

A simulation-based method to inform serosurvey design to estimate dengue force of infection using existing blood samples

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Aim of the study

Develop a novel **simulation-based method** to estimate the number and age-distribution of blood samples to test for obtaining **accurate FOI estimates** when leveraging existing blood samples. We present an application of our framework to inform the design of a dengue serosurvey in **Ghana**.

Background

- Age-stratified **seroprevalence surveys** are the gold standard for estimating the:
 - force of infection (FOI)**
 - unobserved **burden of dengue** infection
- Limited number** of dengue serosurveys conducted globally so far (~100), due to extensive resource required
- Leveraging existing blood samples** to test for anti-dengue antibodies to assess historical circulation patterns, reconstruct the immunity profile of the population and quantify dengue FOI.

Materials and Methods

- Simulation-based framework based on **catalytic model** equation:

$$z_a = 1 - e^{-\lambda a}$$

- Test effect of **different sample sizes** and age distributions (named scenarios 0, A, B, C, D and E) on accuracy of estimated FOI accounting for test specificity and sensitivity
- Select sampling scheme that **maximises accuracy** whilst reducing number of samples to test in selected age-groups (optimal scenario)

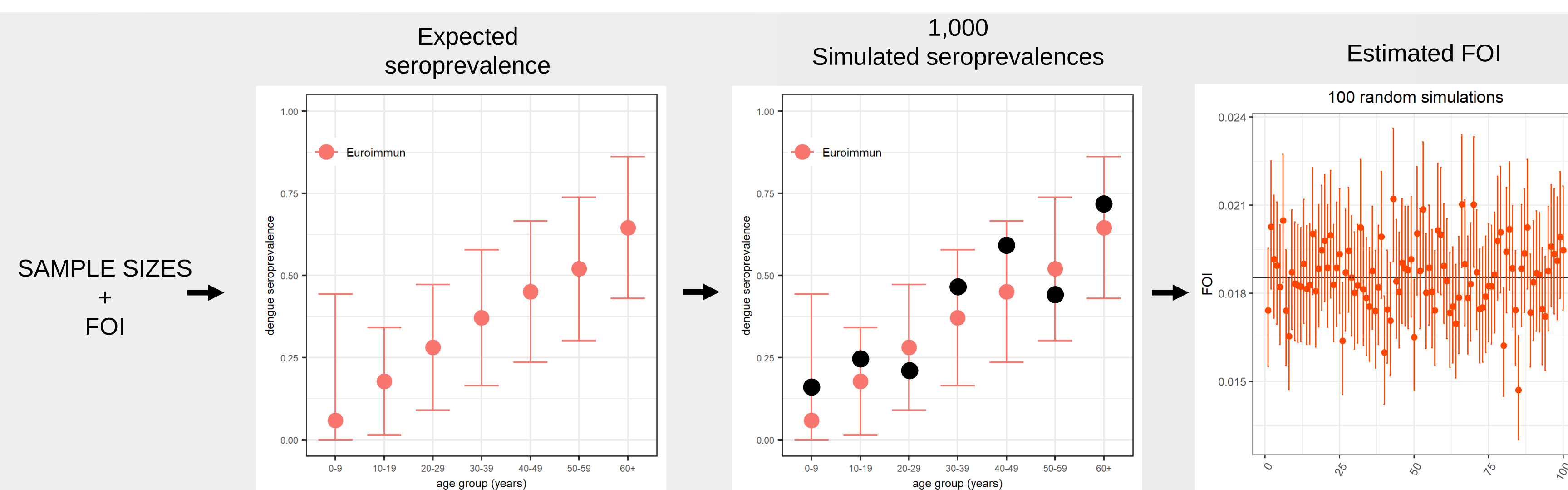


Figure 1 Steps of the simulation-based framework: the sample sizes of the selected sampling scenario coupled with the FOI are used to produce the expected seroprevalence, from this 1,000 simulated seroprevalences are designed accounting for test specificity and sensitivity and feed into the catalytic model to get the FOI estimate. These scenario-specific FOI estimates are compared with the one of the baseline scenario to determine the optimal sampling strategy.

Figure 2 Blood sample distribution across several scenarios for the city of Accra using the 5-year age category.

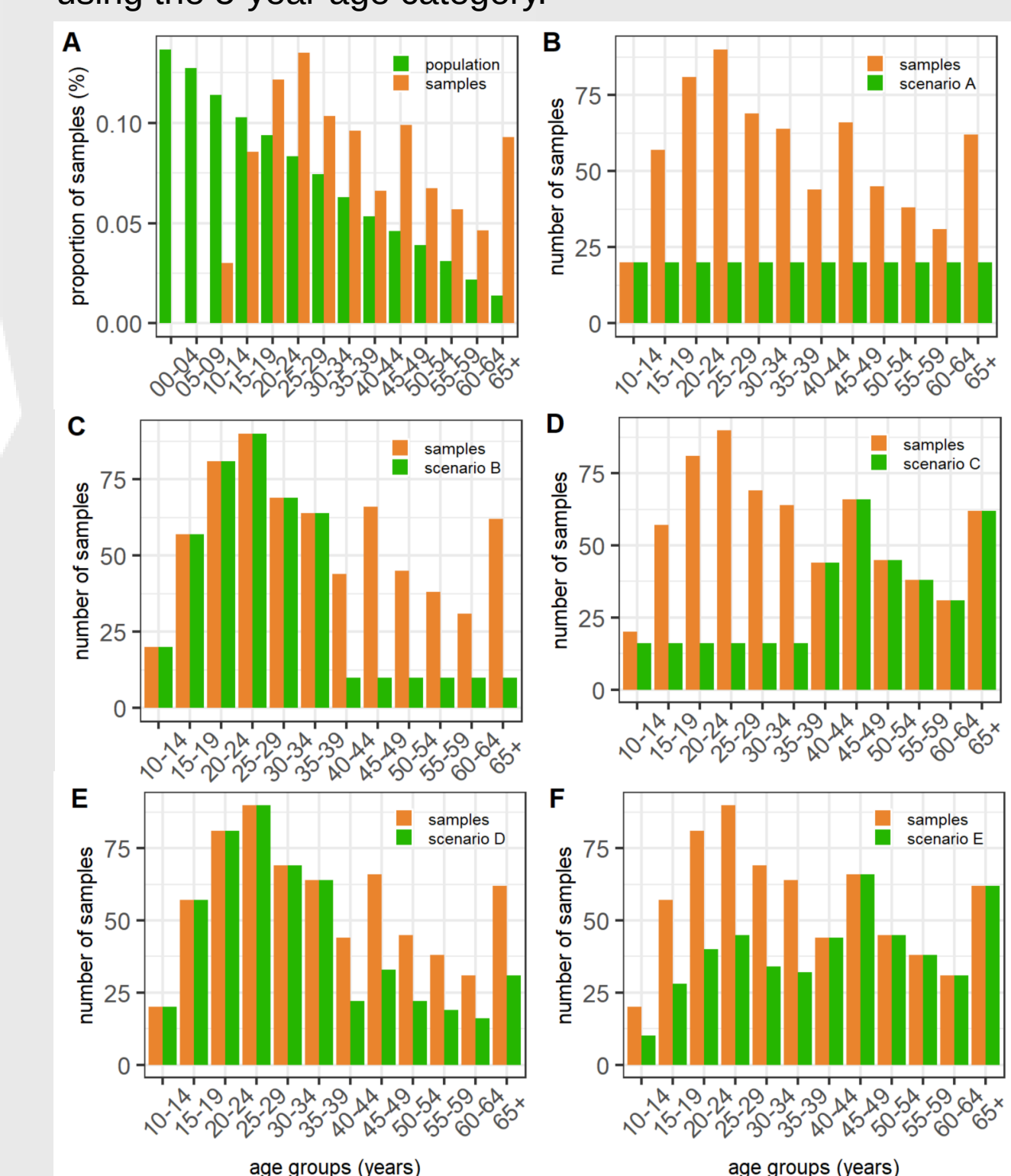


Figure 3 Summary of the accuracy metrics obtained for Accra across scenarios; the optimal scenario is highlighted in green.

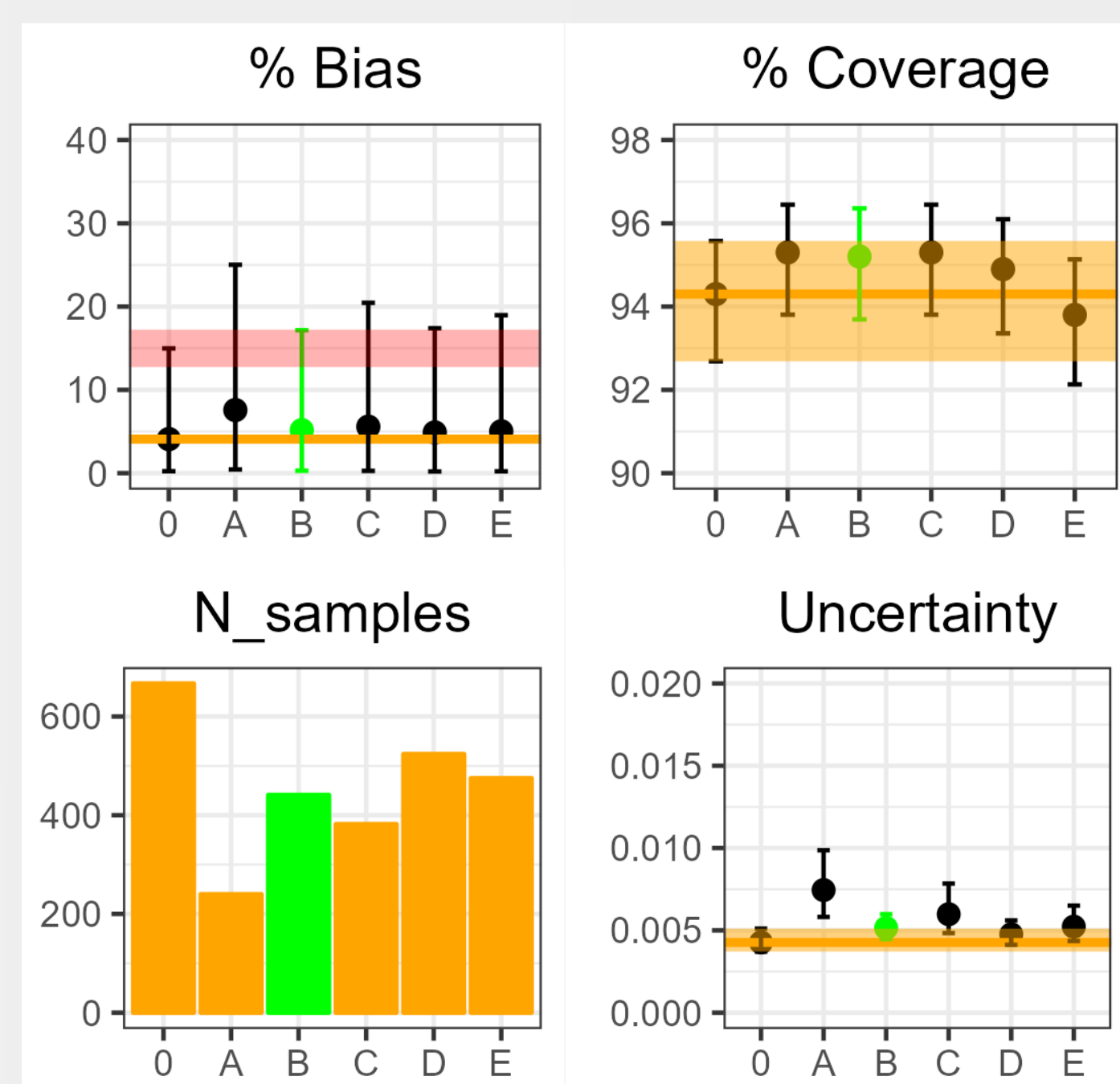
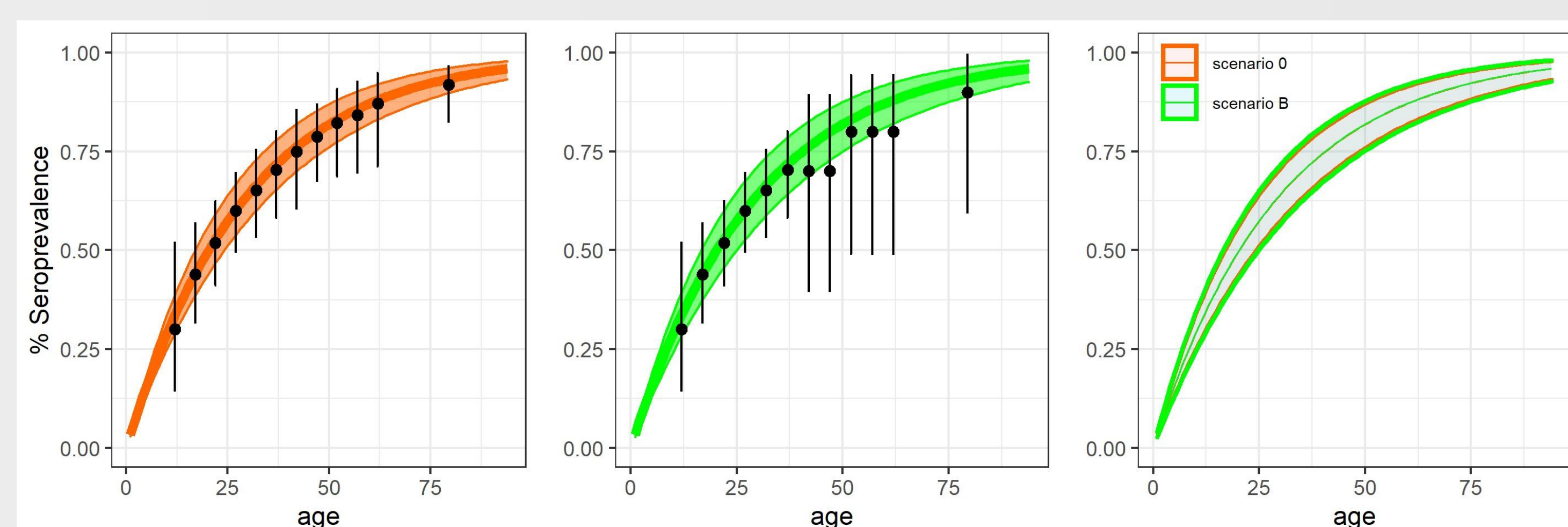


Figure 4 Model fit of the age-stratified seroprevalence for Accra under the 5-year age categorization with baseline scenario (scenario 0, green) and optimal sampling scenario (scenario B, orange).



Results

- As a result of our analysis, under the optimal scenarios, the **total sample size** of the study in Ghana was **reduced** from 2,051 to 1,487
- According to our analysis, in high-transmission settings testing younger age-groups is preferable, while in low-transmission settings testing of older age-groups is required to get accurate FOI estimates
- Two-step approach** recommended in locations with no prior information on FOI, as shown in Figure 5.

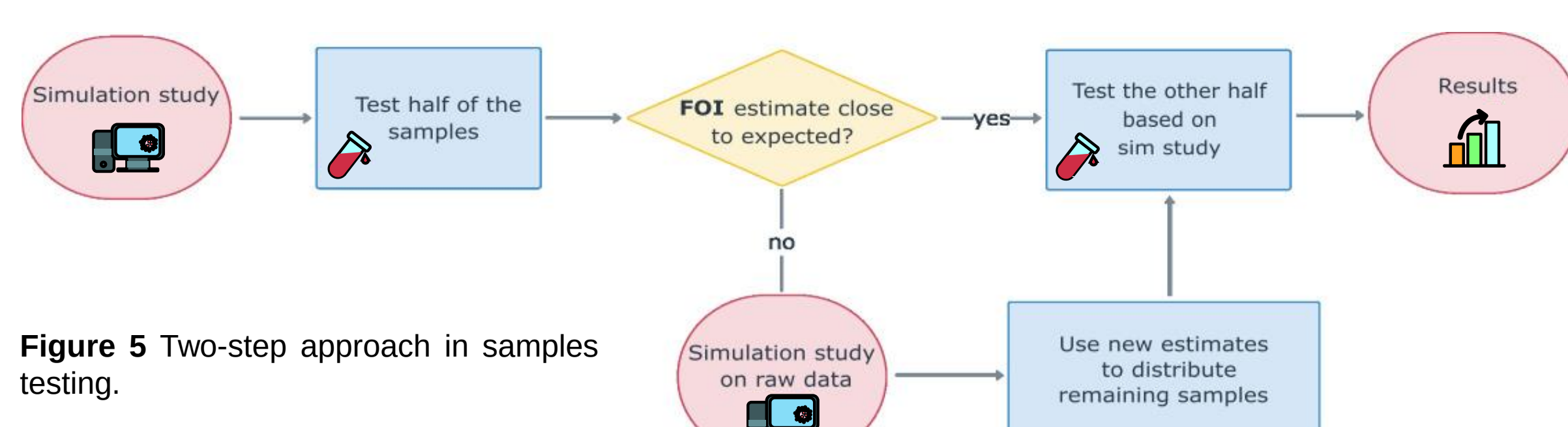


Figure 5 Two-step approach in samples testing.

Conclusions

- Accurate FOI estimates** can be obtained with selected age-distribution and reduced sample sizes
- The method can be applied to **other viruses**, also when there is evidence of immunity decay and/or changes in FOI in time
- See **QR code** to access our preprint and get in touch with any questions (a.vicco21@imperial.ac.uk and Twitter.com/anna_vicco).

