measles/vaccination.html (accessed on April 16, 2017).
17. U.S. CDC, Recommended immunization schedules for persons aged 0 through 18 years, http://www.cdc.gov/vaccines/schedules/downloads/child/0-18yrs-childcombined-schedule.pdf (accessed on April 16, 2017).
18. W.H. Organization, A guide to introducing a second dose of measles vaccine into routine immunization schedules, 2013,http://apps.who.int/iris/bitstream/10665/85900/1/WHO_IVB_13.03_eng.pdf (accessed on April 16, 2017)
19. https://www.cdc.gov/vaccines/vpd/measles/index.html#:~:text=Measles%20can%20be%20prevented%20with,through%206%20years%20of%20age.
20. National Institute Communicable Diseases, VACCINE INFORMATION FOR PARENTS AND CAREGIVERS, 2016, https://www.nicd.ac.za/assets/files/NICD_Vaccine_Booklet_D132_FINAL.pdf

21. R.M. Anderson, R.M. May, Immunisation and herd immunity, Lancet 335 (1990) 641â645.

22. National Institute Communicable Diseases, VACCINE INFORMATION FOR PARENTS AND CAREGIVERS, 2016, https://www.nicd.ac.za/assets/files/NICD_Vaccine_Booklet_D132_FINAL.pdf

23. M. Martcheva. An Introduction to Mathematical Epidemiology, Springer, New York (2015)

24. R.M. Anderson and R.M. May Infectious Diseases of Humans: Dynamics and Control, Oxford University Press (1992)

25. Diekmann, O. and Heesterbeek, J.A.P., 2000. Mathematical epidemiology of infectious diseases: model building, analysis and interpretation (Vol. 5). John Wiley Sons.

26. National Institute Communicable Diseases. OUTBREAK RESPONSE UNIT, DIVISION OF PUBLIC HEALTH SURVEILLANCE AND RESPONSE; CENTRE FOR VACCINE AND IMMUNOLOGY. 2002. https://www.nicd.ac.za/wp-content/uploads/2022/06/Measles-Vaccine-FAQ-_20220608.pdf

27. W.H. Organization, Measles fact sheet, march 2017, http://www.who.int/mediacentre/factsheets/fs286/en/(accessedonApril16,2017).

28.

29.

30.

31.

32.

33.

34.

35.