MODELING THE INFLUENCE OF ENVIRONMENT AND INTERVENTION ON CHOLERA IN HAITI

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ABSTRACT. We propose a simple model with two infective classes in order to model the
cholera epidemic in Haiti. We include the impact of environmental events (rainfall, temperature
and tidal range) on the epidemic in the Artibonite and Ouest regions by introducing
terms in the force of infection that vary with environmental conditions. We fit the model on
weekly data from the beginning of the epidemic until March 2012. We then used this model
to obtain epidemic projections from April 2012 through September 2013, and then modified
these projections incorporating the vaccination programs that were recently undertaken in
the Ouest and Artibonite regions to compare with actual cases.

Using real-time daily rainfall we found lag times between precipitation events and new
cases that vary seasonably, ranging from 5.0 to 11.8 weeks in Artibonite, and 5.8 to 8.5 in
Ouest. In addition, it appears that, in the Ouest region, tidal influences play a significant
role in the dynamics of the disease.

Intervention efforts of all types have reduced case numbers in both regions, however, per-
sistent outbreaks continue. In Ouest, where the population at risk seem particularly besieged
and the overall population is larger, vaccination efforts seem to be taking hold more slowly
than in Artibonite, where a smaller core population was vaccinated. The model implement-
ing the vaccination program predicted that in mid March 2013, the mean number of cases
in Artibonite would be about 88 hundred, and in Ouest by 34 hundred less than predicted
by the model without vaccinations. The actual numbers of cholera cases were only about
18 hundred less than no-vaccine model predictions in both departments. We also found that
vaccination is best when done in the early spring, and if resources are limited in scope, it
may be better done in the third or fourth years of the epidemic if other interventions can be
successfully applied in the interim.

Cholera; Haiti; tides; precipitation; epidemic model; vaccination

1. INTRODUCTION

On January 12, 2010, a 7.0 magnitude earthquake struck near Haiti’s capital, Port-au-
Prince. The poorest nation in the Western Hemisphere, the earthquake shattered Haiti’s
already weak infrastructure. Thousands of Haitians were killed and even more were forced
to flee to resettlement camps.

In October 2010, the first case of cholera was reported in Haiti. A later UN investigation
revealed the specific strain of *V. cholerae* came from South Asia. The UN investigation and
epidemiological literature suggest that the epidemic began outside of a UN peacekeeper camp
near Mirebalais in the Centre department, along the Artibonite River. As *V. cholerae* is a
waterborne pathogen, the Artibonite River is the ostensible route through which the disease
spread throughout Haiti’s ten administrative regions, called departments.

Anecdotal news reports describe the dismal situation for thousands of Haitians that still
remain displaced months after the earthquake. Sewage of millions of people flow through
open ditches. Human waste from septic pits and latrines is dumped into the canals, and after
it rains, ends up in the sea. Those living close to the water use over-the-sea toilets, and next to these outhouses, fishing boats unload and sell the fish from plastic buckets.

Haiti’s two most populous regions, Ouest and Artibonite, were also the two regions hardest hit by the epidemic. Cases in Ouest and Artibonite account for 60% of the total burden of cholera in Haiti. For this reason, we chose to focus our analysis on the Ouest and Artibonite regions. By April 7, 2012, cholera had affected 5.7% of the total population in Ouest and 6.9% of the population in Artibonite.

1.1. Previous Research. We reviewed the literature dealing with cholera, modeling, and climatic conditions (rainfall, precipitation, and tides) in Haiti at the beginning of this study and again at the end. We did multi-database searches in the Biology, Medicine, and Health fields and found four modeling papers of which the first three used variations of a basic system of differential equations proposed in 2001 by Codeço. At that time, none of these models took environmental conditions directly into account. Two other papers have since appeared that do take one of the environmental conditions, precipitation, into account in cholera. The first is a spatiotemporal Markov chain model using seasonal rainfall which was outside our purview. The second deals specifically with Haiti and was done by the same group that produced one of the earlier papers. In they looked at the reliability of the earlier studies, and they found that although those models do well in capturing the early dynamics of the epidemic, they fail to track latter recurrences forced by seasonal patterns. As a follow up, Rinaldo et al. add a precipitation forcing function to their original model along with other modifications such as the river network and population mobility. These modifications produce a better fit to the observed pattern of case but predict recurring large outbreaks tracking the seasonal precipitation patterns.

The three models proposing a variation on the SIWR model, proposed by Codeço in 2001, explain cholera transmission through susceptibles’ contact with a water reservoir, rather than susceptibles’ contact with infectious individuals. The models proposed by Tuite, et al. and Bertuzzo, et al. both incorporated a “gravity” term to study the interaction among departments. The model proposed by Andrews and Basu accounted for a bacterial “hyperinfectivity” stage, following research by Hartley, et al. in 2006 showing that V. cholerae initially has a higher infectivity before it decays to a lower infective rate in the aquatic reservoir. The fourth model by Chaoa, et al. was an agent based approach designed to look at various vaccination strategies.

In addition, all these models assessed the impact of potential intervention strategies, including vaccination. Bertuzzo found that a vaccination campaign aiming to vaccinate 150,000 people after January 1, 2011 would have little effect, in part because of the late timing and in part because of the large proportion of asymptomatic individuals who would need to get vaccinated. Both the models proposed by Tuite, et al. and Andrews and Basu suggest that vaccination campaigns would have modest effect. In March 2012, Partners in Health began vaccinating 100,000 individuals with Shanchol, a two-dose cholera vaccine. The size

*Note: population data for Haiti is from 2009, one year before the earthquake.
of the campaign was limited by the size of the global stockpile of Shanchol. The vaccination campaign is targeted at 50,000 individuals living in the slums of Port-au-Prince, where population density is thought to increase the rate of cholera exposure, and at 50,000 individuals living in the Artibonite River valley, where the epidemic began. Chao et al. showed that a targeted vaccination strategy would have the best results for this limited supply of vaccine, and by vaccinating 30% of the population the cases could be reduced by as much as 55%.

In 2001, Codeço proposed introducing an oscillating term to model seasonal variability. However, none of the four Haiti-specific models accounted for seasonality. Haiti experienced flooding in June 2011, October 2011, and March 2012. As cholera has reached an endemic state in Haiti, an analysis of cholera’s seasonality as it relates to Haiti’s rainy season is pertinent. Moreover, mathematical models should incorporate seasonality in order to more accurately predict the course of the epidemic and to simulate the effects of potential interventions. In April 2012 Rinaldo et al. reexamined the above four models (including their own) and concluded that, among other factors, seasonal rainfall patterns were necessary to account for resurgences in the epidemic. They use long-term monthly averages to augment the bacterial growth term of contaminated water-bodies.

Other papers dealing with environmental factors were (1) a study of cholera in Zanzibar, East Africa that demonstrated 8 weeks fixed delay between rainfall and cholera outbreaks, and (2) a study in Bangladesh that reports a somewhat shorter delay (4 weeks). Both these studies use a statistical approach with seasonal data. Both also made note of the potential influence of ocean environmental factors, and the Reyburn et al. paper included sea surface height and sea surface temperature in their analysis but failed to find any significant relationship. In a third paper Koelle et al. (2005) model very long time periods, more than a year, in Bangladesh. This model also uses seasonal precipitation and models changes in the susceptible fraction of the population due to demographics and loss of immunity.

1.2. Our Model. In this paper we use detailed and current rainfall, temperature, and tidal records to model cholera in the Artibonite and Ouest regions. We forego a bacterial compartment in favor of an a posteriori approach using climatic data directly to estimate infection rates. This has the advantage of more tractable temporal estimates without over parameterizing and including compartments that are essentially unmeasurable. This paper is also the first, that we know of, that uses tidal range in a model of cholera dynamics.

These long term trends and environmental influences establish the pattern of response of the epidemic in Artibonite and Ouest. Thus parameters were chosen and model calibration set prior to a vaccination program being implemented. We then used the model to evaluate the performance of the vaccination program against the backdrop of an alternative history without vaccination.

2. Material and Methods

For Ouest and Artibonite, we investigated the correlations between reported cholera cases and rainfall, temperature, and, in the case of Ouest, tidal range. We wanted to determine
• if such correlations exist,
• the time delay between environmental conditions and recorded cholera outbreaks,
• if effectiveness of a recent vaccination program could be assessed by use of this model.

2.1. Model. We take a combined mechanistic and phenomenological approach to our model.

The mechanistic part is a standard SIR type model where individuals move from Susceptible (S) to Infected (I) to Recovered (R) classes. An infectious individual may either be symptomatic (I) or asymptomatic (A). The probability, ρ, of asymptomatic infection is 0.79. Both symptomatic and asymptomatic individuals move to the recovered group, R, at a rate γ. Symptomatic individuals die from cholera at a rate µ (dead are denoted by D).

The phenomenological approach comes from estimating the force of infection, \( \beta(t) \), by fitting the number of cases predicted by the model (both incidence and cumulative cases) to the data. We chose not to incorporate water bodies and environmental bacterial populations explicitly since this requires the estimation of extra compartments and half dozen or so other parameters for which there are no data. The feedback effects, though, are included as time lags in the action of precipitation and tides. These and all other parameters are discussed below and values are given in Table 1 and Table 2.

This paper evaluates Artibonite and Ouest separately, in order to capture the different dynamics in each region. In each case we use the following system of non-autonomous ordinary differential equations, and the components to be fitted: \( N = S + A + I + R + D \), where \( N \) is the initial population of the region, \( t \) is time since beginning of the epidemic (week starting 17-October-2010), and \( \Delta t \) is the time interval for reporting new cases (1 week). (For the purposes, and time scale, of this study we chose to ignore the demographics of the population.)

System of equations

\[
\begin{align*}
\frac{dS}{dt} &= -\beta(t) S \\
\frac{dA}{dt} &= \rho \beta(t) S - \gamma A \\
\frac{dI}{dt} &= (1 - \rho) \beta(t) S - (\gamma + \mu) I \\
\frac{dR}{dt} &= \gamma (A + I)
\end{align*}
\]

Variables to be fitted

\[
\begin{align*}
\text{new cases} &= (1 - \rho) \int_{t - \Delta t}^{t} \beta(t) S(t) \, dt \\
\text{total cases} &= (1 - \rho) \int_{0}^{t} \beta(t) S(t) \, dt
\end{align*}
\]

*Conceptually the underlying model is a variation on the SIWR model, which assumes that cholera is spread through susceptibles’ contact with contaminated water, food or fomites. This model uses the amount of water consumed as a proxy for all possible modes of transmission, and the concentration of bacteria in the water consumed modifies the infection rate by a dose-response expression (see 19 with a base model 11).
2.2. Environmental Effects. Significant rain events will cause overflowing of river and stream banks, which we assume will increase direct contact the bacteria via contaminated water, or indirectly via soils, vegetation, and pathogen-carrying insects, etc., that have been contaminated or have consumed cholera bacteria. We also assume that temperature plays a dual role by increasing the infection rate and decreasing the lag time between environmental events (precipitation and tidal range) and disease outbreaks. We speculate that decreases in time lags with warmer temperatures are due to more rapid growth, better survival, and more active bacteria and transmission agents. People also more frequently contact sources of contamination due to the variety of increased activities that warmer weather engenders.

Additionally, in the Ouest region there are commercial areas, tent-cities and slums that have raw waste directly discharging to Port-au-Prince Bay, or to the bay via rivers (e.g. Froide, Momance, and Grise), and numerous open sewage canals. We hypothesize that there may be additional disease generated when large tidal ranges stir up contaminated sediments or cause blooms of plankton in these coastal or estuarine waters. Again, the chain of infection may be complex and include direct contact with water, insects, plankton, benthos or consumption of contaminated seafood, etc. Why tidal range would have a significant effect and not tidal height is curious. There are a number of possible explanations. It may be that a larger bottom area is scoured by the breaking surface waters along the beaches, or more fresh and brackish water from river outflows and estuaries can contact the bottom sediment as the water falls and rises again, or a combination of actions. In any event it may warrant closer examination in the field.

To incorporate these effects, we modify the force of infection term, $\beta$, as follows

\begin{equation}
\beta(t) = u(t) \left[ \alpha_p H(t) P(t - \tau_p, \theta_p) + \alpha_m M(t - \tau_m, \theta_m) \right],
\end{equation}

where $P$ is a moving average of the amount of daily rainfall, and $M$ is a moving average of the maximum semi-diurnal tidal range, $H$ is a heat index based on mean air temperature, $\tau_p$ is the lag time for precipitation (which is itself affected by temperature), $\tau_m$ is the lag time for tides, $\theta_p$, and $\theta_m$ are the respective averaging periods, and $\alpha_p$ and $\alpha_m$ are the corresponding proportionality constants.

In the above formula, we also include an expression for improvement of conditions over time, either through reducing the effective susceptibles, or reduction in the infection rate, or both. These factors would be due to increased access to clean water, increased personal hygiene, decreased contamination of the environment, vaccination, and rapid treatment of new cases, or any other means of removing risk. We model this by assuming that the force of infection is reduced by an exponential function

\begin{equation}
u(t) = u_0 + (1 - u_0)e^{-rt}.
\end{equation}
In this formula \( r \) is the rate of improvement in conditions, \( 1 - u_0 \) is the initial fraction of the population whose risk is eradicable, and \( u_0 \) is the initial fraction of the population that is chronically indigent.

This approach is tantamount to having the susceptible, or at-risk population reduced directly by public health improvements. In this interpretation the at risk population would be \( S_R = u(t) S \), the \( R \) subscript indicating the at-risk subgroup of the larger susceptible population\(^1\). The at-risk population starts out equal to the entire susceptible population and declines asymptotically to the remaining number of indigent susceptibles as conditions improve.

2.3. Data.

2.3.1. Cholera cases. The source of the epidemic data was the Haitian Ministry of Public Health and Population and compiled by the Pan American Health Organization. The available data sets from the above source, used for this study, consist of cumulative cholera cases, and new cholera cases. New cholera cases are calculated based on the difference between the latest report and the previous one. Cholera case definition also includes suspected cholera cases and deaths in addition to confirmed cases and deaths. As such, data posted on the website are periodically updated with minor corrections. Cases are reported on weekly basis with the reporting week beginning on Sunday.

Reported hospitalized cases and hospitalized deaths are probably more accurate, but for the purposes of this study, less useful, since we want to track the progress of the epidemic, and increases in access to treatment biases the data. No data is available for new or total cases (\( TC \)) during the first four weeks, however hospitalized case data is available. In order to estimate the number of new and total cases during the first four weeks of the epidemic, we regressed, for the subsequent 8 weeks (14-Nov-10 through 2-Jan-11), the reported total cases against hospitalized cases (\( HC \)). For the Ouest region \( TC_O = 2.2HC_O \) \((R^2 = 0.99)\), and for the Artibonite region \( TC_A = 2.59HC_A + 497 \) \((R^2 = 1.00)\). Then using these formulas, we back-calculated the approximate number of new cases during the the first four weeks of the epidemic.

2.3.2. Environmental data. We compared rainfall, temperature and tide data to the pattern of new cholera cases reported each week. The rainfall data comes from NASA using centrally located points in each region as our datum point, given by \((\text{latitude, longitude})\). For Artibonite our datum point is (19.125, −72.625) and for Ouest, it is (18.625, −72.375). Precipitation estimates provided in the TRMM_3B42_daily.007 data product are a combination of remote sensing and ground verified information reported with a spatial resolution of 0.25 × 0.25 degrees and a temporal resolution of 1 day, further details are available on the website.\(^{22}\)

\(^{1}\)We will use this interpretation exclusively when we talk about vaccination. See appendix for the related system of equations using this interpretation.
Temperature data is mean daily air temperature at Port-au-Prince, and is reported by the Weather Underground. We used a sine function fit to the annual cycle in simulations. This has the advantage of allowing us to extrapolate temperature patterns for model projections. Unfortunately, only temperatures from Port-au-Prince were available. The temperature index derived from Port-au-Prince data were used for both Ouest and Artibonite.

Tide data is for Port-au-Prince Bay (StationId: TEC4709). These numbers are predictions from NOAA’s tide model for this location and are not direct measurements. NOAA’s web site allows one to download tide numbers for any date starting from 2010 and extending through 2014. Again, only data from Port-au-Prince is available.

2.3.3. Data analysis. The initial modeling was done by comparing data sets in the frequency (Fourier) domain for new cases and rainfall in order to find any suggestions of matching periodicity and/or time-lags. After that code was written in Berkeley Madonna to simulate the dynamical system and study the environmental data in order to match predictions to data. Rainfall data was available only to week of 27-January-2013 (week 119) because of the lag between the timing of rainfall events and what had been processed at the time we accessed it.

2.4. Model calibration. All modeling and calibration was done in Berkeley Madonna. When possible we used ranges for each parameter as established by previously published research ($\rho$, $\gamma$, $N_0$, $S_0$, $I_0$, $A_0$, $R_0$, $D_0$, $t_0$, and $u_0$; see Table 1). Since our model contains several fitted parameters ($\theta_p$, $\tau_p$, $\alpha_p$, $\theta_m$, $\tau_m$, $\alpha_m$, $M_0$, and $r$; see Table 2), we needed to supply a plausible range and initial value for each parameter in order to efficiently search the parameter space for a best fit. These ranges and initial values were chosen by visually fitting the new case output of the model to reported new cases. The Berkeley Madonna curve fitting algorithm was then used to minimize the root mean square difference between model predictions of number of cumulative cases and reported cumulative cases. Confidence and prediction intervals were calculated using the delta method.

2.5. Parameters from literature. Table 1 displays parameter values for each region obtained from published or online sources.

2.6. Environmental components of the force of infection.

When we discuss the output of our model, will use the term “prediction” to indicate the numbers generated during the calibration phase of the model and “projection” to indicate the extrapolation of the model past cases used for the calibration.
2.6.1. Artibonite. Meteorological influences on infection rate are a product of precipitation rate and a heat index. Daily precipitation $p(t)$ is averaged over an interval $\theta_p$ so the running average precipitation rate is

$$P(t - \tau_p, \theta_p) = \frac{1}{\theta_p} \sum_{j=0}^{\theta_p} p(t - \tau_p - j),$$

where $\tau_p$ is the delay in precipitation’s affect on infection rate (see below). For the delay we used a simple sine function to model a mean temperature index throughout the year. (Temperature data from.) The mean air temperature index given by

$$T_{air}(t) = \sin \left( \frac{2\pi (7t + 187)}{365.25} \right),$$

where $t$ is in weeks from 17-Oct.-2010.

This is then used to create a delay functions that varies from a minimum of $\tau_{p,lo}$ during summer and $\tau_{p,hi}$ during winter

$$\tau_p = ((\tau_{p,hi} + \tau_{p,lo}) - (\tau_{p,hi} - \tau_{p,lo}) T_{air}(t)) / 2.$$

In other words, infections follow a key set of weather and climatic variables. This would be expected since warmer temperatures mean faster growth rates for bacteria and some of their invertebrate hosts (bacterial dormancy is probably not an issue since the climate is tropical).

In addition, there is a direct influence of temperature on the infection rate. We use a heat index, $H(t)$, rather than temperature itself. This heat index is a linear function of the normalized temperature pattern with a mean (intercept) of 1 and the slope, $k$, is a parameter to be fit. This index is used as a multiplicative factor modifying the infection rate: the mean temperature has no effect on the infection rate.

| Parameter | Artibonite | Ouest | Units or calculation | References |
|-----------|-----------|-------|----------------------|------------|
| $\rho$    | 0.79      | 0.79  | fraction becoming asymptomatic | [20,26]    |
| $\gamma$  | 1.4       | 1.4   | fraction recovered per week | [4]        |
| $N_0$     | 1,571,020 | 3,664,620 | – | [2] |
| $S_0$     | 1,534,338 | 3,663,699 | $N - (A_0 + I_0 + R_0 + D_0)$ | [6] |
| $I_0$     | 7,653     | 193   | regression on early hospitalized cases | [6] |
| $A_0$     | 28,790    | 726   | $\frac{\rho}{1 - \rho} I_0$ | [6] |
| $R_0$     | 0         | 0     | – | [6] |
| $D_0$     | 239       | 2     | – | [6] |
| $t_0$     | 17-Oct.-2010 | 17-Oct.-2010 | 290th day of the year | [6] |
| $u_0$     | 0.05      | 0.05  | persistent fraction of pop. at risk | [24] |

Table 1. Parameter values obtained from literature, simple calculation, or by definition (sources in last column).
low temperatures decrease the infection rate, and high temperatures increase it. Thus we have
\[ H(t) = 1 + kT_{\text{air}}(t). \]
Therefore, the infection rate is given by
\[ \beta_A(t) = u(t) \alpha_p H(t) P(t - \tau_p, \theta_p). \] (3)
The tide term, \( \alpha_m M(t - \tau_m, \theta_m) \), is not included since we had no tidal range data for the Artibonite coast, and the tidal range data we had (Port-au-Prince) was not found to explain a significant amount of variance in the number of cases in Artibonite.

2.6.2. Ouest. For the Ouest region we use the same formulation as in Artibonite, however, we found that tidal range appeared to significantly affect infection rates as well. The maximum tidal range each day (there are two) \( m(t) \) is averaged over an interval \( \theta_m \) so the running average tidal range is
\[ M(t - \tau_m, \theta_m) = \frac{1}{\theta_m} \sum_{j=0}^{\theta_m} m(t - \tau_m - j) - M_0, \]
where \( \tau_m \) is the delay in the tide’s effect on infection rate. Here, \( \tau_m \) is fixed, the effect of temperature (water or air) on lengthening or shortening the response in infection rate was not found to be sufficient to warrant adding another function and additional parameters. Thus, the overall infection rate for Ouest is
\[ \beta_O(t) = u(t) \left[ \alpha_p H(t) P(t - \tau_p, \theta_p) + \alpha_m M(t - \tau_m, \theta_m) \right]. \] (4)

3. RESULTS

3.1. Parameter Fitting and Model Selection. Table 2 displays parameter values for each region obtained through curve-fitting to cumulative reported cases.

| parameter | Artibonite | Ouest | units | description |
|-----------|------------|-------|-------|-------------|
| \( \theta_p \) | 4.61 (0.319) | 1.96 (0.526) | weeks | averaging window for precip. |
| \( \tau_{p,\text{lo}} \) | 0.4019 (0.3261) | 3.800 (0.3757) | weeks | minimum delay for precip. effects |
| \( \tau_{p,\text{hi}} \) | 7.1805 (0.2056) | 6.500 (0.4240) | weeks | maximum delay for precip. effects |
| \( k \) | 0.5198 (0.0177) | 0.5812 (0.03050) | unitless | temp.-precip. interaction level |
| \( \alpha_p \) | 6.8806 (0.1690) \times 10^{-4} | 1.1502 (0.08582) \times 10^{-4} | (mm\times week)^{-1} | infection rate per mm rain |
| \( \theta_m \) | - | 1.00 (0.91) | weeks | averaging window for tidal range |
| \( \tau_m \) | - | 1.960 (0.494) | weeks | delay for tidal range effects |
| \( \alpha_m \) | - | 2.8128 (1.3360) \times 10^{-4} | (cm\times week)^{-1} | infection rate per cm tide range |
| \( M_0 \) | - | 24.791 (24.094) | cm | baseline of tidal range effect |
| \( r \) | 0.06100 (0.00147) | 0.02610 (0.00139) | week^{-1} | decrease in susceptibles per week |

Table 2. Parameter values obtained from model calibration. Numbers in parentheses are 95% confidence intervals (CI’s).
Plausible ranges for time lags were initially obtained from the Fourier analysis, then parameter ranges and initial values were further refined by visually fitting the new cases predicted by the model to the new cases data. We then used the Berkeley-Madonna curve-fitting routine to find a parameter set that minimized the sum of the square differences (SSD) between model output for cumulative cases and cumulative case data.

The Artibonite model with tide was not included in Table 2 since inclusion of tide did not improve the model (see Tables 3 and 4). The statistics for the model fit are given in the following two tables. Table 3 is for cumulative cases predicted by the model compared to cumulative case data.

| statistic     | Artibonite (tide) | Artibonite (no tide) | Ouest (tide) | Ouest (no tide) |
|---------------|-------------------|----------------------|--------------|-----------------|
| data points   | 74                | 74                   | 74           | 74              |
| parameters    | 10                | 6                    | 10           | 6               |
| adj RMSD      | 2210.37           | 2214.42              | 3708.59      | 6336.53         |
| adj $R^2$     | 0.9904            | 0.9909               | 0.9968       | 0.9908          |
| AIC           | 1148.99           | 1141.20              | 1271.40      | 1352.56         |

Table 3. Model predictions versus data statistics for cumulative number of cases: Root mean squared deviations (RMSD), Coefficient of determination ($R^2$), and Akaike information criterion (AIC). Degrees of freedom for the statistics are adjusted by the number of parameters fit in the calibration process.

For the full model in either region (model including tides) the parameters $\theta_m, \tau_m, M_0,$ and $\alpha_m$ are added and the model is re-optimized. For Artibonite an $F$-test for the nested models gives the following results $F = 0.045$ $d.f. = (4, 64)$ and the $p$ value is 0.9960, indicating the inclusion of the extra detail had almost no effect and would be unjustified. For the Ouest region an $F$-test for the nested models gives the following results $F = 33.63$ $d.f. = (4, 64)$ and the $p$ value is $4.208 \times 10^{-15}$, indicating the tidal data significantly improved the model fit.

Table 4 is for new cases predicted by the model compared to new case data. The statistics in Table 4 are done on the square roots of the values in order to produce more uniformly distributed data and stabilize the variance somewhat. The $F$-test for the Artibonite nested models using new cases gives the following results $F = 0.0903$ $d.f. = (4, 64)$ and the $p$ value is 0.9852. For Ouest the difference is again highly significant with $F = 3.9599$ $d.f. = (4, 64)$ and the $p$ value is 0.0062.

3.2. Lag times. The total delays in response to precipitation and tides are the sum of the averaging window and the delay function. For precipitation the minimum and maximum delays for Artibonite are 5.0 and 11.8 weeks, and for Ouest they are 5.7 and
8.5 weeks, respectively. The shorter delays are very similar in the two regions during the warmer months but during the cooler months the response time in Artibonite is 3 weeks longer. These long delays are similar in magnitude to delays reported from a study of Cholera in Zanzibar, East Africa (8 weeks fixed delay)\textsuperscript{16} and the shorter delays (4 weeks) to those in Bangladesh\textsuperscript{17}. For Ouest estimated delay from response to changes from tidal range was about 3 weeks. But since influence of tidal range has not been quantitatively reported elsewhere in the literature, we have nothing to compare this number to.

Although, rainfall data was available only to week of 27-Jan-2013 (week 119), we run the simulations using contemporaneous data lag period is over (around 7 weeks). This is just before the data for new cases ends.

3.3. Vaccination. A program to vaccinate the most at risk populations began in the 2nd week of April and ended in mid June. Each site (Ouest and Artibonite Dept) vaccinated about 50,000 persons, and each site had about 91% 2nd dose coverage. The administration of the first dose was staggered by age groups (beginning first with 10 year olds and up) because the Ministry of Health had a measles, rubella and polio vaccine catch-up campaign for children under 10 years of age that was taking place at the same time last April\textsuperscript{18}\textsuperscript{.}

In the Ouest Department, GHESKIO\textsuperscript{¶} vaccinated adults, adolescents and children over 10 years of age from April 12-23, 2012 and children under 10 from May 26 - June 3. The first dose of vaccine was given to 52,357 persons (of which 47,520 received the second dose), living in the slums of Port-au-Prince and surrounding villages\textsuperscript{.}.

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|}
\hline
\textbf{statistic} & \textbf{Artibonite (tide)} & \textbf{Artibonite (no tide)} & \textbf{Ouest (tide)} & \textbf{Ouest (no tide)} \\
\hline
data points & 74 & 74 & 74 & 74 \\
parameters & 10 & 6 & 10 & 6 \\
adj RMSD & 9.118 & 8.871 & 21.30 & 23.08 \\
adj $R^2$ & 0.7621 & 0.7755 & 0.3932 & 0.3681 \\
AIC & 336.37 & 328.79 & 461.92 & 470.28 \\
\hline
\end{tabular}
\caption{Model predictions versus data statistics for \textit{new cases}: Root mean squared deviations (RMSD), Coefficient of determination ($R^2$), and Akaike information criterion (AIC). Degrees of freedom for the statistics are adjusted by the number of parameters fit in the calibration process.}
\end{table}

\textsuperscript{8}Communicated by Jordan Tappero, MD, MPH (CDC/CGH/DGDDER, Atlanta, GA). Nov. 29, 2012.
\textsuperscript{ ¶}Groupe Haitien d’Etude du Sarcome de Kaposi et des Infectieuses Opportunistes
\textsuperscript{ ¶}Communicated by Jean W. Pape, MD (GHESKIO, Weill Cornell Medical College, Port-au-Prince, Haiti). Nov. 29, 2012.
In the Artibonite Department, PIH\textsuperscript{**} vaccinated 32183 people in rural Bocozel and 13185 people in Grand Saline with 90.8% of those people confirmed to get the 2nd dose (or 41194 for both locations). The campaign started April 15th 2012 and ran until June 10 2012. Here too, children under 9 year old were vaccinated in the second half of the time period because of the MMR and Polio vaccination campaign\textsuperscript{††}.

With these basic facts we constructed a crude vaccination schedule (Table 5) using the following assumptions:

1) approximately 25% of the population is under 10 years old;
2) the second dose was administered 14 days after the first dose was given;
3) the immune response took hold about 8.5 days after the second dose was given;
4) we used the average number of people vaccinated per day over a 12 day period for adults and 9 days for children.

| Ouest                   |
|-------------------------|
| Adult 1\textsuperscript{st} dose | 39,268 | April 10 - April 23 |
| Adult 2\textsuperscript{nd} dose | 35,640 | April 26 - May 7   |
| Adult immune response | 65 – 85% | May 4 - May 15    |
| Child 1\textsuperscript{st} dose  | 13,089 | May 26 - June 3   |
| Child 2\textsuperscript{nd} dose  | 11,880 | June 9 - June 17  |
| Child immune response  | 65 – 85% | June 17 - June 25 |

| Artibonite              |
|-------------------------|
| Adult 1\textsuperscript{st} dose | 34,026 | April 15 - April 26 |
| Adult 2\textsuperscript{nd} dose | 30,896 | April 29 - May 10   |
| Adult immune response | 65 – 85% | May 7 - May 18    |
| Child 1\textsuperscript{st} dose  | 11,342 | May 19 - May 27   |
| Child 2\textsuperscript{nd} dose  | 10,298 | June 2 - June 10  |
| Child immune response  | 65 – 85% | June 10 - June 18 |

Table 5. Simulated vaccination schedule for Artibonite and Ouest

We ran simulations following the above schedule as closely as the simulation would allow by subtracting the numbers of at risk persons (given below) from the susceptible compartment (\(S\)).

In Ouest the vaccination algorithm involved removing 2970 at risk persons per day starting on 4-May-2012 and ending on 15-May-2012, or 35640 total (these correspond to the vaccination of persons over age 10). Then the algorithm removed 1320 at risk

\textsuperscript{**}Partners in Health
\textsuperscript{††}Communicated by Louise Ivers, MD (Partners in Health/ZL, Cange, Haiti). Nov. 29, 2012.
persons per day starting on 17-June-2012 and ending on 25-June-2012, or 11880 total (children).

In Artibonite the vaccination algorithm removed 2574.67 at risk persons per day starting on 7-May-2012 and ending on 18-May-2012, or 30896 total (over age 10), then the algorithm removed 1144.22 persons per day starting on 10-June-2012 and ending on 18-June-2012, or 10298 total (these correspond to the vaccination of the at risk children). These simulations roughly follow the actual vaccination schedules given in Table 5.

Since the efficacy of the vaccine (oral Shanchol) is between 65 and 85% we did three runs 65, 75, and 85% for each department. The 75% run was our mean. To get the prediction intervals on the numbers of cases in the vaccination model, the upper bound on the interval is the 95% prediction interval determined for 65% run and the lower bound is the 95% prediction interval for the 85% run.

3.4. Simulations and Projections. We list the time line for particular events in Table 6. Curve fitting (parameter estimation) was done between model output and data from week 3 to week 76, we refer to model output during this period as “predictions”, simulation from week 76 through week 150 are referred to as “projections”. We were able to use rainfall data that ended in week 199 for another six weeks (to week 125) due to the delay of new infections from the time of the rain fall events. By “immune response for first...” and “immune response for last...” we mean this is when we begin and end removing susceptibles from the at risk group respectively.

| Event                                      | Date (week of epidemic) |
|--------------------------------------------|-------------------------|
| Begin epidemic                             | 17-Oct-10 (0)           |
| Begin case data                            | 14-Nov-10 (4)           |
| End model fitting                          | 1-Apr-12 (76)           |
| Immune response for first adult vaccinated  | 7-May-12 (81.1)          |
| Immune response for last adult vaccinated   | 18-May-12 (82.7)         |
| Immune response for first child vaccinated  | 10-Jun-12 (86)          |
| Immune response for last child vaccinated   | 18-Jun-12 (87.1)         |
| End precipitation data                     | 27-Jan-13 (119)         |
| End precipitation data with delay          | 8-Mar-13 (124.7)         |
| Begin random average rain fall data        | 9-Mar-13 (124.9)         |
| End case data                              | 17-Mar-13 (126)         |
| End simulation                             | 1-Sept-13 (150)         |

Table 6. Time line for modeling events.
3.4.1. *Predictions compared to observations for cumulative and new cases.* The following Figures 1 and 2 show the model predictions compared to observations for cumulative number of cases in Artibonite and Ouest regions, respectively. Similarly, Figures 3 and 4 show the model predictions compared to observations for new number of cases in Artibonite and Ouest regions, respectively. Prediction intervals were calculated only for the cumulative numbers, since the final model fitting was done on these numbers. Confidence intervals are shown for incidence. The match for the trends in new cases match fairly well, the slope of the expected (model) regressed against observed (data) is nearly one in both departments (see Figures 5 and 6) even though there is a substantial amount of unexplained variance. Whether this is due to the crude spatial resolution or other factors remains to be seen.

Prediction intervals (PIs) and confidence intervals (CIs) were calculated using the delta method adapted for differential equations (see, for example, Ramsay et al.25). After 27-Jan-2013 rainfall data from NASA was unavailable, for simulations after that date we did 13 runs using rainfall patterns from each of the 13 prior years. The mean of those simulations was used and the variance of the 13 runs, at each time step, was added to the variance from the estimation procedure before computing the PIs.

3.4.2. *Epidemic projections for Artibonite.* The model projected that by the mid March 2013, Artibonite would have seen between 120 and 128 thousand cholera cases without vaccine, and between 112 and 122 thousand with the implemented vaccination program (a decrease in about 7 thousand cases; see Figure 7). The models (with and without vaccination) show a marginal difference in how well they match cumulative number of cases data. There seems to be moderate agreement between the projected and observed incidence as well (see Figure 8) where the number of new cases is below what would have occurred without vaccination.

The actual number of cases is only 1,883 less than the predicted mean number of cases without vaccination. If we assume the model without vaccine is correct an average of 15,016 people would have gotten sick between 6-May-2012 and 13-Mar-2013. Over that period of time 13,143 people actually did get sick. This represents a 12% reduction in the number of people that would have gotten cholera.

3.4.3. *Epidemic projections for Ouest.* For Ouest, the model projected that by mid March 2013, Ouest would have seen between 247 and 266 thousand cholera cases without vaccine, and between 244 and 264 thousand with the implemented vaccination program (a decrease in almost 3 thousand cases; see Figure 9). The model also predicted that with vaccination about 32,839 people would have gotten ill between the onset of the immune response (6-May-2012) and the last rainfall data week (17-Mar-2013), whereas 35,613 would have gotten sick without vaccination. This represents about a 7.8% decrease in the number of people that would have gotten cholera. The different models (with and without vaccination) do not substantially differ in how well
Figure 1. Artibonite. The predicted cumulative number of *symptomatic* individuals, against total reported cases to 1-Apr-2012. Projections are from then to end of February. Projections using the vaccination schedule (red) begin on 7-May-2012, approximately three weeks after beginning the vaccination program in Artibonite. All projections after 11-Nov-2012 are based on runs using prior 13 years of precipitation, and PI’s include the variance of those data (see text).

They match cumulative number of cases data. Note that this *does not mean* that the vaccination program did not have an impact, but only that the model at this point in time could not distinguish between a scenario with and without vaccination.

The actual number that got ill between 6-May-2012 and 17-Mar-2013 was 38,910. This is 3,297 *more* than the model without vaccination predicted! There was a slowdown in number of new cases in starting in mid February 2012 and running through March 2012 which dropped the cumulative case number below the mean model projections (but still within the prediction interval), however, this occurred *before* the vaccination program took place. There was another smaller slowdown in July but then new cases increased rapidly again in November (see Figure 9). It would seem
Figure 2. Ouest. The predicted cumulative number of *symptomatic* individuals, against total reported cases to 1-Apr-2012. Projections are from then to end of February. Projections using the vaccination schedule (red) begin on 4-May-2012, approximately three weeks after beginning the vaccination program in Ouest. All projections after 11-Nov-2012 are based on runs using prior 13 years of precipitation, and PI’s include the variance of those data (see text). Note that for the Ouest region, the model begins at the fourth week. We assume that the low initial numbers in the first three weeks are a result of immigration of cases from the Artibonite region. The model therefore uses data for the first four weeks – assumed immigration numbers for the first three weeks and the initialization of the model from data for the fourth week.

that these oscillations are in spite of, rather than because of vaccination, since the model predicts a steady, albeit slow, additional decline in new cases (see Figure 10). It would seem that such a small percentage of the at risk population vaccinated, although probably beneficial to those individuals receiving the vaccine, may have had negligible impact in bestowing any broader community benefits.
3.5. **Vaccination scenarios.** We looked at changing the number of people vaccinated and the timing of vaccination to see if there is some optimal schedule that can be applied.

3.5.1. **Changing the number of people vaccinated.** The first experiment was to change the number of people vaccinated. We completed, in the model, all vaccinations within a 5 week period. The second round of vaccination was assumed to begin on epidemiological week 80 and the immune response was assumed to begin a week later on week 81 with a 75% efficacy. This was to approximately match the timing of the initiation of the actual vaccination second dose. In Artibonite we varied the number vaccinated from 0 to 65,000 and in Ouest we varied the number vaccinated from 0 to 450,000. The results are illustrated in Figures 11 and 12. Numbers vaccinated are shown on
the x-axis and percent decrease in cases on the y-axis. We show the percent decrease of cases at weeks 100, 125, and 150 of the epidemic. These correspond to 20, 45, and 70 weeks after the second dose of vaccine was administered.

In both departments the percent decrease in number of cases increases steadily until the number vaccinated reaches the number of people remaining in the at risk group. At this point there are no more people to be vaccinated but 25% of those people that were vaccinated are still susceptible. The curves level off at this point.

The curve increases almost as a straight line (almost, because the vaccination takes place over a finite period of time rather than instantaneously), indicating that the potential benefit to each person remains constant. The optimal amount to have vaccinated at 80 weeks would have been one and a half times what was done in Artibonite and nine-fold greater in Ouest. However, the costs of vaccinating every person at risk is certainly not a linear function and a cost-benefit analysis would be necessary to

**Figure 4.** Ouest. The new symptomatic individuals, vs. time. Circles - observed; solid line - model prediction; Dashed lines - 5, 50, and 95 percentiles for model projections based on past 13 years precipitation records.
determine if, and at what point the money and efforts would be better expended in other control measures.

3.5.2. Changing the timing of vaccination. To investigate the best timing of vaccination we ran two scenarios: the first, vaccination near the number to optimize vaccination at 80 weeks; and the second, vaccination near the numbers actually vaccinated.

We start by beginning the second round of vaccination at the 3rd and then increasing the timing to the 247th week. We then compare the decrease in cases for various weeks in the epidemic. The total numbers vaccinated in Artibonite was 60 thousand and in Ouest was 400 thousand.

The maximum reduction in number of cases in the 100th and 125th weeks occur when the vaccine second dose is given in the 29th week (8-May-2011) in Artibonite and 27th week (24-April-2011) in Ouest. The maximum reduction in number of cases after the 125th week occur when the vaccine second dose is given beginning in the 79th week (22-April-2012) in Artibonite and the 75th week (25-March-2012) in Ouest. However, this may belie the true best timing since the timing from vaccination to response is different for each week of the epidemic. For example for vaccine given at week 100
Figure 6. Ouest. The predicted new *symptomatic* individuals, against weekly reported cases to 1-Apr-2012 (square root transformed). A regression line matching the 45° line would show an optimal fit, the discrepancy is due in part to fitting on the cumulative numbers.

There is a large reduction in cases in the 225\textsuperscript{th} week but no reduction at all in the 100\textsuperscript{th} week since the immune response will not ever occur until the 101\textsuperscript{st} week.

Alternatively, if we look at fixed intervals relative to when vaccination is done, a different picture emerges, see Figures 15 and 16. Again there are global maximums when vaccine is given in week 29 (8-May-2011) in Artibonite and week 27 (8-May-2011) in Ouest 78 weeks (1.5 years) later. However, now there are periodic local maxima occurring each year occurring between late March and early May. At 26 weeks after vaccination (a half a year) the peak reduction in number of cases is approximately the same each spring for the first three years in Artibonite, and was greatest the first spring in Ouest.

The half year and one and a half year intervals match vaccination during a seasonal low with response in a seasonal high and vice versa. Thus they show the extreme seasonal pattern, whereas the one and two year offsets match low with lows and high with highs, so the percent differences display a minimal of seasonal pattern. Nevertheless, even in the whole number offsets there is still an annual periodicity where vaccination in early spring has an advantage over other times of the year. The early spring is marked by slightly cooler temperatures and less rain then later in the
summer. Thus it is just before new cases start to increase in the summer months. This appears to be the optimal time of year to vaccinate.

A examination of the timing response with the number vaccinated more closely matched to the actual numbers is seen in Figures 17 and 18. Here though the global maximums occur in the third year in Artibonite, and in the fourth or fifth year in Ouest.

There reason is clear when we consider again Figures 11 and 12. Here the maximum percent decrease in cases is when the number vaccinated matches the number remaining at risk. Thus when we vaccinated at a lower level the optimal time for the this level of vaccine is at a later date, and preferably in April, when other measures have reduced the at risk population to a size comparable to the number that can be vaccinated. Thus it appears that vaccination programs, as they actually occurred,
Figure 8. Artibonite. The projected new symptomatic individuals, vs. time. Circles - observed; solid line - model prediction; Dashed lines - 95 percentile confidence intervals for model projections. Red line is projections with 75 percent vaccine efficacy.

occurred at nearly the best time of year, but may have been slightly more effective this year in Artibonite, or even next year in Ouest.

4. Discussion

Modeling the dynamics of cholera in Haiti has been hampered by the lack of easily accessible detailed historical meteorological data. We use NASA satellite data to address this problem. This study shows that with environmental data of sufficient detail and quality, projections of disease progression can be made with sufficient lead time to prepare for outbreaks. The lag times of over five weeks means that if even rudimentary but reliable meteorological and coastal records are kept, preparations and resources can be more focused. The gathering of basic weather information is simple and inexpensive and should be made standard procedure when any agency takes part
in interventions, particularly when the environmental component of the epidemiology is so well established.

In addition we explored the hypothesis that, at least in the Ouest region, tidal influences play a significant role in the dynamics of the disease. It appeared that tidal range rather than the height of the tide itself had the strongest influence. Some connection to tidal influences should be expected where large populations are in close contact with bays and estuaries, and humans are consuming local seafood.\textsuperscript{17,28} It is not surprising that there was no effect of tidal range found in Artibonite since the tide model was for off the coast of Port-au-Prince. Again the lack of readily available
detailed historical tide records or even a model for various regions along the coast hinders a thorough investigation of possible factors in the disease dynamics.

We also affirmed the longer time lags (8 - 10 weeks) found in previous studies from Africa[16] and shorter ones (4 weeks) in Bangladesh.[17] Delays in the effects of precipitation on the infection rates varied for Artibonite between 5.0 and 11.8 weeks, and for Ouest they ranged from 5.8 to 8.5 weeks. The shorter delays occurring in the two regions during the warmer months but differing by up to 3 weeks during the cooler months. One possible explanation of the difference in the two regions may be due to greater sensitivity to the density of infected population in cooler months and little sensitivity in warm months. Or, to state it another way, there could be a low sensitivity to temperature changes when infected density is high, and high sensitivity to temperature changes when there are relatively less people infected. The relatively high numbers of infected in Ouest keep the lag times short no matter what the weather,
whereas in Artibonite where the infection rate is a quarter to half that of Ouest cooler weather has more of an impact in slowing the disease cycle.

Over the course of the epidemic the incidence has been tapering off. There has been steady and continued effort to improve hygiene and living conditions, however, the areas where the greatest strides are made are those where people leave the camps to return to normal living conditions and employment. The declining numbers of those at risk in the overall population belie the fact that many local populations are still without basic hygienic facilities. This was reflected in the model by setting a level $u_0$ to 5% of the original number of susceptible. This value matches the approximate 5% of the population that still remain displaced after the 2010 earthquake.

On top of predicting when and how many cholera cases will increase with Haiti’s weather patterns and tides, any modeling to predict the effectiveness of interventions (such as vaccination) should consider these patterns. Considering that cholera may

**Figure 11.** Artibonite. The percent decrease in the total number of cases at week 100, 125, and 150 for the total number vaccinated indicated on the abscissa. The onset of the immune response was assumed to begin in week 81 and complete in week 85. We assume 75% efficacy of the vaccine. The actual number completing vaccination (41,194) is indicated by the vertical line.
be maintained in the environment outside the human chain of infection is essential to planning effective prophylaxes and interventions.

Using these models we were able to assess, to some degree, the relative effectiveness of the recent vaccination program in Artibonite and Ouest. The discrepancy between the apparent effectiveness of vaccination in the two regions is perhaps not that puzzling when one considers the number vaccinated relative to the size of at risk population. In Artibonite about 41 thousand people and in Ouest about 47 thousand people received both doses of the vaccine. However, our model suggests that in Artibonite the at risk population by 6-May was about 61 thousand whereas in Ouest it was still over 428 thousand, seven times the number in Artibonite. Thus in Artibonite 67% of the most at risk population apparently received the vaccine, while in Ouest only 11% did. Further, in both regions 100 people receiving vaccination does not mean 100 people protected. The vaccine is about 75% effective, and only 21% of people who are infected
with cholera show symptoms, $0.75 \times 0.21 = 0.1575$. So as a rough calculation we might expect $0.1575 \times 41,000 = 6457.5$ in Artibonite, and $0.1575 \times 47,000 = 7402.5$ people in Ouest protected directly. Any additional protection would be due to the reduction in environmental loading of cholera bacteria and the force of infection. Although ultimately more people will be protected in Ouest any of the secondary effects of vaccination will probably be lost due to dilution of the vaccinated group.

4.1. Conclusion. Although progress has been made in the past two years in modeling the Haitian cholera epidemic, only one model, so far, has accounted for seasonal variation due to precipitation, and none of the model of the current Haitian epidemic have examined temperature or tidal influences. Our paper shows that with basic climatic and tidal records and a relatively unsophisticated modeling procedure, not only can these factors be accounted for but also the time lags between climatic events and outbreaks can be identified. This approach looks at specific climatic events on the scale of a week rather than just seasonal patterns. We use daily tidal range as a predictive
The decrease in the total number of cases by week 100 through 225 for the week beginning the second round of vaccination indicated on the abscissa. The onset of the immune response was assumed to begin a week later. We assume 75% efficacy of the vaccine.

factor for cholera epidemics for the first time in a modeling paper, and we use real time daily precipitation estimates. These provide a level of detail of environmental events in conjunction with the lag times and estimates of core population size that can help evaluate intervention (such as vaccination) and public hygiene efforts. In order to show this we examined recent vaccination efforts in the Haitian cholera epidemic. Complex environmental patterns incorporated in epidemic models allow us to remove a large source of variability and bring into relief intervention efforts by identifying deviations from the unaltered flow.
Figure 15. Artibonite. The percent decrease in the total number of cases 26, 52, 78 and 104 weeks after the beginning the second round of vaccination indicated on the abscissa. The onset of the immune response was assumed to begin a week later. We assume 75% efficacy of the vaccine.
Figure 16. Ouest. The percent decrease in the total number of cases 26, 52, 78 and 104 weeks after the beginning the second round of vaccination indicated on the abscissa. The onset of the immune response was assumed to begin a week later. We assume 75% efficacy of the vaccine.
Figure 17. Artibonite. The percent decrease in the total number of cases 26, 52, 78 and 104 weeks after the beginning of the second round of vaccination indicated on the abscissa. The onset of the immune response was assumed to begin a week later. We assume 75% efficacy of the vaccine.
Figure 18. Ouest. The percent decrease in the total number of cases 26, 52, 78 and 104 weeks after the beginning the second round of vaccination indicated on the abscissa. The onset of the immune response was assumed to begin a week later. We assume 75% efficacy of the vaccine.
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APPENDIX

System of equations using a reduction in the at-risk group. We have \( u = u_0 + (1 - u_0) e^{-rt} \) as before, and \( \frac{d}{dt} u = -r (u - u_0) \). The equation for the entire susceptible population is the same also, that is \( \frac{d}{dt} S = -u \beta_R S \), but here we keep improvement factor \( u \) and the crude force of infection \( \beta_R \) separate, where

\[
\beta_R = \alpha_p H(t) P(t - \tau_p, \theta_p) + \alpha_m M(t - \tau_m, \theta_m).
\]

The improvement factor, \( u \), represents the fraction of the population that remains at risk at time \( t \). Thus

\[
S_R = u S.
\]

Differentiating with respect to time we have

\[
\frac{d}{dt} S_R = u \frac{d}{dt} S + S \frac{d}{dt} u = -u^2 \beta_R S - r (u - u_0) S - u \beta_R S_R - r \left(1 - \frac{u_0}{u}\right) S_R.
\]

New cases are as before \( u \beta_R S \) which equals \( \beta_R S_R \). Note that the number of new cases is the same in both interpretations but the force of infection is reduced (\( \beta = u \beta_R \)) in the original interpretation and we use the crude force of infection (\( \beta_R \)) and the reduced at-risk susceptible population (\( S_R \)) here.

With vaccination we have

\[
\frac{d}{dt} S_R = -u \beta_R S_R - r \left(1 - \frac{u_0}{u}\right) S_R - V = -u^2 \beta_R S - r (u - u_0) S - V,
\]

where \( V \) is the number vaccinated per unit time. But

\[
\frac{d}{dt} S = \frac{1}{u} \left( \frac{d}{dt} S_R - S \frac{d}{dt} u \right) = \frac{1}{u} \left(\left(-u^2 \beta_R S - r (u - u_0) S - V\right) + r (u - u_0) S\right)
\]

\[
= -u \beta_R S - \frac{V}{u}.
\]

New cases are still \( u \beta_R S \) which equals \( \beta_R S_R \) and the \( V/u \) term represents the number of all susceptibles that would have needed to have been vaccinated in the original, reduced force of infection, interpretation of the model in order to have an equivalent impact on the number of new cases.
In order to include efficacy of vaccination, $f$, in the model we need to introduce a new compartment, $Q$, for vaccinated but still susceptible. The set of differential equations for the system then become,

$$\frac{dS}{dt} = -u\beta(t) S - \frac{V(t)}{u}$$
$$\frac{dQ}{dt} = -u\beta(t) Q + (1 - f) \frac{V(t)}{u}$$
$$\frac{dA}{dt} = \rho u\beta(t) (S + Q) - \gamma A$$
$$\frac{dI}{dt} = (1 - \rho)u\beta(t) (S + Q) - (\gamma + \mu) I$$
$$\frac{dR}{dt} = \gamma (A + I)$$

New and total cases are

new cases = $(1 - \rho) \int_{t-\Delta t}^{t} u(t) \beta(t) (S(t) + Q(t)) \, dt$

total cases = $(1 - \rho) \int_{0}^{t} u(t) \beta(t) (S(t) + Q(t)) \, dt$