Mathematical Analysis of the Transmission Dynamics of Measles with a Two-Dose Vaccination and Quarantine

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Abstract
Measles is an infectious disease that results from a paramyxovirus. Known to be highly contagious, it can be transmitted through contact with an infected person. It is a viral respiratory infection that attacks the immune system of an infected person. In this research, a dual model for the elimination of measles with some control strategies was proposed. The first model was with quarantine, while the second model was developed and analyzed with first and second stages of measles vaccination. Sensitivity analysis as well as the numerical simulation of both models were carried out. The study determined the disease free equilibrium (DFE) point and the endemic equilibrium (EE) point from the system of the equations. Appropriate model reproduction numbers were computed and interpreted. Numerical simulations showed that two-stage vaccination fot the disease was able to inhibit the disease spread. Concerning the Reproduction number R_m^e, it was confirmed that when $R_m^e > 1$, the disease will persist, and that when $R_m^e = 1$, this indicates a threshold between the extinction and the persistence of the disease. It was also established that effective treatment plan, red rash identification rate, effective cost factoring and active mechanism for case finding were parameters that positively impacted the burden of measles infection, and had the potentials to reduce the prevalence of this disease in a population, irrespective of the values assumed by other parameters contributing to R_m.

Keywords: Measles, red rash identification, quarantine, vaccination, reproduction number.

1. Introduction

Measles is a viral respiratory infection that attacks an immune system and anybody not immuned to it will likely be infected when exposed. In children, this infection has been known to result in blindness, deafness or impaired vision [1]. After recovery from the disease, it confers permanent immunity from further attacks. Measles is generally known for an incubation period of between 8 to 12 days closely followed by symtons of kopliks spots, fever, coryza, conjunctivitis and cough. This incubation period occurs before the appearance of red rash. After this period, the symptoms are then followed by the presence of red rash that starts from the face, then spreads to the neck and other parts of the body [2,3,4]. Children within five years bracket in age are mostly at risk, and it is estimated that measles are contracted by about 30 to 40 million children each year with a mortality exceeding one million, and often with complications like pneumonia, diarrhoea and malnutrition [2]. In order to prevent measles, it has been recommended by health institutions that children should be vaccinated against measles. Vaccines for measles on children and

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adults include MMR (Mumps, Measles and Rubella) vaccines. It has been asserted that one dose of MMR vaccine is 93% effective against measles and that two doses of same is 97% protective against measles [4]. Another effective way of controlling measles is the use of quarantine. Quarantine helps to reduce the transmission of the infection such that infected individuals do not come in contact with susceptible individuals.

Standard mathematical distributions and models have been enhanced with flexibility and adapted to analyze the outcomes of intervention programmes on the dynamics of several infectious diseases. From probability theory to applied statistics, models have been used extensively to optimize human efforts. For instance, a generalized generating function was developed and used to generate the moments of the attributes of a population distribution in [5], while [6] developed a general method via moment generating functions for obtaining moments of random variables with both integer and fractional powers. In epidemiological studies of populations, [7] used a numerical collocation approach to analyse a four-compartmental disease transmission model, while [8] developed a model to consider the dynamics of COVID-19 in Ghana and to consider the impact of testing and quarantining of immigrants, contact tracing and isolation as measures in the mitigation of the spread of the disease. In an applied study, [9] developed a lifetime hybrid probability distribution with established survival and hazard rate functions and applied the hybrid distribution to estimate recovery rates and mortality rates arising from the Covid-19 pandemic in Nigeria. Along the same line, a time series model was employed to analyse infant mortality rates in some regions of Nigeria [10]. All these are instances of applications of mathematical models in explaining population related issues, just like [11] who developed a mathematical Model for the dynamical control of Malaria fever in Nigeria, and [12] who investigated how community lockdown and social distancing protocols could impact the spread of Covid-19 disease. In [13] a compartmentalized epidemiological model was used to explain the dynamics of poverty, cybercrime and prostitution. while [14] investigated the relationship between model assumption violation and regressional multi-collinearity, and used illustrations to show the role of variance inflation factor (VIF) in detecting model violations.The concurrent study of population growth is essential for any nation due to the effect it can have on the country's planning and budget allocation for health exigencies such as disease outbreak and control strategies. Many countries rely on periodic censuses to get this important data, but the process is oftentimes, very costly, involving a lot of people and technologies [15].

With particular emphasis on Measles, mathematical models have been useful in planning, proposing, implementing and comparing various control strategies. A Study [1] proposed an SEIR model that investigated the impact of exposed class of individuals at latent periods on the transmission dynamics of measles and discussed the modeling impact of vaccines on the rate of spread of measles. Another study [16] formulated a four-compartment mathematical model for spread of measles that accommodates two-step of vaccination and quarantine. Findings show that receiving two steps of vaccine can reduce measles transmission much better rather than only one step vaccination. Similarly, [17] developed a model that simulated the dynamics of measles transmission, using an SEIR model to discuss the infection and to address the stability of the disease free and endemic equilibriums. Also, a mathematical model [18] was proposed for measles dynamics under vaccination and two-stage infectiousness. The study adopted the SIR approach and showed that disease extinction is possible if all susceptible individuals were vaccinated. It noted that while achieving a 100% vaccination coverage may be impracticable, a coverage of at least 94% vaccination might just be enough. Another study is [19] which centred on assessing the impact of vaccination protocols on the transmission dynamics of measles.

It is obvious from literature that a lot has been done in the field of mathematical moedels for measles transmission. However, this research proposes a dual model for the elimination of measles with some control strategies. This paper developed and analyzed the first model with quarantine, while the second model was developed and analyzed with first stage and second stage of measles vaccination.

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Sensitivity analysis and numerical simulations for both models were evaluated.

1.1 Basic Model Assumptions

The total population at time t, denoted by N(t) is divided into the following epidemiological compartments: susceptible class, S(t); individuals exposed to measles (E(t)); individuals already infected with measles, I(t); recovered individuals with permanent immunity, R(E); and the quarantined individuals, Q(t); so that

$$N(t) = S(t) + E(t) + I(t) + R(t) + Q(t) \quad (1)$$

It is assumed that rate of recruitment of susceptible persons is □ (a constant), as well as individuals that are born at a rate π. Susceptible individuals become exposed to measles infection at rate ʎ following effective contact with infected persons.

Hence, the force of infection is given by

$$\lambda = \frac{BaI}{N} \quad (2)$$

where B represents the transmission probability of an infected individual becoming infectious, and 'a' is the marginal contact rate.

Exposed individuals upon developing clinical signs and symptoms move to the infectious class at a rate Ɛ. We assume that individuals in the exposed class cannot be moved the quarantined class since, they are still in their asymptomatic state. Infectious individuals upon display of clinical signs and symptoms are moved to the quarantined class at a rate $p = \alpha + v\sigma$ (where α accounts for active case finding rate, v accounts for cost factor and σ red rash identification rate).

Individuals in infectious class recover at a rate r_2. All human compartments suffer from natural death at a rate $\varkappa$**, and** disease induced death at a rate δ.

Table 1: Variables and Parameters for the models

Variables / parameters	Description
S(t)	Individuals susceptible to measles
E(t)	Class of persons exposed to measles
I(t)	Class of persons infected with measles
R(t)	Class of persons who have recovered from measles
Q(t)	Quarantined individuals
$V_1(t)$	Class of persons who took the first stage of vaccine
$V_2(t)$	Class of persons who took the second stage of vaccine
B	Probability of an infected person becoming infectious
A	Marginal contact rate
E	Rate of asymptomatic persons becoming symptomatic
A	Active case finding rate
V	Cost factor
Σ	Red rash identification rate
r_1	Rate of recovery from measles by infectious individuals
r_2	Rate of recovery from measles by quarantined individuals
Q	Rate of administering first stage of vaccine to recruited individuals
Θ	Rate of administering first stage of vaccine to newborns
P	Fraction of persons who receive the second stage of vaccine
Ø	Rate of receiving first dose of vaccine
C	Waning rate of first dose of vaccine
K	Rate of receiving second stage vaccine
Δ	Disease induced death rate
$\varkappa$	Natural death rate
Λ	Recruitment rate of individuals
Π	Birth rate of newborns

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On the basis of the above assumptions, we have the following deterministic set of non-linear differential equations.

$$\frac{ds}{dt} = \pi + \Lambda - (\lambda + \varkappa)s$$
$$\frac{dE}{dt} = \lambda s - (\varepsilon + \varkappa)E$$
$$\frac{dI}{dt} = \varepsilon E - (\alpha + v\sigma + r_1 + \varkappa + \delta_1)I \quad (3)$$
$$\frac{dQ}{dt} = (\alpha + v\sigma)I - (r_2 + \varkappa + \delta_2)Q$$
$$\frac{dR}{dt} = r_1 I + r_2 Q - \varkappa_n R$$

1.2 Demographic Parameters

This section provides the Nigeria demographic data that was employed for the numerical simulations. The Nigerian average lifespan $(1/\varkappa)$ was assumed to be 80 years [20]. Thus $\varkappa$ = 0.02041. The birth into the popualtion was calculated as 154,567 [21] for the 200,963,599 individuals in Nigeria [22]. Thus, the recuitment rate of individuals is calculated 3,947,100 individuals per year. Furthermore, the initial conditions used in the numerical simulation of model (3) were:

S(O) = 180, 896, 161, E = 7438 [23], I = 10,000, Q = 50,000 and R=20,000,000

so that the total population is 200,963,599.

For model (17), the same initial conditions were used for the numerical simulation.

Lemma 1:

The model (3) preserves positivity of solutions.

That is, the solutions with positive initial conditions will remain positive for all time, t > O

Proof:

Suppose $t_1 = \text{Sup}\{> 0: (st) > 0, E(t) > 0, I(t) > 0, Q(t) > 0, R(t) > 0\} > 0$

From the first component of the model (3), we have that

$$\frac{ds}{dt} = \Lambda + \pi - (\lambda + \varkappa)s \geq \pi - \lambda s - \varkappa s$$

This translates as

$$\frac{ds}{dt}\{s_1(t)\exp[\varkappa tr\int_0\lambda(\hat{I})d\hat{I}]\} \geq \Lambda\left\{\exp\left(\varkappa t\int_0^t\lambda(\hat{t})\,d\hat{i}\right]\right\}$$

Thus, $S_1(t_1)\exp\left[\varkappa t_1 + \int_0^{t_1}\lambda(\hat{i})d\hat{i}\right] - S_1(O) \geq \int_0^{t_1}\Lambda\{\exp[\varkappa y + \int_0^y\lambda(\hat{t})d\hat{t}]\}dy$

So that

$$S_1(t_1) \geq +(O)\exp\left[-\varkappa t_1 + \int_0^{t_1}\lambda(\hat{i})d\hat{i}\right] + \{-\exp[-\varkappa t_1 - \int_0^{t_1}\lambda(\hat{i})d\hat{i}]\int_0^t\Lambda\{\exp[\varkappa y + \int_0^y\lambda(\hat{t})d\hat{t}]\}dy > 0$$

Similarly argument is adopted to show that E(t) > 0, Q (t) > 0 and R (t) > 0 for all time t > 0.

Therefore, all solutions of (3) remain positive for all non-negative initial conditions.

Lemma 2:

The closed set $D = \{(S, E, I, Q, R)ER_+^S : N \leq \frac{\Lambda+\pi}{\varkappa}\}$ is positively invariant and attracting with respect to the model (3)

Proof:

Adding all the equations in model (3) gives

$$\frac{dN}{dt} = \pi + \Lambda - \varkappa N - \delta_1 I + \delta_2 Q \quad (4)$$

$$\text{Since } \frac{dN}{dt} \leq \Lambda + \pi - \varkappa N \quad (5)$$

It follows that

$$\frac{dN}{dt} < O \text{ if } N(t) > \frac{\Lambda+\pi}{\varkappa}$$

We can use the standard comparison theorem [24] to show that

$$N(t) \leq N(O)e^{-\varkappa(t)} + \frac{\Lambda+\pi}{\varkappa}[1 - e^{-\varkappa(t)}] \quad (6)$$

And especially that, $N(t) \leq \frac{\Lambda+\pi}{\varkappa}$ if $N(O) \leq \frac{\Lambda+\pi}{\varkappa}$

Thus, D is positively invariant.

Further, if $N(t) \leq \frac{\Lambda+\pi}{\varkappa}$, then either the solution enters *D* in infinite time,

or N(t) approaches $\frac{\Lambda+\pi}{\varkappa}$ and the infected variables E, I, Q tends to zero.

Hence *D* is attracting and all solutions in R_+^S eventually enter D.

Thus in the closed set D, the model is epidemiologically meaningful and mathematically well posed. Hence, it is sufficient to study the dynamics of the model (3) in *D*

2. Existence and Stability of Equilibria

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2.1 Disease-Free Equilibrium (DFE)

The model (3) has a DFE which is given by

$$\mathcal{E}_o = (S^*, E^*, I^*, Q^* R^*) = \left(\frac{\Lambda+\pi}{\mu}, 0, 0, 0, 0\right) \quad (7)$$

We use the next generation operator method [25] to establish the linear stability of $\mathcal{E}_o$ for (3). The matrices F, for the new infection, and V for the transition terms are given as follows:

$$F = \begin{bmatrix} 0 & Ba & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \quad \text{and} \quad V = \begin{bmatrix} g_1 & 0 & 0 \\ \epsilon & g_2 & 0 \\ 0 & \alpha + v\sigma & g_3 \end{bmatrix}$$

Where $g_1 = \epsilon + \mu, g_2 = \alpha + v\sigma + r_1 + \mu + \delta_1, g_3 = r_2 = r_2 + \mu + \delta_2$

Hence, the associated reproduction number becomes

$$R_m = p\,(FV^{-1}) = \frac{Ba\epsilon}{g_1 g_2} \quad (8)$$

Where P is the dominant eigenvalue in magnitude or spectral radius of FV^{-1}.

The following theorem follows [25].

Lemma 3

The DFE, E_0, of the model (3), is locally asymptotically stable (LAS) if $R_m < 1$, and unstable if $R_m < 1$

The value R_m represents the mean number of new infections generated by an infected person when introduced into a susceptible population, the implication of this is that the disease can be effectively managed in the population (when $R_m < 1$) if the initial sizes of the sub-populations can be in the basin of attraction of E_0. Thus effective control of measles in Nigeria is independent of the initial sub-populations sizes as portrayed in model (3). If $R_m < 1$, then infection over it's infectious period and this leads to an outbreak of the disease.

2.2 Analysis of the Reproduction Number

With the threshold R_m, it is to investigate the influence of treatment, rate of identification of red rash and its cost factor, and active case finding techniques on the spread of measles in the population. By this we may be able to glean some effective control strategies that include the parameters characterizing these effects. The effect of these parameters is evaluated by differentiating R_m with respect to these parameters (r_1, v, σ, α). The results are given below

$$\frac{\partial R_m}{\partial r_1} = \frac{\partial R_m}{\partial \alpha} = \frac{-\beta a \varepsilon}{(\varepsilon+\mu)(\alpha+v\sigma+r_1+\mu+\delta_1)^2} \quad (9)$$

$$\frac{\partial R_m}{\partial v} = \frac{-\beta a \varepsilon \sigma}{(\varepsilon+\mu)(\alpha+v\sigma+r_1+\mu+\delta_1)^2} \quad (10)$$

$$\frac{\partial R_m}{\partial \sigma} = \frac{-\beta a \varepsilon v}{(\varepsilon+\mu)(\alpha+v\sigma+r_1+\mu+\delta_1)^2} \quad (11)$$

It follows form (9), (10) and (11) that R_m is a decreasing function of $r_1, \alpha, v \text{ and } \sigma$. Since a decrease in value of the reproduction number may well signify decrease in disease burden [19]. This shows that treatment, red rash identification rate and its cost factor, and active case finding technique will all have positive impacts in reducing measles disease burden in the population.

2.3Endemic Equilibrium Point (EEP)

We solve the model (3) at an arbitrary equilibrium, denoted by

$$\xi_o^* = (S^*, E^*, I^*, Q^*, V^*) \quad (12)$$

Which gives

$$S^* = \frac{\Lambda+\pi}{\Lambda^*+\mu} \quad \text{and} \quad E^* = \frac{(\Lambda+\pi)\lambda^*}{g_1(\Lambda^*+\mu)} \quad (13)$$

$$I^* = \frac{E(\Lambda+\pi)\lambda^*}{g_1\, g_2(\Lambda^*+\mu)}$$

$$Q^* = \frac{E(\Lambda+\pi)(\alpha+v\sigma)\lambda^*}{g_1\, g_2\, g_3(\Lambda^*+\mu)}$$

$$R^* = E(\Lambda+\pi)\lambda^*\left[\frac{r_1\ g_3 + r_2(\alpha+v\sigma)}{g_1\, g_2\, g_3(\Lambda^*+\mu)}\right]$$

$$\lambda = \frac{\beta a I^*}{S^*, + E^* + I^* + Q^* + R^*} \quad (14)$$

Substituting (13) into (14) reveals that the endemic equilibria of (3) satisfies the polynomial (in terms of λ):

$$\lambda^*[A\lambda^* + B] = O \quad (15)$$

Where $A = g_2\, g_3 + (I + r_1\varepsilon g_3 + \varepsilon(\alpha + +v\sigma)(1 + r_2)$ and $B = g_1\, g_2\, g_3\,[1 - R_m]$

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The root λ^* of (15), corresponds to the DFE ε_0 (whose stability has already been analyzed). Thus it follows from (15) that the non-zero equilibrium of the model aligns with

$$F(\lambda^*) = A\lambda^* + B = O \quad (16)$$

Clearly, A > O and $B \geq O$ whenever $R_m < 1$ so that $\lambda^* = \frac{-B}{A} \leq O$.

Therefore, whenever $R_m < 1$, the model will have an endemic equilibrium This result implies the impossibility of backward bifurcation in (3), because of the absence of endemic equilibrium when $R_m < 1$.

3 A Vaccination Model for Measles

In this section, model (3) is extended to incorporate a class of vaccinated persons. Vaccination against measles comprises of two doses. According to [4], one dose of MMR (Mumps, Measles and Rubella) vaccine is 93% effective, whilw a second dose of MMR vaccine is 97% effective against measles. Based on this fact, we include two vaccinated subs population, $V_1(t)$ (persons who receive the first dose) and $V_2(t)$ (persons who receive second dose) of the vaccine. Susceptibles receive the first dose of vaccine at a rate $\emptyset$. Since the first dose of vaccine is not 100% protective, persons in class V_1 become exposed to measles at a rate of $\Lambda\gamma$ (where γ accounts for reduction in infectiousness). Persons in the V_1 class receive the second dose of vaccine at a rate PK (where P represents a fraction of vaccinated persons who have received the first dose and k accounts for the rate of the second dose of vaccine). Persons in the V_1 class may revert back to the susceptible class at a rate (1-p)c (where c is the waning rate of the first dose of the vaccine).

Under the hypotheses above, the following model is obtained for the dynamics of measles transmission

$$\frac{dS}{dt} = (1-q)\Lambda + (1-\theta)\pi + (1-p)cv_1 - (\lambda + \emptyset + \mu)S$$
$$\frac{dE}{dt} = \lambda S + \gamma\lambda V_1 - (\varepsilon + \mu)E$$
$$\frac{dI}{dt} = \varepsilon E - (\alpha + v\sigma + r_1 + \delta_1 + \mu)I$$
$$\frac{dQ}{dt} = (\alpha + v\sigma)I - (r_2 + \delta_2 + \mu)Q$$
$$\frac{dV_1}{dt} = (\theta\pi + q\Lambda + \phi S - (c(1-p) + PK + \gamma\lambda + \mu)V_1$$
$$\frac{dV_2}{dt} = PKV_1 - NV_2 \quad (17)$$
$$\frac{dR}{dt} = r_1 I + r_2 Q - NR$$

Where $\lambda = \frac{BaI}{N}$

The analysis of the vaccination model (17) above will be done in the region:

$$D_0 = \{(S,E,I,Q,V_1,V_2,R) \in \mathbb{R}_+^7 : N_H \leq \frac{\Lambda + \pi}{\mu}\}$$

As shown earlier in section 2.1, the region D_0 is positively invariant and attracting. The disease-free equilibrium (DFE) of model (17) is given by

$$E_0^v = (S^*, E^*, I^*, Q^*, V_1^*, V_2^*, R) = S_0^*, O, O, O, V_1^{**}, V_2^{**}, O) \quad (18)$$

Where

$$\frac{S_0^v = ((1-q)\Lambda + (1-\theta)\pi[(Pk + c(1-p) + \mu)(\emptyset + \mu) - \emptyset(1-p)] + (1-p)[\mu(\theta\pi + q\Lambda) + \emptyset(\Lambda + \pi)]}{(PK + C(1-p) + \mu)(\emptyset + \mu) - \emptyset\alpha(1-p)}$$

(19)

$$V_1^{**} = \frac{\mu(\theta\pi + q\Lambda) + \emptyset(\Lambda + \pi)}{(PK + C(1-p) + \mu)(\emptyset + \mu) - \emptyset\alpha(1-p)} \quad (20)$$

$$V_2^{**} = \frac{PK[\mu(\theta\pi + q\pi) + \emptyset(\Lambda + \pi)]}{\mu[(Pk + c(1-P) + \mu)(\emptyset + \mu) - \emptyset\alpha(1-P)]} \quad (21)$$

Now $S_0^* + V_1^{**}, + V_2^{**} = 1$

To establish the linear stability of ε_0^v using the method of next generation operator on model (17). The matrices F and V are given by

$$F = \begin{bmatrix} 0 & \beta a S_0^* \\ 0 & 0 \end{bmatrix} \text{ and } V = \begin{bmatrix} g_1 & 0 \\ \varepsilon & g_2 \end{bmatrix}$$

$$FV^{-1} = \begin{bmatrix} \frac{\beta a \varepsilon S_0^*}{g_1 g_2} & \frac{\beta a \varepsilon S_0^*}{g_2} \\ 0 & 0 \end{bmatrix} \quad (22)$$

Thus

R_m^e is the effective reproduction number of model (17) as it contains all the control strategies. In the absence of control strategy, then $\theta = p = q = k = \emptyset = \alpha = c = v = \sigma = o$ so that the basic reproduction number becomes

$$R_m = \frac{\beta a \varepsilon(\Lambda + \pi)}{\varepsilon + \mu)(r_1 + + \delta_1} \quad (23)$$

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Lemma 4
The DFE, ε_0^v, of model (17) is locally asymptotically stable if $R_m^e < 1$, and unstable if $R_m^e > 1$,

3.1 Analysis of the Reproduction number under Different Control Strategies

In this section, we discuss various scenarios that involve the presence of control measures based on the effective reproduction number. Using the threshold parameter R_m^e, we investigate the effect of treatment, rate of first dose of vaccine, rate of second dose of vaccine, newborns who are vaccinated as well as the proportion of immigrants who take first dose of vaccine on the dynamics of measles within the population.

It is evident from (22) that as $\emptyset \to \infty, c \to 0, k \to \infty, q \to 1, \theta \to 1$

$$LimR_m^e = \frac{\beta a \varepsilon[(1-q)\Lambda+(1-\theta)\pi]}{g_1 g_2} \quad (24)$$

And as $q \to 1, \theta \to 1$, $LimR_m^e = 0$
(25)

From (25), it obvious that total eradication of measles is almost achievable. An important strategy is to effectively combine rates of first and second dose of the measles vaccine, reduction of the waning rate of first dose of vaccine by administering second dose of the vaccine, ensuring high rate of vaccination for newborns and immigrants (that is, $\emptyset \to \infty, c \to 0, k \to \infty, q \to 1, \theta \to 1$). It is important to note that a similar conclusion can be reached if a control strategy focuses on vaccinating all new births and immigrants as well as a high rate of administering the second dose of the vaccine to all who have been vaccinated once.
The above strategies could be unrealistic and prohibitive especially in countries that are still finding their feet. However, an alternative strategy that can be from equation (24) can be applied to the target population, in reducing the spread of measles in the population. For example the limit in (24) does not necessarily require the vaccination of all newborns immigrants especially when it is cost effective.
We now compute the partial derivatives of R_m^e with respect to its key parameters $(\emptyset, k\ q, \theta, c)$ to reveal the likely effects of these parameters.

Computing the partial derivatives of R_m^e with respect to K yields

$$\frac{\partial R_m^e}{\partial k} = \frac{-g_1 g_2 \beta a \varepsilon P c (1-p)(\emptyset+\mu)[\mu(\theta\pi+q\Lambda)+\emptyset(\Lambda+\pi)]}{g_1 g_2 g_3} \quad (26)$$

Where $g_3 = (PK + c\,(1-p) + \mu)(\emptyset + \mu) - \emptyset c(1-p)$

The results above reveals that $\frac{\partial R_m^e}{\partial k} < O$ unconditionally. Therefore, an increased rate of receiving the second dose of measles vaccine will have a positive impact in reducing the disease burden in the population. Thus we have the following lemma.

Lemma 5
A higher rate of the second dose of vaccine to individuals who have received the first dose of vaccine will positively impact the burden of measles in the population. It will reduce the prevalence of the infection in the population irrespective of values of other parameters contributing to the effective reproduction number.
Similarly, considering the partial derivative of R_m^e with respect to $\emptyset$, we have

$$\frac{\partial R_m^e}{\partial \emptyset} = \frac{g_1 g_2 \beta a \varepsilon \pi c (1-p)[(1-q)\Lambda+(1-\theta)\pi][\Lambda+\pi) g_3 - (PK+\mu)[\mu(\theta\pi+q\Lambda)+\emptyset(\Lambda+\pi)]}{{g_1}^2 {g_2}^2 {g_3}^2} < 0$$

If $D_1^* > D_1 = g_3 \equiv \frac{(PK+\mu)[\mu(\theta\pi+q\Lambda)+\emptyset(\Lambda+\pi)]}{(\Lambda+\pi)}$
(28)

Or $D_2^* < D_2 = PK + \mu \equiv \frac{g_3(\Lambda+\pi)}{\mu(\theta\pi+q\Lambda)+\emptyset(\Lambda+\pi)}$
(29)

The above partial derivative implies that a high rate of first dose of vaccine by some of the susceptible individuals will positively impact the burden of measles in the population of $D_1^* > \mathrm{D}_1 (D_2^* < \mathrm{D}_2)$, and that the strategy of using only first dose of vaccine will not significantly reduce the burden of measles in the population if $D_1^* = \mathrm{D}_1 (D_2^* = \mathrm{D}_2)$. In fact, it can increase R_m^e, if $D_1^* < \mathrm{D}_1 (D_2^* < \mathrm{D}_2)$, thereby leading to a detrimental effect on the population. The result is summarized as follows:

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Lemma 6

An increase in rate of first dose of the vaccine by susceptible class will have a positive impact in reducing the burden of measles in the population only if $D_1^* > \mathrm{D}_1 (D_2^* < \mathrm{D}_2)$, no impact if $D_1^* = D_1^* (D_2^* = \mathrm{D}_2)$, and a negative impact if $D_1^* < \mathrm{D}_1 (D_2^* > \mathrm{D}_2)$.

In the same vein, considering the partial derivatives of R_m^e with respect to c, we have

$$\frac{\partial R_m^e}{\partial c} = \frac{\beta a \varepsilon g_1 g_2 (1-p)[(1-q)\Lambda + (1-\theta)\pi][\mu(\theta\pi + q\Lambda) + \emptyset(\Lambda+\pi)]g_3 - (\mu(1-p))]}{g_1{}^2 g_2{}^2 g_3{}^2} \quad (30)$$

The above partial derivative implies that a high waning rate of the first dose of vaccine by susceptible individuals will have a positive impact on the burden of measles in the population if $g_3 < c\mu(1-p)$. The strategy of administering first dose of vaccine will not reduce the burden of measles in the population if $g_3 = c\mu(1-p)$. It will rather have a detrimental effect on the population by increasing the value of R_m^e, if $g_3 > c\mu(1-p)$. The result is thus summarized below.

Lemma 7

A high waning rate of the first dose of vaccine by susceptible individuals will have a positive impact in reducing the burden of measles in the population only if $g_3 > c\mu(1-p)$, no impact if $g_3 = c\mu(1-p)$ and a negative impact if $g_3 > c\mu(1-p)$.

Finally, considering the partial derivative of R_m^e with respect of q and θ gives

$$\frac{\partial R_m^e}{\partial q} = \frac{\beta a \varepsilon \Lambda [c\mu(1-p) + g_3]}{g_1\, g_2\, g_3} \quad (31)$$

$$\frac{\partial R_m^e}{\partial \theta} = \frac{-\beta a \varepsilon \mu [c\mu(1-p) + g_3]}{g_1\, g_2\, g_3} \quad (32)$$

From (31) and (32) above, we have that $\frac{\partial R_m^e}{\partial q} < O$, $\frac{\partial R_m^e}{\partial \theta} < O$ unconditionally. The results reveals that increasing the fraction of newborns as well as recruited persons who take first dose of vaccine will positively impact to reduce the disease burden. The result is summarized below.

Lemma 8

Increasing the fraction of newborns as well as recruited persons who take the first dose of vaccine will significantly impact on the burden of measles in the population and will reduce the prevalence of the disease.

4.Simulations

In this section, a sensitivity analysis of all the parameters in model (3) and (17) were carried out using the reproduction numbers ($\mathrm{R_m}$ and R_m^e) as functions of focus. It is followed by the Numerical simulation of the models.

4.1 Sensitivity Analysis

There are 15 parameters in the reproduction numbers ($\mathrm{R_m}$ and R_m^e). We try to determine how sensitive, these parameters are in relation to the model. Sensitivity analysis enables us to estimate the robustness of predictions to model parameter values. Hence, we use it to ascertain the level of impact of each parameter on the reproduction numbers ($\mathrm{R_m}$, R_m^e) . We use the method by [26] to derive the appropriate expressions for the sensitivity of $\mathrm{R_m}$ and R_m^e to each parameter which is obtained as follows

$$\partial_\beta^{R_0} = \frac{\beta}{R_m} \times \frac{\partial R_m}{\partial \beta} = \frac{\beta}{R_m^e} \times \frac{\partial R_m^e}{\partial \beta} = +1$$

$$\partial_a^{R_0} = \frac{a}{R_m} \times \frac{\partial R_m}{\partial a} = \frac{a}{R_m^e} \times \frac{\partial R_m^e}{\partial a} = +1$$

The other sensitivity indices for all other parameters in $\mathrm{R_m}$ and R_m^e are computed similarly and are all given as in Table 2.

Table 2: Sensitivity indices for parameters of both models using $\mathrm{R_m}$ and R_m^e as response function

Parameters	Sensitivity index $\mathrm{R_m}$
β	+ 1
a	+ 1
ε	+ 0.14066
α	- 0.64199
v	-0.32099
σ	-0.32099
r_1	-0.018342

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δ	- 0.016049
μ	- 0.14298
q	- 0.8486
θ	- 0.6061
k	- 0.1043
$\emptyset$	0.0000054
C	0.0007944

From Table 2 and for model (3), the parameters that play dominant role in the dynamics of the disease (in terms of the reproduction number R_m) are the rate of transmission (β), per capital contact rate (c), as well as the rate at which asymptomatic individuals become symptomatic (ε). This implies that any increase in the values of $\beta, c \; or \; \varepsilon$ will have a commensurate effect on R_m. Thus $\beta, c \; and \; \varepsilon$ are $\alpha, v, \sigma, r, \delta, \mu < 0$ thus, these parameters are inversely proportional to R_m. Thus the order of sensitivity from the highest includes $\beta, c, \varepsilon, \delta, r_1, \mu, v, \sigma \; and \; \alpha$. Hence, to minimize measles transmission via contact, this study establishes that persons infected with measles should be identified and quarantined, because placing infected individuals in quarantine reduces the likelihood of susceptible individuals being in contact with them.

In the same vein, as observed from table 2, for model (17), the order of sensitivity from the highest includes $\beta, c, \varepsilon, c, p, k, \theta, q$. A public health take-away from this is that measles can be effectively controlled by having a two-stage vaccination of all susceptible individuals, including newborns and recruited individuals..

4.2Numerical Simulation

Numerical simulations of models (3) and (17) were done to illustrate the effects of varying some key parameters the model. The parameter values listed in Table 3 were used for the simulations, and were either assumed or adapted from literature. Also, the demographic parameters relevant to Nigeria were used. As at end of 2019, the total population of Nigeria was estimated to be 200,963,599 [22]. The birth rate for 2019 stood at 37.684 births per 1000 individuals [21]. Thus the number of new births per year was calculated as 154,567.

Since the total population is given as $N = \frac{\Lambda+\pi}{\mu}$, it follows that $200{,}963{,}599 = \frac{\Lambda+154{,}567}{0.02041}$.

Thus the recruitment rate of individuals is obtained as $\Lambda = 3{,}947{,}100$.

Table 3: Parameter Values

Parameters	Nominal values per year	References
Λ	3947100	[22]
π	154,567	[21]
β	0.33	[27]
a	0.09091	[28]
ε	0.125	[28]
α	5	[29]
v	0.5	[29]
σ	5	[29]
r_1	0.14286	[28]
r_2	0.2	Assumed
q	0.7	[30]
θ	0.5	[30]
p	0.5	[30]
$\emptyset$	0.7	[30]
c	0.167	[31]

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k	0.8	[30]
δ	0.125	[32]
μ	0.02041	[20]

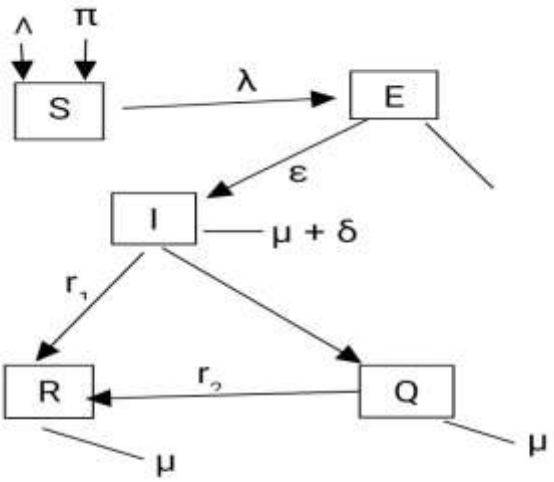

Figure 1: flow diagram of model (3)

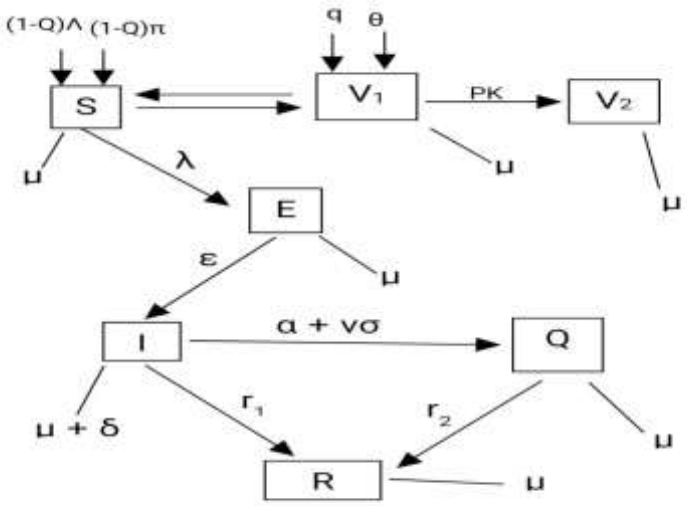

Figure 2: flow diagram of model (17)

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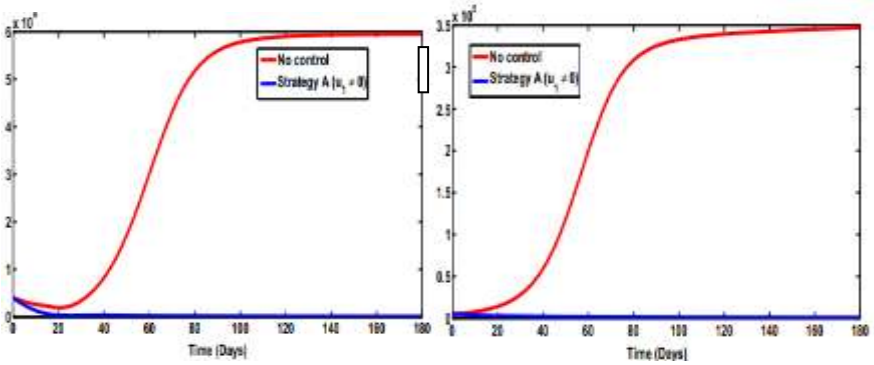

Figure 1: plots of the infected and exposed class with first and second dose of vaccination (α) infected class (a) [$\emptyset = 1$ red line and $k = 1$ blue line] (b) exposed class (a) [$\emptyset = 1$ red line and $k = 1$ blue line].

Figure 1 reveals that taking the first dose of measles vaccine is not sufficient enough to decrease the incidence of measles in the population. With a near perfect second dose vaccine coverage, the incidence of the disease will be drastically reduced. Thus, after participating in the first stage of vaccination, it was necessary to also take the second dose of the vaccine, although a near perfect vaccine community wide coverage is almost impractical

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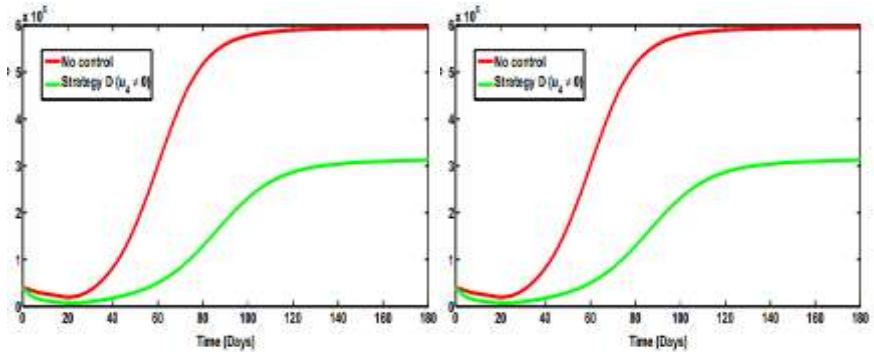

Figure 2: plots of the infected class with varied active case finding and red rash identification rate (α) (a) [$\alpha = 0$ red line and $\alpha = 5$ blue line] (b) red rash identification rate$\sigma = 0$ (red line) $\sigma = 5$ (blue line).

Figure 2 reveals that increasing the active case finding rate through red rash identification will equally reduce the incidence of measles in the population. It is pertinent to note that pursuing this strategy will be capital intensive as we also consider the cost of actively finding infectious individuals with measles through red rash identification via screening and tests done in the hospital.

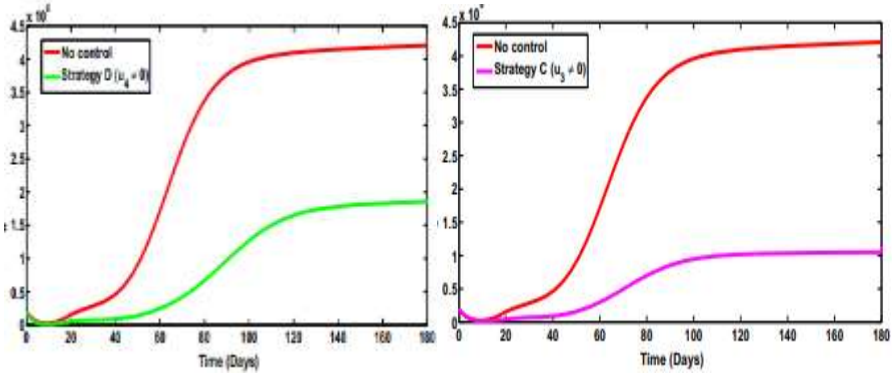

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Figure 3: plots of the recovered class with varied rate of treatment (r_1) (a) [$r_1 = 1$ red line and $r_1 = 0$ blue line] (b) recovery rate for quarantined individuals $r_2 = 1$ (red line) $r_2 = 0$ (pink line).

Figure 3 shows that high rate of treatment received by the infectious class and quarantined class will decrease the disease burden of the population.

5.Results and Discussion

Numerical simulations of two related models were carried out to graphically establish the trend of exposed, infected, and recovered populations. The Tables and figures presented were to illustrate how the set of parameter values were affected and the state variables which were used in order to support the analytical results. Assuming vaccination was to be effective in protecting susceptible individuals, Figures 1 show that vaccine can reduce the peak of infected compartment drastically especially when the second dose is also administered. Figure 2 reveals that combining a high rate of active case finding through red rash identification and the required cost will see to the reduction of the incidence of measles in the population. Figure 3 shows the dynamics of recovered compartment with high rates of treatment for the infectious and quarantined class. This rapid decline in the number of infected individuals could be attributed to early detection, high treatment rates and higher rate of coverage by second dose of vaccine.

5.1 Conclusion

In this paper we have developed a mathematical model for the transmission of measles infection by considering two dose vaccine impact and effect of quarantine. The disease free equilibrium and its stability was presented and analysed to show its connection with the basic reproduction number and vaccination reproduction number. The simple Numerical simulation confirms that vaccination in two stages was able to positively impact the control strategy that inhibits the spread of the disease. Furthermore, this study established that when $R_m^e > 1$, then the disease will persist, while $R_m^e = 1$ remains the threshold between the extinction and the persistence of the disease.

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Declaration on Conflict of Interest

The authors declare that there is no conflict of interest whatsoever.

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