Pertussis Human Challenge Studies

Tod Merkel, PhD

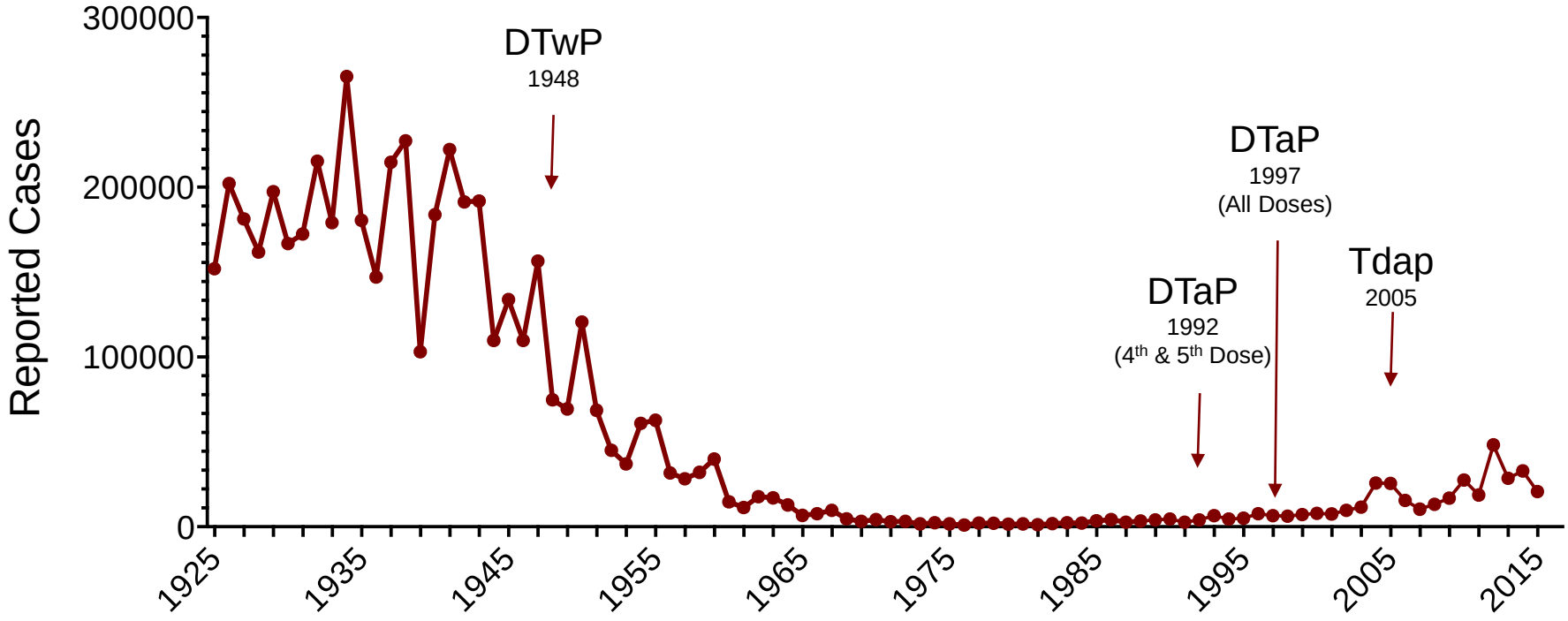
CBER / FDA
Silver Spring, Maryland

My comments are an informal communication and represent my own best judgment. My comments do not bind or obligate the FDA.

Pertussis (Whooping Cough)

- Highly contagious respiratory infection caused by *Bordetella pertussis.*
- Nearly universal by school entry in the pre-vaccine era
- Approximately 1 in 10 cases resulted in mortality. Responsible for more deaths than measles and polio combined.
- Still a common cause of infectious disease worldwide. Modeling for the period 2000 to 2015 estimated approximately 56,700 deaths annually in children under five years of age worldwide .

Reported Pertussis Cases



Source: **CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive reports to the Public Health Service**

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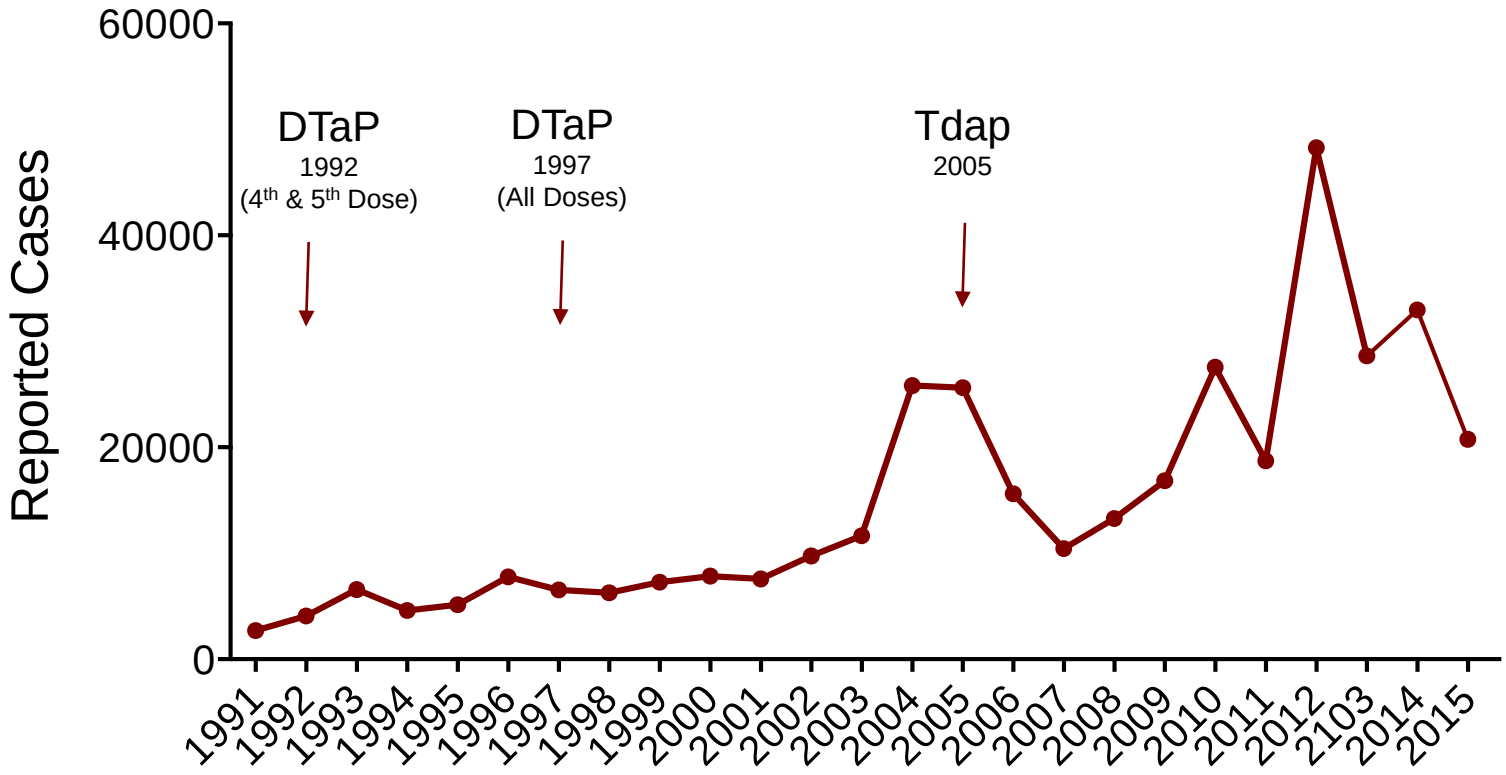

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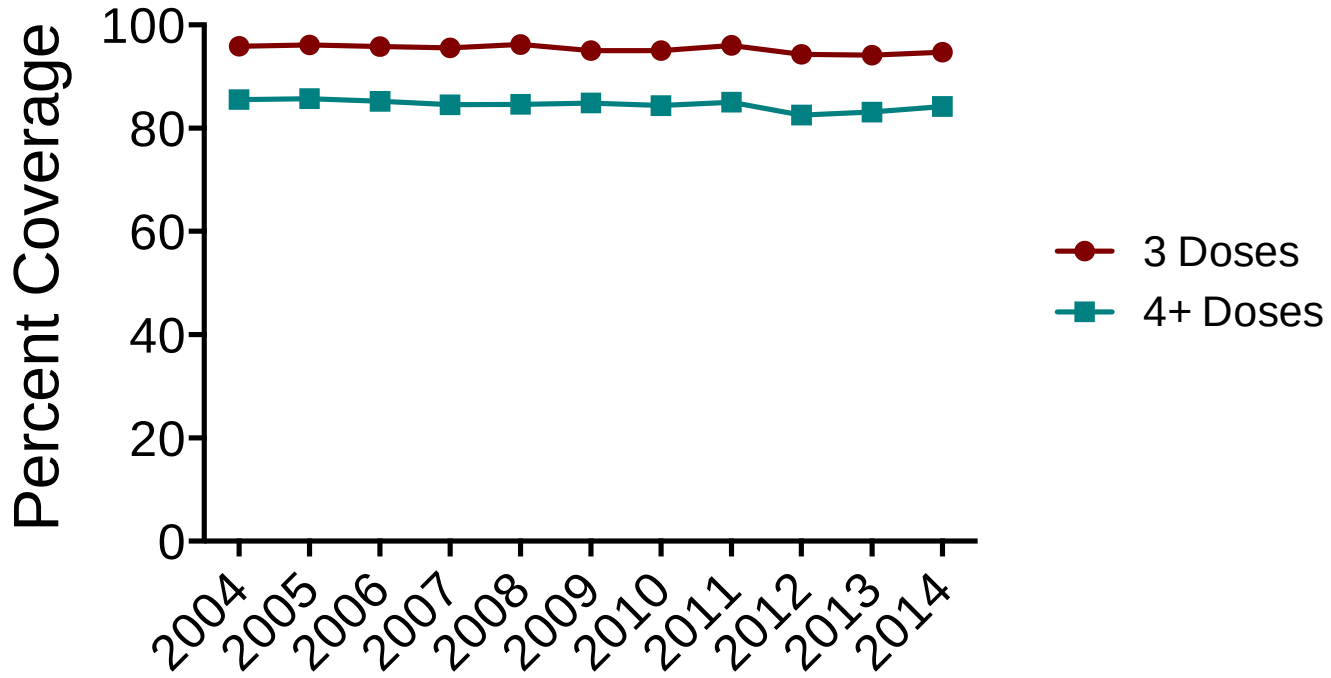
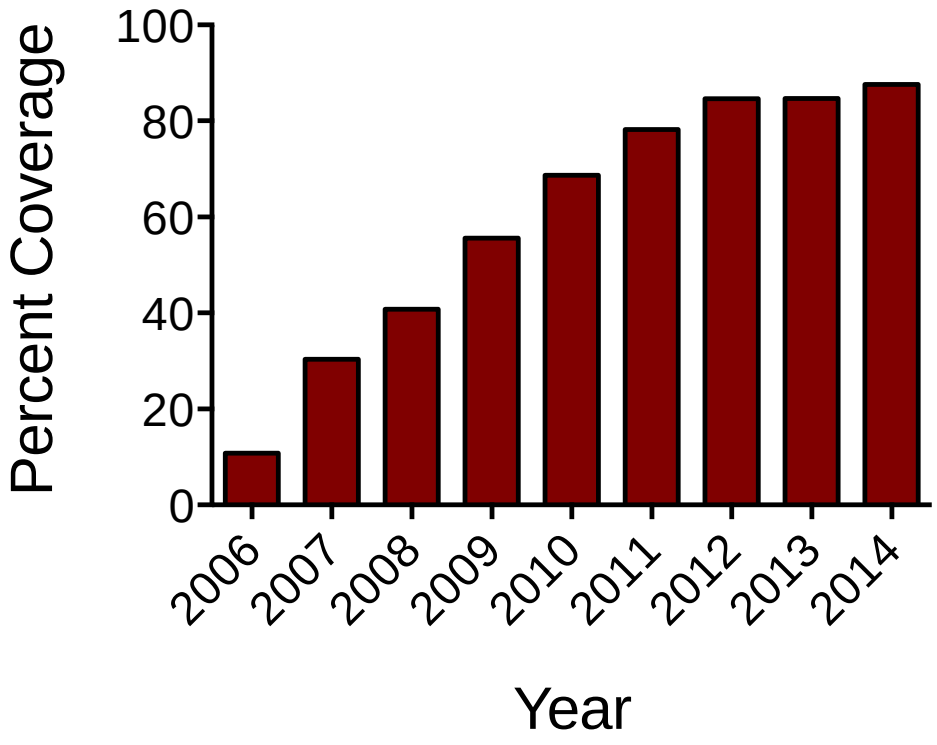
DTaP Coverage



Source: CDC National Immunization Survey

Tdap Coverage



Source: CDC National Immunization Survey

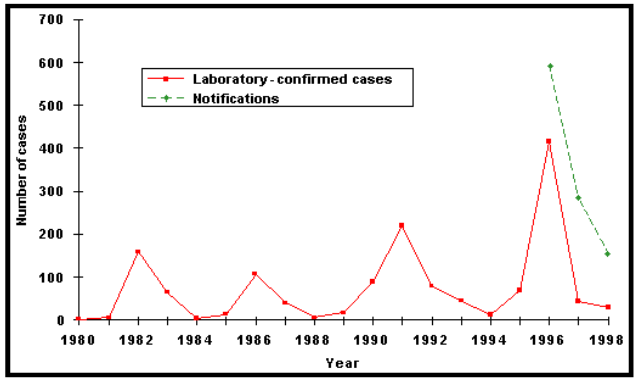
Insights From the Baboon Model of Pertussis

- The licensed acellular pertussis vaccines prevent disease but not colonization, carriage or transmission.
- These data suggest that acellular-vaccinated individuals act as a reservoir for *B. pertussis* circulation.
- Hypothesis: Increased circulation in aP-vaccinated populations leads to increased exposure of unvaccinated, under-vaccinated and non-responding individuals.

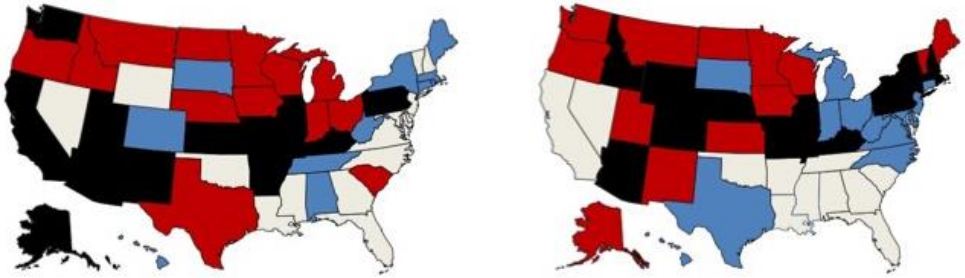
New pertussis vaccines are required to reduce B. pertussis circulation in the population.

Need for Pertussis Human Challenge Studies

- Incidence of pertussis is low
- Pertussis incidence varies over time



- Pertussis incidence varies geographically.



Uses for Pertussis Human Challenge Studies

- Characterize early clinical manifestations
- Study the immune response
- Study transmission (?)
- Identify and test new protective antigens
- Identify and evaluate correlates of protection
- Evaluate new diagnostic tests
- Evaluate new therapeutics
- Evaluate next generation vaccines
- Provide clinical data to support approval of novel vaccines

Pertussis-specific Considerations

- Pertussis is an airborne pathogen that transmits efficiently across a room. Therefore containment of subjects and protection of subject contacts important.
- Although pertussis is typically mild in adults, disease can be severe.
- Point of no return?

University of Southampton Pertussis Human Challenge Study

P.I. Robert Read

Single centre, first in human

Phase A (35 volunteers, or until 10 colonised with one standard dose)

Aims:

- Assess safety of inoculation with *B. pertussis*
- Find the inoculum dose to get 70% colonisation
- Assess the specific immune response
- Assess environmental shedding

Source: Dr. Robert Read, University of Southampton

Southampton Human Challenge Study Inclusion criteria

- Healthy adults aged 18 to 45 years inclusive on the day of screening
- Willingness to take a curative antibiotic regimen after inoculation with *B. pertussis* according to the study protocol
- Agreement to be admitted to the NIHR-WTCRF Southampton for 17 days (from inoculation until two days after the eradication therapy is given)

Source: Dr. Robert Read, University of Southampton

Southampton Human Challenge Study Exclusion criteria

- Individuals (and household contacts) can't rule out contact with::
  - unimmunised or partially immunised children and infants aged < 1 year
  - pregnant women >32 weeks who have not received pertussis vaccination at least a week prior to contact
- Individuals who have anti-PT IgG ELISA >20 IU/mL
- Individuals who are *B. pertussis* positive
- Individuals received pertussis vaccination in the last 5 years
- Individuals who have a history of never receiving pertussis vaccination

Source: Dr. Robert Read, University of Southampton

Southampton Human Challenge Study Challenge Strain

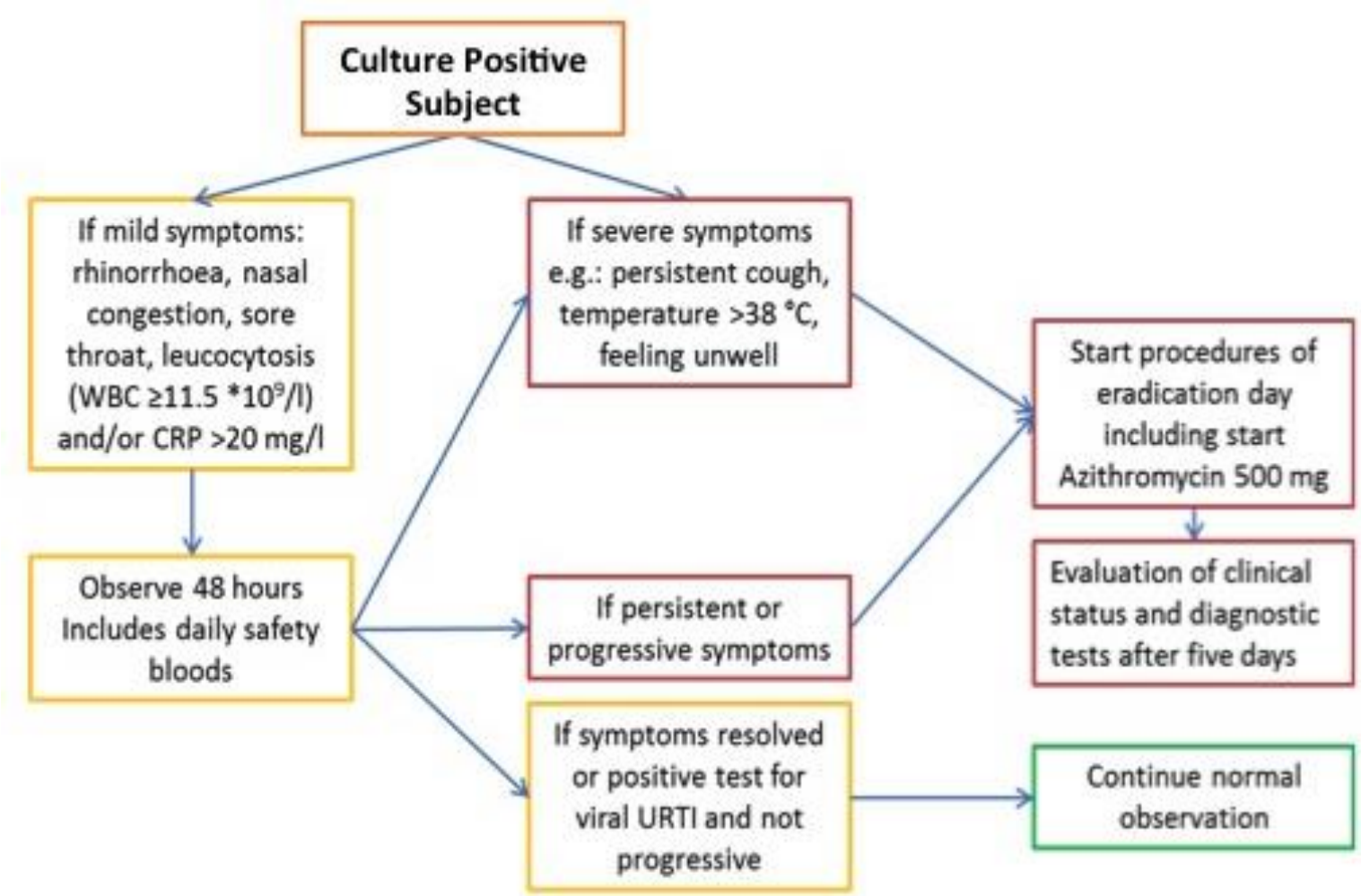
- Strain B1917
- Representative of current clinical isolates in Europe
- Sensitive to azithromycin *in vitro*
- Prepared by Q Biologicals
  - GMP standard
  - Licensed cGMP facilities
  - Free of animal-derived products
- Vials containing 1.1 mL at 10^6 cfu/ml

Source: Dr. Robert Read, University of Southampton

Southampton Human Challenge Study Infection prevention

- Admission to the NIHR-WTCRF for 17 days Visitors allowed between 8:00 AM and 10.00 PM (PPE required)
- Allowed off unit 2 x 2 hrs a day with escort. Mask required.
- Use of PPE
- Vaccination of staff
- Sampling of staff

Source: Dr. Robert Read, University of Southampton



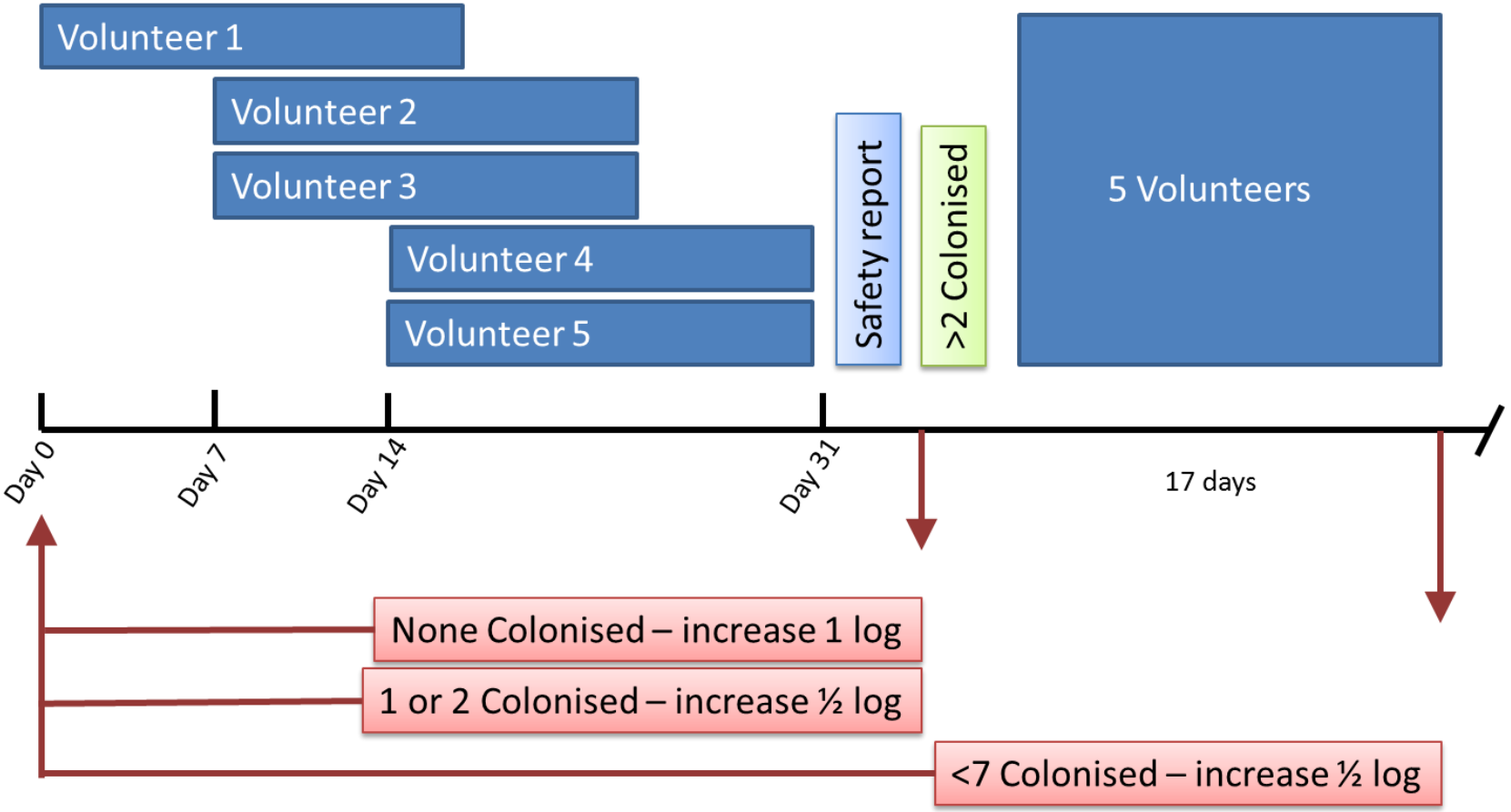
Source: Dr. Robert Read, University of Southampton

Southampton Human Challenge Study Eradication Therapy

- Azithromycin 500 mg orally once a day for three days
- On day 14, or when early *B. pertussis* disease is suspected.

Source: Dr. Robert Read, University of Southampton

Southampton Human Challenge Study
Escalating the Dose



Source: Dr. Robert Read, University of Southampton

Southampton Human Challenge Study Phase B

45 Subjects:

- Intervention group (n=30). Standard inoculum identified in Phase A
- Control group (n=15). Sham inoculum, no admission

Aims:

- Confirm the standard inoculum
- Assess the specific immune response

Source: Dr. Robert Read, University of Southampton

Canadian Center for Vaccinology in Halifax Pertussis Human Challenge Study

P.I. Scott Halperin

Open Label, Single Center:

Up to 28 volunteers, or until 6/8 colonised with one standard dose

Aims:

- Assess safety of inoculation with *B. pertussis*
- Identify the inoculum dose that achieves 75% colonisation

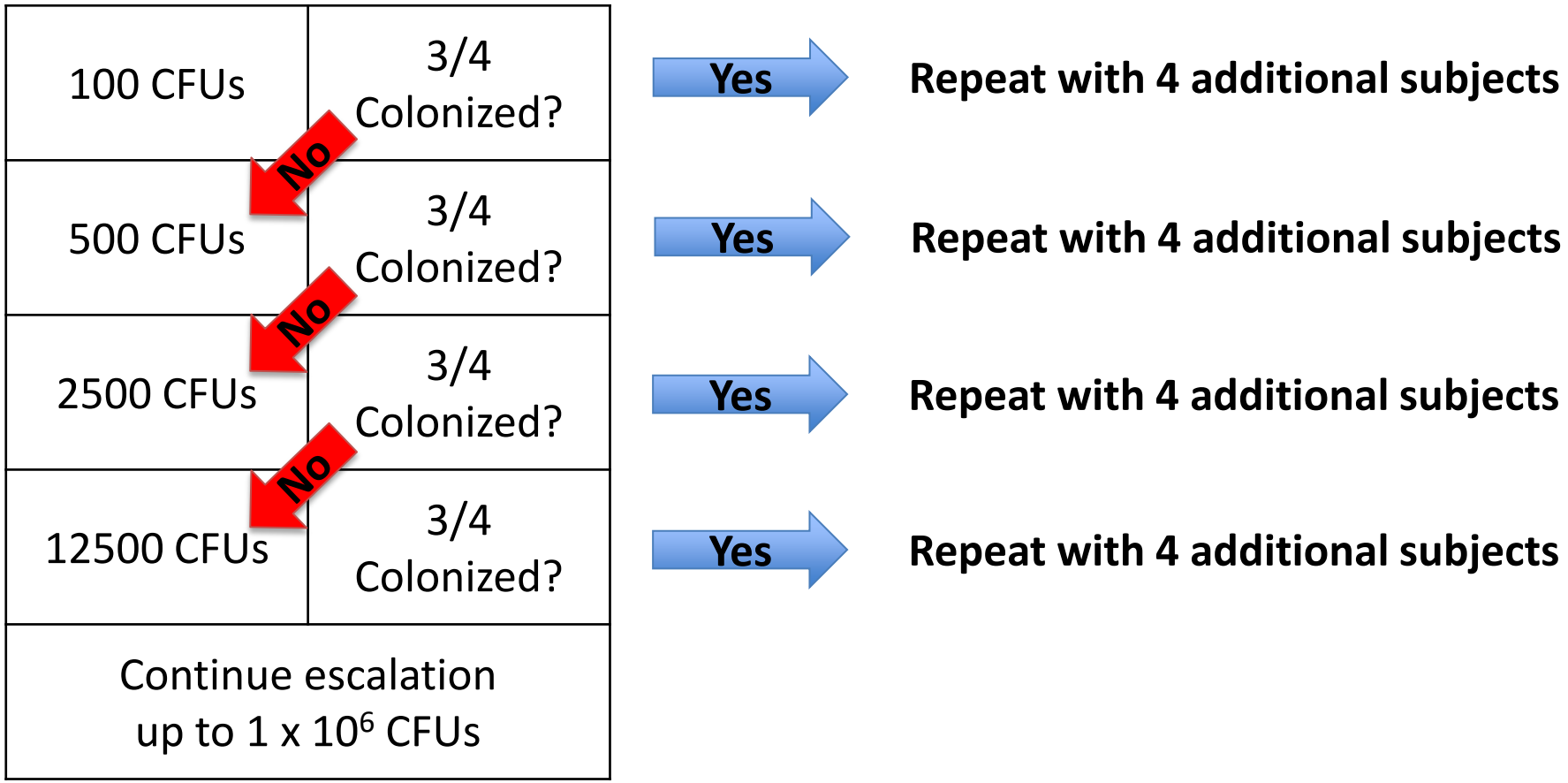
Source: Dr. Scott Halperin, Canadian Center for Vaccinology in Halifax

Halifax Human Challenge Study
Study Overview

- Healthy adults aged 18 to 40 years inclusive on the day of screening.
- Challenge with *B. pertussis* strain D420. Clinical isolate representative of strains circulating in North America.
- In-patient
- Antibiotic therapy with azithromycin initiated within 24-48 hours of onset of symptoms or at the end of the in-patient period.

Source: Dr. Scott Halperin, Canadian Center for Vaccinology in Halifax

Halifax Human Challenge Study
Escalation of Challenge Dose



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Acknowledgements

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