Optimized Oral Cholera Vaccine Distribution Strategies to Minimize Disease Incidence

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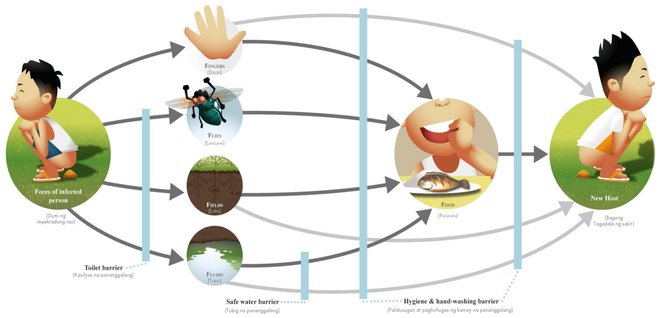
Introduction

Cholera Worldwide

1.4-4.3 million cases of cholera per year, leading to 28,000-142,000 deaths (WHO, 2014)

Cholera Transmission

Oral-Fecal Pathway[1]



Cholera Outcomes

Severe diarrhea, dehydration, and potentially death

Cholera Prevention

- Improved water, sanitation, and hygiene (WASH) strategies
- Vaccination with an oral cholera vaccine (OCV)

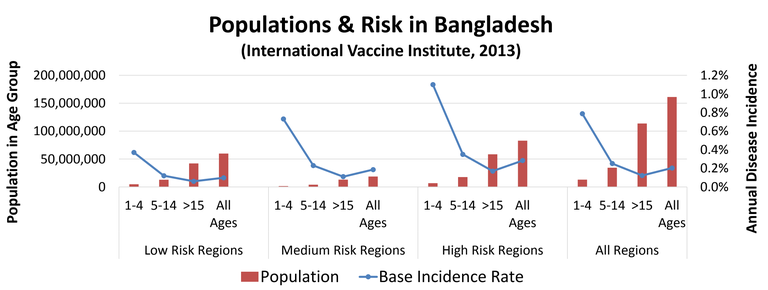
Currently, there is no systematic method for finding the best OCV distribution strategy under limited resources.

Methods

For systematic distribution of OCVs over multiple populations and multiple years:

- Mixed integer programming model
- Distribution strategy analysis, considering groups by:
  - Age
  - Region
  - Age & region
- Investigation of age & region strategy with:
  - Varying supply
  - Complete vaccination (best coverage)
  - Partial vaccination
  - Varied vaccine efficacy
- Cost-effectiveness analysis

Case Study: Bangladesh



1. "F-diagram-01" by UNICEF Philippines and Luis Gatmaitan / 2014 / Gilbert F. Lavides - https://www.flickr.com/photos/gtzecosan/17125224489/in/set-72157648282032913. Licensed under CC BY 2.0 via Wikimedia Commons - https://commons.wikimedia.org/wiki/File:F-diagram-01.jpg#/media/File:F-diagram-01.jpg

Optimization Model

Basic model assumptions:

- OCV Shanchol
  - $2 US /dose
  - 65% fixed vaccine protective efficacy over 5 years (Bhattacharya et al., 2013)
- .5%-1.5% case fatality rate
- Crude birth rate 20/1000, crude death rate 6/1000 (Worldbank, 2012)

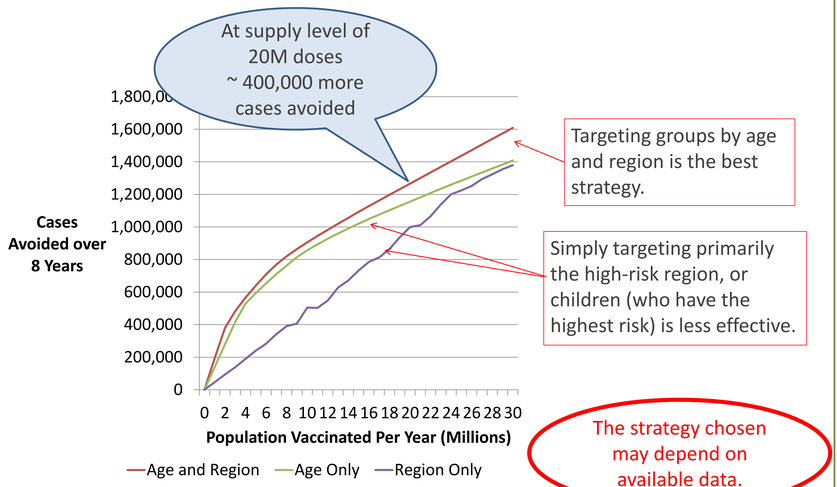
Primary model constraints:

- Vaccinations administered ≤ Production capacity
- Cost ≤ Budget
- Vaccinations administered ≤ Population

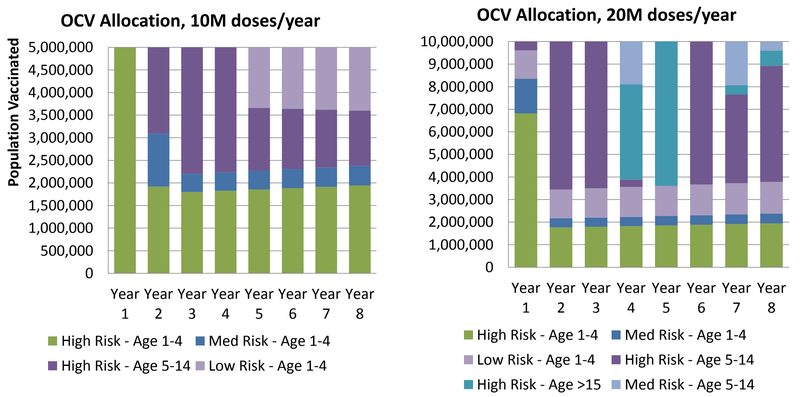
Objective: Minimize cases of (or deaths from) cholera

Results

Distribution Strategies



Complete Vaccination (2 doses per vaccinated person)



Vaccination priorities:

1. High risk 1-4 year-olds
2. Medium risk 1-4 year-olds
3. Low risk 1 year-olds and/or high risk 5-14 year-olds
4. Other groups in order of risk (if vaccine remaining)

High risk 5-14 year-olds have slightly lower risk than low risk 1-4 year-olds, but children in the age 1-4 group move quickly to a group with lower risk than the age 5-14 group.

Results (continued)

Partial Vaccination (1 or 2 doses per vaccinated person)

Two doses are recommended per vaccinated person unless a single dose is at least 51% as effective as two doses. In that case, a single dose is recommended for some individuals in order to vaccinate more people.

Varied Vaccine Efficacy

	Age (years)			Year Since Vaccination				
	1-4	5-14	15+	1st	2nd	3rd	4th	5th
Vaccine Protective Efficacy (2 doses) (Bhattacharya et al., (2013))	42%	68%	74%	45%	76%	66%	58%	80%

Priority is given to groups receiving the most vaccine benefit:
vaccine benefit = (base incidence rate) * (vaccine efficacy)

Cost-Effectiveness Analysis of Distribution Strategies

	Case Fatality Rate (CFR)	Age and Region	Age Only	Region Only
Cost per DALY avoided (20M doses/yr)	0.5%	$2,526	$2,615	$5,326
	1.0%	$1,263	$1,307	$2,663
	1.5%	$842	$872	$1,775

Cost Effective

DALY = disability-adjusted life year

Very cost effective if ≤ $830 (gross domestic product (GDP))

*Cost effective if ≤ $2,490 (3 * GDP)*

- No strategy is cost effective if CFR is 0.5%
  - Age and region and age only strategies are cost effective over 8 years at 0.5% CFR if:
    - investment in OCV vaccination for 7 years or less

    or
    - at most 15 million doses/year
  - The region only strategy is cost effective for 0.5% CFR if maximum price of $.90/dose
- Strategies may be more cost effective if we consider herd immunity

Conclusions

- Detailed and reliable surveillance data can produce OCV distribution strategies that prevent thousands of deaths
- Allocating vaccines by region and age group (or in order of vaccine benefit) is the most life-preserving and cost-effective strategy
- Mathematical modeling is a useful tool for helping optimize OCV distribution strategies

For additional details:

Smalley, H.K., P. Keskinocak, J. Swann, and A. Hinman. "Optimized oral cholera vaccine distribution strategies to minimize disease incidence: A mixed integer programming model and analysis of a Bangladesh scenario." *Vaccine*. 2015