Oxford Vaccine Group
University of Oxford

Preliminary results from an oral vaccine in the Paratyphoid Human Challenge Model

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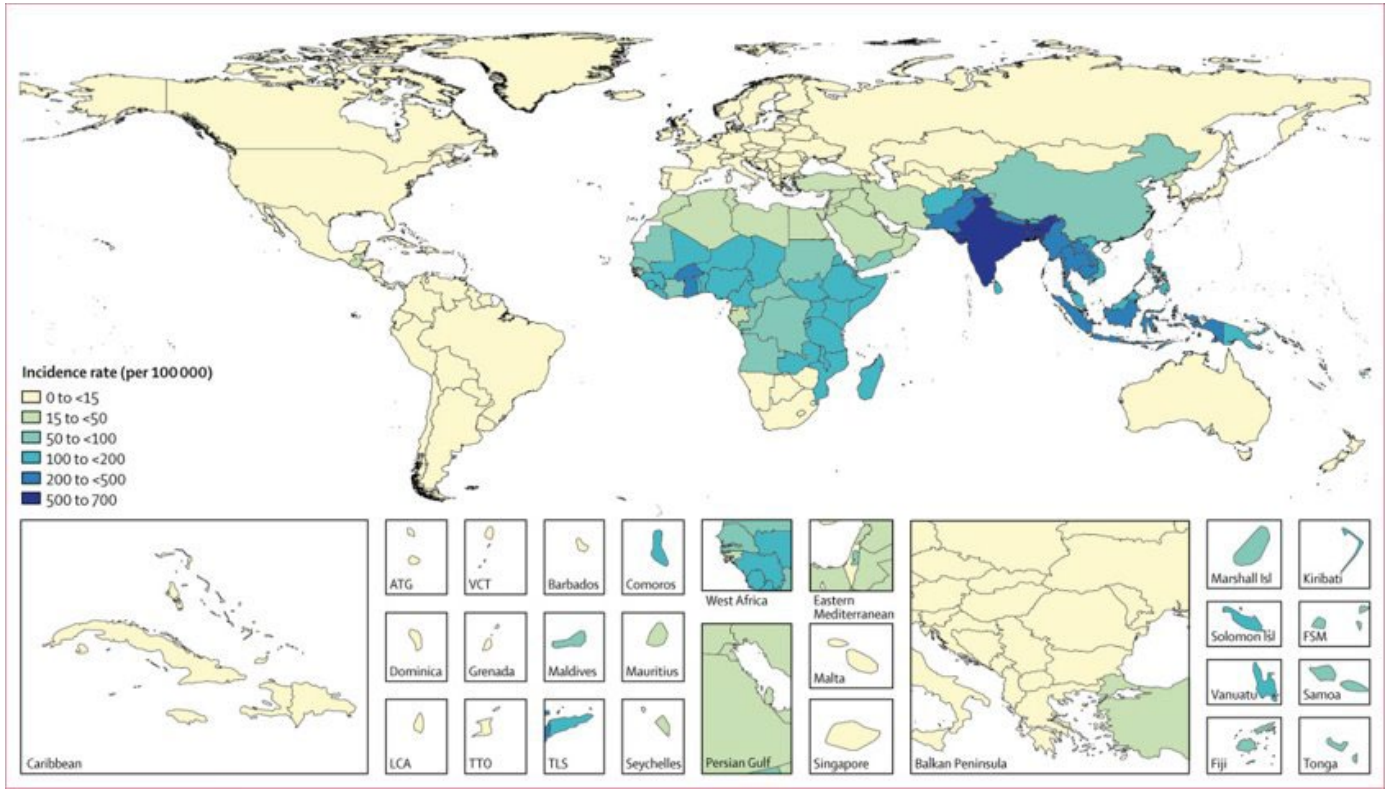
S. Paratyphi A – unmet need for vaccines

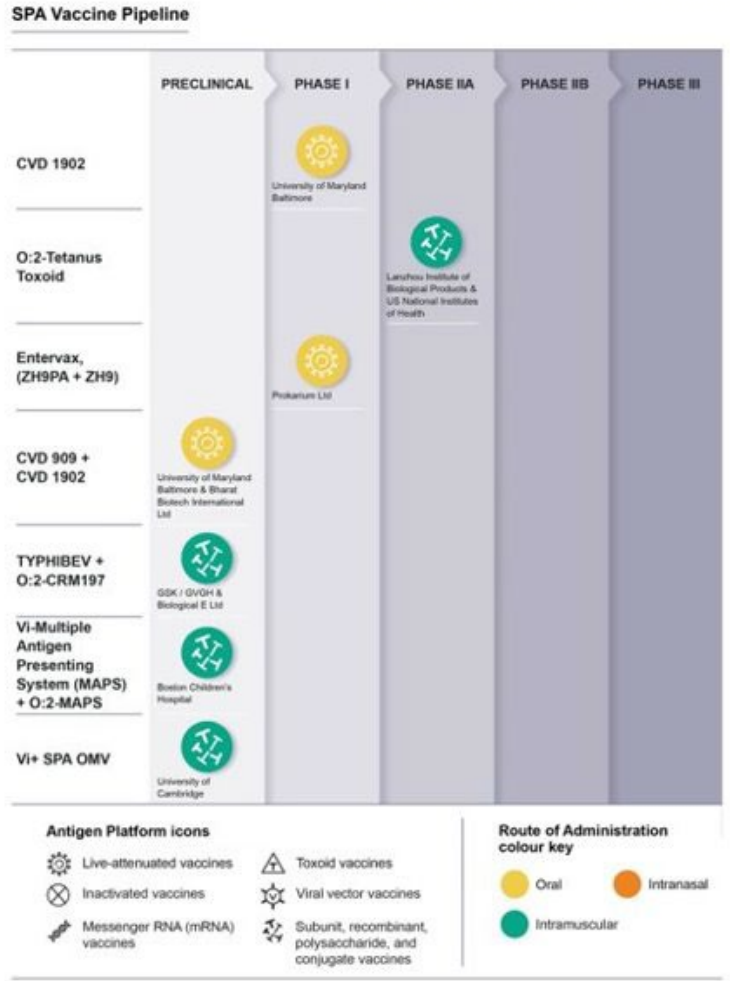


Stanway et al, Lancet ID, 2019

3.8 million cases

~30% of enteric fever

World Health Organization



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CHIM is a valuable method to assess efficacy of *S.* Paratyphi A vaccine candidates

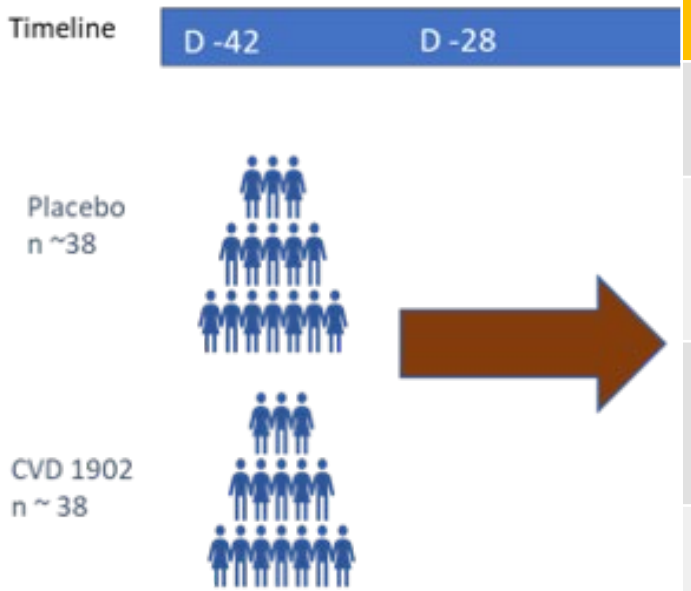
World Health Organization

Demonstration of vaccine efficacy against *S.* Paratyphi A is considered difficult, as a low attack rate means that an efficacy study will need around 100,000 – 250,000 participants. A CHIM for *S.* Paratyphi A has been developed and can potentially be a valuable way to assess the efficacy of the current paratyphoid vaccine candidates. Licensure of bivalent typhoid-paratyphoid vaccines can be supported on the basis of of Phase II efficacy (from CHIM) and field immunogenicity for the *S.* Paratyphi A component to demonstrate non-inferiority (on immunogenicity) to licensed typhoid conjugate vaccines. Such an accelerated pathway would likely require post-licensure effectiveness studies.

Updated April 30, 2022

VASP trial to assess CVD 1902

- Testing efficacy of **CVD 1902**, **live attenuated vaccine** against SPA
- Observer-participant blinded randomised, placebo-controlled trial



Paratyphoid fever is diagnosed if ANY of the following apply
A positive blood culture for S. Paratyphi A from 72 hours post-challenge
A positive blood culture for S. Paratyphi A within 72 hours post-challenge, with one or more signs/symptoms of paratyphoid infection (such as recorded temperature ≥38.0°C)
Persistent positive blood cultures (two or more blood cultures taken at least 4 hours apart) for S. Paratyphi A within 72 hours post-challenge.
Oral temperature ≥38.0°C persisting for 12 hours

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Objectives

Sample size – 66-76 participants

PRIMARY

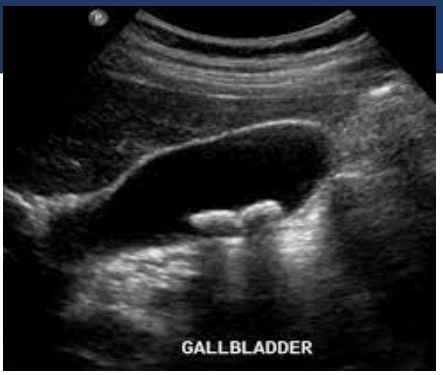
- **Determine relative protection of 2 doses of CVD 1902 vs placebo**

SECONDARY

- Compare clinical and laboratory features of host response following challenge in vaccinated vs placebo
- Compare host immune response following vaccination in those vaccinated vs placebo
- Compare host immune response following challenge in those vaccinated vs placebo
- To assess safety and tolerability of CVD 1902
- To investigate immunological correlates of protection for S. Paratyphi A

Strict inclusion/exclusion criteria

- Healthy adult volunteers (18-55)
  - Gallstones excluded

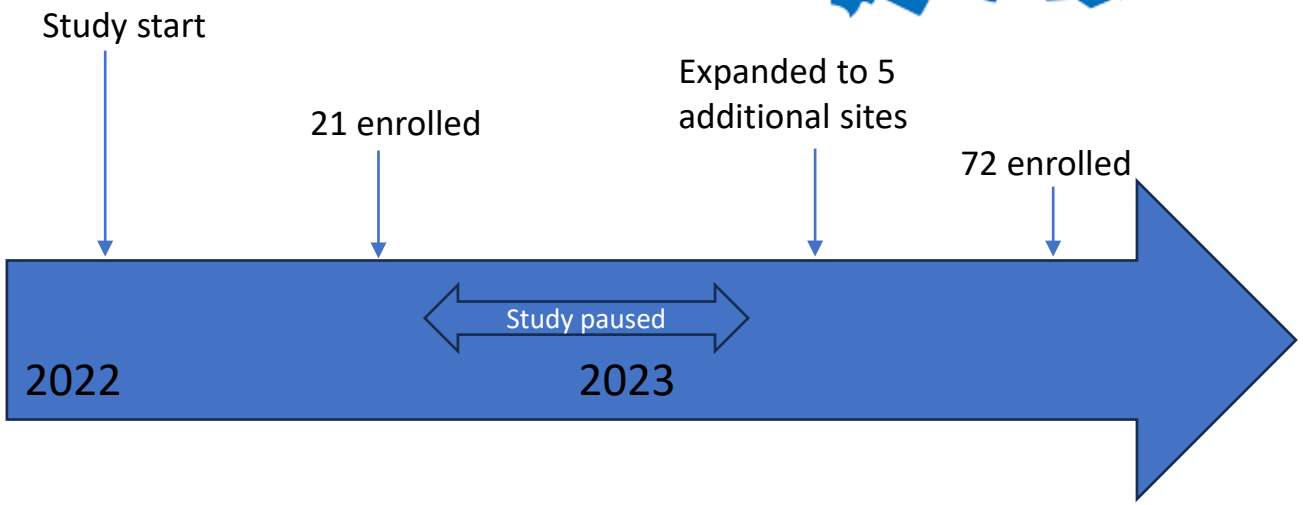


https://radiopaedia.org/cases/gallstones-1

- Not putting others at risk
  - Occupation
  - Household contacts

- Not affect study outcomes
  - Prior challenge/infection

Recruitment completed



Enrolled / recieved first vaccination =72

Received second vaccination = 55

Been challenged = 52

Completed challenge = 42

Reached D90 =33

Completed 1 year follow-up = 18

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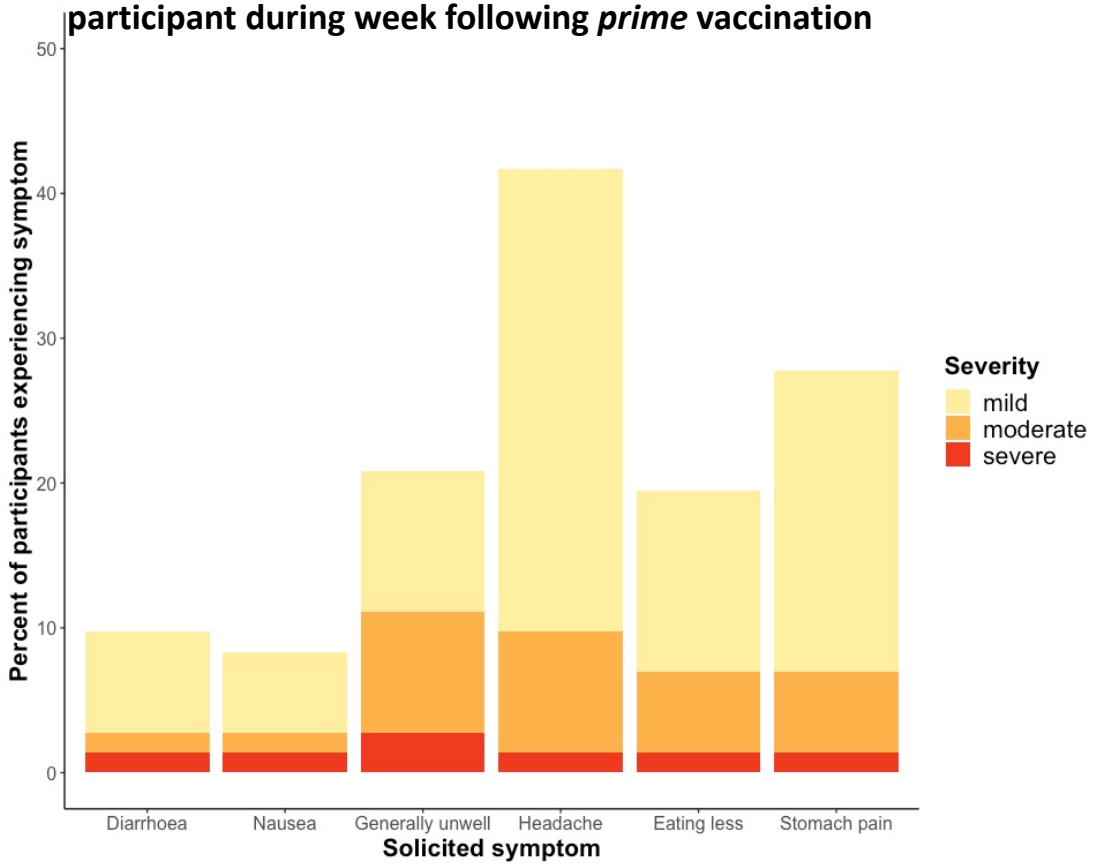
Demographics

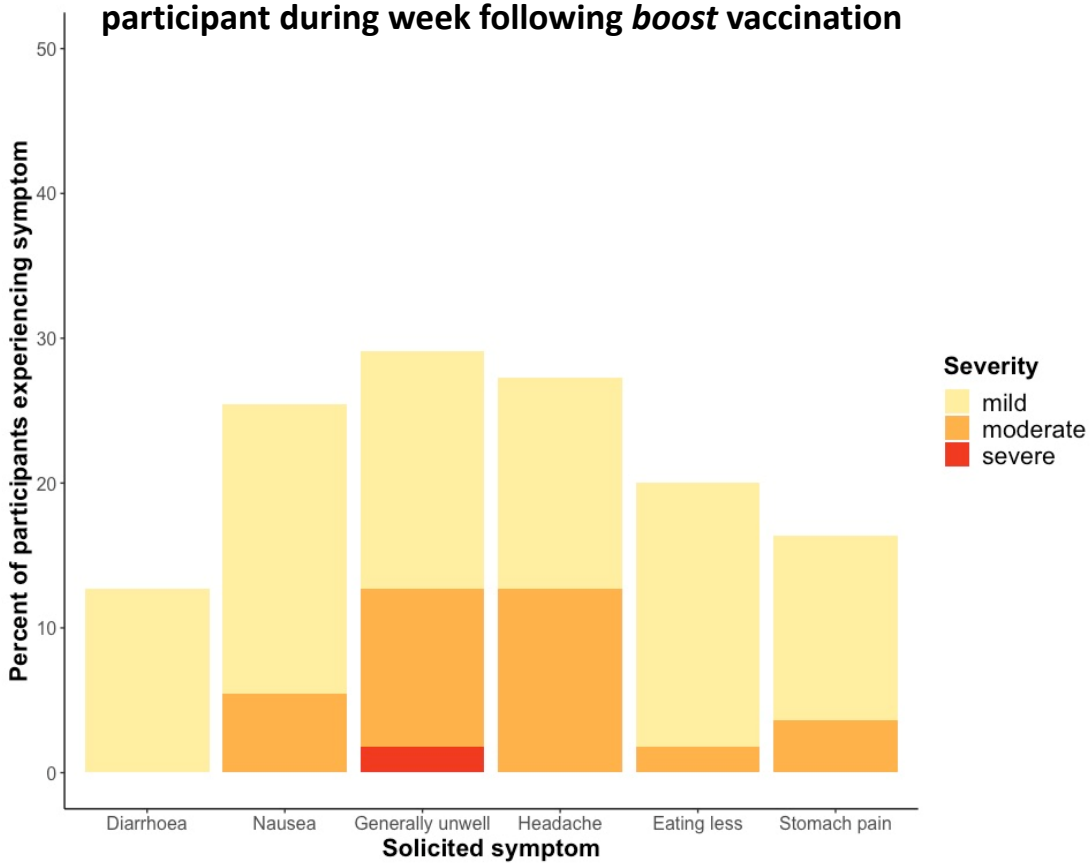
Characteristic	N (%) or median (range)
Age, median (range)	31.5 (20-54)
Sex at birth	
Female	33 (46%)
Male	39 (54%)
Ethnic origin	
White British	51 (71%)
White other	9 (12.5%)
Mixed	6 (8%)
Asian	3 (4%)
Other	3 (4%)
Occupation	
Student	20 (28%)

CVD 1902 appears to be well-tolerated

Maximum severity of solicited symptoms experienced by participant during week following *prime* vaccination



Maximum severity of solicited symptoms experienced by participant during week following *boost* vaccination



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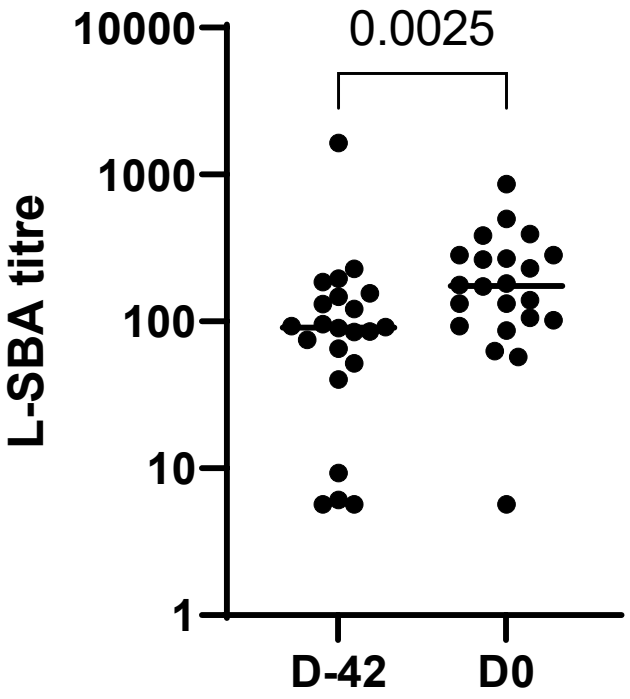
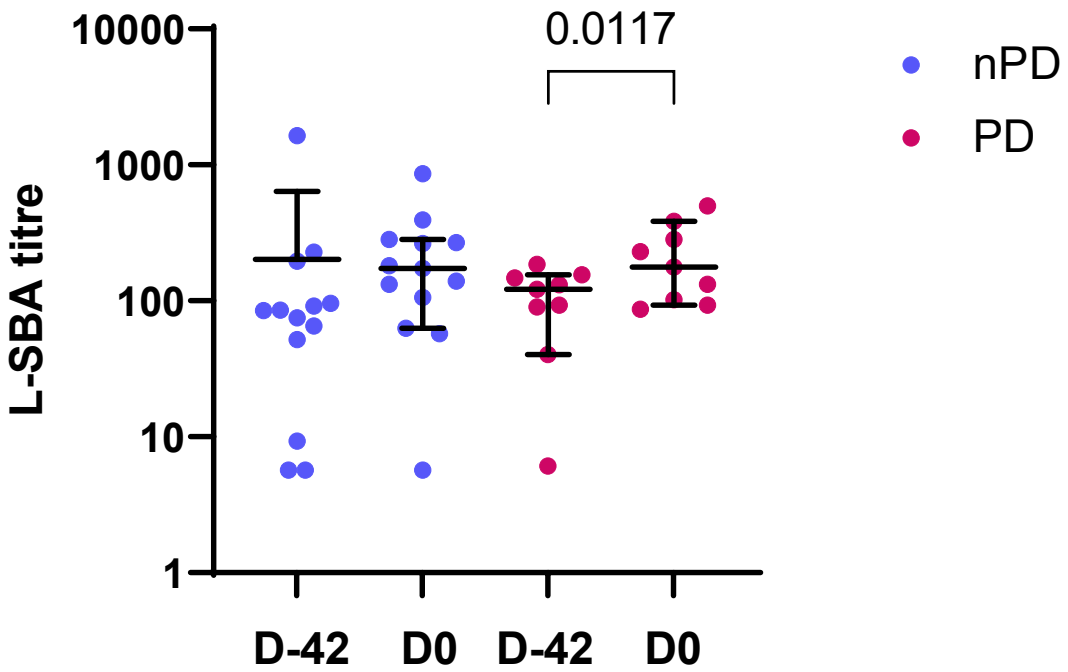
Significant rise in SBA titres following CVD 1902 vaccination





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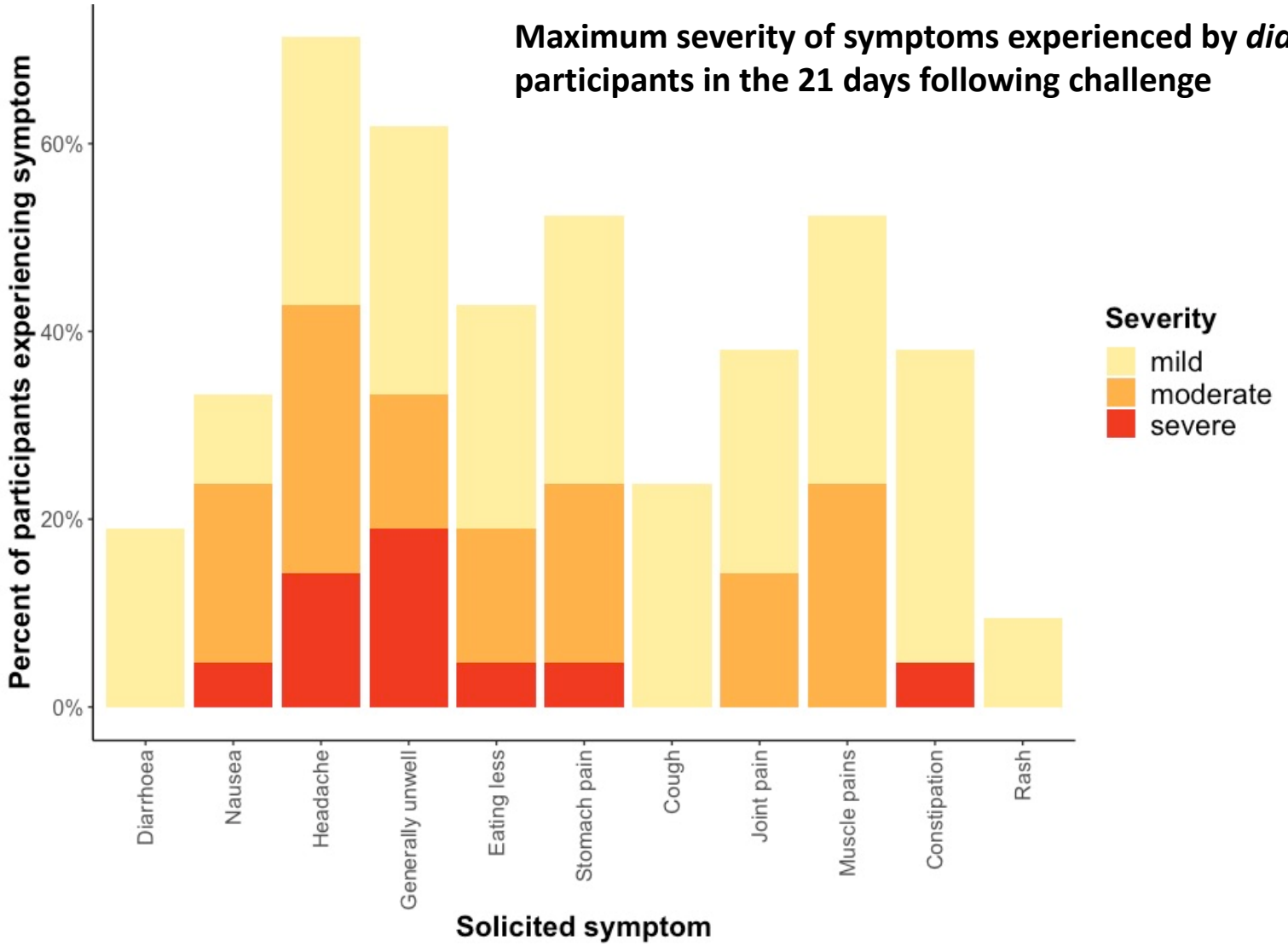
Paratyphoid A in CHIM causes predominantly mild disease

Current attack rate 50%

No hospital admissions

No severe disease



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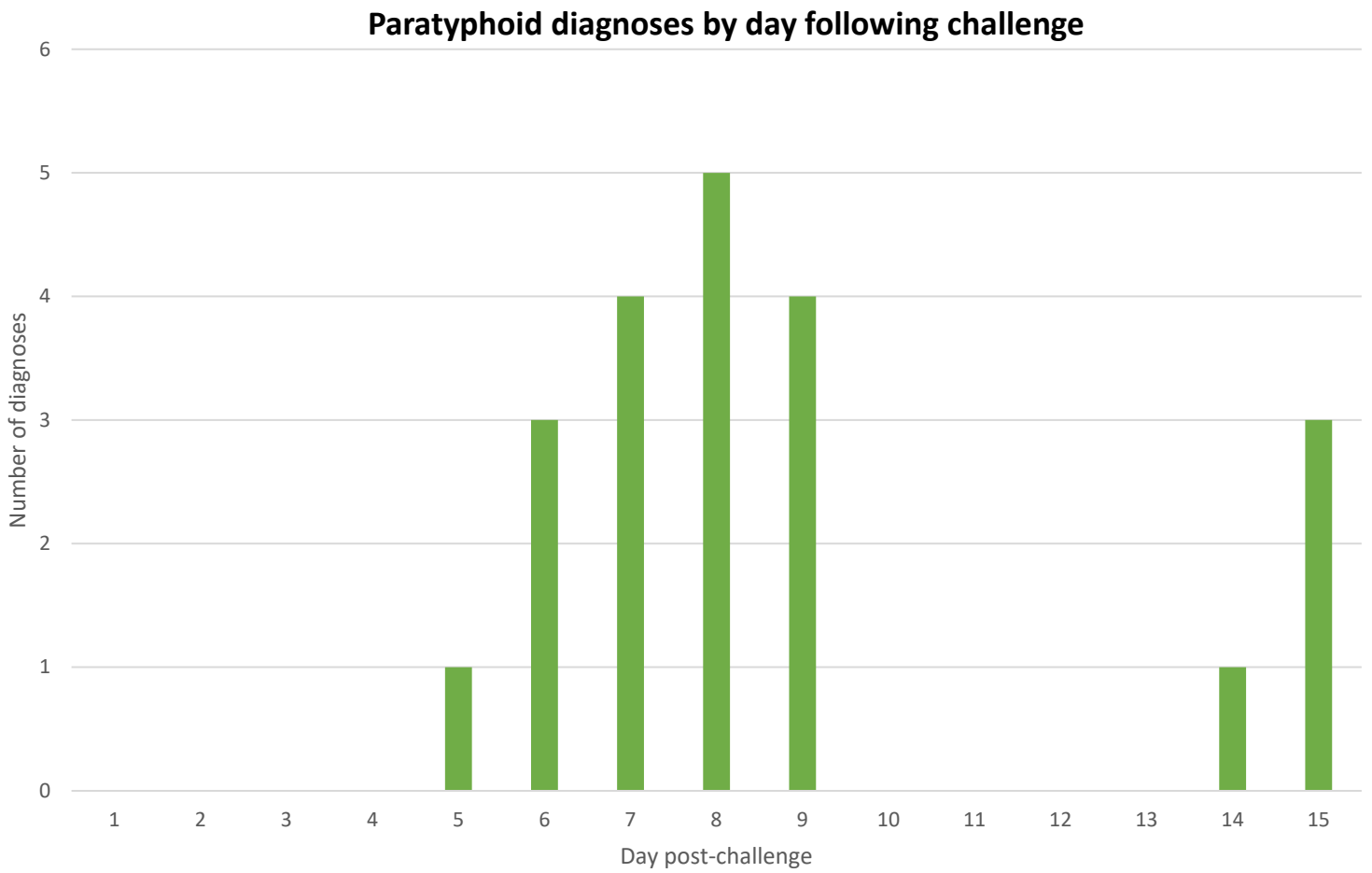
Majority of diagnoses are microbiological

90% diagnoses microbiological

Fevers in 29%

Median day of diagnosis = D8

Median days of bacteraemia = 3



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Summary

- CVD 1902 appears safe, well-tolerated & immunogenic
- *S.* Paratyphi A in CHIM model is usually mild
- Success of first multi-site enteric challenge model

Next steps

- Study completion 2024
- Efficacy data presentation/publication mid-2024
- Towards bivalent vaccination
- Immunology & sequencing work investigating correlates of protection
- Validated model for testing of other paratyphoid vaccine candidates

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