

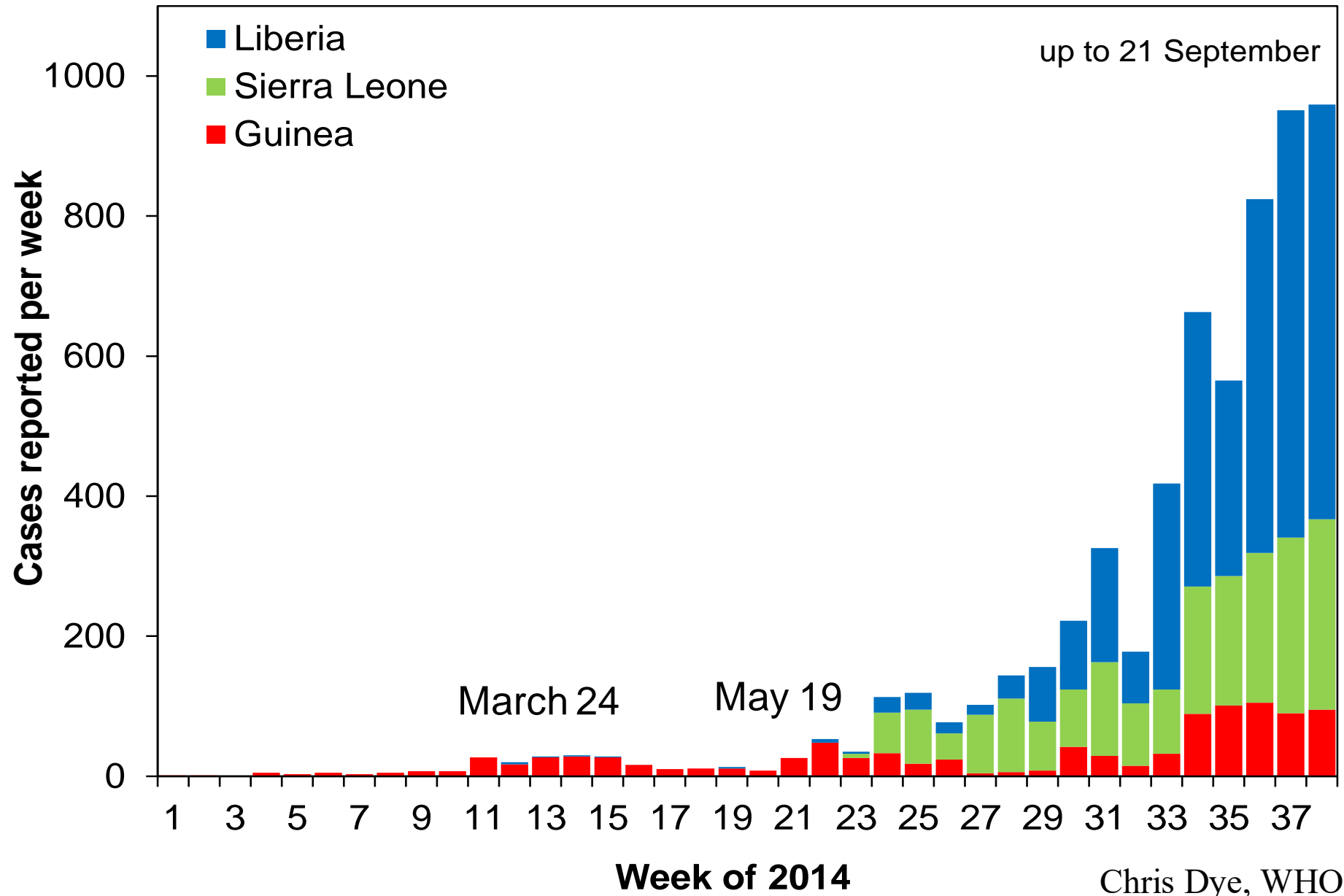


Assessing Impact of Access to mRNA Vaccines in LMICs

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An Exploding Ebola Outbreak in mid-2014

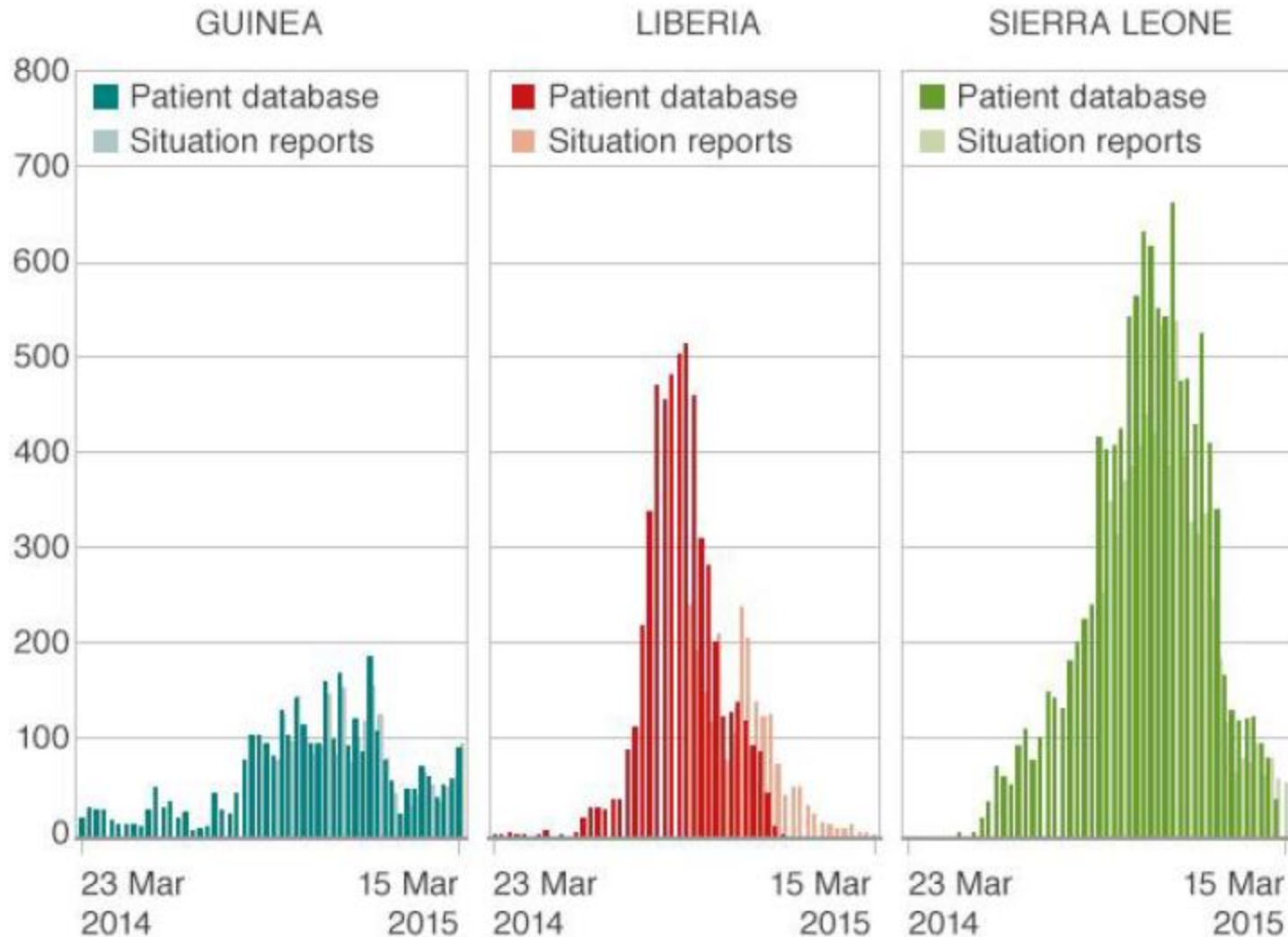


Ebola Vaccine Trial Timeline

| | |
|--------------|---------------------------------------|
| 14 August | Grant application submitted |
| 26 August | Award letter |
| 30 August | Vaccine filled |
| 2 September | Trial file submission to UK regulator |
| 5 September | Ethics meeting |
| 8 September | Ethical approval |
| 9 September | Regulatory approval |
| 11 September | Vaccine shipping |
| 15 September | Vaccine labelled |
| 16 September | Trial contract signed |
| 17 September | 1 st vaccinee |
| 18 November | 60 th vaccinee |



Declining Case Incidence



Vaccine trials in the outbreak area delayed until April 2015

Only one vaccine was tested:
Merck's VSV-vectored vaccine
expressing Ebola glycoprotein

Very high efficacy

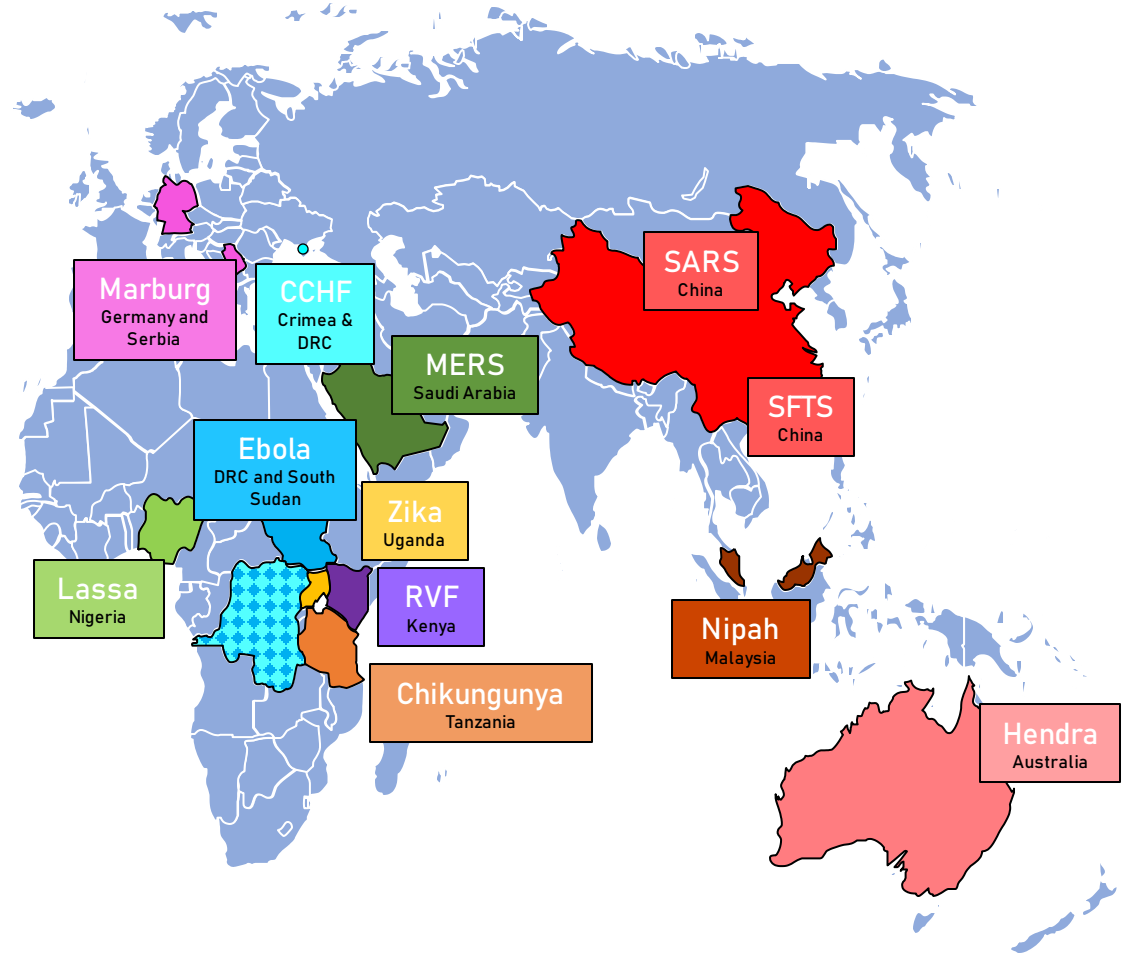
Requires ultra-low temperature
storage, manufacturing process
not scaled-up

J&J vaccine now also licensed

Vaccines cover Ebola Zaire
only

Outbreak Pathogens

| Virus | Country of first identification | Year of first identification |
|--|---|------------------------------|
| Crimean Congo haemorrhagic fever (CCHF) | Crimea and Congo | 1967 |
| Ebola | South Sudan and Democratic Republic of Congo | 1976 |
| Marburg | Germany and Serbia (from NHPs imported from Uganda) | 1976 |
| Lassa fever | Nigeria | 1969 |
| SARS-CoV-1 | China | 2003 |
| SARS-CoV-2 | China | 2020 |
| MERS-CoV | Saudi Arabia | 2012 |
| Nipah | Malaysia | 1999 |
| Rift Valley fever (RVF) | Kenya | 1931 |
| Zika | Uganda | 1947 |
| Severe fever with thrombocytopenia syndrome (SFTS) | China | 2009 |
| Chikungunya | Tanzania | 1952 |
| Hendra | Australia | 1994 |

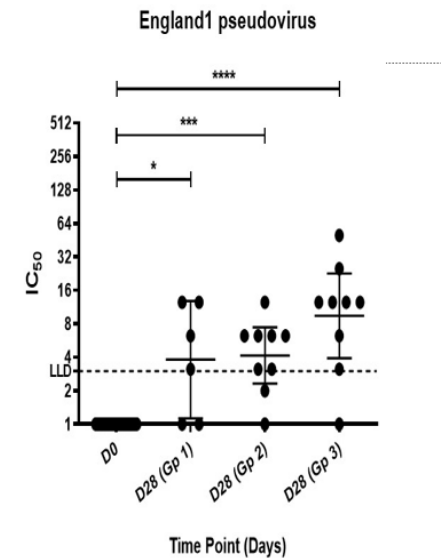
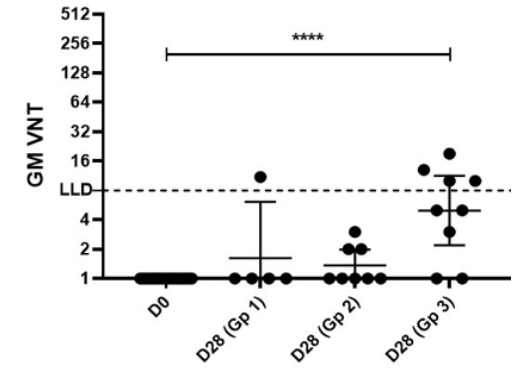
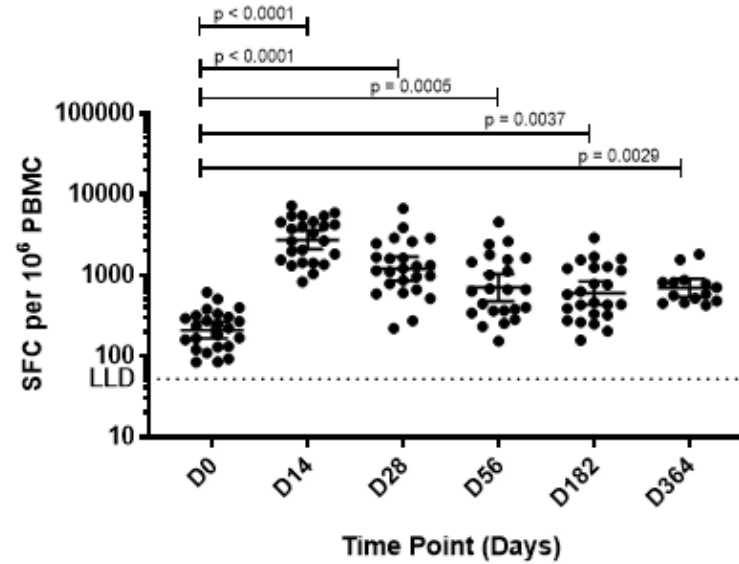
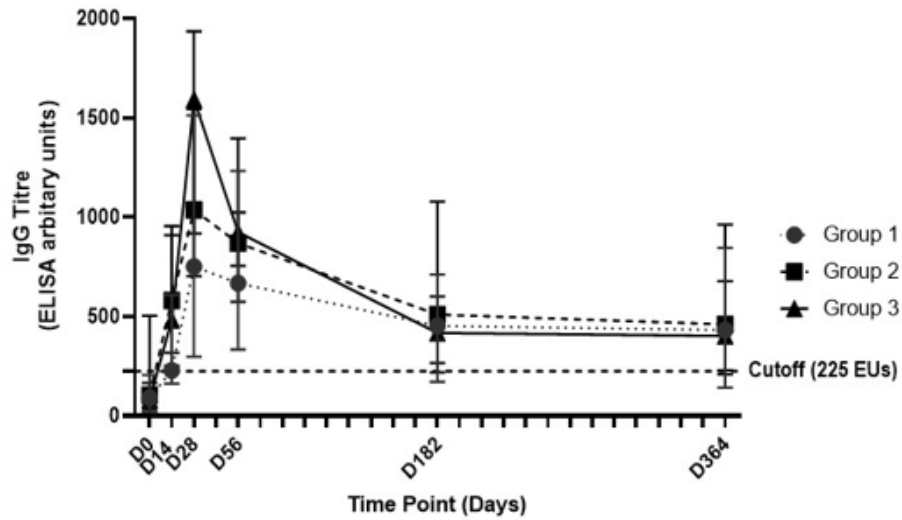


Middle East Respiratory Syndrome coronavirus (MERS-CoV)

- More than 2250 cases of severe acute respiratory disease, 800 deaths in 27 countries
- Camels are the source of zoonotic infections
 - Occupational exposure can lead to seroconversion
 - Severe disease in the immunocompromised
 - Hospital outbreaks
- Major surface antigen is the Spike (S) protein



ChAdOx1 MERS immunogenicity



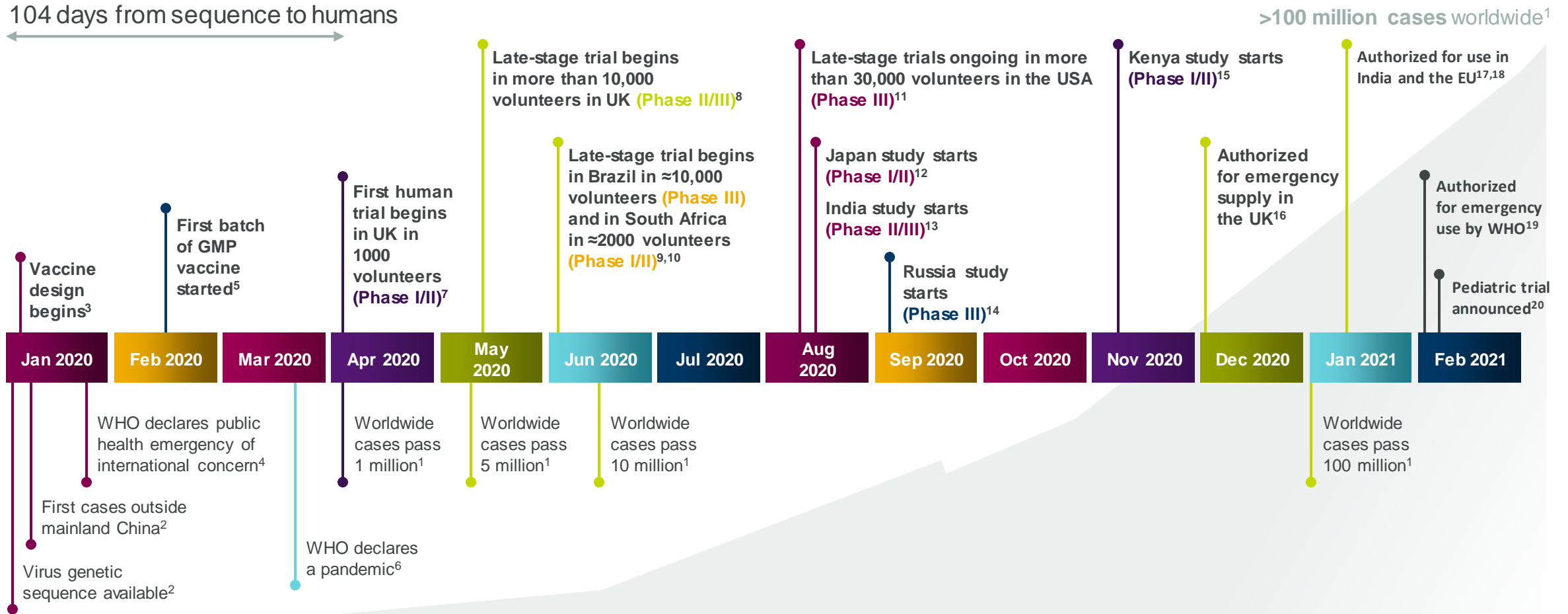
| Dose Group | % Seropositivity | | | | | |
|---------------|------------------|---------|----------|----------|---------|---------|
| | D0 | D14 | D28 | D56 | D182 | D364 |
| Group 1 (n=6) | 17% (1) | 50% (3) | 83% (5) | 83% (5) | 67% (4) | 60% (3) |
| Group 2 (n=9) | 33% (3) | 78% (7) | 89% (8) | 89% (8) | 78% (7) | 63% (5) |
| Group 3 (n=9) | 0% (0) | 89% (8) | 100% (9) | 100% (9) | 89% (8) | 83% (5) |

Numbers in parenthesis represent total seropositive individuals.

Folegatti et al., Lancet Inf Dis 2020

From the ChAdOx1 platform to a vaccine candidate against COVID-19

104 days from sequence to humans



Collaboration has made this possible²¹



EU = European Union; GMP = Good Manufacturing Practices; UK = United Kingdom; USA = United States of America; WHO = World Health Organization.
 1. COVID-19 Dashboard. Johns Hopkins University website. Accessed June 25, 2020; 2. Novel coronavirus situation report – 1. World Health Organization website. Accessed June 22, 2020; 3. University of Oxford press release. Published March 18, 2020; 4. Global research and innovation forum consensus. World Health Organization website. Accessed June 22, 2020; 5. University of Oxford press release. Published February 7, 2020; 6. COVID-19 situation report – 51. World Health Organization website. Accessed June 22, 2020; 7. Study NCT04324606. ClinicalTrials.gov website; 8. Study NCT04400838. ClinicalTrials.gov website; 9. University of Oxford press release. Published June 28, 2020; 10. Study NCT04444674. ClinicalTrials.gov website; 11. Study NCT04516746. ClinicalTrials.gov website; 12. Study NCT04568031. ClinicalTrials.gov website; 13. Study CTRI/2020/08/027170. Clinical Trials Registry – India website; 14. Study NCT04540393. ClinicalTrials.gov website; 15. University of Oxford press release. Published October 30, 2020; 16. AstraZeneca press release. Published December 30, 2020; 17. AstraZeneca press release. Published January 6, 2021; 18. AstraZeneca press release. Published January 29, 2021; 19. AstraZeneca press release. Published February 15, 2021; 20. University of Oxford press release. Published February 13, 2020; 21. COVID-19 Oxford vaccine trial – sponsors and partners. University of Oxford. Accessed June 25, 2020.

Equitable access strategy delivers vaccine at no profit to over 170 countries: over 25 manufacturers in 15 countries



First AZ vaccine doses have been delivered (solid circle) / First AZ vaccine doses not yet delivered (hatched circle)

CEPI-Gavi / COVAX - Countries eligible to receive AZ vaccine through COVAX



Supporting equitable access, globally

Key points

- 128 approvals and emergency authorisations in ~100 countries to date
- More than 2.8 billion doses released for supply to 180 countries
- Collaboration with more than 20 partners across over 15 countries
- 424 million doses to approx 130 countries via COVAX
- Approx. 2/3 doses to low and lower middle income countries



Covax Rollout: Ivory Coast, 1st March 2021

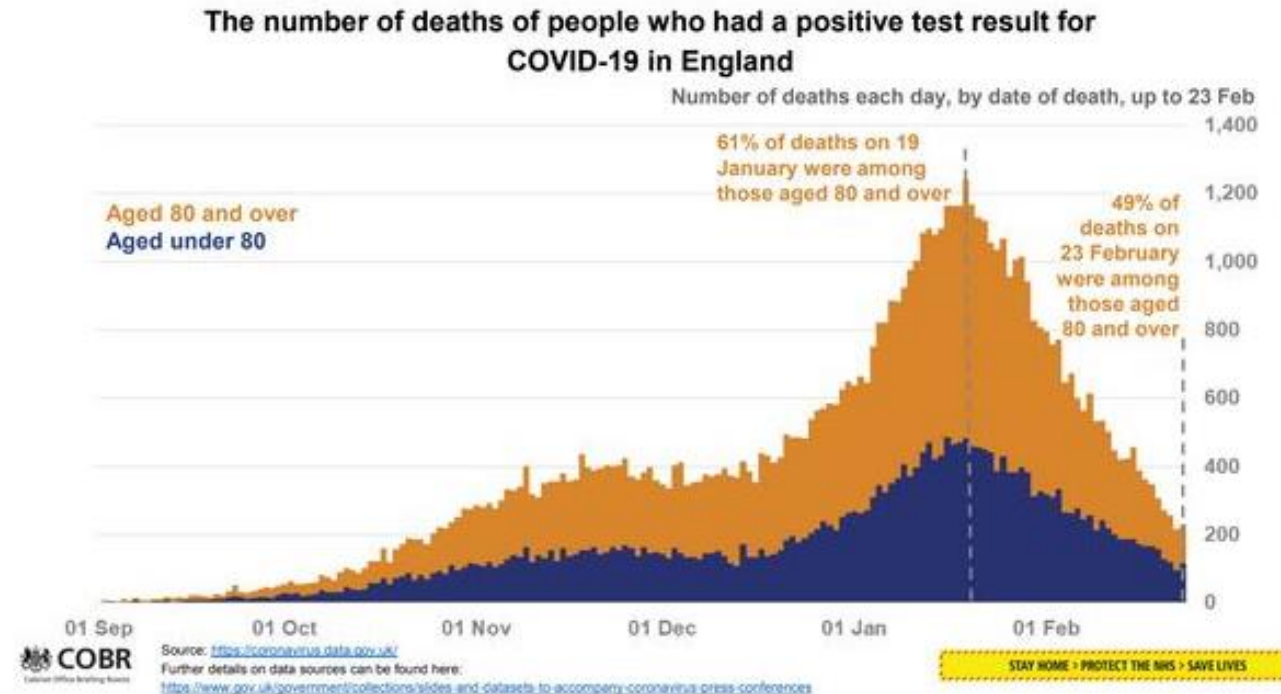


Of the first 38 million doses administered via Covax, 37 million doses were ChAdOx1 nCoV-19



Vaccine effectiveness data

- Public Health England data released March 1st.
- In England, in over 70s who have received one dose, from 28 days, at least 60% protection against symptomatic PCR +ve disease (ChAdOx1 nCoV-19 and also BNT162b2)
- In over 80s, hospitalisation reduced by 80% (ChAdOx1 nCoV-19 and also BNT162b2)
- Deaths in over 80s reducing faster than in younger age groups (combined effect of ChAdOx1 nCoV-19 plus BNT162b2)



Why produce mRNA vaccines in LMICs?

In outbreak/epidemic scenarios

- Rapid access
- Rapid deployment
- Ability to control pricing
- Independent planning of vaccine development and stockpiling
 - or plans for rapid production when needed

For routine vaccination programmes

- Control of supply locally
- Ability to control pricing
- Development of sustainable industry
- Advancement of the technology is possible
 - Ambient temperature storage?
 - Mucosal delivery?

What challenges can be expected?

- Intellectual Property
- Regulatory concerns
 - Local regulatory capacity must be strengthened
 - Distributed manufacturing results in a complex situation for regulators
 - Ultra-local manufacturing presents further challenges
- For routine vaccinations, prices may be higher
- Secure supply of raw materials
- For outbreak pathogens,
 - how to prioritise? Local planning.
 - how to plan for efficacy testing? Global planning.
 - how to plan for rapid response? Local and global planning.
- Facilities must be 'kept warm'
- Should livestock vaccines be produced and rolled out?

PANDEMIC SCIENCES INSTITUTE (PSI)

- The Pandemic Sciences Institute will draw upon lessons learnt from COVID-19 pandemic **to identify and counter future pandemic threats**
- **Partnership** between academia, industry & public health organisations across the world
- Create science-led innovations to
 - accelerate the understanding
 - develop new diagnostics, treatments, vaccines & digital control tools
- Focus on **equitable** access

