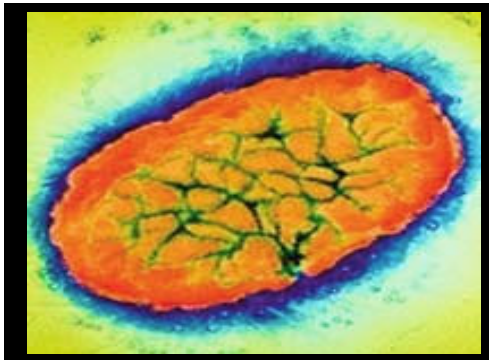
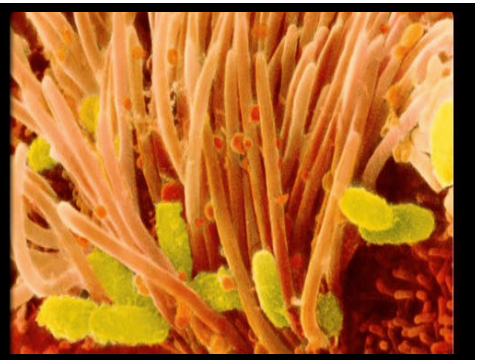
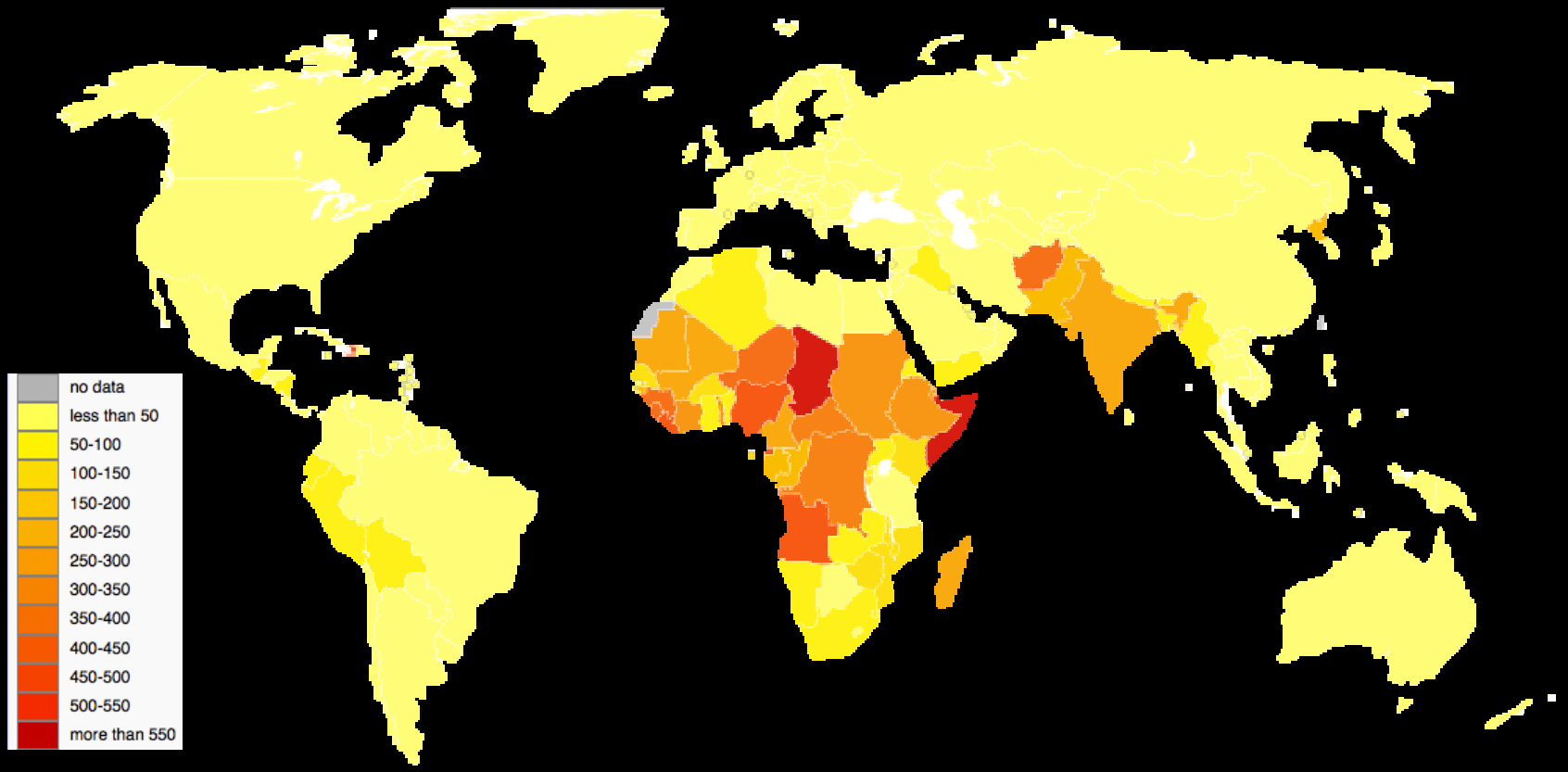




Pertussis: the importance of loss of immunity to endemicity

Ashleigh Tuite and David Fisman
University of Toronto

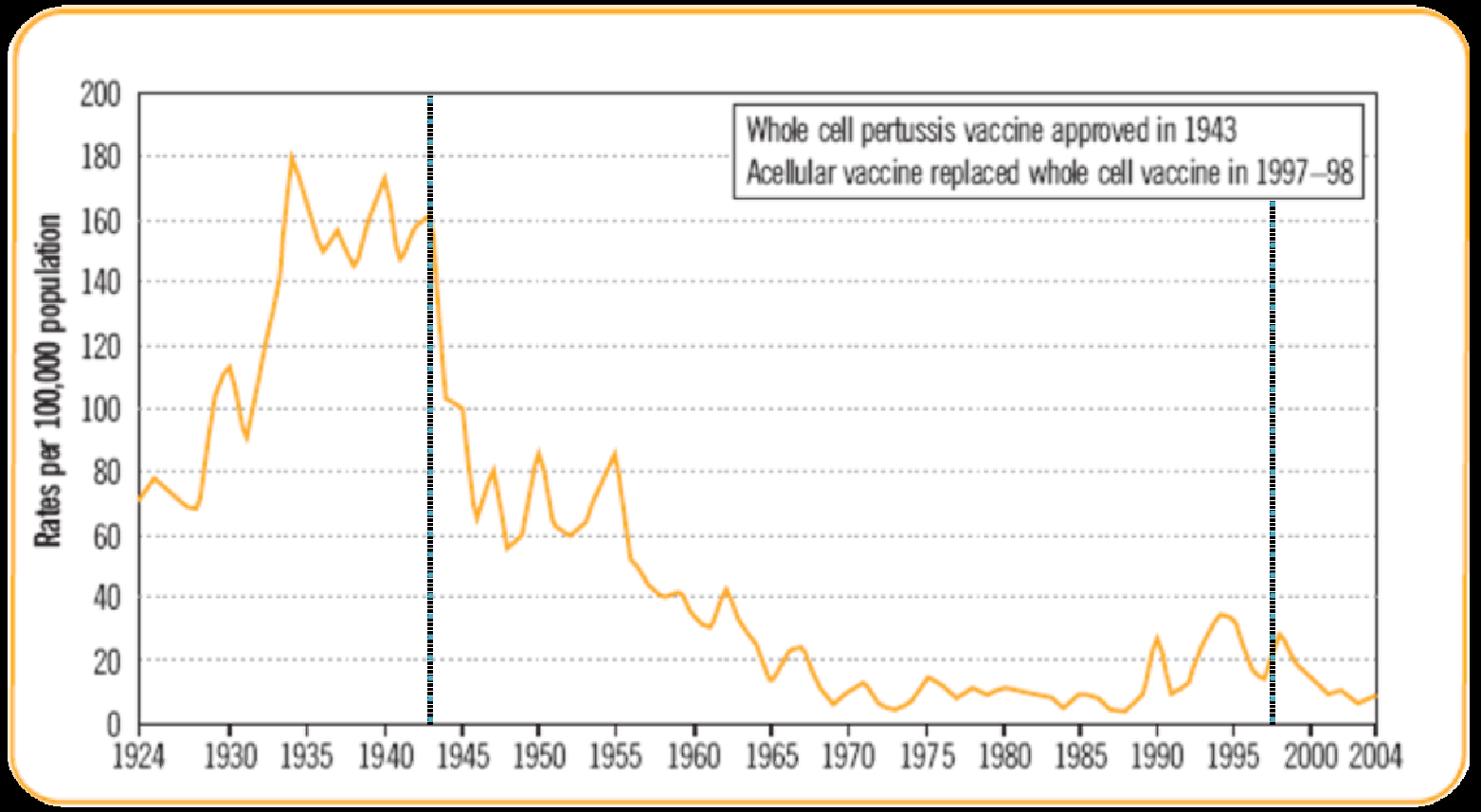


50 million cases
300,000 deaths
CFR in low-income countries as high as 4% in infants

Global burden of pertussis: DALY per 100,000

Source: WHO, 2004

Pertussis in Canada: 1924 to 2004



- Pertussis ongoing medical/public health challenge
  - despite introduction of vaccine in Canada in 1940s and high coverage
- Increases in incidence
- Outbreaks in Australia, Ireland, UK, US (California)
- Reasons for persistence?
  - Aging of under-vaccinated cohort
  - Vaccine effectiveness
  - Test sensitivity/testing patterns
  - Waning immunity & under-diagnosis in adolescents and adults

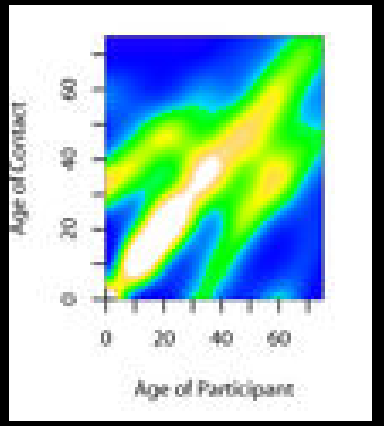
Estimation of the degree of under-reporting of pertussis in the GTA

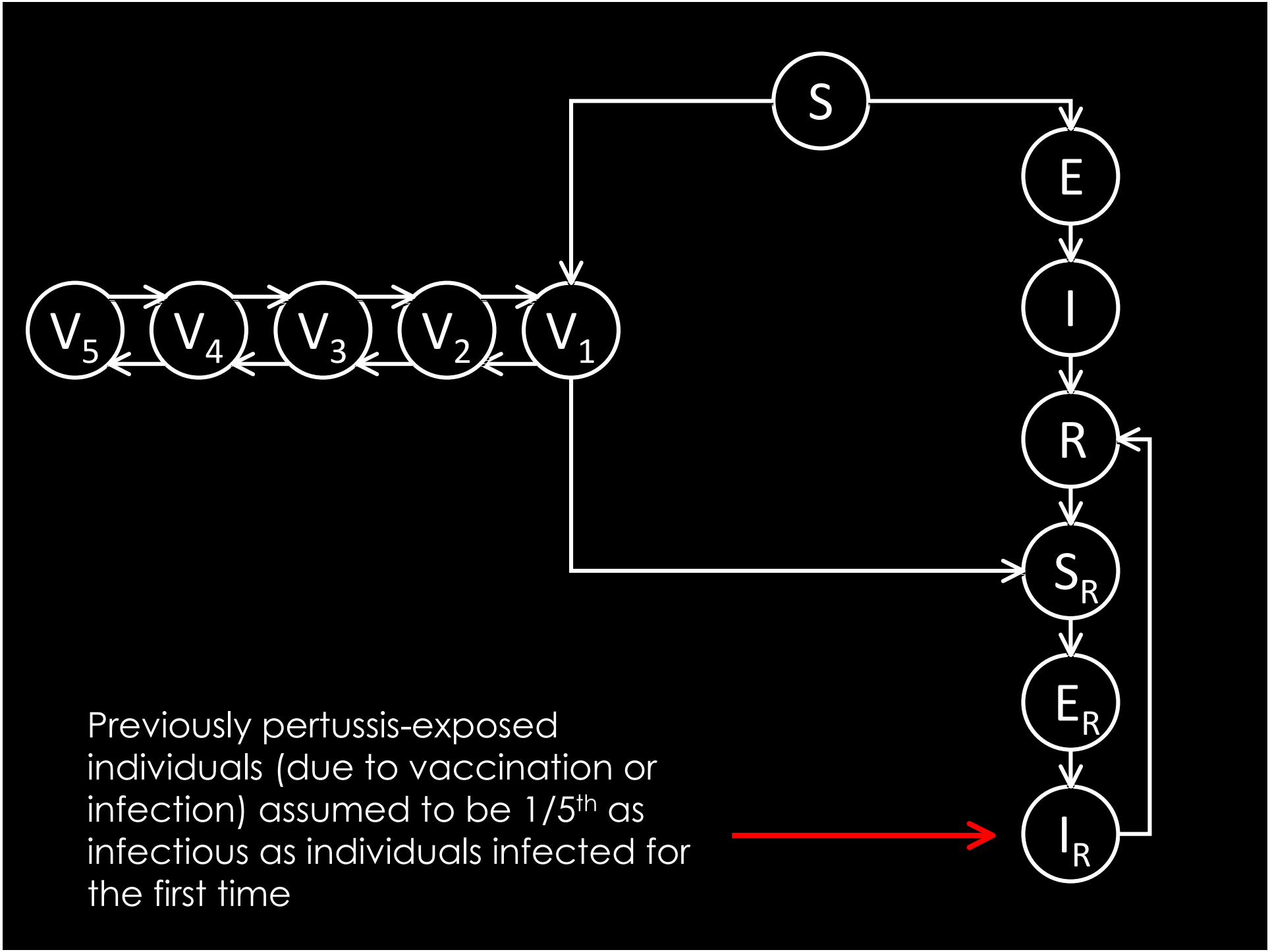
- Objective: To better understand how under-recognition of pertussis in adults may be contributing to observed disease patterns

- Approach: Use a mathematical model to describe the transmission of pertussis in the Greater Toronto Area and to estimate the underlying burden of pertussis in the population

Model overview

- Age-structured compartmental model
  - Includes births and deaths, and introduction of pertussis vaccine
  - 10 age groups (to allow for modeling of existing pertussis vaccination schedule)
  - Mixing within and between age groups based on population-based prospective study of contact patterns in 8 European cities(Mossong et al., 2008)




S
E
I
R
S_R
E_R
I_R
V_1
V_2
V_3
V_4
V_5
Previously pertussis-exposed individuals (due to vaccination or infection) assumed to be 1/5th as infectious as individuals infected for the first time

Calibration

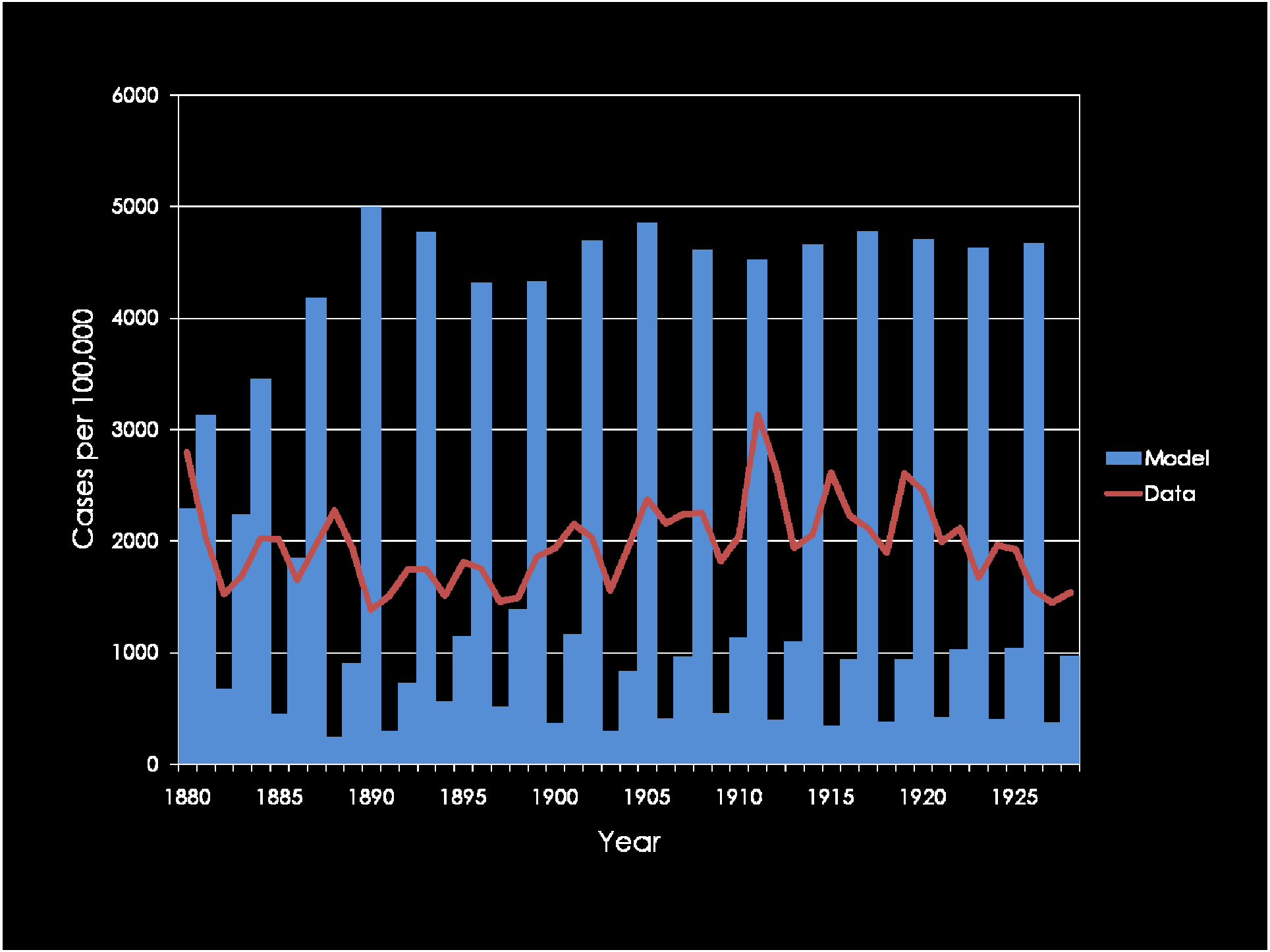
- Stage I:

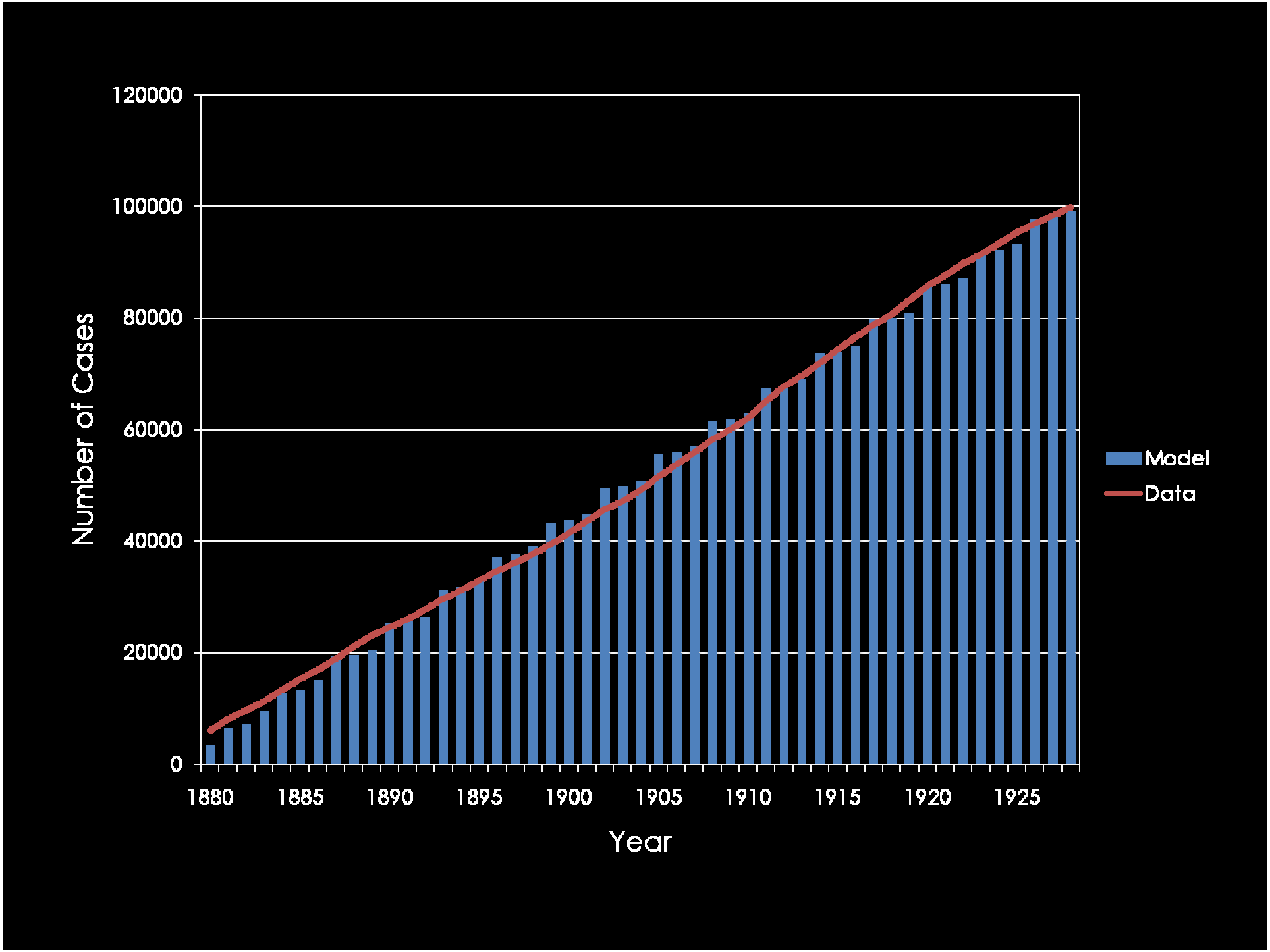
  Natural history in pre-vaccination era
  - Used Ontario pertussis mortality rates and contemporary case-fatality rates from 1880 to 1929
- Stage II:

  Epidemiology during vaccination era
  - Model calibration to reproduce observed case counts in < 2 year-olds (greater severity, more accurate reporting)
    - Data from CPHL/SickKids

Calibration 1.

PRE-VACCINATION ERA


6000
5000
4000
3000
2000
1000
0
Cases per 100,000
1880
1885
1890
1895
1900
1905
1910
1915
1920
1925
Year
Model
Data

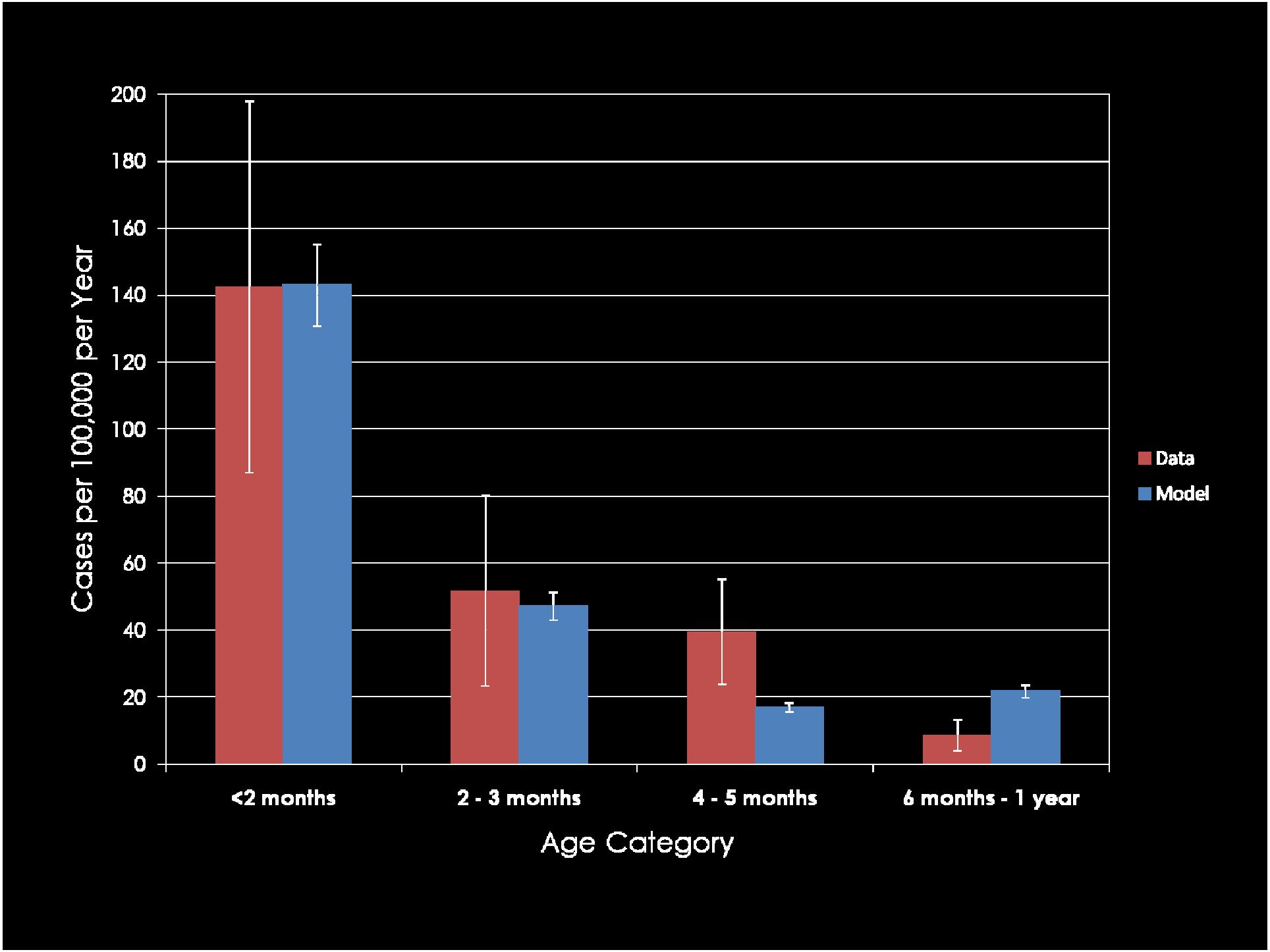

120000
100000
80000
60000
40000
20000
0
Number of Cases
1880
1885
1890
1895
1900
1905
1910
1915
1920
1925
Year
Model
Data

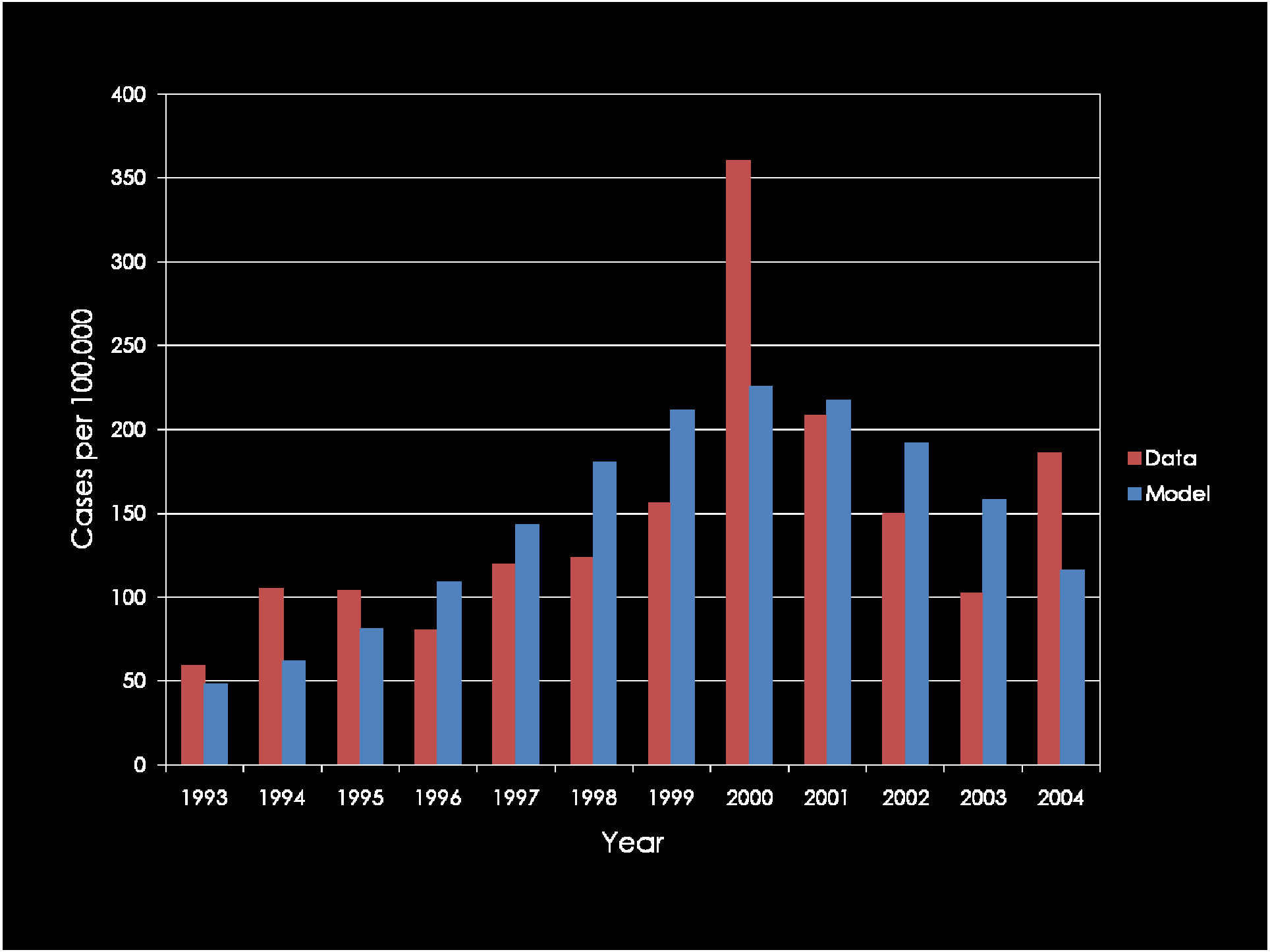
Calibration 2.

VACCINATION ERA

Vaccination Coverage at 7 years of age

Number of doses	Recommended age at vaccination	Reported (PHAC)	Model
0	-	0.04	0.034
1	2 months	0.02	0.022
2	4 months	0.04	0.043
3	6 months	0.06	0.067
4	1.5 years	0.19	0.183
5	4-6 years	0.65	0.652

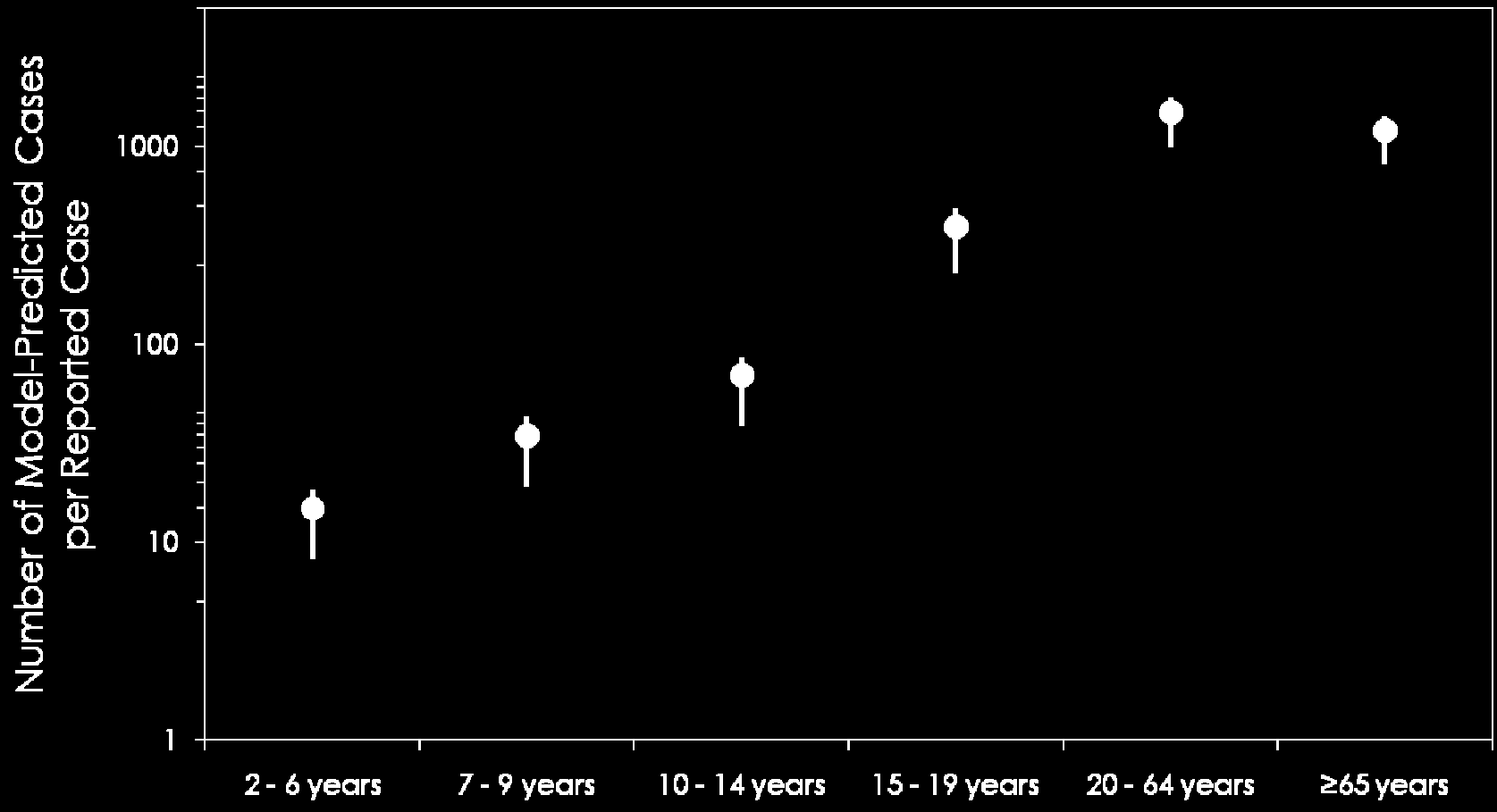

200
180
160
140
120
100
80
60
40
20
0
Cases per 100,000 per Year
<2 months
2 - 3 months
4 - 5 months
6 months - 1 year
Age Category
Data
Model


400
350
300
250
200
150
100
50
0
Cases per 100,000
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
Year
Data
Model

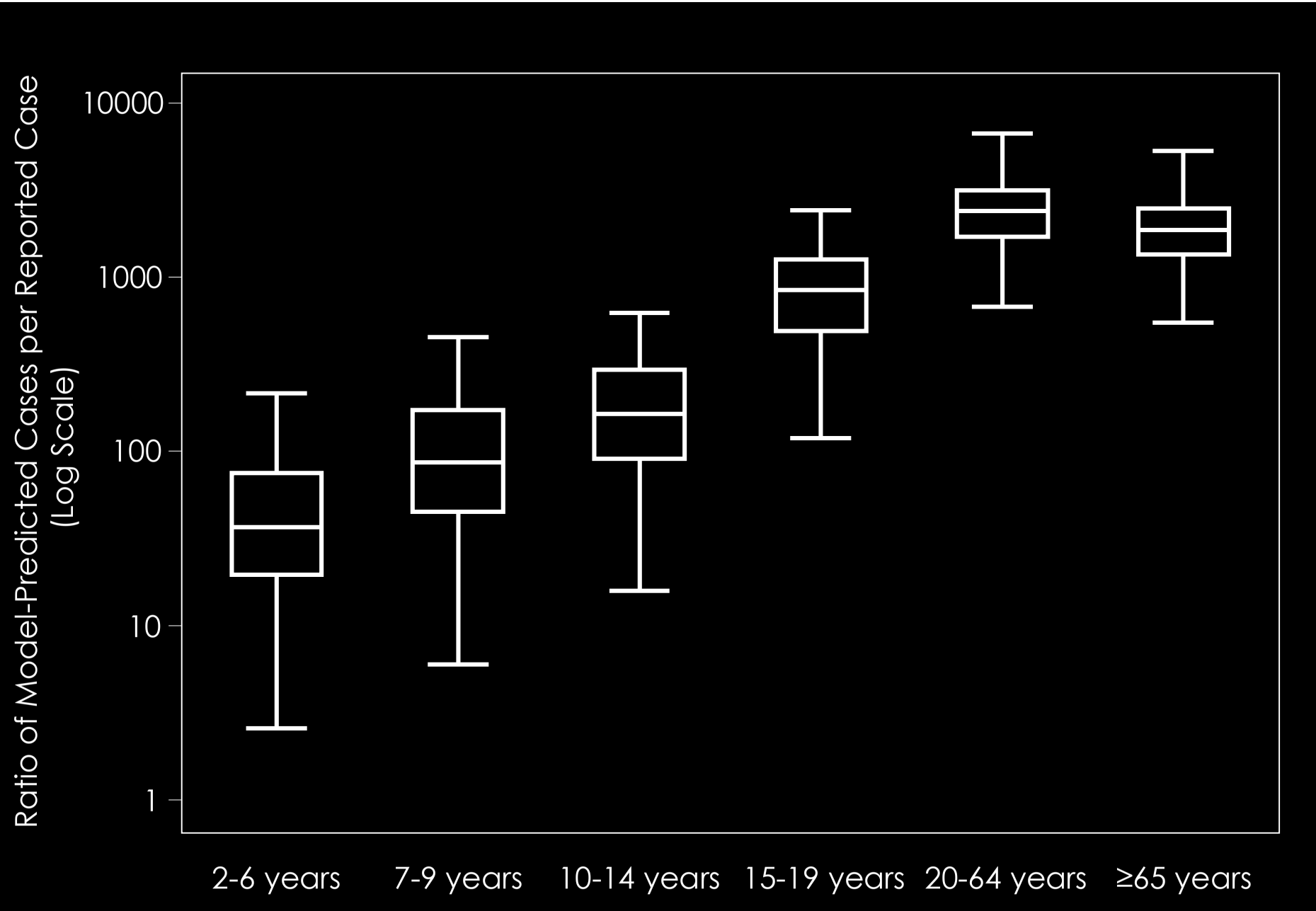
Parameters

Parameter	Best-fit value (plausible range)	Source
Latent period (days)	8	Nguyen and Rohani, 2008(26)
Infectious period (days)	15	Nguyen and Rohani, 2008(26)
Duration of immunity following infection (years)	24.2 (10 – 50)	Model calibration; Wendelboe et al., 2005(32); Wearing and Rohani, 2009(37)
Duration of immunity following complete immunization (years)	16.5 (2 – 25)	Model calibration; Wendelboe et al., 2005(32)
Relative infectiousness of individuals re-challenged with pertussis (following loss of naturally-acquired or vaccine-induced immunity)	0.2	Assumption
Reproductive number	5.5 (5.2 – 5.7)	Kretzschmar et al., 2010(30)
β_1	0.365 (0.35 – 0.38)	Kretzschmar et al., 2010(30)
β_2, relative amplitude of seasonal forcing	0.16 (0.10 – 0.3)	Model calibration; Nguyen and Rohani, 2008(26)
Life expectancy (years)	75	Assumption

Estimated under-detection of pertussis cases



- Average number of model-predicted cases to reported cases between 1993-2004
- Assumed completeness of reporting in <2 age group of between 0.4 and 1



- 1000 simulations: varied duration of immunity after infection and vaccination and R_0.

- Estimated proportion of force of infection in infants attributable to individuals previously exposed to pertussis (either via vaccination or infection): 74%

Even assuming marked reductions in infectiousness of individuals with prior pertussis, their large number and relative connectedness means these 'partially immune' individuals contribute significantly to force of infection

Implications

- Maintenance of pertussis endemicity in the face of high rates of vaccine coverage dependent on:
  - Relatively short duration of immune protection from *both* natural infection and immunization
  - Continued susceptibility to infection throughout the lifespan

- Ongoing pertussis boosting in adults may be necessary for optimal control of this disease in children