

PB59 Proving efficacy in microbicide trials: What design, how many women and for how long?

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ABSTRACT TEXT

Issues:

Several candidate microbicides are currently in Phase III trials but presently there is no microbicide with demonstrated effectiveness. How can proof of efficacy best be achieved?

Description:

What should the comparator be? The no-gel arm control would at first seem an attractive option. There may, however, be serious disadvantages to this approach because of likely behaviour change and differential follow-up rates. The size of the study population required will be determined by factors including incidence rates and effectiveness. In a 2 arm study the number of woman-years required to demonstrate efficacy, at the 5% level with 90% power, assuming a control arm incidence of 4/100 years, increases from about 3000 for a 50% reduction in incidence to more than 3 times as many if the reduction is only 30%. We must also take into account losses to follow-up and withdrawals for pregnancy. Maintaining good adherence over time is also likely to be difficult because of the need to continually reinforce the message that we do not know whether product use will protect. This could lead to a further reduction in effectiveness. A shorter duration trial could be more efficient due to the reduction in woman-years required, and the ability to work with higher estimates of effectiveness. Suppose there is a 3% increase in loss of woman-years every 3 months and a reduction in overall effectiveness from 50% over 3 months to 42.5% over 12 months. The total number of woman-years required (given a control arm incidence of 4/100 years) would decrease by almost 40% in a 3 month study compared to a 12 month study. The 3-month follow-up requires fewer woman-years but the total number of women enrolled would be over 12,000; in areas of high HIV-prevalence, this could mean having to screen over 25,000 women. The strategy adopted in the MDP301 trial will be discussed.

Conclusion:

Microbicide trials are complex and costly. To maximise the chance of demonstrating an effect it may be better to enrol large numbers for a relatively short duration of follow-up. This has to be weighed against the feasibility of delivering such a design.

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