IMPACT OF NONMEDICAL VACCINE EXEMPTION POLICIES ON THE HEALTH AND ECONOMIC BURDEN OF MEASLES

Results from an Agent Based Transmission Model

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Acknowledgements

- Jon Campbell, PhD
- Allison Kempe, MD, MPH
- Amanda Dempsey, MD, PhD, MPH
- Rachel Herlihy, MD, MPH

Whittington MD, Kempe A, Dempsey A, Herlihy R, Campbell JD. Impact of Nonmedical Vaccine Exemption Policies on the Health and Economic Burden of Measles. Academic Pediatrics.

Learning Objectives

1. Describe the implications of geographic variation in vaccination coverage.
2. Compare and contrast nonmedical vaccine exemption policies.
3. Describe the impact of vaccine exemption policies on the likelihood, magnitude, and cost of a measles outbreak.

BACKGROUND

Measles Virus

- Causes an infection of the respiratory system[1]
  - Symptoms:[1]
    - Fever
    - Cough
    - Runny nose
    - Red eyes
    - Rash
  - Severe Complications:[1]
    - Pneumonia
    - Encephalitis
    - Hospitalization
    - Death

- Highly Contagious
  - Spread by coughing and sneezing[1]
  - 90% of non-immune contacts will become infected[1]

Preventing Measles

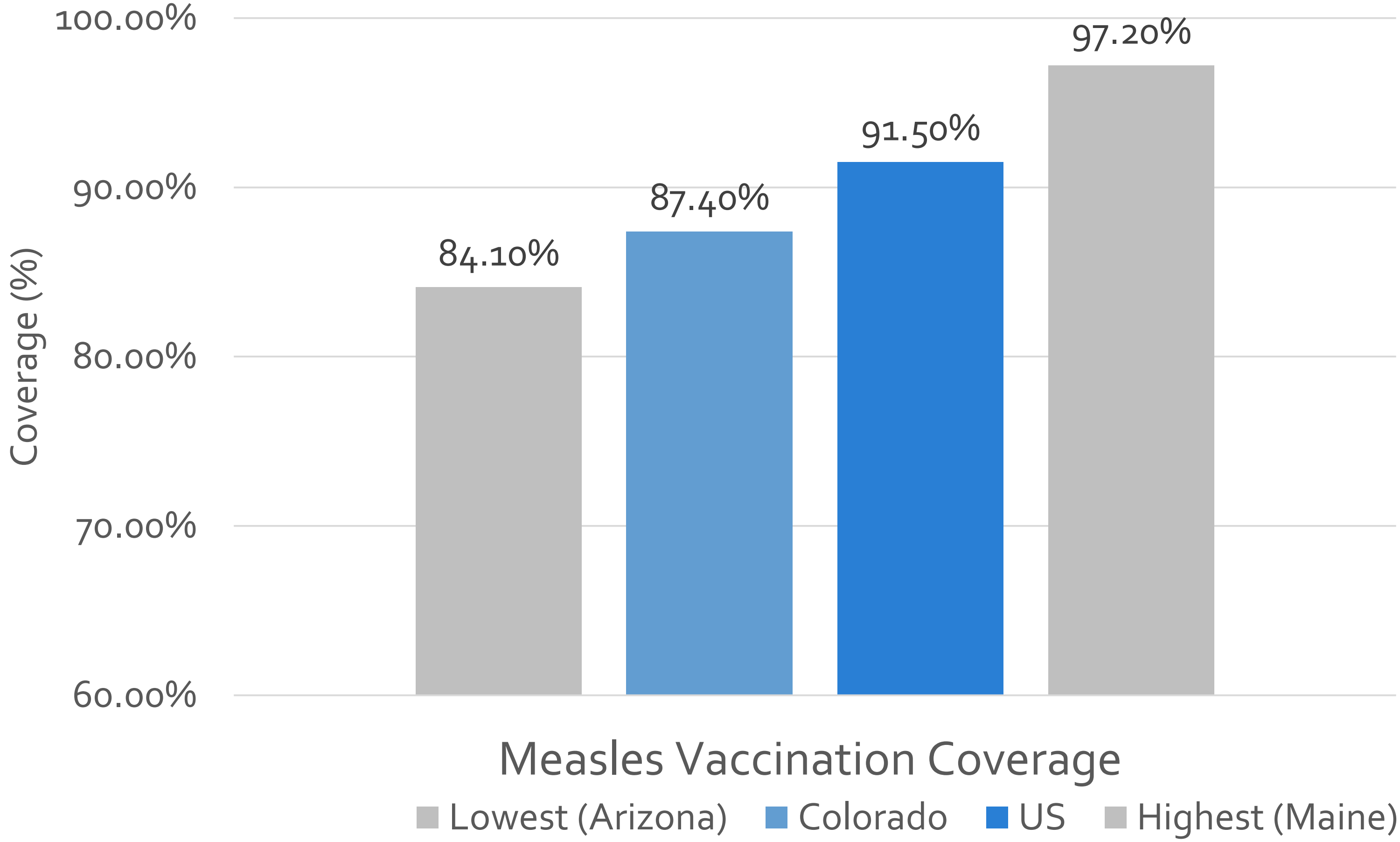
- **High Vaccination Coverage**
  - Vaccine effectiveness:
    - One Dose: 94-98%[2]
    - Two Doses: 98-100%[2]
  - Community immunity threshold: 93-95%[2]

- **Contact Tracing by Public Health**
  - Post-exposure prophylactic MMR vaccine[3]
    - within 72 hours of exposure, greater than 6 months of age
  - Post-exposure prophylactic immune globulin[3]
    - within 6 days of exposure, any age
  - Home quarantine[3]
    - exposed persons contacted more than 7 days after exposure

Measles Vaccination Coverage

- Relatively high national vaccination coverage: 91.5% of children aged 19 to 35 months have received at least one dose[4]
- Geographic variation in vaccination coverage
  - Maine: 97.2% with at least one dose[4]
  - Arizona: 84.1% with at least one dose[4]
- Variation also exists within each state
- Geographic variation results in clusters of susceptibility
  - Outbreaks typically occur in low vaccination coverage regions

Variation in Vaccination Coverage



Source: 2014 National Immunization Survey, children 19-35 months MMR

Vaccine Exemption Categories

- Easy: parent signature on standardized form[5]
- Medium: parent's signature on form from local health department, attendance at a vaccine education session with a school nurse, and/or a statement of objections[5]
- Difficult: medium restrictions plus having the form or letter notarized[5]

Literature on Policies and Vaccination Coverage

Blank et al., 2013[5]

- Rates of nonmedical exemptions in states with easy exemption policies were:
  - **1.9 times higher** than rates in states with medium exemption policies
  - **2.6 times higher** than rates in states with difficult exemption policies

Omer et al., 2009[6]

- In areas with higher rates of nonmedical exemptions, more outbreaks of vaccine-preventable diseases occur

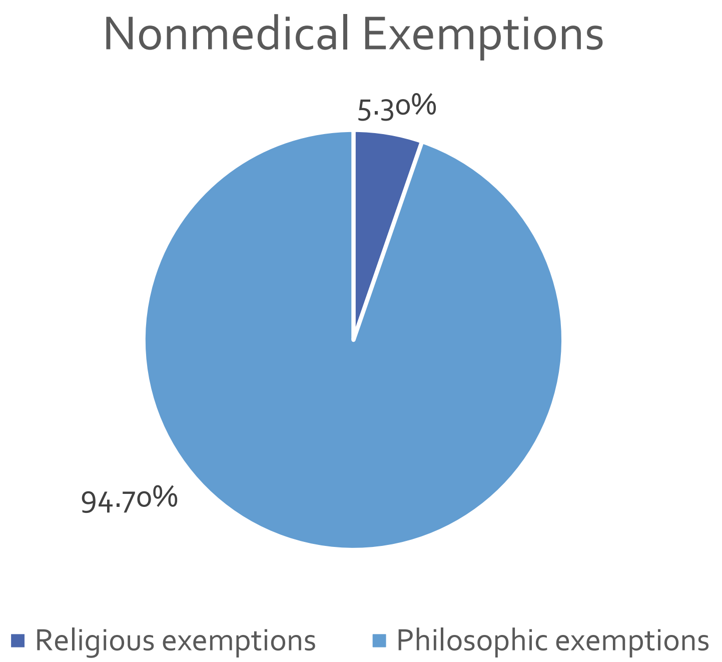
Glasser et al., 2016[7]

- Vaccinating individuals with nonmedical exemptions has been effective in decreasing the realized reproduction number of measles outbreaks

Colorado Exemption Policy

CO allows non-medical exemptions to vaccines

- Difficulty of obtaining: Easy[8]
- Rate of non-medical exemptions: 5.4%[9]



Source: CDC 2014-2015 school year data, children enrolled in public & private kindergarten

STUDY DESIGN

Research Questions

- What is the likelihood, magnitude, and cost of a measles outbreak in a state with vaccination coverage less than herd immunity and easy non-medical exemption policies?
- What impact does strengthening the nonmedical vaccine exemption policy have on the likelihood, magnitude, and cost of a measles outbreak?

Study Design

- Agent-based transmission model (ABTM) to simulate scenarios following the introduction of a measles index case in an urban area (Denver, CO)
  - Capability to model heterogenous problems, assign population and spatial characteristics, and monitor time
  - Measles transmission is dependent on spatial and temporal characteristics
  - ABTM simulates how disease propagates through space and over time among nonhomogenous populations
  - Modeling events and outcomes at individual level to generate predictions for a community

Data Sources

- Vaccination coverage rates
  - CDC's 2014 National Immunization Survey[4]
  - Random-digit dialing mechanism to call households with children between the ages of 19 and 35 months
  - Parents provide consent for child's provider to be contacted
  - Provider completes a survey about vaccination status
- Non-medical exemption rates
  - CDC's 2014-2015 school year data
  - Analyze kindergarten enrollment vaccination data collected by federally funded state, local and territorial immunization programs to monitor exemption levels
  - Colorado used a simple random sample of 350 (0.5%) kindergarteners
- Published medical literature (vaccine effectiveness, contract tracing effectiveness, outcomes associated with infection, etc.)

Inputs

Parameter	Value
Duration of Incubation Period	10 days
Duration of Infectious Period	9 days
Infectiousness of Measles	90%
Acquired Natural Immunity	100%
Probability of Hospitalization if Infected	20%
Probability of Death if Infected	0.1%
Rate of Recovery	99.9%
Vaccine Effectiveness*	98%
Effectiveness of Contact Tracing¥	88.3%
Probability a Case Stays Quarantined	75%
Contacts per Day	3-20
Population Size (Denver county)	649,495

*weighted by percentage receiving one dose and percentage receiving two doses
¥weighted by effectiveness of the three different interventions

Model

- Random mixing transmission model following introduction of one measles index case in Denver County
- Observes contact interactions and transmission of measles
- Accounts for community immunity, infectiousness of pathogen, duration of incubation, duration of communicable period, rate of recovery
- Modeled contact tracing and quarantine by public health
- Tracked interactions until transmission stopped

Model (cont.)

- Three different models were evaluated
  - Denver, Colorado under easy non-medical exemption policy
  - Denver, Colorado under simulated medium non-medical exemption policy
  - Denver, Colorado under simulated difficult non-medical exemption policy

- All inputs held constant except vaccination coverage
  - Assumed that the Colorado nonmedical exemption rate would decrease to the average nonmedical exemption rate for states with medium (1.5%) and difficult (1.1%) nonmedical exemptions[5]
  - Reductions in nonmedical exemptions would be absorbed by an increase in vaccination coverage

Random Variation

- Variation in Model Inputs:
  - Each model environment was run 100 times with a different random seed
    - Seed: number stated at beginning of the model that initializes the random number sequence
    - Same 100 seeds were used with each model
- Variation in Number of Contacts
  - 10 contacts a day for base-case
  - Varied from 3-20 contacts per day

Outcomes

- Number of Cases
- Number of Secondary Cases
- Occurrence of Outbreak
  - 3 or more cases connected in time and space
- Number of Hospitalizations
- Number of Deaths

Quantification of Economic Burden

- Outcomes from the 100 model iterations for each model scenario were monetized
- All costs normed to 2015 USD

Cost Component	Value
Cost to Public Health	$13,326 - $33,316 per case[10]
Outpatient Visit	$92 - $553 per visit[11]
Hospitalization	$4,236 - $48,392 per hospitalization[11]
Indirect Costs	$988 per case[12]

Model Validation

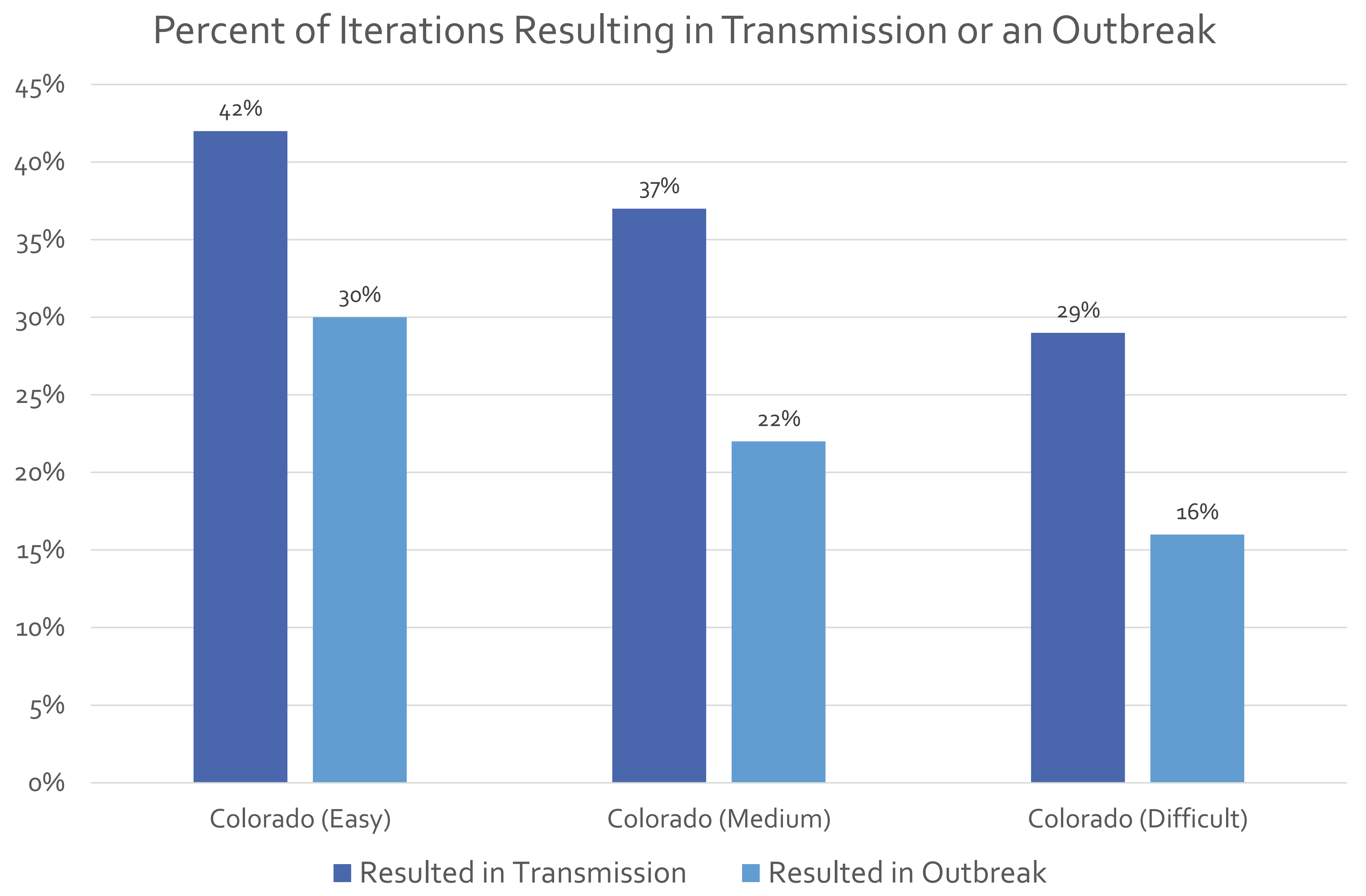
- Herd immunity established at 95%
- Compared simulated cases with confirmed cases in previous outbreaks
  - 16 outbreaks in 2011[10]
    - 107 confirmed cases[10]
    - Number of Cases per Outbreak
      - Minimum: 3 confirmed cases per outbreak[10]
      - Maximum: 22 confirmed cases per outbreak[10]
      - Mean: 7 confirmed cases per outbreak[10]
      - Median: 6 confirmed cases per outbreak[10]
- Compared simulated costs with reported costs in 2011 outbreaks
  - Median cost to public heath ranged from $71,598 to $178,996[10]

RESULTS

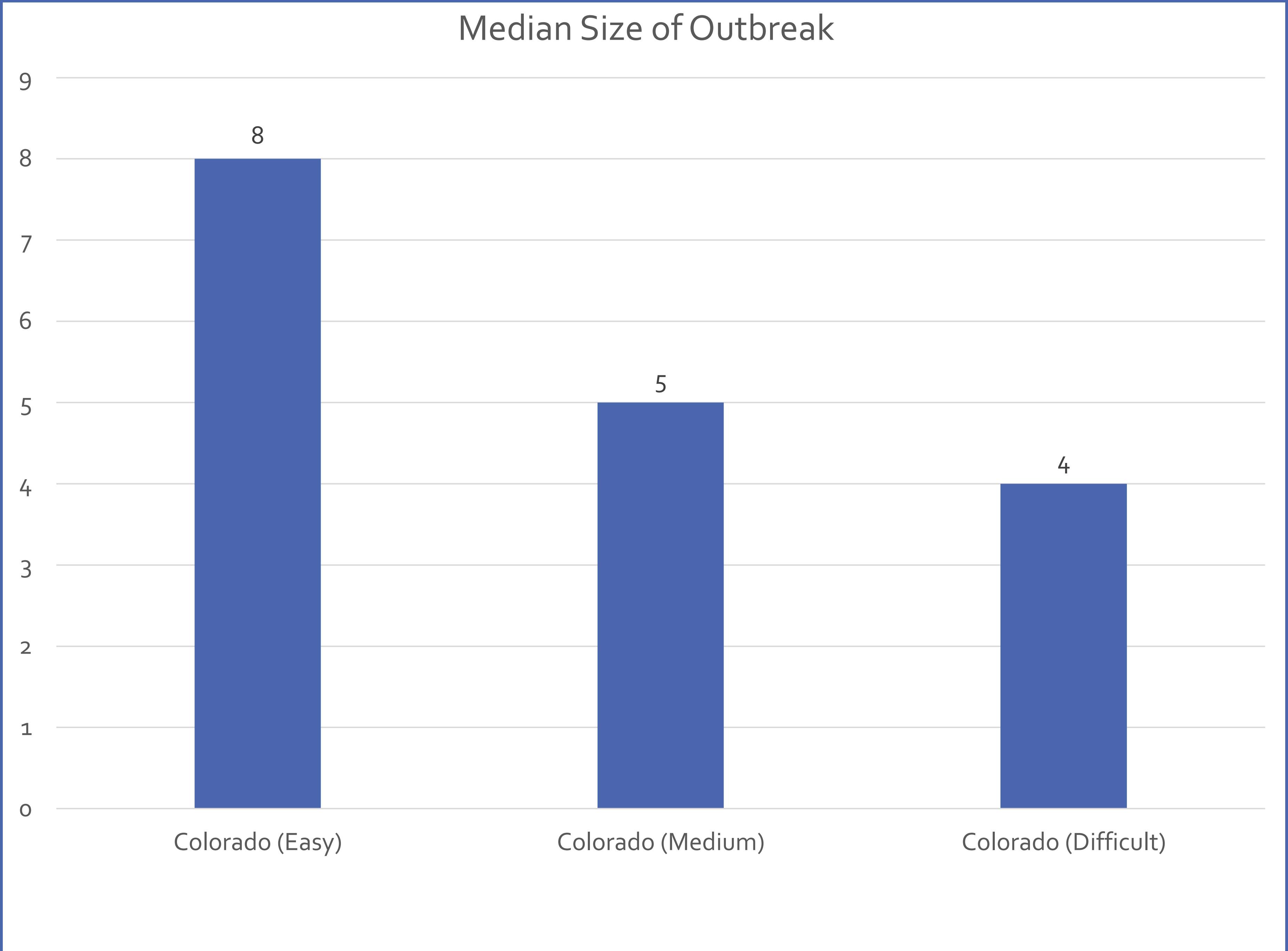
Likelihood and Magnitude of a Measles Outbreak

	Vaccination Coverage	Percent Spread*	Percent Outbreak†	Median Size of Outbreak	Median Duration of Outbreak
Easy Policy	87.4%	42%	30%	8 cases	61 days
Medium Policy	91.3%	37%	22%	5 cases	38 days
Difficult Policy	91.7%	29%	16%	4 cases	35 days

*Percent of iterations with at least one secondary case.
†Percent of iterations with at least three total cases.



Percent of Iterations Resulting in Transmission or an Outbreak
45%
40%
35%
30%
25%
20%
15%
10%
5%
0%
42%
30%
37%
22%
29%
16%
Colorado (Easy)
Colorado (Medium)
Colorado (Difficult)
Resulted in Transmission
Resulted in Outbreak


Median Size of Outbreak
9
8
7
6
5
4
3
2
1
0
8
5
4
Colorado (Easy)
Colorado (Medium)
Colorado (Difficult)

Varying Number of Contacts

- Similar trend after varying the number of contacts per day
- With 3 contacts per day, there were fewer outbreaks for all models than when 10 contacts per day were assumed; however, there were still nearly twice as many outbreaks in the easy policy model compared with the difficult policy model
- With 20 contacts per day, there were more outbreaks than when 10 contacts per day were assumed; however, there were still nearly twice as many outbreaks in the easy policy model compared with the difficult policy
- The median size of each outbreak was not sensitive to the number of contacts assumed per day

Economic Burden of Measles Transmission

		Above $100,000		Above $200,000	
	Vaccination Coverage	Public Health Costs*	Societal Costs†	Public Health Costs*	Societal Costs†
Easy Policy	87.4%	23%	30%	15%	15%
Medium Policy	91.3%	9%	22%	4%	5%
Difficult Policy	91.7%	8%	16%	3%	4%

*Public health costs include the costs to public health departments such as their contact tracing efforts, outbreak investigations, and post-exposure prophylaxis.

†The societal costs include the public health costs, as well as the direct medical costs and indirect costs to the patient.

DISCUSSION

Interpretation of Results

- As the degree of difficulty for the non-medical vaccine exemption policy increased
  - likelihood of the infection being transmitted decreased
  - magnitude of the resulting outbreaks decreased
- Strengthening policy reduced the economic burden of measles transmission to public health and to society
  - Nearly 3x as many iterations from the easy policy model cost more than $100,000 compared to the difficult model
  - Nearly 5x as many iterations from the easy policy model cost more than $200,000 compared with the difficult model

Addition to Literature

- Simulates the impact of strengthening nonmedical vaccine exemption policies as a way to increase vaccine uptake and thus reduce the health and economic burden of measles outbreaks.
- Used national data to simulate vaccination coverage under different existing policy scenarios to assess the effect of the policy using real data.
- Targets policy, not just vaccination coverage, and includes health as well as economic outcomes.

Policy Implications

- Strengthening non-medical vaccine exemption policies can reduce the health and economic burden of measles outbreaks by increasing the vaccination rate.
- Reducing the clusters of susceptibility because of large geographic vaccine variation should be a priority because a measles outbreak is more likely to occur in areas with low vaccination coverage.
- Increasing the complexity of obtaining a non-medical exemption could greatly reduce the likelihood and magnitude of an outbreak.
  - Adding education component
  - Requiring a written statement of objection
  - Requiring notarization of standardized form

Limitations

- Simulated average result for Denver, Colorado and thus uniform characteristics assumed for all people in the environment
- State-level data used to simulate regional transmission
- Data inconsistencies in vaccination coverage and exemption rates
- Public health efforts and response held constant for all simulations
- Indirect costs included only for those who became infected

Possible Future Directions

- Given the current analysis is an average across Denver County, interesting applications could include limiting the population to certain subpopulations (school districts, areas with immunity clustering).
- This analysis holds public health efforts constant between simulations and varies the vaccination coverage. The public health response could be varied in future analyses, including the addition of a lag time in identifying the first few cases of an outbreak and the effectiveness of contact tracing efforts.
- The current analysis only includes indirect costs for individuals who become infected. Future work could expand indirect cost considerations to contacts that are quarantined as well.

Application to Minnesota Outbreak

- High state-level vaccination coverage
- Strong non-medical vaccine exemption policies
- 69 confirmed cases by May 22, 2017
- Clusters of susceptibility/low vaccination coverage in specific populations

Conclusions

- Measles cases and outbreaks are an issue again in the US because of clusters of low vaccination coverage
- Outbreaks associated with negative health consequences and a large economic burden
- One way to increase vaccination coverage at a state level is to strengthen nonmedical vaccine exemption policies
- Adding components to vaccine exemption requirements can increase vaccination coverage which can reduce likelihood, magnitude and cost of a measles outbreak
- States exploring options for decreasing their vulnerability to outbreaks of vaccine-preventable diseases should consider more stringent requirements
- Strengthened policies might protect population health and financial resources

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Questions?

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Whittington MD, Kempe A, Dempsey A, Herlihy R, Campbell JD. Impact of Nonmedical Vaccine Exemption Policies on the Health and Economic Burden of Measles. Academic Pediatrics.