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What is the efficacy of RTS,S?

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Whitty's insightful editorial [1] puts the recent phase III RTS,S malaria vaccine trial results [2] in the wider context of malaria control. While vaccines are an important potential component of this effort, they are not necessarily the complete solution. RTS,S is clearly a big step in the right direction, although further advances are needed towards the goal of a highly effective malaria vaccine. [1]

The decision to publish interim efficacy data from an ongoing phase III study is unusual, [3] and others have questioned the headline efficacy figure of around 50% in time to first malaria episode. [4] Efficacy estimates will critically influence decisions on the public health role for RTS,S, and we wish to clarify some aspects of the published analysis.

A readily interpretable method of vaccine efficacy analysis involves calculating the risk ratio (the proportion of malaria in the intervention group over the control group). [5] Using this approach efficacy against clinical malaria in older children is more modest at 34% (intention-to-treat) or 36% (per-protocol).

RTS,S is thought to reduce the risk of infection from each exposure, rather than conferring "all or nothing" protection on a proportion of recipients. [5] By this hypothesis, everyone vaccinated will eventually experience malaria if transmission is high enough. [5] In other words, the vaccine should have a greater effect on the incidence rate of the first or total episodes of clinical malaria than on the overall proportion of people experiencing it, a conclusion supported by the phase III data. [2] While analysis of hazard and incidence rate ratios are completely valid [5], the risk ratio for clinical malaria provides additional highly relevant information to both policy makers and parents of immunised children, and should also be reported.

References

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Conflict of Interest: AVSH is a named inventor on patent applications covering malaria vectored vaccines and immunisation regimes.

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