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# A Mathematical Model on Cholera Dynamics with Prevention and Control

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***Abstract***: In this paper, we present and analyze a cholera epidemiological model with modifications to Fung (2014) cholera model. The extended model incorporates preventive and control measures as well as the possibility of disease transmission from person-to-person. Equilibrium analysis is conducted for the extended model for two cases of epidemic equilibrium and endemic equilibrium to establish disease free equilibrium state (DFE) and endemic equilibrium state (EE) respectively. We derive the basic reproduction numbers and establish the local asymptotical stability for the two models. We later use the results to compare the models at the DFE states as regards the effects of control on the extended model. The endemic equilibrium state (EE) of the extended model is also studied and found to be locally asymptotically stable when the basic reproduction number . This shows that cholera can be eliminated in a population only if the preventive and control measures are strong enough.

***Keywords***: model, equilibrium, reproduction number, stability

## Introduction

Cholera is an acute intestinal water-borne infectious disease. It is a potentially epidemic and life-threatening secretory diarrhea that is caused by the bacterium Vibrio Cholerae, first identified by Robert Koch in 1883 during a cholera outbreak in Egypt and characterized by numerous, voluminous watery stools, often accompanied by vomiting and resulting in hypovolenic shock and acidosis (Finkelstein, 2013). Though cholera is preventable and curable, the current global cholera report indicates that there are an estimated 3 – 5

million cholera cases and 100 000 – 120 000 deaths due to cholera every year [1].

The complexity of cholera dynamics stems from the fact that both direct (i.e. human-to –human) and indirect (i.e. environment-to-human) routes are involved in the disease transmission [2]. The environment-to-human way of transmitting cholera is mainly through ingesting Vibrio Cholerae bacteria from contaminated food or water while human-to-human way of cholera transmission is mostly unhygienic contact with cholera patient'sfaeces, vomit or corpse [3]. Although cholera is well prevented in developed countries of the world, recent data show that the global outbreak of cholera is rising in Africa and the entire less developed countries. This rise may be attributed to inadequate access to safe drinking water supply, improper treatment of reservoirs and improper sanitation [4].

While cholera has been a recognized disease for more than a century, its occurrence in developing countries including Nigeria has been alarming and has become a subject of concern. In 1971, 22,931 cases of cholera and 2,945 deaths with a case fatality rate (CFR) of 12.8% were recorded in Nigeria. The disease reoccurred in 1991 in which 59,478 cases and 7,654 deaths were reported. The CFR was 12.9% which remains the highest rate reported by the country to date. Also, in 2009, Nigeria reported 13,691 cases and 431 deaths [5]. Furthermore, in 2005, Nigeria had 4,477 cases and 174 deaths and in 2008, there were reported cases of 6,330 and 429 deaths [6].

Several mathematical models have been proposed to understand the transmission dynamics and control of cholera [3, 6]In all of these models, the use of vaccination and antibiotics to control cholera are played down. Nevertheless, the place of vaccination and antibiotics in fighting against the propagation of infectious diseases cannot be underestimated. Vaccination reduces the number of fully susceptible individuals, reduces infectiousness (i.e the rate of contamination of the water supply), and reduces the probability of becoming symptomatic when infected. Also, antibiotics administration shortens the duration of illness and perhaps reduces the concentration of Vibrios excreted during illness [7].

Chao et al. (2011) claimed that the use of vaccines would likely have minimized the calamity that befell Haiti in 2010 in terms of reduction in morbidity and mortality of cholera, but such vaccines were in short supply and little was known about effective vaccination strategies for epidemic cholera. The researchers also examined prevaccination strategies in which vaccination occurs well before the epidemic starts and reactive vaccination strategies in which vaccination begins after the epidemic has started and discovered that randomly prevaccinating a fraction of the population well before the epidemic begins can reduce the number of cases roughly in proportion to the number of individuals vaccinated and delay the epidemic peak.

Benefits from an intervention are a combination of direct effects on those receiving the intervention and indirect effects on those with reduced exposure because others received the intervention. In the context of

vaccination, producing immunity through vaccination of only a part of the population may stop an epidemic because chains of transmission are broken – a concept known as "herd protection"[7]. Concentration of prevaccination in areas at high risk of cholera, such as along rivers and other bodies of fresh water can help achieve critical vaccination threshold – the proportion of the population one would need to vaccinate effectively to stop an epidemic [8]. The cholera vaccines are safe, effective and have an efficacy against clinical disease of over 65% lasting at least 3 – 5 years [9]

The study conducted by the research arm of the international medical humanitarian organization [10] and the Guinean Ministry of Health revealed that an oral cholera vaccine (i.e. Shanchol) protected individuals by 86% during the 2012 cholera outbreak in Guinea (MSF, 2012). Since most existing cholera models exclude the use of vaccination and antibiotics as measures against cholera despite their roles in fighting against the propagation of infectious diseases, this work is aimed to better understand the effects of these measures so as to gain useful guidelines to the effective prevention and intervention strategies against cholera epidemics. To that end, we study cholera dynamics with prevention and control measures as well as the possibility of disease transmission from person-to-person incorporated into the model of [11] which involve only the environment-to-human transmission mode

## Material and Methods

### Formulation of model

Let S(t), I(t) and R(t) represent the susceptible, the infected, and the recovered human populations, respectively. The total human population N = S + I + R is closed, which is a reasonable assumption for a relatively short period of time and for low – mortality diseases like cholera. For example, WHO states that "In 2012, the overall case fatality rate for cholera was 1.2 %"[12] Also, let B denote the concentration of the Vibrios in the environment (i.e. contaminated water). The following assumptions are made to extend [11] cholera model:

(i) Vaccination is introduced to the susceptible population at a rate v1(t), so that v1(t)S(t) individuals per time are removed from the susceptible category and added to the recovered population.

(ii)Therapeutic treatment and vaccination are applied to the infected people at a rate

(t), and v2(t) respectively so that (t)I(t) and v2(t)I(t) individuals per time are removed from the infected class and added to the recovered class. Therapeutic treatment is in the form of administration of antibiotics or rehydration salts. As a result of modifications, the new model equations are as follows:

$$\left.\begin{aligned}
\frac{dS}{dt} &= \pi - \mu S - \varphi S - \gamma_1 S + \sigma R \\
\frac{dI}{dt} &= \varphi S - (\mu + \mu_c + \gamma_2 + \rho + \gamma) I \\
\frac{dR}{dt} &= \gamma I - \mu R + \gamma_2 I + \gamma_1 S + \rho I - \sigma R \\
\frac{dB}{dt} &= \varepsilon I - \delta B
\end{aligned}\right\} \quad (1)$$

$$\varphi = \left[\frac{\beta_1 B}{(B+\aleph)} + \beta_2 I\right] \quad (2)$$

Where
$S(0) > 0, B(0) \geq 0, I(0) \geq 0, R(0) \geq 0.$
All the parameters are non-negative and $\beta_1 > \beta_2$.
$\pi$ is the recruitment rate of susceptible individuals, $\gamma$ is the natural recovery rate , $\mu$ and $\mu_c$ are death rates, unrelated to cholera and due to cholera respectively, $\sigma$ is the rate of losing immunity, $\varphi$ is the force of infection, $v_1$ and $v_2$ are vaccination rates, before and after the outbreak respectively, $\rho$ is the rate of applying therapeutic treatment, $\varepsilon$ is the rate at which infectious individuals contribute V. cholerae to the water reservoir, $\delta$ is the death rate of V. cholerae unrelated to water treatment, $\aleph$ is the concentration of V. cholerae in the water reservoir that will make 50% of the susceptible population ill and $\beta_1 and \beta_2$ represent rates of ingesting Vibrios from the contaminated water and through human – to – human interaction, respectively

**Equilibrium analysis**

For the special case when the rates of prevention and control are positive constants,
i.e v(t) = $v_1 > 0$, $v_2 > 0$ and $\rho(t) = \rho > 0$, the model eqn. (1) using eqn. (2) is reduced to an autonomous system

$$\frac{dS}{dt} = \pi - \mu S - \frac{\beta_1 B}{B+\aleph} S - \beta_2 IS - v_1 S + \sigma R \quad (3)$$

$$\frac{dI}{dt} = \frac{\beta_1 B}{B+\aleph} S + \beta_2 IS - (\mu + \mu_c + v_2 + \rho + \gamma) I \quad (4)$$

$$\frac{dB}{dt} = \varepsilon I - \delta B \quad (5)$$

$$\frac{dR}{dt} = \gamma I - \mu R + v_2 I + v_1 S + \rho I - \sigma R \quad (6)$$

Permanent immunity is assumed therefore, equation (6) is not needed in the model analysis. This is done for convenience of discussion [12,13]. Besides in (3) is dropped since compartment R is not included in the analysis.
This allows us to conduct a careful equilibrium analysis to investigate the effects of protection and control on the epidemic and endemic dynamics of cholera.

**Epidemic Dynamics**

The disease-free equilibrium (DFE) for the model is given by

$$E_0 = \left(\frac{\pi}{\mu+v_1}, 0, 0\right). \quad (7)$$

Having determined the disease free equilibrium point $E_0$, we proceeded to compute the basic reproduction number for the two models using the method of [14]. The associated next generation matrices are given by

$$F = \begin{pmatrix} \beta_2 S & \frac{\beta_1 S}{B+\aleph} - \frac{\beta_1 BS}{(B+\aleph)^2} \\ 0 & 0 \end{pmatrix}, V = \begin{pmatrix} (\mu+\mu_c+v_2+\rho+\gamma) - & 0 \\ -\varepsilon\delta & \end{pmatrix} \quad (8)$$

The basic reproduction number is then determined as the spectral radius of $FV^{-1}$, which yields

$$R_0^{\,q} = \rho(FV^{-1}) = \frac{\pi\varepsilon\beta_1+\pi\aleph\delta\beta_2}{\aleph\delta(\mu+v_1)(\mu+\mu_c+v_2+\rho+\gamma)} \quad (9)$$

The superscript q is used to emphasize the model with controls. Compared to the basic reproduction number for the original no-control model (Fung, 2014) which is given as

$$R_0 = \frac{\mu_b\beta N}{\aleph\mu_d(\gamma+\mu_c+\mu_d)} \quad (10)$$

Clearly, $R_0^{\,q} \leq R_0$ and the result in (9) shows that, mathematically, each of the controls can reduce the value of $R_0^{\,q}$ below 1 so that the disease will be eradicated though the combination of the two interventions would achieve better result.

It follows from theorem 2 in [15] that the disease- free equilibrium is locally asymptotically stable when $R_0^{\,q} < 1$. In contrast, if the controls are weak such that $R_0^{\,q} > 1$, then the disease-free equilibrium is unstable and a disease outbreak occurs.

**Local Stability of the Disease Free Equilibrium (DFE)**

If the controls are assumed to be weak and an outbreak occurs then there is a need to compare the outbreak growth rates between the original no - control model and the model with controls. We shall use the linearization approach to analyze the effect of weak prevention and control measures on the extended model. The positive (dominant) eigenvalue of the Jacobian matrix at the DFE characterizes the initial outbreak growth rate [16].

For the system of equations (3) – (5), the Jacobian matrix at the DFE is given by

$$J(E_0) = \begin{bmatrix} \frac{-\beta_1 S}{B+\aleph} - \beta_2 I - \mu - v_1 & -\beta_2 S & -\frac{\beta_1 S}{B+\aleph} + \frac{\beta_1 BS}{(B+\aleph)^2} \\ \frac{\beta_1 S}{B+\aleph} + \beta_2 I & \beta_2 S - (\mu+\mu_c+v_2+\rho+\gamma) & \frac{\beta_1 S}{B+\aleph} - \frac{\beta_1 BS}{(B+\aleph)^2} \\ 0 & \varepsilon & -\delta \end{bmatrix} \quad (11)$$

At the disease free equilibrium state, using the expression $E_0$ i.e put eqn. (7) in eqn. (11), we obtain

$$J(E_0) = \begin{bmatrix} -\mu - v_1 & \frac{-\pi\beta_2}{(\mu+v_1)} & \frac{-\pi\beta_1}{\aleph(\mu+v_1)} \\ 0 & \frac{\pi\beta_2}{(\mu+v_1)} - (\mu+\mu_c+v_2+\rho+\gamma) & \frac{\pi\beta_1}{\aleph(\mu+v_1)} \\ 0 & \varepsilon & -\delta \end{bmatrix} \quad (12)$$

The characteristic equation in λ is obtained from the Jacobian determinant thus,

$$(\mu + v_1 + \lambda)\left[\lambda^2 + (\mu+\mu_c+v_1+\rho+\gamma+\delta-\beta_2 S_0)\lambda + \delta(\mu+\mu_c+v_2+\rho+\gamma) - \left(\frac{\varepsilon\beta_1}{\aleph} + \delta\beta_2\right)S_0\right] = 0, \quad (13)$$

where $S_0 = \frac{\pi}{(\mu+v_1)}$.

The necessary and sufficient conditions for the DFE of the model to be locally asymptotically stable is for all the eigenvalues of eqn. (13) to be negative

Clearly the first eigenvalue is:

$$\lambda_1 = -(\mu + v_1)$$

The remaining part of the characteristic equation is given as:

$$\left[\lambda^2 + (\mu+\mu_c+v_2+\rho+\gamma+\delta-\beta_2 S_0)\lambda + \delta(\mu+\mu_c+v_1+\rho+\gamma) - \left(\frac{\varepsilon\beta_1}{\aleph} + \delta\beta_2\right)S_0\right] = 0$$

In the absence of the disease (i.e. DFE), there is no transmission of infection either from person-to-person or from water-to-person which makes $\beta_1$ and $\beta_2$ to be zero in the above equation hence, all the eigenvalues in eqn. (13) are negative and the DFE of the extended model is locally asymptotically stable for $R_0{}^q < 1$.

As speculate earlier, suppose the controls are weak and there is an outbreak i.e $\beta_1 \neq 0$ and $\beta_2 \neq 0$ such that $R_0{}^q > 1$ then there will be at least one positive eigenvalue for eqn. (13). Let $\lambda_+{}^q$ denote the eigenvalue and it exists if and only if $\delta(\mu + \mu_c + v_2 + \rho + \gamma) <$ $\left(\frac{\varepsilon\beta_1}{\aleph} + \delta\beta_2\right) S_0$. This is the sufficient condition for the product of the remaining roots of eqn. (13) to be negative.

In terms of graph, the value of $\lambda_+{}^q$ is the slope of the ascending infection curve when $R_0{}^q > 1$ and the higher the $\lambda_+{}^q$ the higher the severity of disease outbreak. Obviously, $\lambda_+{}^q > 0$ when $R_0{}^q > 1$ and $\lambda_+{}^q < 0$ when $R_0{}^q < 1$. This result can be interpreted by the values of the controls. The disease easily breaks out and easily sustained if $v_1 = v_2 = \rho = 0$ whereas the initial disease outbreak growth rate is prevented or eradicated if the strength of $v_1, v_2$ and $\rho$ is strong enough.

For the purpose of comparison, the quadratic part of the characteristic equation of the original no-control cholera model for $R_0 > 1$ is evaluated in a similar way as in eqn. (13) and it is given as

$$\left[\lambda^2 + (\mu_d + \mu_c + \gamma + \delta)\lambda + \delta(\mu_d + \mu_c + \gamma) - \left(\frac{\varepsilon\beta}{\aleph}\right)S_0\right] = 0, \quad (14)$$

where $S_0 = \frac{\mu_b N}{\mu_d}$. If $\lambda_+$ is the positive eigenvalue of the original no-control cholera model then, $\lambda_+{}^q \leq \lambda_+$ if $v_1 \geq 0,\ v_2 \geq 0$ and $\rho \geq 0$ while $\lambda_+{}^q \geq \lambda_+$ if $v_1 = 0, v_2 = 0$ and $\rho = 0$. Hence, the severity of outbreak will be lower when $R_0{}^q > 1$ than when $R_0 > 1$ .The above inequalities hold from the elementary algebra since $\delta(\mu + \mu_c + v_2 + \rho + \gamma) \geq \delta(\mu_d + \mu_c + \gamma)$.

Finally, the summary of the results of analysis of disease-free equilibrium states is that the disease-free equilibrium of the system of equations (3) – (5) is locally asymptotically stable if $R_0{}^q < 1$ ; whereas it is unstable, with a lower outbreak growth rate than that of the original no-control model whenever $R_0{}^q > 1$ .

**Endemic dynamics**

Assuming that the disease-free equilibrium of the extended model is unstable and the disease is sustained in the population then there is need to investigate the long-term behavior of the disease dynamics for $R_0{}^q > 1$ . Suppose the endemic equilibrium of the model equations (3) - (5) is denoted by

$$E^* = (S^*, I^*, B^*) \quad (15)$$

Where and represent the population of each compartment at endemic equilibrium. Hence, the model equations (3) – (5) are written in terms of the endemic state as

$$\pi - \mu S^* - \frac{\beta_1 B^*}{B^* + \aleph} S^* - \beta_2 I^* S^* - v_1 S^* = 0 \quad (16)$$

$$\frac{\beta_1 B^*}{B^*+\aleph} S^* + \beta_2 I^* S^* - (\mu + \mu_c + v_2 + \rho + \gamma) I^* = 0 \quad (17)$$

$$\varepsilon I^* - \delta B^* = 0 \quad (18)$$

Note that $\sigma R$ is dropped in eqn. (16) due to the fact that the compartment R is not included in the model analysis as stated earlier under eqn. (6)

From eqn. (18),

$$B^* = \frac{\varepsilon I^*}{\delta} \quad (19)$$

Solving for the remaining compartments at endemic equilibrium (i.e. $S^*$and $I^*$), their values are positive since each compartment and parameter is assumed non-negative.

**Local asymptotic stability of the endemic equilibrium**

Theorem 1: The endemic equilibrium state $E^*$ is locally asymptotically stable if $R_0{}^q > 1$.

The linearization approach shall be employed to investigate the stability of the endemic equilibrium state $E^*$.The approach shall be employed to show that the endemic equilibrium state $E^*$ is locally asymptotically stable. To achieve this, eqn. (11) is used, so that, substituting $B^*$ for B and $S^*$ for S and replacing $\frac{\beta_1 B^*}{B^*+\aleph} + \beta_2 I^* > 0$ by M and $\frac{\beta_1 \aleph S^*}{(B^*+\aleph)^2} > 0$ by N, the Jacobian matrix eqn. (11) is reduced to

$$J(E^*) = \begin{bmatrix} -M-(\mu+v_1) & -\beta_2 S^* & M+N+\beta_2 I^* \\ M & \beta_2 S^* - (\mu+\mu_c+v_2+\rho+\gamma) & M-N+\beta_2 I^* \\ 0 & \varepsilon & -\delta \end{bmatrix} \quad (20)$$

The characteristic equation in $\lambda$ of eqn. (20) is evaluated as follows

$$(M + \mu + v_1 + \lambda [(\lambda+\delta)[-\beta_2 S^* + (\mu+\mu_c+v_2+\rho+\gamma+\lambda)] - \varepsilon(M-N+\beta_2 I^*)] = 0 \quad (21)$$

On simplification, eqn. (21) can be written as

$$a_0\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0 \quad (22)$$

Where

$$a_0 = 1$$

$$a_1 = M + 2\mu + \mu_c + v_1 + v_2 + \rho + \gamma + \delta$$

$$a_2 = (M+\mu+v_1)(\mu+\mu_c+v_2+\rho+\gamma+\delta) + \delta(\mu+\mu_c+v_2+\rho+\gamma-\beta_2 S^*) - \varepsilon(M-N+\beta_2 I^*)$$

$$a_3 = (M+\mu+v_1)(\delta(\mu+\mu_c+v_2+\rho+\gamma-\beta_2 S^*) - \varepsilon(M-N+\beta_2 I^*))$$

The Routh-Hurwitz criterion inTian*et al.*(2010) and Liao and Wang (2011) requires

$$a_1 > 0,\ a_2 > 0,\ a_3 > 0 \text{and}$$

$$a_1 a_2 - a_0 a_3 > 0 \quad (23)$$

as the necessary and sufficient conditions for the local asymptotical stability of the endemic equilibrium of the model; i.e., all the solutions of eqn. (22) must have negative real parts.

$a_1 > 0$is obvious. Meanwhile, to establish the validity of eqn. (23) for the local asymptotic stability of the extended model, eqn. (17) and eqn. (19) shall be considered and eqn. (19) will be substituted into eqn. (17) to obtain

$$(\mu + \mu_c + v_2 + \rho + \gamma) = \beta_2 S^* + \frac{\beta_1 S^* \varepsilon}{\varepsilon I^* + \aleph\delta} \quad (24)$$

From (24),

$$(\mu + \mu_c + v_2 + \rho + \gamma) - \beta_2 S^* > 0 \quad (25)$$

Since all the model parameters as well as M and N are positive andeqns (24) and (25) hold then all the inequalities in (23) are true. Hence, the endemic equilibrium of the extended model is locally asymptotically stable. The implication of the local asymptotical stability of the endemic equilibrium state $E^* under R_0{}^q > 1$ as proved above is that even though the prevention and control measures are not strong enough to remove the epidemic, they have the effect of

reducing the size of the infection, particularly for the long-term disease dynamics. We expect that when $I^*$ is close to zero, an endemic state would be unlikely to occur or persist in reality, since practical endemism requires a reasonably higher value for $I^*$ (Tian *et al.*, 2010)

**Results and Discussion**

In our analysis, there exists a disease free equilibrium state and theendemic equilibrium state. We established that if$R_0{}^q$ <1 then disease free equilibrium state is locally asymptotically stable, which implies that the prevention and control measures are potent enough to inhibit the emergence of secondary infections. The United States of America is one of the several countries that has been maintaining stability in terms of cholera outbreak both locally and globally for more than a century. Even though there are occasional sporadic cases of cholera resulting from several people who traveled abroad to countries where cholera is endemic and contracted the disease either by drinking the water or eating some food that was contaminated and developed illness on returning to the United States but at large, no secondary transmission has been recorded within the United States. We also established that an endemic equilibrium state exists if $R_0{}^q$ >1 which implies that the prevention and control measures are not strong enough to break the chain of transmission of the disease and the population experienced mild waves of cholera epidemic. The frequent outbreak of cholera in most developing countries of the world is as a result of carefree attitude towards cholera prevention and control. Despite availability of cholera measures in these countries, the measures are being handled with levity hands.

**Conclusion**

In this work we modified the model by Fung [11] to incorporate vaccination and therapeutic treatment as prevention and control strategies against cholera transmission. We derive the basic reproduction number and conduct a careful equilibrium and stability analyses. Both the disease free equilibrium state and the endemic equilibrium state are found to be locally asymptotically stable. From the results obtained from the study we conclude that the most effective way to curb cholera outbreak is to ensure the effectiveness and wide coverage of cholera vaccination as well as cholera treatment through the use of drugs in cholera endemic regions. The availability and potency of these interventions are capable of averting 120 000 deaths due to cholera yearly.

**References**

1. Azman, A. S., Rudolph, K. E., Cummings, D. A. T., Lessler, J. (2012). The incubation period of cholera: A system review. Journal of Infection, 66, 432-438.
2. Mukandavire, Z., Liao, S., Wang, J., Gaff, H., Smith, D. L. and Morris, J. G. Jr (2011). Estimating the reproductive numbers for the 2008-2009 cholera outbreaks in Zimbabwe. Proc. Natl Acad. Sci. USA, 108(21), 8767- 8772.
3. Fakai, S. A., Ibrahim, M. O. and Siddiqui, A.M.(2014). A deterministic model on cholera dynamics and some control

strategies. International Journal of Scientific Engineering and Technology, 3(8), 1115-1118.

4. Posny, D. and Wang, J. (2014). Modeling cholera in periodic environments.Journal ofBiological Dynamics, 8(1), 1-1

5.World Health Organisation, (2012).Global Task on Cholera Control. Cholera Country Profile: Nigeria. Retrieved from: http:/www.who.int/cholera countries/Nigeria country profile 2011.pdf

6. Fatima,S., Krishnarajah, I., Jaffar, M. Z. A. M., Adam, M. B. (2014). A mathematical model for the control of cholera in Nigeria. Research Journal of Environmental and Earth Sciences,6(6), 321 – 325.

7. Grad, Y. H., Miller, J. C. and Lipsitch, M. (2012).Cholera modeling: challenges to quantitative analysis ans predicting the impact ofintervention. Epidemiology, 23(4), 523-530.

8. Chao, D. L., Holloran, M. E. Longini, I. M. Jr. (2011). Vaccination strategies for epidemic cholera in Haiti with implications for the developing world.Proc. Natl Acad. Sci. USA, 108,7081-7085.Azman,

9. Azman, A. S., and Lessler, J. (2014). Reactive vaccination in the presence of disease hotspot.Pro.R. Soc. B. http:/rspb.royalsocietypublishing. org Emerging themes in epidemiology. htpp://www.et online.com./content/11/1/1.

10.Me'decinsSanFrontie'res (MSF, 2012). Oral cholera vaccines highly effective during outbreak in Guinea.Retrieved from: http:/www.msf.org.

11 Fung, I. C-H.(2014). Cholera transmission dynamic models for public health practitioners. Fung

12.Wang, J. and Modnak, C. (2011).Modeling Cholera Dynamics with Controls.Canadian Applied Mathematics Quarterly.19(3), 255-273

13. Tian, J. P., Liao, S. and Wang, J. (2010). Dynamical Analysis and Control Strategies in Modelling Cholera.Retrieved from:ath.wm.edu/jptian/tain-liao-wang.

14. Tian, J. P. and Wang, J. (2011), Global Stability for Cholera Epidemic Models. Mathematical Biosciences 232, 31-41.

15. van den Driessche, P. and Watmough, J. (2002). Reproduction number and sub – threshold endemic equilibria for compartmental models of disease transmission.Math.Biosci. 180,29 – 48.

16.Tien, J. H. and Earn, D. J. D. (2010). Multiple transmission pathways and disease dynamics in a waterborne pathogen model.Bull. Math.Biol.72, 1502 – 1533.

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