Determination of the Most Cost Effective Pre-Outbreak Immunization Rate through a Novel Approach

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Abstract

This research sought to improve the cost effectiveness of Pre-Outbreak Immunization (POI). This end was achieved through the development of a novel quantification for cost effectiveness, the Morbidity Avoidance Ratio (MAR), which can be widely applied in impoverished nations most affected by vaccine preventable diseases. Using a simulation for disease spread programmed into MS Excel, I calculated the MAR for idealized cases of measles, mumps, and rubella. I also determined based upon this analysis that the most cost effective POI rate is the herd immunity threshold, and found that as the POI rate increased, the cost effectiveness increased up until the threshold is reached. This research demonstrates a novel approach to analyzing POI and can help improve the cost effectiveness of outbreak control.

INTRODUCTION

Vaccines provide the opportunity to greatly reduce the disease burdens of nations around the world [1]. Unfortunately, vaccination programs are costly [2] and thus place extreme financial burdens on the health systems of impoverished nations, which are most affected by Vaccine Preventable Diseases (VPDs) [3]. In recognition of this problem, this research seeks to improve the cost effectiveness of VPD outbreak control with the goal that funds preserved through increased cost effectiveness can be applied to other areas of dire medical need.

The primary aspect of outbreak control discussed in this paper is vaccination. There are two windows of time during which a vaccination program may be implemented: Pre-Outbreak Immunization (POI) and Outbreak Response Immunization (ORI – occurs during the outbreak). This paper seeks to optimize the cost effectiveness of the POI approach.

Several measures of cost effectiveness exist and have been thoroughly studied. Chief among them are the “life years gained” and “quality adjusted life years (QALY),” both of which quantify the output value of a certain medical intervention [4]. However, both approaches have been shown to be inefficient at properly analyzing the true cost effectiveness of medical programs [5]. In addition, the cost effectiveness of immunization campaigns for measles, mumps, and rubella has been calculated previously; however, this prior approach involved sometimes arbitrary quantifications of monetary benefits and was conducted in the U.S. using the U.S. monetary system [6], thus limiting its applicability to impoverished nations. The cost effectiveness of measles immunization specifically also has been studied extensively, with most applying the U.S. monetary system again [7,8]. In most cases these cost effectiveness analyses concern one outbreak or immunization approach specifically, thus further limiting their scope of applicability [7,8].

In this research, I developed a novel approach to quantifying the cost effectiveness of different POI rates. In addition, I generated formulas with which POI campaigns can be tailored to each individual VPD in order to maximize their cost effectiveness.

METHODS

In order to quantify the cost effectiveness of Pre-Outbreak Immunization (POI), a method was developed that took into account the limitations of previous methods discussed earlier. This novel quantification was named the Morbidity Avoidance Ratio (MAR). I based it upon the notion that the primary goal of immunization is to reduce the number of infections (morbidities). The cost of the immunization campaign is assumed to be directly proportional to the number of vaccines deployed.

Morbidity Avoidance Ratio

Figure 1

$$\text{MAR} = \frac{\text{\# of infections avoided}}{\text{\# of successful immunizations}}$$

The MAR was tested using a previously developed SIRV Model reproduced below [10]:

Figure 2

$$\frac{dS}{dt} = -\lambda SI - \rho S$$

$$\frac{dI}{dt} = \lambda SI - \delta I$$

$$\frac{dR}{dt} = \delta I$$

$$\frac{dV}{dt} = \rho S$$

Where S is the fraction of the population susceptible, I is the fraction of the population infectious, R is the fraction of the population recovered, V is the fraction of the population immunized during the outbreak, t is time, ? is the infection rate, ? is the recovery rate, and ? is the immunization rate.

A cost effectiveness analysis using the MAR was performed for three VPDs: measles, mumps, and rubella. Using published estimates [9] for the infection and recovery rates for each of the diseases, I programmed into MS Excel a simulation of the SIRV Model [10] shown above by creating a recursive definition for each of the differential equations. The total population for each of these simulations was set at 10,000 persons with basic reproduction numbers of 18 for measles, 5 for mumps, and 7 for rubella [9].

The simulation was run for each disease initially without any POI or ORI. In other words, the disease ran its natural course without any outbreak control interference. The total number of infections having occurred through the entirety of the outbreak was recorded. The simulation was then rerun with POI coverage set at 10% and successive values at increments of 10 (i.e. 10%, 20%, …. 90%, 100%). The total number of infections caused by the outbreak at each POI rate was recorded.

The difference between the total infections without immunization and the total infections with immunization was used to determine the "# of infections avoided" term in the MAR formula. Using this data, the POI rate yielding the maximum MAR was determined for each disease. Each disease had a unique maximum MAR as well as a different POI rate resulting in this maximum MAR. Based upon these differences, it was hypothesized that both the POI rate that maximizes the MAR and the actual maximum value of the MAR are dependent upon the basic reproduction number (R), which differs for each disease. Upon further investigation, the following relationships were determined:

POI rate resulting in maximum MAR

Equation (1):

Figure 3

$$V = 1 - \frac{1}{R_0}$$

Maximum value of MAR

Equation (2):

Figure 4

$$MAR \cong 1 + \frac{1.2}{R_0}$$

RESULTS

The data resulting from my SIRV Model simulation runs on MS Excel is shown below in Figure 1. The maximum MAR for measles occurred with an 94.44% POI rate and was 1.055. That for mumps was 1.237 at an 80% POI rate, and for rubella 1.160 at an 85.71% POI rate.

Figure 5

Figure 1: Graph demonstrating the effects of POI rate on the MAR.

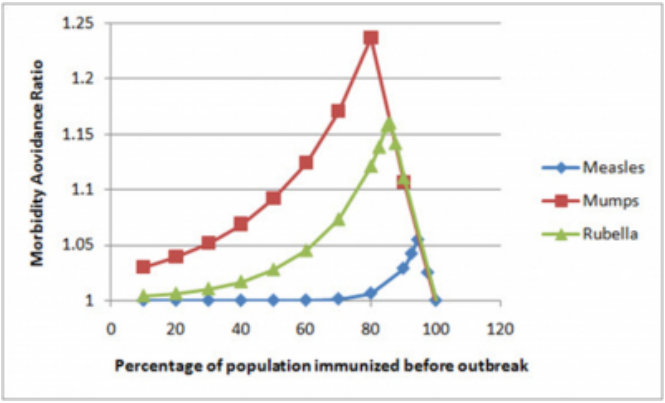


Figure 6

Figure 2: Graphical representation of the relationship between the basic reproduction number and the most cost effective POI rate.

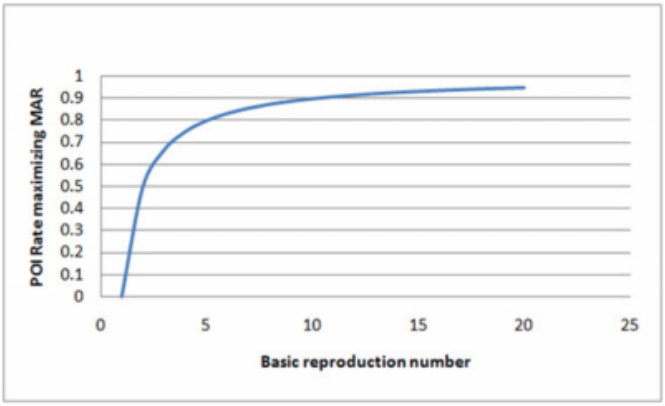
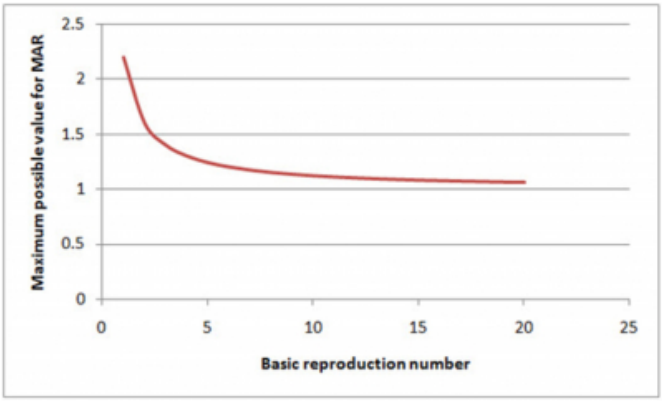


Figure 7

Figure 3: Graphical representation of the relationship between the basic reproduction number and the highest possible MAR for the certain disease.



Equations (1) and (2) are graphically represented in Figures 2 and 3, respectively. These equations were tested against the actual data from the SIRV Model simulation. Data from this comparison, demonstrating the accuracy of equations (1) and (2), is displayed in Table 1 below. As can be seen, both equations (1) and (2) are highly accurate, with extremely low percent error values.

Figure 8

Table 1: Data generated from MS Excel SIRV Model simulation demonstrating accuracy of developed models (1) and (2) for the optimum POI rate and maximum possible MAR for each studied disease.

Disease / basic reproduction number	Modeled optimum POI rate (%) using (1)	Actual optimum POI rate (%)	Modeled maximum value of MAR using (2)	Actual maximum value of MAR	Percent error of model (2) for max MAR (%)
Measles / 18	94.444	94.444	1.067	1.055	1.137
Mumps / 5	80.000	80.000	1.240	1.237	0.243
Rubella / 7	85.714	85.714	1.171	1.160	0.948

DISCUSSION

The novel approach to determining the cost effectiveness of different POI rates (through the Morbidity Avoidance Ratio) achieved the goals of this research. The use of the MAR facilitated the development of a concise formulation with which an outbreak control agency may easily determine the optimum POI rate. While that formula (1) was widely known previously as an elementary formula to determine the herd immunity threshold, a novel purpose, to determine most cost effective POI rate, was found for it in this research.

The fact that the herd immunity threshold and the most cost effective POI rate coincide is quite logical, due to the fact that if the herd immunity threshold has been achieved, an outbreak cannot begin. Another important aspect of Figure 1 is its demonstration of the partial contribution of higher POI rates to increased cost effectiveness. In other words, as the POI rate increases towards the herd immunity threshold, the MAR increases as well. Therefore, outbreak control agencies can know that although they may not be able to attain the full herd immunity threshold, the cost effectiveness will still be greater for a higher POI rate than a lower one. However, the peaks in Figure 1 must be noted as well. At POI rates in excess of the herd immunity threshold, the MAR actually decreases.

As seen in Figure 3, the basic reproduction number for a specific disease and the maximum MAR for that disease are inversely proportional. This fact illustrates an important aspect of improving the cost effectiveness of vaccination programs. The MAR analysis demonstrates that immunizing against a VPD with a lower basic reproduction number is more cost effective (as evidenced by the higher maximum MAR) than immunizing against a VPD with a higher basic reproduction number.

One notable drawback with regard to the cost effectiveness analysis presented herein is that the SIRV simulation assumed homogenous mixing of the population and the mass action principle [$_{10}$]. In other words, the cost effectiveness of idealized versions of measles, mumps, and rubella was calculated. These values would most likely differ given real world variability and heterogeneity. However, it appears as though the general trends would remain relatively unchanged.

It should be noted that the reason the MAR approach does not involve a specific cost is due to the high variability of monetary systems and costs of vaccine implementation across the wide spectrum of impoverished nations. Instead, it was assumed that the cost, regardless of the nation, would be directly proportional to the number of vaccines deployed. In other words, the MAR approach is more widely applicable to impoverished nations than one rooted in strictly defined pecuniary measures, such as those discussed in the Introduction.

Overall, the MAR analysis represents a novel approach to determining the most cost effective immunization rate. It accomplishes the overall goal of this research, that of creating a quantification for cost effectiveness that is widely applicable to impoverished nations. In addition, the MAR analysis of several VPDs revealed important trends and revelations concerning improving the cost effectiveness of outbreak control.

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