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Establishing herd immunity against Ebola through vaccination

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ABSTRACT

Objectives: In response to recent concern regarding Ebola outbreaks, this study aims to (1) determine the relationship between vaccination coverage and herd immunity, (2) determine the vaccination coverage necessary to establish herd immunity for previous Ebola viruses, and (3) recommend vaccination coverage thresholds for future Ebola viruses.
Methods: Herd immunity thresholds needed to block transmission of Ebola virus were determined using vaccine efficacy and number of secondary cases per infected case during an entire infectious period.
Results: In past Ebola outbreaks 42.2–63.0% of the population would need to be vaccinated in order to prevent transmission and outbreaks. Assuming 80% vaccine efficacy as reported by phase I clinical trials, 52.7–78.7% of the population would require vaccination coverage in order to establish herd immunity. In recent ring vaccination trials which considered the vaccine to be 100% effective after 10 days, 42.2–63.0% of the population would need to be vaccinated.
Conclusion: For future Ebola outbreaks, the spread of the virus can be prevented by vaccinating certain percentages of the population depending on vaccine efficacy and number of secondary cases per infected case.

1. Introduction

In 2014 the largest Ebola epidemic in history spread through West Africa with additional cases reaching the United States [1]. The first case of Ebola was recognized in 1976 in the Democratic Republic of Congo as a rare and severe illness with fatal potential. The virus is transmitted from wild animals to people and spreads through the population from human-to-human transmission. Due to the dangerous nature of the virus, it is important to prevent its transmission through vaccination. Vaccination can reduce the risk of Ebola virus contraction and its related complications, physician visits, hospitalizations and death. By vaccinating a certain proportion of the population against the virus, transmission of Ebola in the community can be blocked through the establishment of herd immunity.

Vaccines can affect more than just the individual who is vaccinated; vaccines can also protect people who have not been immunized. The concept of "herd immunity" refers to an indirect protection of an entire community from disease by immunizing a critical proportion of the populace. Herd immunity breaks the chain of an infection's transmission so that outbreak does not occur [2]. For example, transmission of measles can be blocked by vaccinating 92–95% of a given community [3]. The remaining 5–8% of the community who are unvaccinated and susceptible to measles receive "conferred immunity" from the vaccinated individuals. Given the proportion of vaccinated individuals, in terms of vaccination coverage, above a pre-determined herd immunity threshold, transmission of measles is blocked within the community.

The threshold for herd immunity needed to block transmission of Ebola virus in the population is currently unknown. Herd immunity is established when the prevalence of protected persons (I) is higher than the herd immunity threshold ($I > I_c$) [3,4]. When this occurs, Ebola virus transmission is blocked within the given population. However when prevalence is lower than the threshold, the number of infections is able to grow exponentially, thus spreading the virus within the population. Recent early phase trials of Ebola vaccinations report the efficacy of the vaccines, which can be used to determine the percentage of the population that requires vaccination in order to reduce community outbreaks and prevent transmission [5,6].

The objectives of this study are to determine the relationship between Ebola vaccination coverage and herd immunity,

Abbreviations: V_c, critical vaccination coverage; I_c, herd immunity threshold; R_0, basic reproductive number; E, vaccine efficacy.

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Table 1
Average number of secondary cases per infected case (R_0) and prevalence of protected persons necessary to establish herd immunity (I_c) for studied Ebola virus outbreaks.

Ebola virus	R_0, CI	I_c (%), CI
1995 Democratic Republic of the Congo epidemic [5]	2.7 (1.9–2.8)	63.0% (47.37–64.3%)
2000 Uganda epidemic [5]	2.7 (2.5–4.1)	63.0% (60.0–75.6%)
2014 Liberia epidemic [6]	1.73 (1.66–1.83)	42.2% (39.8–45.4%)

Where $I_c = [1 - (1/R_0)]$.
I_c = herd immunity threshold and R_0 = basic reproductive number.

determine the vaccination coverage necessary to establish herd immunity for previous Ebola viruses, and provide suggestions for vaccine coverage needed for future Ebola viruses.

2. Methods

This study mathematically determined the herd immunity threshold required to prevent transmission of Ebola. It was determined by accounting for the number of secondary cases per infected case (R_0) during the entire infectious period in a completely susceptible population, or basic reproductive number, in past outbreaks and the vaccine effectiveness. When $R_0 > 1$, outbreaks and resulting epidemics occur.

When vaccinations are administered within a specified population or community, the vaccine protects only a proportion (E) of the vaccinated individuals. The proportion of protected individuals who were vaccinated represents the effectiveness of the vaccine against infection transmission.

Using the mentioned variables, the critical proportion of protected individuals needed to establish herd immunity in a completely susceptible community can be determined from the equation $I_c = 1 - (1/R_0)$ [2–4]. The critical vaccination coverage (V_c) needed to establish herd immunity can next be determined by dividing the herd immunity threshold (I_c) by the level of vaccine effectiveness (E): $V_c = I_c/E = [1 - (1/R_0)]/E$ [2,4].

Citing R_0 values from past Ebola epidemics (Table 1), it is possible to mathematically derive the herd immunity threshold, and the number of protected persons required to establish herd immunity in a completely susceptible population.

After determining herd immunity thresholds for previous epidemics, data was pulled from phase I and III clinical trials in order to determine the critical vaccination coverage needed to establish herd immunity in past outbreaks given vaccine efficacy. Vaccine efficacy in early phase I clinical trials was measured by percentage of subjects with positive enzyme-linked immunosorbent assay results at week 12 after vaccination. Antibodies directed against specific antigens were measured throughout the trial and an end point titer with a background-corrected optical density reading of ≥30 was considered a positive result [7]. A more recent phase 3 trial of Ebola ring vaccination determined efficacy of ring vaccination based on zero cases of Ebola virus disease at 10 days or more post-randomization and vaccination [8].

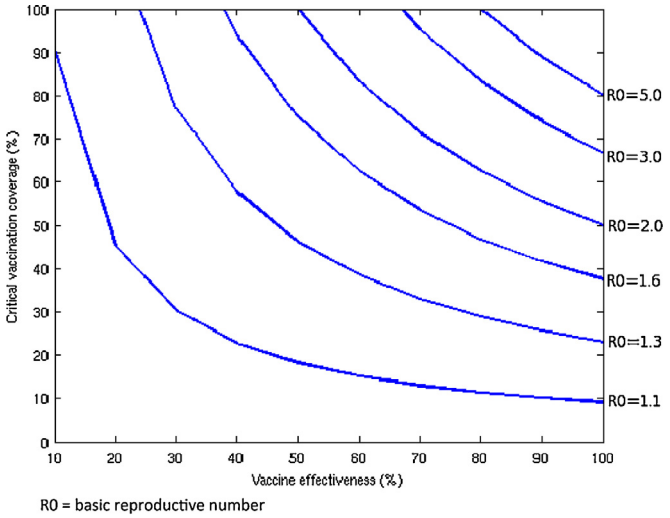

Fig. 1. Critical vaccination coverage (%) needed to provide herd immunity against varying Ebola viruses and variable vaccine efficacy. R_0 = basic reproductive number.

3. Results

In past Ebola virus epidemics, the prevalence of protected persons needed to establish herd immunity ranged from 42.2% in the most recent epidemic to 63.0% in earlier epidemics (Table 1).

The required vaccination coverage to establish herd immunity for past Ebola epidemics varied depending on vaccine efficacy. The required vaccination coverage to establish herd immunity for these past Ebola epidemics ranges from 52.7% to 78.7% assuming the vaccine is 80% effective as reported by a phase I clinical trial [7]. A 2015 phase-3 ring vaccination cluster-randomized trial reports the efficacy of the vaccine in different scenarios. In individuals who randomly received the ring vaccination, the vaccine was considered to be 100% efficacious after 10 days [8] which requires 42.2–63.0% of the population to be vaccinated in order to provide herd immunity. The 2015 study reports an estimated 75.1% and 76.3% overall vaccine efficacy in all eligible participants, which equates to a critical vaccination coverage of 56.2–83.9% and 55.2–82.6% respectively.

To account for real-world human error and varying degrees of efficacy, Table 2 reports the vaccination coverage that would have been required to establish herd immunity against past epidemic Ebola viruses for different levels of vaccine effectiveness.

The vaccination coverage required to establish herd immunity against future Ebola viruses for varying levels of vaccine effectiveness and differing R_0 values is demonstrated in Fig. 1. For example, when the number of secondary cases per infected cases, R_0, is equal to 1.1 and the vaccine is approximately 90% effective, only about 10% of the given population will have to be vaccinated in order to provide herd immunity against the virus.

Table 2
Vaccine coverage (V_c) required to establish herd immunity against past Ebola viruses for varying levels of vaccine effectiveness.

Vaccine effectiveness (E)	1995 Democratic Republic of the Congo epidemic	2000 Uganda epidemic	2014 Liberia epidemic
40%	100%	100%	100%
60%	100%	100%	70.3%
80%	78.7%	78.7%	52.7%
90%	70.0%	70.0%	46.9%
100%	63.0%	63.0%	42.2%

Where $V_c = I_c/E$.
V_c = vaccine coverage and I_c = herd immunity threshold.

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