Lessons from zoonoses – future emerging threats & how to respond to them

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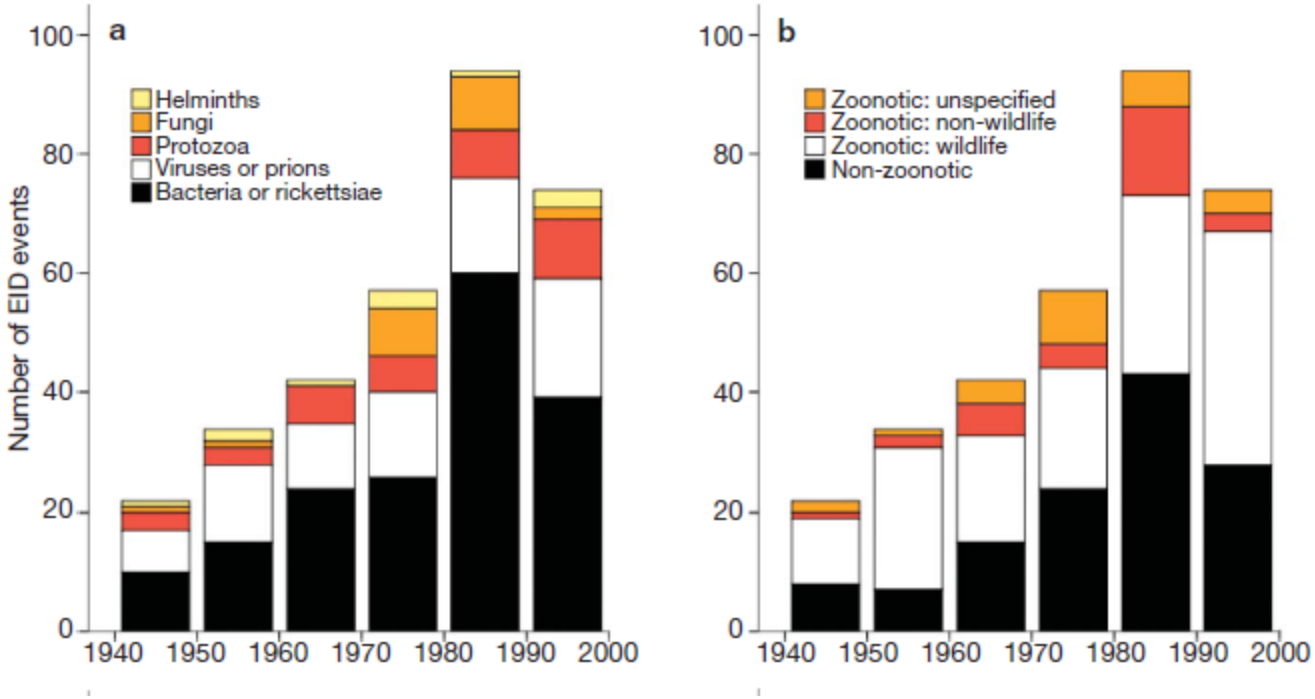
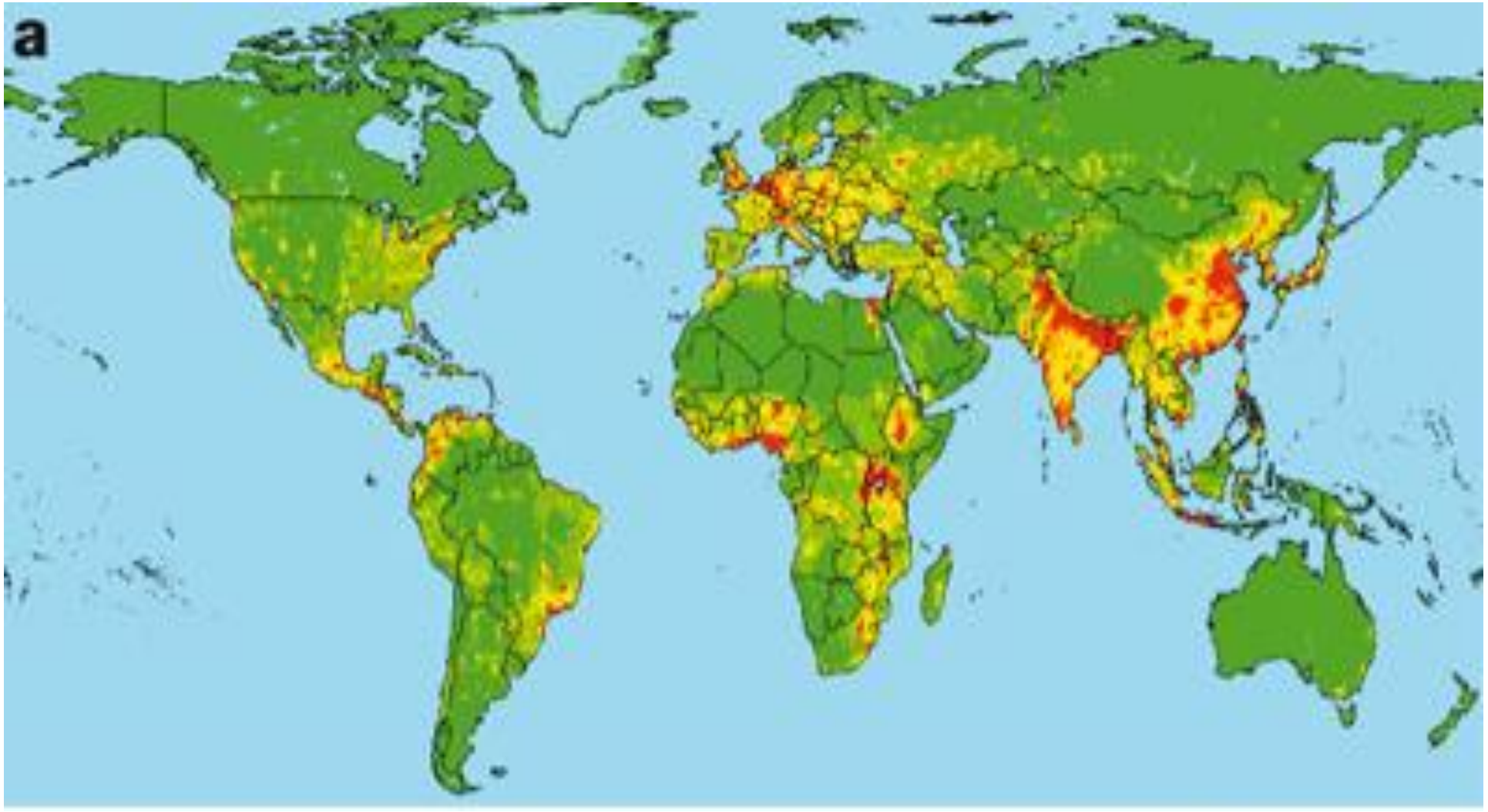
Zoonoses are important for human disease

- 60% human infectious diseases have ‘zoonotic origins’
  - 75% of *emerging* infectious diseases (EIDs) are zoonotic (Taylor)
- 61% of EIDs are zoonotic
  - 72% of these have *wildlife* source (and % increasing) (Jones)



Taylor et al *Phil Trans* 2001;
Jones et al *Nature* 2008

Emerging Zoonotic Pathogens from Wildlife



Plus a further 1-2 million pathogens yet to be discovered….

Jones et al *Nature* 2008

Approaches to mitigating future pandemic impacts

- Vaccination
  - Reactively develop rapid novel, safe vaccines more rapidly even than in 2020
  - Develop cross-reactive vaccines against pathogens known to exist in animals
- Novel medical treatments
  - Need more and novel antimicrobials (viral and bacterial) to protect against a range of pathogens
- Immediate implementation of non-pharmaceutical measures in face of emerging infection outbreaks
  - How fast is fast enough?
  - Initially this was considered for H5N1 in Thailand by Ferguson et al
- Prevent spillover infection events
- Combine all approaches….

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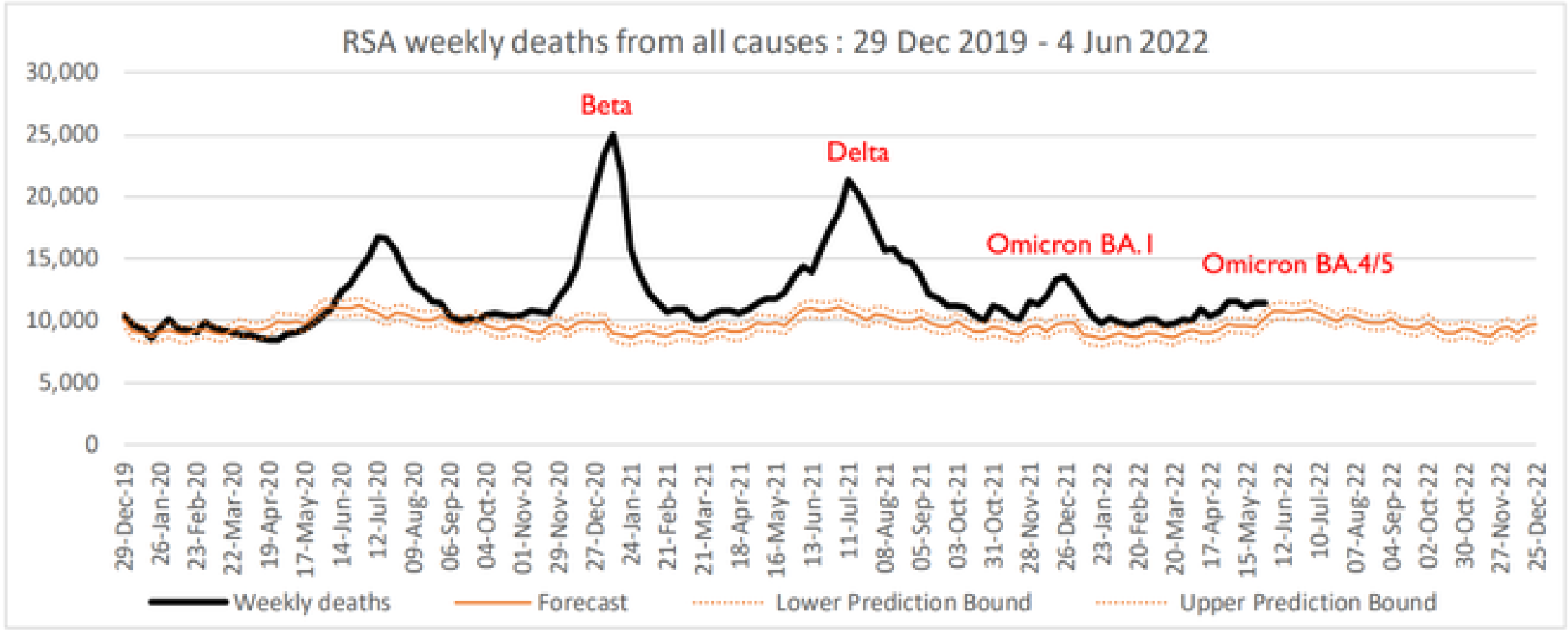
Dependent on prior animal and wildlife surveillance data and then response to this

Transmission in humans

- If any new infection transmits between humans, it will spread
  - This can evolve rapidly (but how rapidly?)
- SARS-COV-2 has demonstrated how quickly a pathogen can adapt for greater transmissibility
  - E.g. Delta -> Omicron -> Omicron.BA.2 (etc)
- So can we detect and intervene effectively at source?

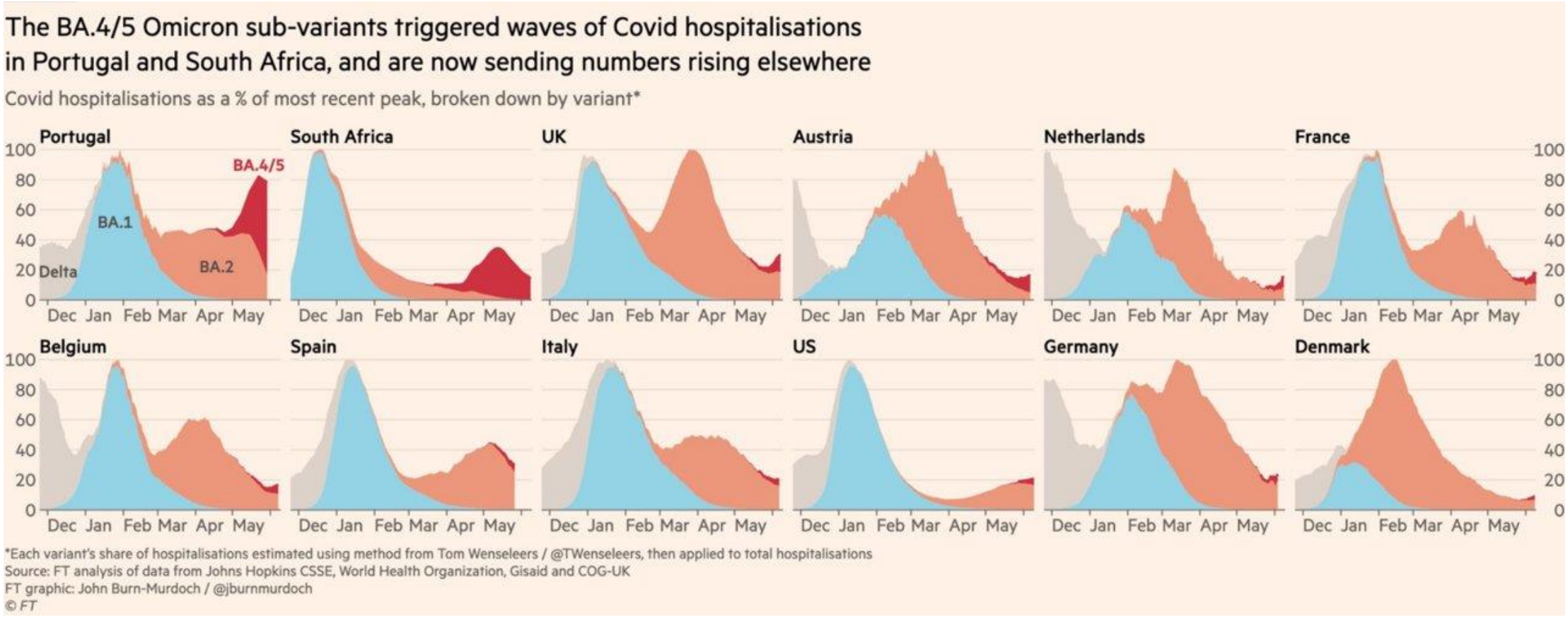
SARS-Cov-2 evolving



Numbers have been scaled to the estimated actual number of death and for the last week has been adjusted for delayed registrations

https://twitter.com/Tuliodna/status/1536058894333759492

Omicron waves demonstrating adaptation



https://www.ft.com/content/8c871596-d3c0-438c-b54c-f47b26aa4b7a

A slide from 2009: how much have we learned?

- Why has MERS not adapted like SARS-COV-2?
- Why did the West Africa Ebola outbreak not persist?
- What happened with 2009 ‘Swine flu’?

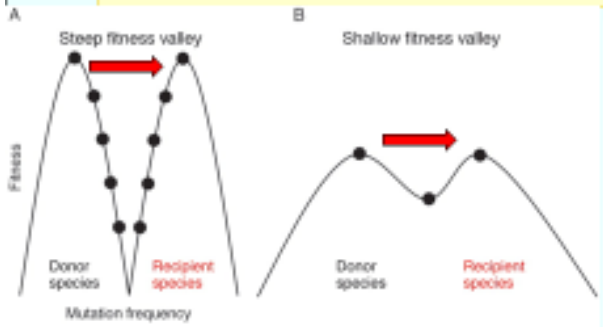
Pathogen Adaptation to cross between Species: Key Factors

Speed of mutation

Efficiency of replication (virus population size)

&

Extent of change required



Correlation with Phylogenetic Distance

- SIVcpz ➔ HIV-1: 1 mutation?
- FPV ➔ CPV: 7 mutations
- Avian influenza ➔ human influenza: 14 mutations?

Images from Grenfell (2003) Phylodynamics paper

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How good are (source) surveillance data?

- A key defence against disease emergence is early detection
- Early detection requires surveillance, which requires
  - primary health care
  - laboratory capacity
  - and access
  - excellent communications
- Can we sequence pathogens from lots of people in contact with animals?
  - For early detection?
  - Or should we focus on pathogens within wildlife?
- Massive challenges in predicting which infections will spillover to humans
  - Prediction of *future seasonal (i.e. endemic)* influenza viruses is challenging enough

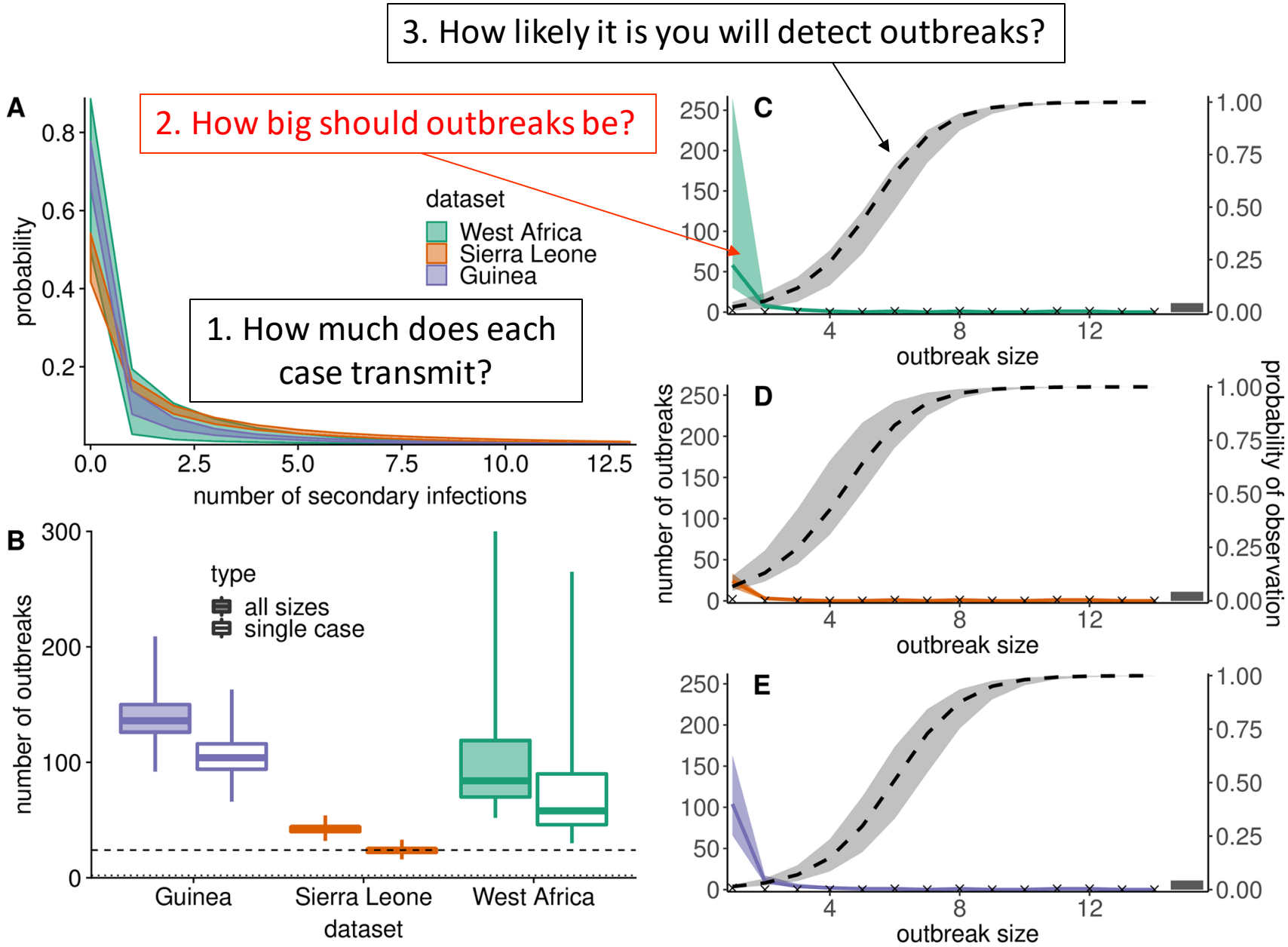
Human health seeking behaviours

- Humans have to seek treatment if they are to contribute to surveillance.
- Buoyem, nr Techiman, Brong Ahafo, Ghana
  - Malaria hyper-endemic rural region
  - 5 month ethnographic study
- Comparison of village and town living
- Different patterns of health care usage
  - Dependent on income, specific signs and disease severity
- Lack of record keeping in clinics, different communication between doctors & patients
  - Frequent retreatment for malaria
  - Only one opportunity for single diagnostic test
- Little or no chance of detection of EIDs

Jephcott et al *Phil Trans Roy Soc* 2017

How good are Ebola surveillance data?

- We know how big the detected outbreaks are
- We can predict how big outbreaks should be, given how transmissible the infection is (in outbreaks)
- We can predict what the distribution of outbreak sizes *should be*, given how transmissible the infection is



Glennon et al, PLoS Neg Trop Dis 2019

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- At least half of all spillover events have failed to be reported since Ebola was first recognised
- The probability of detecting outbreaks of different sizes, is less than 10% for single-case spillover event
- Strong evidence for need to invest in primary health care

Glennon et al, PLoS Neg Trop Dis 2019

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- So can we detect and intervene at source?
  - **UNLIKELY TO BE EFFECTIVE FOR ACUTE INFECTIONS with R0>1**
- Logically, we must therefore intervene to prevent spillover transmission
  - Reduce biodiversity loss, extractive industries, care with intermediate (agricultural) hosts etc etc

What is role of wildlife farming?

- Farming and trade of live palm civets was responsible for SARS-CoV-1 outbreaks
  - Extended epidemic in traded palm civets caused multiple spillover events into humans
  - Palm civet acted as intermediate hosts
- Was there a role for farmed wildlife – common in the Hunan Seafood Market – in causing the onset of the SARS-CoV-2 pandemic?
- Is this different to more conventional agriculture?
  - Scale of wildlife farming, esp. in South Asia is massive
  - Bridging / intermediate species between wildlife and humans for pathogens
  - But agricultural scale and movement of animals is still a massive risk….

- (What even are farmed wildlife?
  - Animals may be wild caught and fattened, or bred on farms)

Role for massive investigation of pathogens in wildlife?

- It is useful to know what pathogens are present in animals
  - But what will we do with the information?
- Can we predict the next pathogen that will cause a pandemic
  - We cannot accurately predict which influenza strain will cause the next seasonal flu outbreak
- Is it feasible to develop multiple effective cross reactive vaccines?
  - Stock pile them
  - Or stock pile vaccine seeds?
  - Where will resourcing come from?

conclusions

- Important to focus on (post-hoc) pandemic responses
  - Need to consider spillback risks (not discussed today)
- Improve early detection
  - Technology limited by under-investment in global primary health care
- Vital to work to reduce spillover infection risk
  - Reducing biodiversity loss
  - Target live animal trade, extractive industries (including elements of agriculture)
- Politically challenging
  - Largely ignored to date, certainly since 2019, and especially in funding opportunities