MATHEMATICAL ANALYSIS OF DIARRHEA IN THE PRESENCE OF VACCINE

S.O. Adewale, I.A.Olopade, S.O. Ajao and G.A. Adeniran

ABSTRACT: We present four (4) compartmental mathematical models (S, V E, I) to study the effect of vaccine and treatment in the dynamical spread of diarrhea in the community.

The mathematical analysis shows that the disease free and the endemic equilibrium point of the model exist. The model has disease free equilibrium point which is locally asymptotically stable (LAS) whenever the basic reproduction number (R_0) is less than unity. i.e. $(R_0 < 1)$ and unstable when $R_0 > 1$. The basic reproduction number which is the average number of new infected individuals generated by a single infectious individual in the population of susceptible, is a very important tool that helps in determining whether the disease persist and become endemic or dies out in the society.

Numerical simulation was carried out by maple software using Runge – kutta method of order (4) to show the effects of vaccine and treatment on the spread of diarrhea. The results showed the pronounced effect of vaccine and treatment.

Efficacy of vaccine and treatment shows great impact in the total eradication of diarrhea epidemic, as this should be taken serious by medical practitioners/policy health makers.

KEYWORDS: Diarrhea, Critical points, Basic reproduction number, Stability.

INTRODUCTION

Diarrhea disease is the second leading cause of death in children under five years old. In 2008, 16% of death was caused by infectious disease worldwide. [2]. When an infective individual or external vector is introduced into a close population, the infectious disease tends to spread within the population [20]. Diarrhea is responsible for killing around 76,000 children and globally, there are nearly 1.7 billion cases of diarrheal disease [26]. In developing countries, the annual incidence rate of diarrhea disease episodes in children less than five years old is 3.2 episodes per child [3]. It kills more young children than HIV, malaria and measles combined [23]. Diarrhea illness alone causes more than 1.5 million deaths annually, thereby making it a worse health threat than cancer or AIDS in terms of death toll [19]. Diarrhea is an abnormal looseness of the stool, changes in stool frequency, consistency, urgency and continence. Sub-Sahara Africa is the most vulnerable region of infectious disease [7], this is due to the fact that the region is greatly affected by climate change which makes it more vulnerable to infectious diseases. Diarrhea outbreaks are associated with periods of rainfall and runoff when subsequent turbidity compromises the efficiency of the drinking water treatment plants [13]. Auld et.al.[1] found out that heavy rainfall increases diarrhea outbreak due to water contaminated distribution. Many waterborne disease outbreaks occur following a period of intense rainfall [11, 12]. Diarrhea could be acute which lasts for 2 weeks and chronic which lasts for more than 2 weeks [22]. It is one of the most common diseases that is transferred through contaminated food and water [6,9]. There are two types of diarrhea which are infectious and non-infectious diarrhea. Infectious diarrhea is caused by virus, parasite or bacterium, which could be canpylobacteria, shiga – toxin producing E. Coli, giardiasis, salmonellosis, shigellosis,Rotavirus, yers inia, cryptosphoridiosis etc. Non-infections is caused by toxins (e.g. food poisoning). This type of diarrhea does not spread from person to person. [17, 18]. The immunity after infection is temporary and the infection tend to be less severe than the original infection [21]. However, diarrhea is preventable and can be treated.

Diarrhea disease can be prevented by taking safe clean drinking water, by using improved sanitation, washing hands with soap regularly, exclusive breast feeding for the first six months and taking of rotavirus vaccination. It can be treated by rehydration with oral rehydration salt (ORS), by taking Zinc supplement and eating of nutrient rich food [25, 26, 23]. The most important complication of diarrhea is dehydration [9]. It causes death by depleting the body fluids resulting in great dehydration [5, 15]. Various studies have been conducted to investigate diarrheal disease transmission dynamics. Lopman, B. [14] analyzed the dynamic transmission model of nor virus infection disease and immunity. It was found that asymptomatic prevalence of norovirus can change dramatically with small changes in the basic reproduction number R_0. Chaturvedi, O. et. al [6] formulated a continuous mathematical model for shigella outbreaks. They designed the model as an SIRS system comprising of a non-constant population. It was proved that as long as the value of basic reproduction number R_0 is kept minimal, the disease can be eradicated. The model shows that the higher the value of R_0 the more likely an epidemic will spread at higher rate.

In this present work, we incorporate the impact of a vaccination and treatment in the control of the disease. We show the efficacy of vaccination and treatment of infected individuals in the control of the disease.

MODEL FORMULATION

The model considered four (4) compartmental models to gain insight into the effect of vaccine on the dynamical spread of diarrhea disease in a community. The model comprises of Susceptible individuals S(t), Vaccinated individuals V(t), Exposed individuals E(t) and Infected individuals I(t) so that

$$N(t) = S + V + E + I \qquad (1)$$

The Susceptible population is increased by the recruitment of individuals into the population at rate λ, the population decrease by fraction of recruitment for vaccinated individuals at the rate ρ and by susceptible individuals who acquire diarrhea infection with effective contact with people infected with diarrhea, where β is the effective contact rate. The population increased by recovered individuals that has been treated and vaccinated individuals who lost vaccine due to vaccine wanes off at the rate τ and w respectively. The population of susceptible individuals further reduced by natural death at the rate μ. Hence,

$$\frac{dS}{dt} = (1-\rho)\lambda - \beta SI + wV + \tau I - \mu S \quad (2)$$

The vaccinated individuals is increased by the fraction of vaccination from susceptible individuals at the rate $\rho\lambda$. This population is decreased by natural death rate and vaccine wanes off of vaccinated individuals at the rate μ and w respectively.

Then, we have,

$$\frac{dV}{dt} = \rho\lambda - \mu V - wV \qquad (3)$$

Exposed individuals are those that carry the bacterial but not capable of infecting susceptible individuals. The population increased by new infection from susceptible individuals who acquire diarrhea infection with effective contact with people infected with diarrhea, where β is the effective contact rate. The population reduced by natural death μ and progression from exposed class to infected class at the rate σ. Hence,

$$\frac{dE}{dt} = \beta SI - \mu E - \sigma E \qquad (4)$$

The population infected diarrhea individual increases by the exposed individuals who develop disease symptoms (at the rate σ The population later decreased by treatment rate (τ) for diarrhea infected individual and finally reduced by the natural death rate, induced mortality death rate at μ and δ respectively. Thus,

$$\frac{dI}{dt} = \sigma E - \mu I - \tau I - \delta I \qquad (5)$$

Hence we have

$$\left.\begin{aligned}\frac{dS}{dt} &= (1-\rho)\lambda - \beta SI + wV + \tau I - \mu S\\ \frac{dV}{dt} &= \rho\lambda - \mu V - wV\\ \frac{dE}{dt} &= \beta SI - \mu E - \sigma E\\ \frac{dI}{dt} &= \sigma E - \mu I - \tau I - \delta I\end{aligned}\right\} \quad (6)$$

Table 1: Description of Variables and Parameters of The Model

Parameters	Description
S	Susceptible
V	Vaccinated
E	Exposed
I	Infected
δ	Induced disease death rate
ρ	Vaccine rate
λ	Recruitment rate
β	Contact rate
τ	Rate at which infected individual are treated
ω	Rate at which vaccine wanes off
σ	Rate at which exposed individuals become infected
μ	Natural death rate

ANALYSIS OF MODEL EQUATIONS FOR EXISTENCE OF SOLUTION

3.1 Existence and Uniqueness of solution

Theorem 3.1.1: Following (Derrick and Grossman 1976)

Let

$$\left.\begin{aligned}x_1^1 &= f_1(x_1, x_2, \ldots x_n, t), x_1(t_0) = x_{10}\\ x_2^1 &= f_2(x_1, x_2, \ldots x_n, t), x_2(t_0) = x_{20}\\ &:\\ x_n^1 &= f_n(x_1, x_2, \ldots x_n, t), x_n(t_0) = x_{n0}\end{aligned}\right\} \quad (7)$$

Let D denote the region in [(n+1)-dimensional space one dimension for t and n dimensions for the vector x].

If the partial derivatives $\frac{\partial fi}{\partial xj}, i, j = 1,2,\ldots,n$ are continuous in

$$D = \{(x,t), /t - t_0 / \le a, / x - x_0 / \le b\} \quad (8)$$

Then there is a constant $\delta > 0$ such that there exists a unique continuous vector solution

$$\underline{x} = [x_1(t), x_2(t), \ldots x_n(t)] \quad (9)$$

in the interval $/t - t_0 / \le \delta$

Theorem 3.1.2.

Let

$$\left.\begin{aligned}\frac{dS}{dt} &= f_1 = (1-\rho)\lambda - \beta SI + wV + \tau I - \mu S & S(t_0) &= S_0\\ \frac{dV}{dt} &= f_2 = \rho\lambda - \mu V - wV & V(t_0) &= V_0\\ \frac{dE}{dt} &= f_3 = \beta SI - \mu E - \sigma E & E(t_0) &= E_0\\ \frac{dI}{dt} &= f_4 = \sigma E - \mu I - \tau I - \delta I & I(t_0) &= I_0\end{aligned}\right\} \quad (10)$$

$$D = \{(S,V,E,I) // S - S_0 / \le a / V - V_0 / \le b,$$
$$/ E - E_0 / \le c, / I - I_0 / \le d, / t - t_0 / \le e\} \quad (11)$$

Then equation (10) has a unique solution

Proof:

$$\left.\begin{aligned}\left.\frac{df_1}{dS}\right|_{(0,0,0,0)} &= -\mu \\ \left.\frac{df_1}{dV}\right|_{(0,0,0,0)} &= 0 \\ \left.\frac{df_1}{dE}\right|_{(0,0,0,0)} &= 0 \\ \left.\frac{df_1}{dI}\right|_{(0,0,0,0)} &= \tau\end{aligned}\right\}$$

$$\left.\begin{aligned}\left.\frac{df_2}{dS}\right|_{(0,0,0,0)} &= 0 \\ \left.\frac{df_2}{dV}\right|_{(0,0,0,0)} &= -(\mu + w) \\ \left.\frac{df_2}{dE}\right|_{(0,0,0,0)} &= 0 \\ \left.\frac{df_2}{dI}\right|_{(0,0,0,0)} &= 0\end{aligned}\right\}$$

$$\left.\begin{aligned}\left.\frac{df_3}{dS}\right|_{(0,0,0,0)} &= 0 \\ \left.\frac{df_3}{dV}\right|_{(0,0,0,0)} &= 0 \\ \left.\frac{df_3}{dE}\right|_{(0,0,0,0)} &= -(\mu + \sigma) \\ \left.\frac{df_3}{dI}\right|_{(0,0,0,0)} &= 0\end{aligned}\right\}$$

$$\left.\begin{aligned}\left.\frac{df_4}{dS}\right|_{(0,0,0,0)} &= 0 \\ \left.\frac{df_4}{dV}\right|_{(0,0,0,0)} &= 0 \\ \left.\frac{df_4}{dE}\right|_{(0,0,0,0)} &= \sigma \\ \left.\frac{df_4}{dI}\right|_{(0,0,0,0)} &= -(\mu + \tau + \delta)\end{aligned}\right\}$$

Therefore $\left|\frac{\partial f_i}{\partial j}\right|, i, j = 1,2,3$ are continuous and bounded.

Hence the problem has a unique solution and the model (6) is mathematically and epidemiologically well posed.

3.2 DISEASE FREE EQUILIBRUM

At Disease free equilibrium, when there is no infection. i.e. I = E = 0

and at equilibrium point, the normalized model (6) is obtained by setting

$$\frac{dS}{dt} = \frac{dV}{dt} = \frac{dE}{dt} = \frac{dI}{dt} = 0$$

Hence, the disease free equilibrium is given by

$$E_0 = \left(\frac{(1-\rho)\lambda(\mu+\omega) + \omega\rho\lambda}{\mu(\mu+\omega)}, \frac{\rho\lambda}{(\mu+\omega)}, 0, 0 \right) \quad (12)$$

3.3 THE ENDEMIC EQUILIBRIUM POINT

To obtain an endemic equilibrium E^* we set each equation in the model (6) equal to zero

$E^* = (S^*, V^*, E^*, I^*)$ is an endemic equilibrium points.

Hence the endemic equilibrium points are

$$\left.\begin{aligned} S^* &= \frac{C_3 C_4}{\beta\sigma} \\ V^* &= \frac{\rho\lambda}{C_3} \\ E^* &= \frac{C_4\left[C_3 C_4 \mu\ C_2 - w\rho\lambda\beta\sigma - C_1\lambda\beta\sigma C_2\right]}{\beta\sigma\left[\tau\sigma - C_3 C_4\right]} \\ I^* &= \sigma\frac{\left(C_3 C_4 \mu\ C_2 - w\rho\lambda\beta\sigma - C_1\lambda\beta\sigma C_2\right)}{\beta\sigma C_2\left(\tau\sigma - C_3 C_4\right)} \end{aligned}\right\} (13)$$

Where

$(I-\rho) = C_1$, $\mu+w = C_2$, $\mu+\sigma = C_3$, $\mu+\tau+\delta = C_4$

3.4 DERIVATION OF BASIC REPRODUCTION NUMBER (R0)

Computation of basic reproduction number is essential in order to assess the local stability of the system (6).

Basic reproduction number is the average number of secondary infection generated by infectious individual in his or her infectiousness. It is obtained by taking the largest dominant eigen-value of

$$F = \left(\frac{\partial F(E_0)}{\partial x_j}\right)\left(\frac{\partial V(E_0)}{\partial x_j}\right)^{-1} \quad (14)$$

it is given by $R_0 = F.V^{-1}$ where F is the new infection Transfer terms,

V is the non- singular matrix of the remaining transfer terms.

The basic reproduction number R_0 of the model (6) is calculated by using the next generation matrix (Driessche and Watmough, 2002). Using their approach (Driessche and Watmough, 2002), we have,

$$F = \begin{pmatrix} 0 & \left[\frac{\beta(1-\rho)\lambda(\mu+w)+w\rho\lambda}{\lambda(\mu+w)}\right] & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} (15)$$

$$V = \begin{pmatrix} (\lambda+\sigma) & 0 & 0 \\ -\sigma & \mu+\tau+\delta & 0 \\ 0 & 0 & \mu+w \end{pmatrix} (16)$$

The eigen value of $F.V^{-1}$ are $(0,\ 0,\ P)$

Where

$$P = \sigma\beta\left(\frac{(1-\rho)\lambda(\mu+\omega)+\omega\rho\lambda}{\left(\mu(\mu+\sigma+\tau+\delta)+\sigma(\tau+\delta)\right)\mu(\mu+\omega)}\right) (17)$$

Hence, the basic reproduction number R_0 for the normalized model (6) is given by

$$R_0 = \sigma\beta\left(\frac{(1-\rho)\lambda(\mu+\omega)+\omega\rho\lambda}{\left(\mu(\mu+\sigma+\tau+\delta)+\sigma(\tau+\delta)\right)\mu(\mu+\omega)}\right) \quad (18)$$

Corrolary:The disease free equilibrium is locally asymptotically stable if

$R_0 < 1$ and unstable if $R_0 > 1$

3.5 LOCAL STABILITY OF DISEASE FREE EQUILIBRIUM

Expressing the system of equation (1) in Jacobian matrix form

The non singular matrix A is

$$\begin{pmatrix} -\mu & \omega & 0 & \tau-\beta\left(\frac{(1-\rho)\lambda(\mu+\omega)+\omega\rho\lambda}{\mu(\mu+\omega)}\right) \\ 0 & -(\mu+\omega) & 0 & 0 \\ 0 & 0 & -(\mu+\sigma) & \beta\left(\frac{(1-\rho)\lambda(\mu+\omega)+\omega\rho\lambda}{\mu(\mu+\omega)}\right) \\ 0 & 0 & \sigma & (\mu+\tau+\delta) \end{pmatrix} (19)$$

Then the characteristic equation is obtained as $|A-KI|$ =0 where K is the eigen values

$$\begin{pmatrix} -\mu-K & \omega & 0 & \tau-\beta\left(\frac{(1-\rho)\lambda(\mu+\omega)+\omega\rho\lambda}{\mu(\mu+\omega)}\right) \\ 0 & -(\mu+\omega)-K & 0 & 0 \\ 0 & 0 & -(\mu+\sigma)-K & \beta\left(\frac{(1-\rho)\lambda(\mu+\omega)+\omega\rho\lambda}{\mu(\mu+\omega)}\right) \\ 0 & 0 & \sigma & (\mu+\tau+\delta)-K \end{pmatrix} \quad (20)$$

Clearly,

$$K=-\mu,\quad K=-(\mu+\omega)$$

Then, we have the characteristic equation

$$\begin{bmatrix} K^2+K(2\mu+\sigma+\tau+\delta)- \\ \sigma\beta\left(\frac{(1-\rho)\lambda(\mu+\omega)+\omega\rho\lambda}{\mu(\mu+\omega)}\right)+ \\ \mu(\mu+\sigma+\tau+\delta)+\sigma(\tau+\delta) \end{bmatrix}=0$$

Let

$$a_1=(2\mu+\sigma+\tau+\delta)$$

$$a_2=-\sigma\beta\left(\frac{(1-\rho)\lambda(\mu+\omega)+\omega\rho\lambda}{\mu(\mu+\omega)}\right) + \mu(\mu+\sigma+\tau+\delta)+\sigma(\tau+\delta)$$

Thus according to Routh-Hurwitz criteria for a 2*2 system, E_0 is locally asymptotically stable.

If a_1>0 and a_2>0

Then for a_2>0,

We have

$$-\sigma\beta\left(\frac{(1-\rho)\lambda(\mu+\omega)+\omega\rho\lambda}{\mu(\mu+\omega)}\right)> -(\mu(\mu+\sigma+\tau+\delta)+\sigma(\tau+\delta)) \quad (21)$$

Hence,

$$\frac{\sigma\beta\left(\frac{(1-\rho)\lambda(\mu+\omega)+\omega\rho\lambda}{\mu(\mu+\omega)}\right)}{\mu(\mu+\sigma+\tau+\delta)+\sigma(\tau+\delta)}<1, \quad (22)$$

Implying that $R_0<1$

This is locally asymptotically stable.

3.6. NUMERICAL SIMULATIONS

Numerical simulations of the model were carried out by maple 14, using the Runge-Kutta of order four (4).

The set of parameter values in the table below were used to investigate the effect of the vaccine, treatment and effective contact rate on the dynamical spread of diarrhea in the population of Susceptible, Vaccinated, Exposed and Infected individuals.

The values of the vaccine wanes off (w) were first varied, followed by the treatment rate (τ).

Table 2. Parameter Values used in Numerical Simulations

Parameters	Value	Sources
δ	0.2	Assumed
ρ	0.5	Assumed
λ	2000	Assumed
β	0.3	Assumed
τ	0.1	Assumed
ω	0.1	Assumed
σ	0.7	Assumed
μ	0.012	[4]

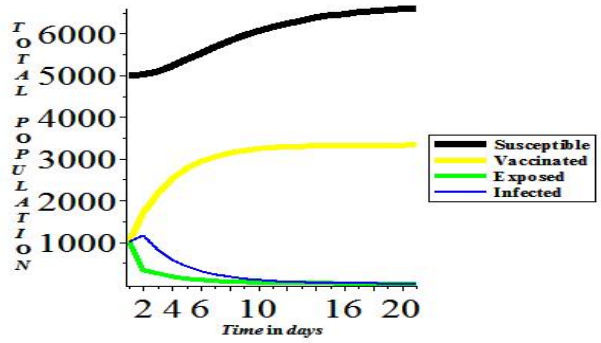

*Fig.*1 *The graph of total population* (S,V,E,I) *against time* (t) *in days where* $\beta = 0.3,\ \tau = 0.1,$ $\rho = 0.5,\ \mu = 0.2,\ \delta = 0.2,\ \sigma = 0.7,\ \omega = 0.1,\ \lambda = 2000$

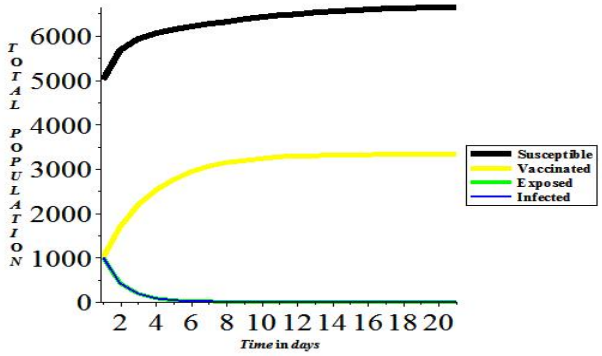

*Fig.*4. *The graph of total population* (S,V,E,I) *against time* (t) *in days where* $\beta = 0.3,\ \tau = 0.5,$ $\rho = 0.5,\ \mu = 0.2,\ \delta = 0.2,\ \sigma = 0.7,\ \omega = 0.1,\ \lambda = 2000$

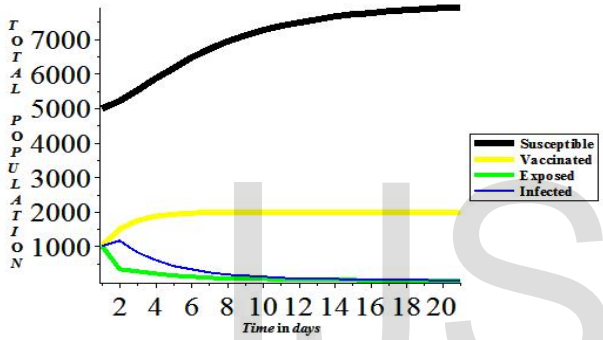

*Fig.*2 *The graph of total population* (S,V,E,I) *against time* (t) *in days where* $\beta = 0.3,\ \tau = 0.1,$ $\rho = 0.5,\ \mu = 0.2,\ \delta = 0.2,\ \sigma = 0.7,\ \omega = 0.3,\ \lambda = 2000$

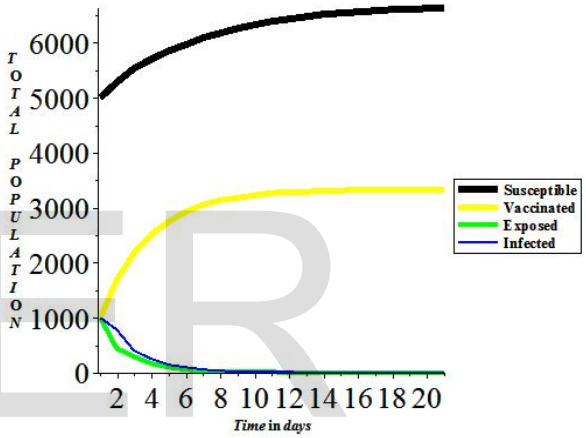

*Fig.*5. *The graph of total population* (S,V,E,I) *against time* (t) *in days where* $\beta = 0.3,\ \tau = 0.9,$ $\rho = 0.5,\ \mu = 0.2,\ \delta = 0.2,\ \sigma = 0.7,\ \omega = 0.1,\ \lambda = 2000$

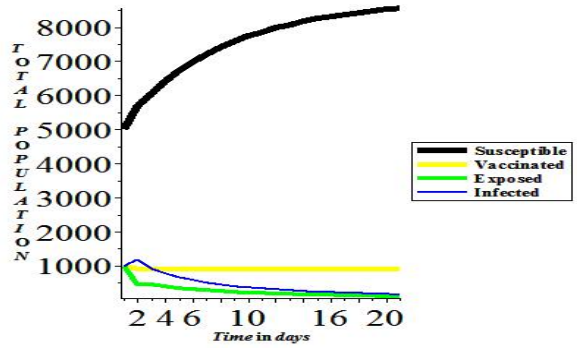

*Fig.*3 *The graph of total population* (S,V,E,I) *against time* (t) *in days where* $\beta = 0.3,\ \tau = 0.1,$ $\rho = 0.5,\ \mu = 0.2,\ \delta = 0.2,\ \sigma = 0.7,\ \omega = 0.9,\ \lambda = 2000$

4 DISCUSSION AND CONCLUSION

A deterministic epidemic model (S, V, E, I) was considered to gain more insight into the effect of vaccine and treatment of infected individuals on the dynamical spread of diarrhea in a population. The research shows the following:

Fig. 1, 2 and 3 show that the lower the vaccine wanes off the lower the susceptible individuals and the lower the infected individuals.

Fig. 4 and 5 show that if the treatment rate is high, the infected individuals decrease and the susceptible individuals increase.

Conclusively, Vaccine plays a vital role in the control of the spread of diarrhea disease, the increase in susceptible individuals is dependent of effectiveness of the vaccine given against diarrhea, if the vaccine wanes off is low, the lower would be the susceptible individuals and the lower would be the spread of the disease but when the vaccine wanes off quickly it increases the number of infected individuals. This suggests that vaccine should be given as early as possible immediately after birth before the exposure to diarrhea infection and vaccine to be given must be effective in order to minimize the spread of the disease and the cost. Also, the drugs should be made available to consumers at a very cheaper rate and efficacy of the vaccine should be considered to reduce the dynamical spread of diarrhea in a community.

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