Are Phase 1a and Phase 1b clinical trials of malaria vaccine candidates justified?

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Background

- Phase 1b trials typically replicate in endemic regions trials previously performed in High-Income Countries (Phase 1a trials)
- Inclusion of 1a trials can both delay vaccine development and increase costs
- We reviewed the literature to explore the rationale for these trials inclusion

Methodology

- The PubMed, Cochrane and Embase databases were searched using pre-specified terms
- Publications from the WHO 'Rainbow Table' of malaria vaccines in development from May 2020 onwards were reviewed
- Arguments relevant Phase 1 vaccine development were extracted

Results

- Several arguments in support of Phase Ia trials were identified:

1) Lack of research infrastructure in malaria-endemic regions prevent safe conduct of first-in-man trials
2) Informed consent for these high risk trials cannot be appropriately obtained from participants in endemic regions
3) Individual's prior exposure to malaria may confound assessment of vaccine immunogenicity

These claims were contested elsewhere, with Argument (1) asserted to be outdated and Argument (2) overly paternalistic. Argument (3), meanwhile, need not necessarily be a barrier—understanding impacts previous malaria exposure on immunogenicity is important for vaccine optimisation.

Conclusions

This review identified no convincing arguments necessitating the routine conduct of Phase Ia trials in non-endemic populations prior to assessment of candidate malaria vaccines in Phase 1b studies in endemic populations.