Unintended consequences: pertussis re-emergence

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Vaccines are essential to controlling pertussis

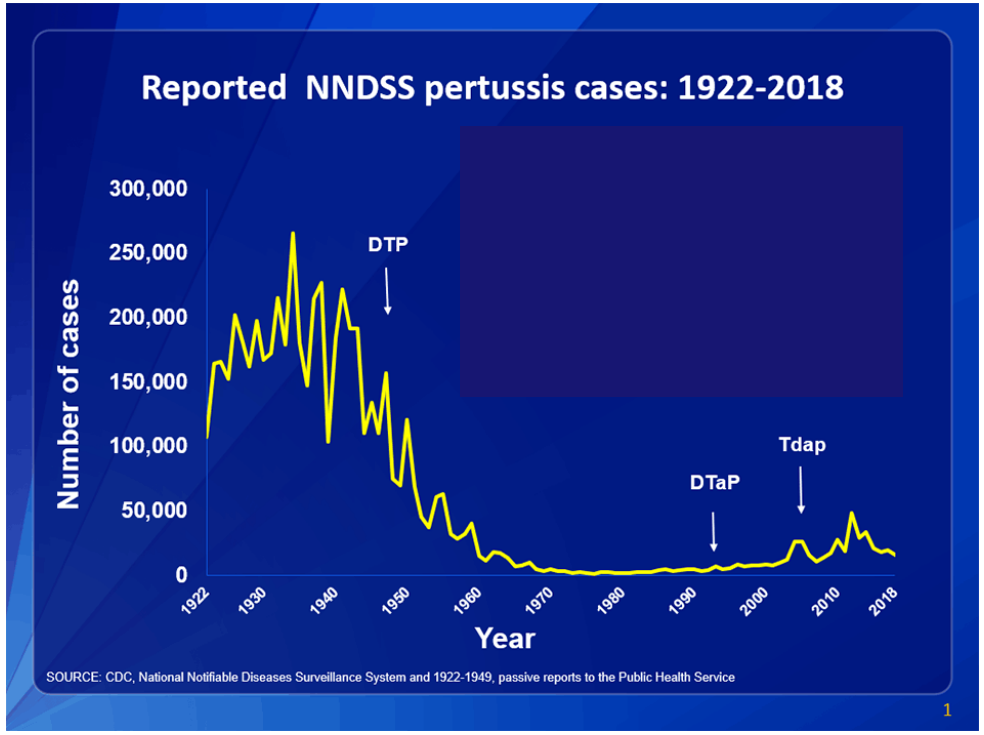
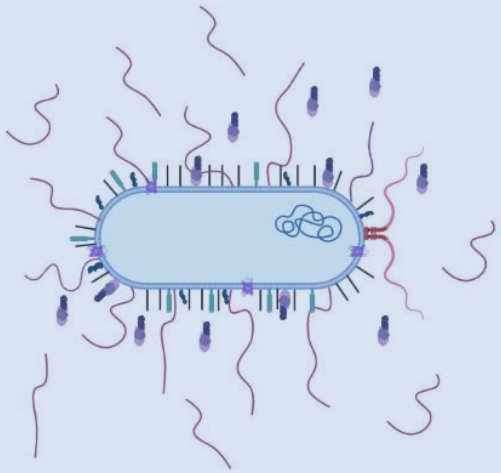


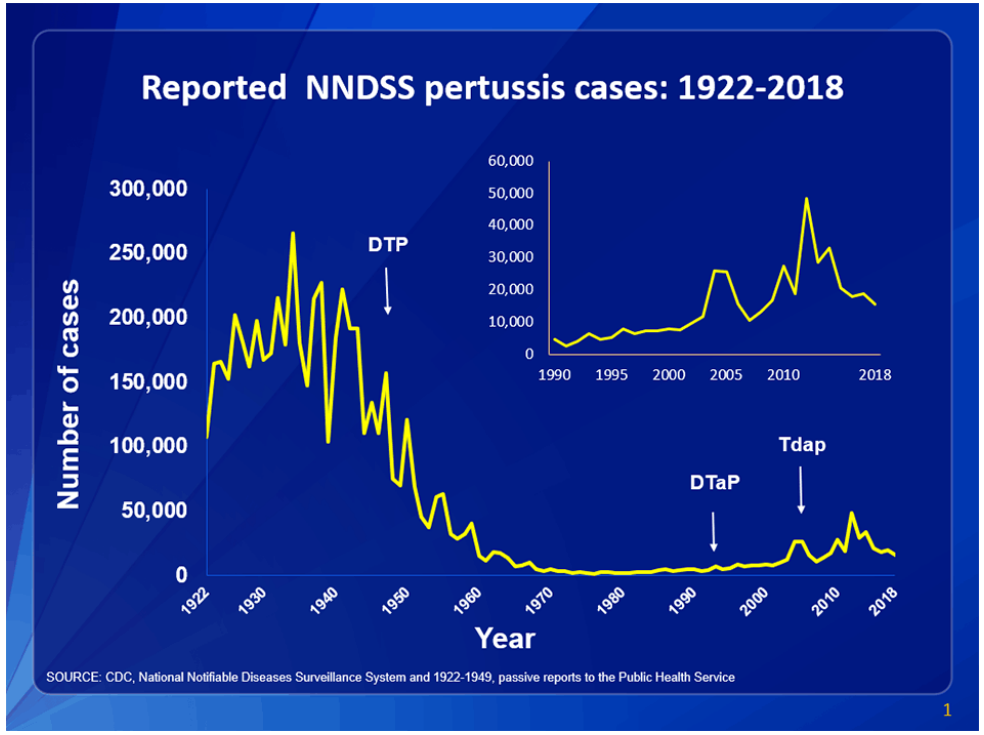
Figure courtesy of CDC, USA.

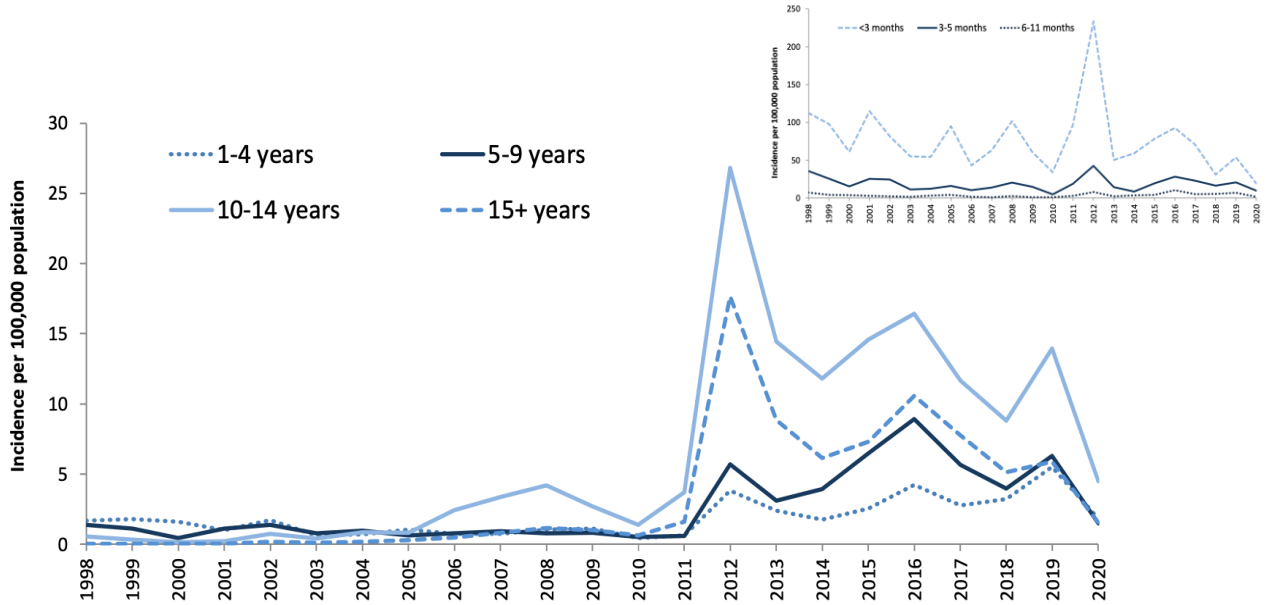
DTP
Whole cell pertussis vaccine



DTaP
Acellular pertussis vaccine
PT, FHA, Prn (Fim)

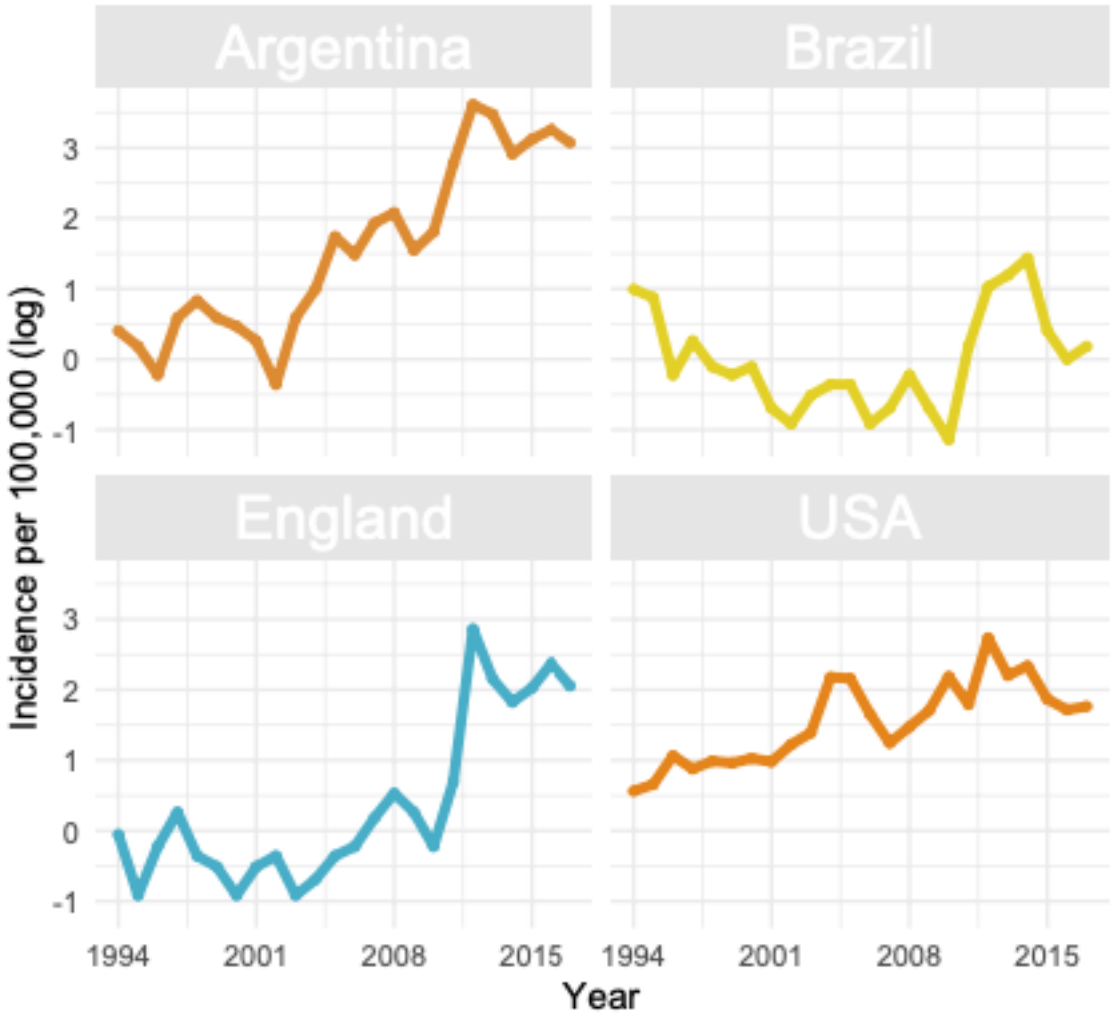
Pertussis is re-emergent, despite continued high vaccine coverage





PHE Laboratory confirmed cases of pertussis in England: Annual report for 2020 supplementary data tables. Accessed Aug 2022

Pertussis is re-emergent across the globe, but with distinct patterns



Associated with early waning of aP induced immunity
Associated with adaptation of BP to aP induced immunity

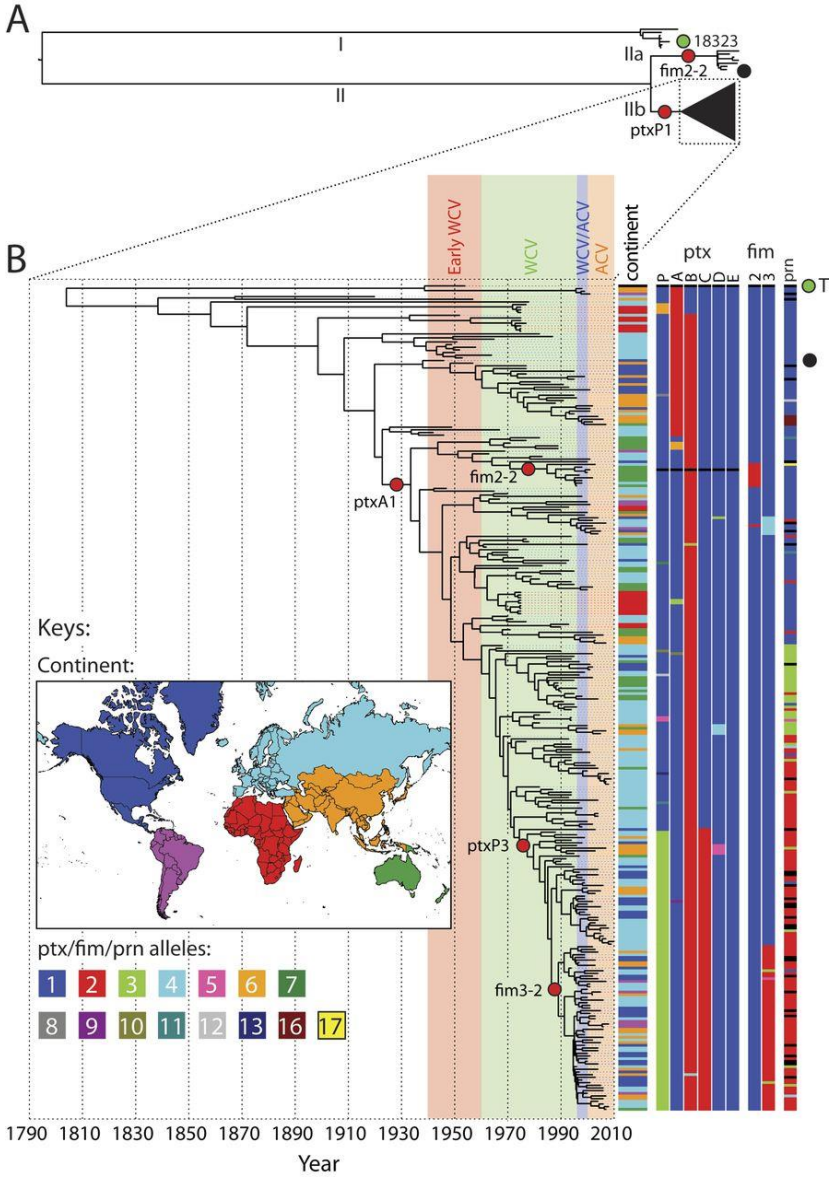
Bento & Preston, unpub.

WCV v ACV

- Th1/Th17 v Th2/Th17
- aP induced immunity wanes earlier than that from WCV
- aP induced immunity protects from disease, but less well against colonization

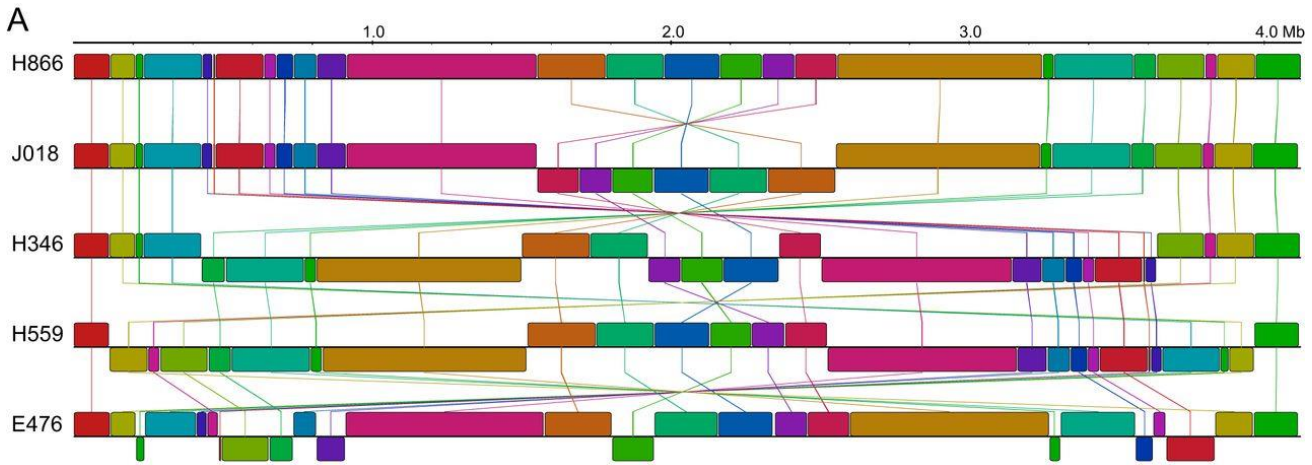
- Does use of aP increase/alter the pool of susceptible hosts?
- Does use of aP increase circulation of *B. pertussis*?

B. pertussis adaptation



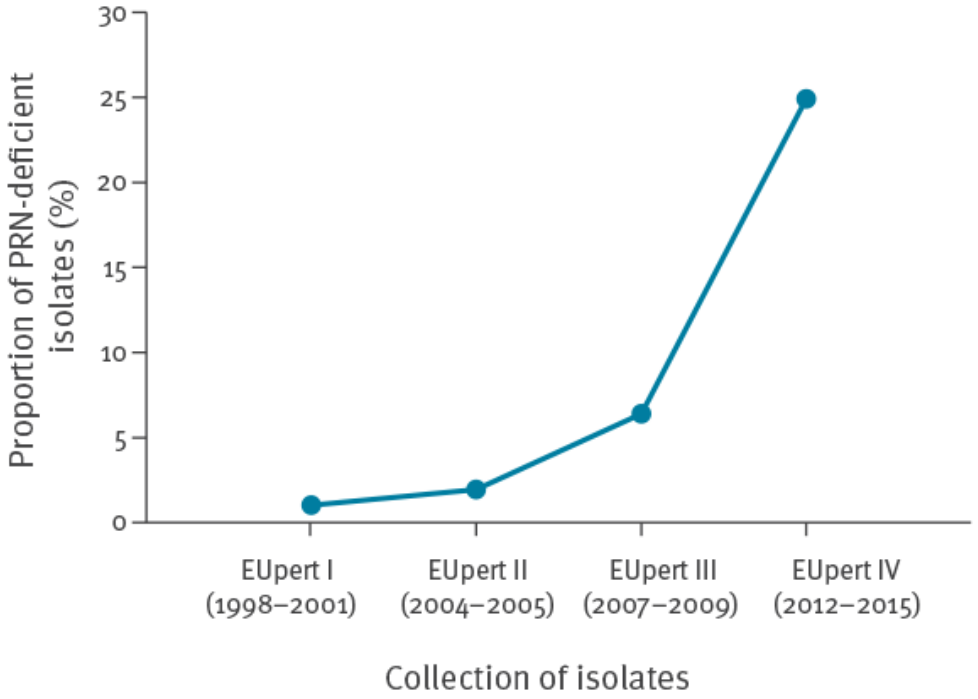
Bart et al. 2014. mBio. DOI: 10.1128/mBio.01074-14

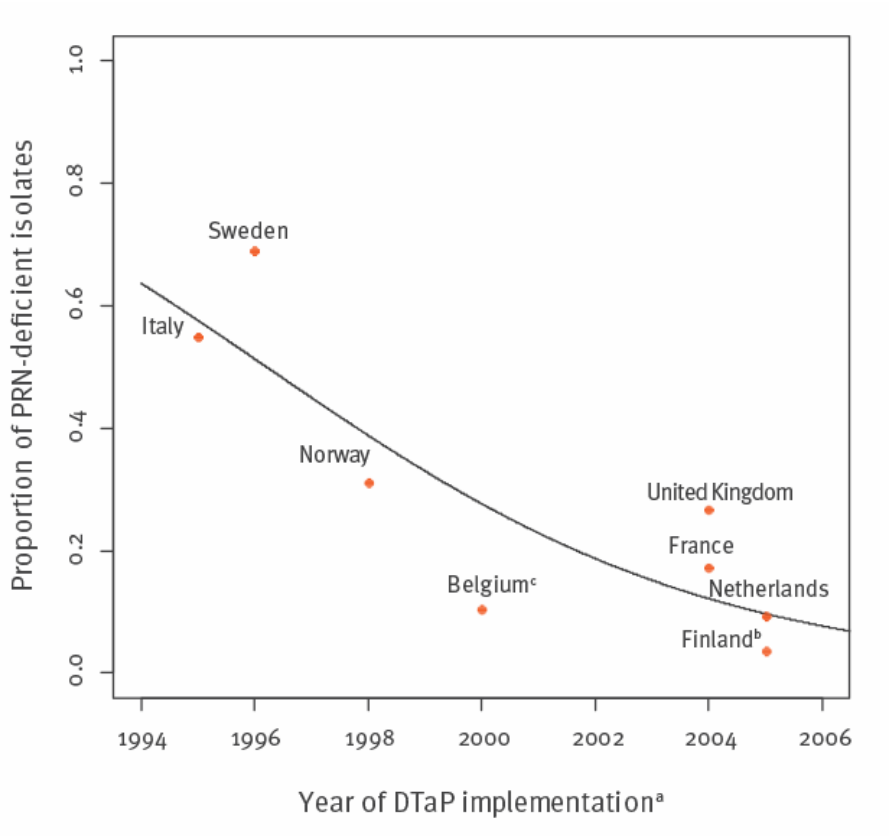
- Certain key SNPs associated with selective sweeps but, mutation rate of *B. pertussis* is low
- Horizontal gene transfer is undetectable
- *B. pertussis* genome is plastic



Weigand et al. 2017. J. Bacteriol.
DOI: https://doi.org/10.1128/JB.00806-16

Pertactin Deficiency





Generally, around 10 years after switch to aP but also observed in some wP countries (e.g. Argentina)

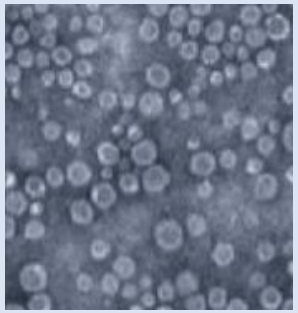
Barkoff et al. 2019. Pertactin-deficient *Bordetella pertussis* isolates: evidence of increased circulation in Europe, 1998 to 2015. Eurosurveillance. 24pii=1700832. https://doi.org/10.2807/1560-7917

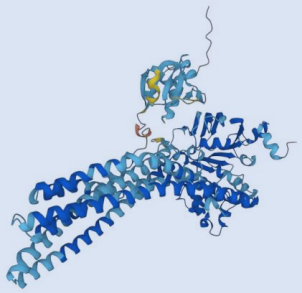
Prn-deficiency

- Prn+ strains are fitter in naïve hosts
- Prn-ve strains are fitter in aP-vaccinated hosts
- Children vaccinated with aP have greater risk of infection by Prn- than Prn+ strain
- No obvious difference in disease presentation due to Prn+ v Prn- strains

So, modified new/vaccines?

More antigens?





OMVs AC - CyaB

Adjuvants?

Th2 ⟶ Th1

BPZE1

Live, attenuated BP
ILIAD Biotech
Regulatory hurdles

Key decision: what do we need from pertussis vaccines?

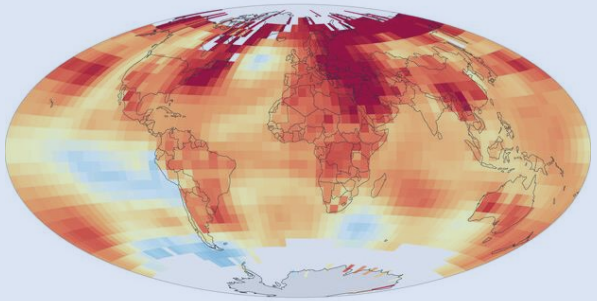
- Protect young babies from disease?
- Lifelong protection from disease?
- Prevention of colonisation (and transmission)?

- What is possible?

Observations

- Changes in host alter selection pressures on the pathogen
- Adaptation will be selected
- Adaptation may be subtle, and may take a long time to manifest
- Before implementing an intervention, can the consequences be anticipated?
  - Modeling
  - Models require data…

The host…human interactions are changing rapidly



Climate change

Changing population epidemiology

Evolving interaction networks

Incidence of pertussis in 2021 was *very* low

Going forward

- Continued (increased) surveillance is essential
  - Pathogen, not disease, focused
  - Global
  - Genomics + metadata
  - Phenotypes (requires isolates and relevant assays)
- Big data offers insight into both host and pathogen
- New models to incorporate all available data
  - Backed up by the ability to test model outcomes
- Lab studies remain essential

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https://periscope-project.eu

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