



**SUPPLEMENTARY FIG. S1.** Decision tree for identifying the most appropriate vaccine efficacy trial design where the NVPM is provided as part of the study intervention. The underlying assumptions are that a combination prevention (Vaccine+NVPM) arm is always of interest, and that if Double-placebo and NVPM-alone arms are warranted, a Vaccine-alone arm is also of interest. Primary objectives for Designs A–E are described in Table 1.