

Randomised controlled trial of different pneumococcal conjugate vaccine schedules in Nepalese infants: challenges to recruitment in Nepal

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INTRODUCTION

A pneumococcal conjugate vaccine (PCV10) immunogenicity study in 2010 showed that a 2+1 schedule (two dose priming at 6 and 14 weeks with a booster at 9 months) was non-inferior to a 3+0 schedule (3 dose priming at 6, 10 and 14 weeks) schedule in early infancy, but superior in late infancy.¹⁻³ The introduction of intramuscular inactivated polio vaccine at 14 weeks of age in Nepal³ has led to the rescheduling of the second priming dose of PCV10 to 10 weeks of age.

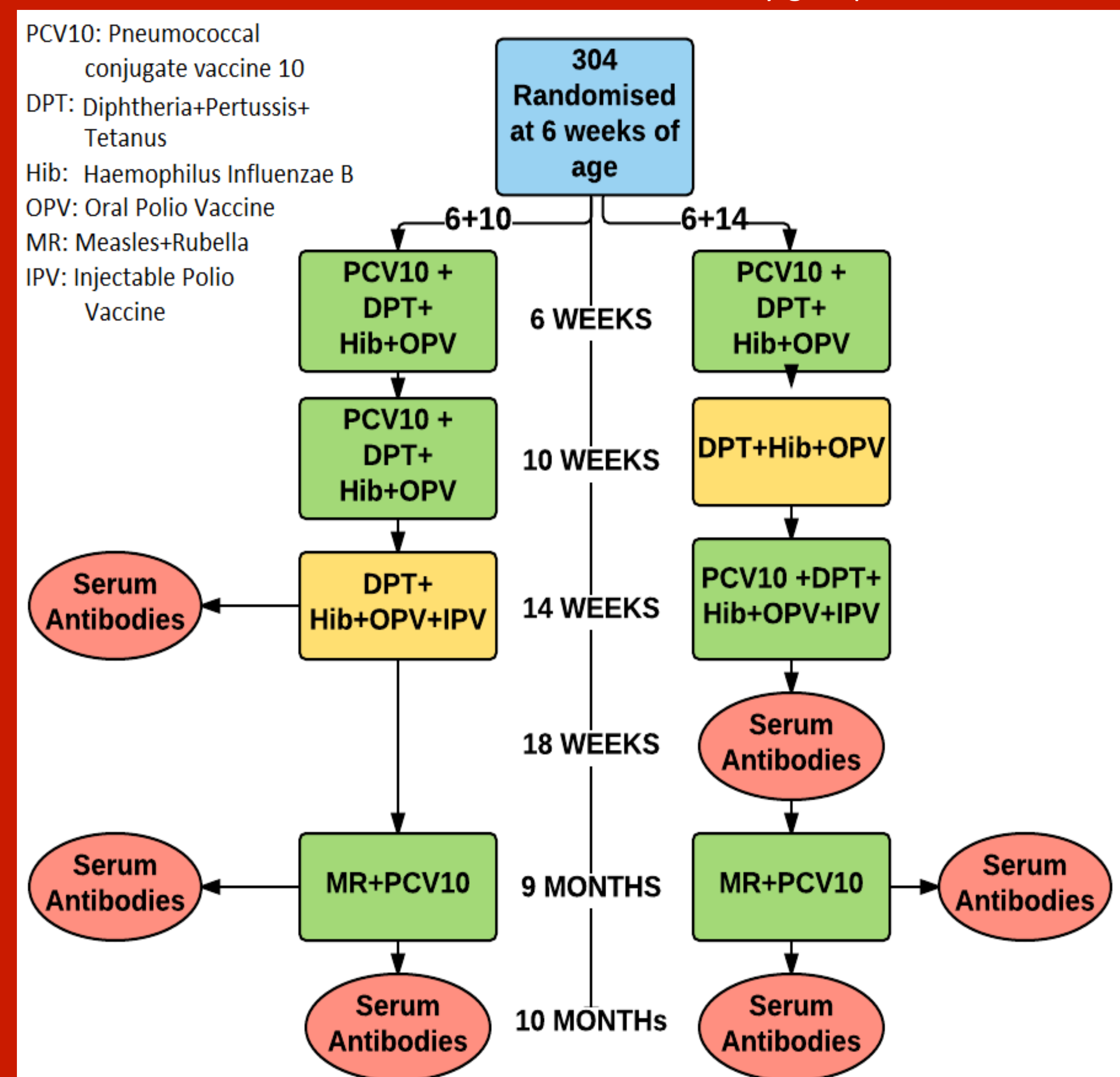
A randomised controlled trial was conducted in Nepalese infants comparing PCV10 priming at 6 and 10 weeks, with PCV10 priming at 6 and 14 weeks of age. Here we address the large scale factors that have influenced study recruitment. In Nepal, prior to the start of enrolment in the study, over 400 earthquakes in April and May 2015 led to population shifts between urban and rural regions as city dwellers moved back to be with their families in the villages. Additionally, a blockade at the Nepal-India border due to a protest in the Terai region from September 2015 led to fuel and consumable shortages making it difficult for parents to attend immunization clinics. Further population shifts occurred during the Dashain festival (an annual Hindu festival during which many individuals leave the cities to be with their family in remote villages).

METHODS

- Total recruitment target was 152 infants in each study arm.
- Parents presenting with their infants (aged 40-60 days) for routine immunizations were approached.
- Infants with good health, whose parents were willing to give informed consent and comply with all study requirements were enrolled.
- The number of participants enrolled each week is calculated to determine the effect of different factors on enrolment.

FIGURE 1

Enrolment flowchart with vaccine timepoint. Figure shows the trial design and schedule of vaccine administration for each study group.

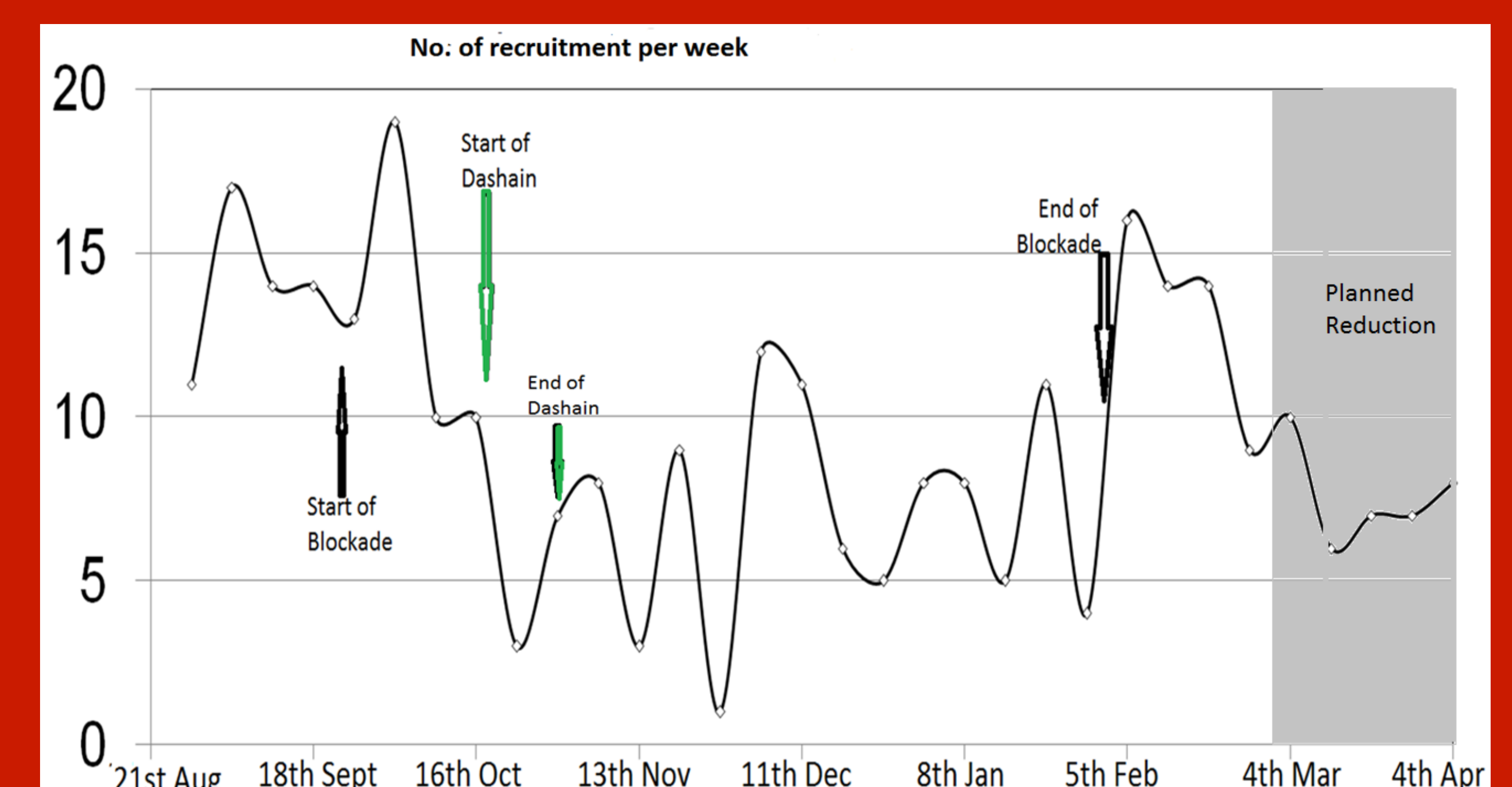


RESULTS

- The recruitment period was 21st Aug 2015 to 4th April 2016.
- The median recruitment rate was 9 infants per week (range of 1-19).
- There was an acute drop in recruitment following the blockade which included period of Dashain festival, from a median recruitment rate of 13.5 per week in the 6 weeks preceding to 5.5 per week in the 6 weeks following.
- Recruitment subsequently modestly increased to median 8 per week.
- After cessation of the blockade, recruitment rates increased to a median of 14 per week for the next five weeks.
- A planned reduction in recruitment rate was introduced at the end of the study to facilitate ongoing study management

FIGURE 2

The number of participants enrolled each week. The recruitment rate dropped following the blockade and the Dashain festival. The rate remained low throughout the blockade and improved after the cessation of blockade.



CONCLUSION

- Nepal has introduced a novel vaccine schedule, leading to the need for a carefully planned study to assess immunogenicity.
- We describe both predictable and unpredictable large-scale challenges which highlight the determination needed to deliver a vaccine trial in this setting.
- Population shifts due to the 2015 earthquake may have affected initial study recruitment as many families had left the city.
- Recruitment fell substantially during the Dashain religious festival period (from mid October).
- Subsequent low recruitment appears to have been due to the hardship caused by a long-term blockade at the Nepal-India border.
- Once all these external factors lifted, recruitment rapidly improved
- Study planning and delivery has to endure considerable disruption for success in these circumstances



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