

BACKGROUND

Sub-Saharan Africa acutely needs enhanced solutions to HIV/AIDS. Retention is crucial in validating efficacy trials. We assessed retention rate-variability, retention strategies and dropout predictors in African efficacy trials.

METHODS

Studies reviewed were those conducted in Africa that individually randomised at-risk HIV sero-negatives, published in English (01/01/1990 to 01/06/2009), achieved ≥50% follow-up, tested either a microbicide, vaccine, HSV-2 suppression, behavioural intervention or STI Periodic Presumptive Treatment (PPT), and had HIV acquisition or risk-reduction as a primary endpoint. Studies were identified through PubMed, Cochrane and AIDSinfo. Data extracted included study population and duration, retention strategies and rates, loss-to-follow-up definitions and dropout predictors.

RESULTS

Seventeen trials involving 26,828 participants aged ≥15years (91.6% female) met eligibility. Ten trials (79% of all participants) tested microbicides. The rest tested HSV-2 suppression, PPT and behavioural-interventions.

Three trials (54% participants) recruited all sexually-active females from the general population. Seven studies recruited self-identified sex workers (25.5% participants), two trials (13.2% participants) recruited as 'high-risk through-own-behaviour', and two (4.2% participants) recruited female recreational-workers.

Only five trials precisely defined loss-to-follow-up and three explicitly stated their retention strategies that included reminder contacts, peer networks, home visits and mobile clinics. Mean retention at study end for all 17 was 80.15% (median=81.50%, range=65.0-98.0%). Retention (≥90% at 1 month) decreased with increasing duration and size of the study (≈60% at 11 to 12 months). However, larger and longer studies beyond 12 months had improved retention (≈80%/≥16months). In contrast, a large phase I/II HIV vaccine trial of 326 participants had 96% retention over the 12 month study. Younger age and shorter sex-work experience frequently predicted dropout.

CONCLUSIONS

While ≥80% retention is achievable in Africa, additional reporting is needed to elucidate the value of different strategies and predictors.

Figure 1. Study Selection

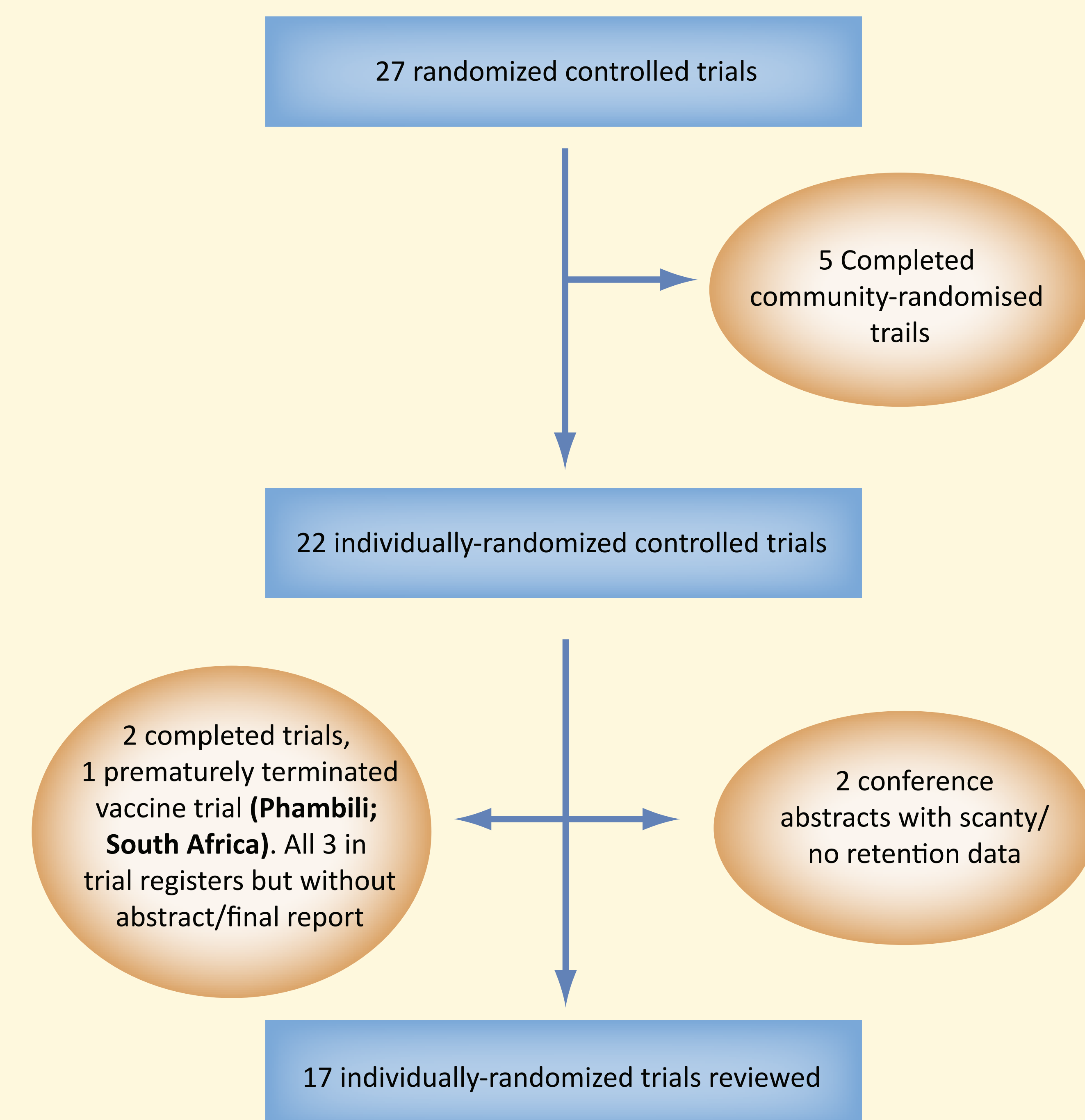


Table 1. Participant Numbers and Sex Distribution, Study Retention Rate-Variability and Regional Distribution by Intervention and Risk Category

Intervention category (number of trials)	Sample size (Number (% of total))	Retention				Region (number of studies)				
		Male	Female	Mean %	Median %	Range %	East Africa	West Africa	South Africa	Multi region
Microbicide (10)	21184* (79)	-	21184	80.10	82.75	65.0-94.5	2	4	2	2b
HSV-2 suppression (2)	4098 (15)	1882‡	2216	84.0	84.0	83.0-85.0	1	-	1	-
Periodic Presumptive Treatment (2)	776 (3)	-	776	77.25	77.25	73.0-81.5	2	-	-	-
Behavioural (3)	770 (3)	358	412	79.7	71.5	69.5-98.0	-	-	3	-
Total (17)	26828 (100)	2240	24588	80.15	81.5	65.0-98.0	5	4	6	2b
Risk Category										
Sex Workers (7)	6852* (25.5)	-	6852	75.2	73.0	65.0-85.5	3	3	-	1
High-risk through own behaviour (2)	3551† (13.2)	-	3551	83.5	83.5	77.0-90.0	-	1	-	1
Recreation workers (2)	1131 (4.2)	-	1131	82.2	82.2	81.5-83.0	2	-	-	-
All Sexually-active female (3)	14524 (54)	1882‡	12642	88.5	86.0	85.0-94.5	-	-	3	-
Illicit drug users (1)	112 (0.42)	-	112	N/A	N/A	N/A	-	-	1	-
Adolescents (1)	515 (2)	236	279	N/A	N/A	N/A	-	-	1	-
STI clinic attendees (1)	143 (0.53)	122	21	N/A	N/A	N/A	-	-	1	-
Total	26828 (100)	2240	24588	80.15	81.5	65.0-98.0	5	4	6	2b

*includes 276 in India, †undisclosed number in Thailand, ‡MSM in Peru and USA, †One trial had sites in India, western, eastern and southern Africa, the other had sites in Thailand, western and southern Africa

Table 2. Vaginal Microbicides/Cervical Barriers Trials

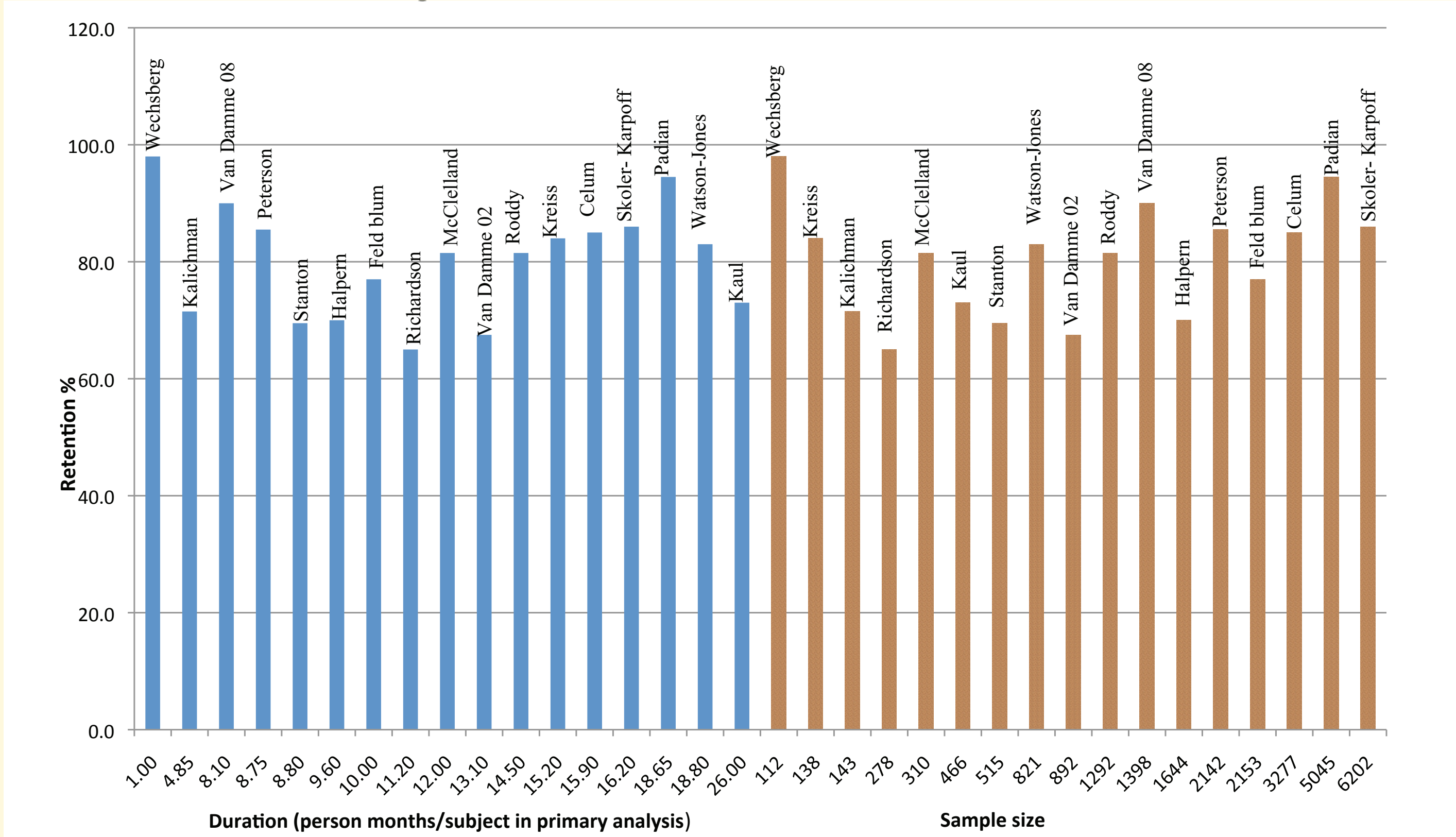
Primary author, reference (product tested)	Country	Age (yrs), risk category	Sample size	Retention (%)	Retention features	Dropout predictors
Van Damme et al. 2008. ¹ (6% cellulose sulphate gel)	Benin, S. Africa, Uganda, India	≥18, risky sexual behaviour	1398†	90.0	Risk-reduction counselling, condoms, STI treatment*	-
Halpern et al. 2008. ² (6% cellulose sulphate gel)	Nigeria	18-35, risky sexual behaviour	1644	70.0	Risk-reduction counselling, condoms, STI treatment, outreach posts' follow-up†	Targeting young, mobile, highest risk, poorly-compliant women thought to have negatively impacted retention
Padian et al. 2007. ³ (Latex diaphragm, lubricant gel)	S. Africa, Zimbabwe	18-49, sexually active	5045	94.5	Risk-reduction counselling, condoms, STI treatment	-
Roddy et al. 1998. ⁴ (Nonoxonyl-9 film)	Cameroon	18-45, sex workers	1292	81.5	Risk-reduction counselling, condoms, STI treatment	-
Van Damme et al. 2002. ⁵ (Nonoxonyl-9 gel)	Benin, C. d'Ivoire, S. Africa, Thailand	≥18 (≥16 S. Africa), sex workers	892*	67.5	Risk-reduction counselling, condoms, STI treatment*	Dropout associated with younger age, more education, shorter sex-work experience
Richardson et al. 2001. ⁶ (Nonoxonyl-9 gel)	Kenya	18-48, sex worker	278	65.0	Risk-reduction counselling, condoms [§]	Dropout associated with shorter sex-work experience. Migration thought to have increased loss-to-follow-up
Peterson et al. 2007. ⁷ (SAVVY C31G gel)	Ghana	18-35, risky sexual behaviour/sex worker [¶]	2142	85.5	3 attempts to contact subject after missed scheduled visit. Risk-reduction counselling, condoms [§]	-
Feldblum et al. 2008. ⁸ (SAVVY C31G gel)	Nigeria	18-35, risky sexual behaviour/sex worker [¶]	2153	77.0	3 attempts to contact subject after missed scheduled visit. Risk-reduction counselling, condoms [§]	-
Skoler-Karppoff et al. 2008. ⁹ (Carraguard)	S. Africa	≥16, sexually active	6202	86.0	Risk-reduction counselling, condoms, STI treatment, pap smears, family planning	-
Kreiss et al. 1992. ¹⁰ (Nonoxonyl-9 sponge [§])	Kenya	Sex Workers	138	84.0	Home visits, peer networks, risk-reduction counselling, condoms, STI treatment.	-

*includes 276 in India, † Trial prematurely stopped due to potential harm, ‡ Includes undisclosed number in Thailand, § study prematurely stopped due to slow enrolment and loss to follow-up issues, ¶ most exchanged sex for money, † trial prematurely stopped due to lower than expected HIV incidence, § Placebo changed due to adverse effects.

Table 3. HSV-2 Suppression, STI Periodic Presumptive Treatment and Behavioural Trials

Primary author, reference (product tested)	Country	Age (yrs), risk category	Sample size	Retention (%)	Retention features	Dropout predictors
Watson-Jones et al. 2008. ¹¹ (Acyclovir 400mg twice daily)	Tanzania	16-35, HSV + HIV -female recreational workers	821	83.0	Family planning, risk-reduction counselling, condoms, STI & minor illness treatment, home visits and mobile clinics	Dropout associated with young age and alcohol consumption
Celum et al. 2008. ¹² (Acyclovir 400mg twice daily)	S. Africa, Zambia, Zimbabwe, + 1882 MSM in Peru, USA	≥18 (≥16 Zambia) HSV + HIV - female sexually active	3277	85.0	Risk-reduction counselling, condoms, STI treatment	-
McClelland et al. 2008. ¹³ (2g Metronidazole + 150mg Fluconazole monthly)	Kenya	18-45, female recreational workers	310	81.5	Risk-reduction counselling, condoms, STI treatment	Dropout associated with younger age, shorter sex-work experience, lower pregnancy rate, more vaginal washing and less vaginal candidiasis.
Kaul et al. 2004. ¹⁴ (1g monthly oral azithromycin)	Kenya	≥18 female sex workers	466	73.0	Risk-reduction counselling, condoms, STI treatment	Mobility thought to have affected retention
Stanton et al. 1998. ¹⁵ (14 abstinence & safer-sex sessions, 12-month delay control)	Namibia	15-18 in-school adolescents	515	69.5	-	Dropout associated with older age
Kalichman et al. 2007. ¹⁶ (60-minute HIV, alcohol risk-reduction skills session, 20-minute HIV education control)	S. Africa	Alcohol-using STI clinic patients	143	71.5	Risk-reduction counselling, condoms, STI treatment	Dropouts in treatment arm were older and less educated than those retained, and those lost and retained in control arm
Wechsberg et al. 2008. ¹⁷ (Women-based risk-reduction, group versus individual delivery)	S. Africa	≥18, black & coloured illicit drug-using women	112	98.0	Certificate of completion, T-shirt, risk reduction kit, participant-staff racial/ethnic identity match for study info/procedure delivery	-

Figure 2. Retention Versus Duration and Size



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