

Randomized Trials of STD Control for HIV Prevention in Adults, Pregnant Women and Infants, Rakai, 1994-98

Results and Supplementary Analyses

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Trial Objective

Objective: to assess whether STD control at the population level would be effective for HIV prevention

- STD Control for HIV Prevention
 - All non-pregnant adults
- Maternal Infant Supplementary Study (MISS)
 - Pregnant women and infants



Trial of STD Control in Adults

- 10 community clusters (each with 3-5 villages) randomized to Intervention (n=5) and Control (n=5) arms. (Genesis of the RCCS)
- Intervention arm received intensive presumptive mass-treatment of STDs via directly observed oral antibiotics and IM penicillin for serologic syphilis.
- **Control arm** received placebo and syndromic STD management.
- Follow-up at 10 month intervals over 20 months via RCCS surveys

Wawer et al. AIDS 1998 Wawer et al. Lancet 1999

Trial of STD Control in Adults: participant compliance

Annual participation rate: 94%

Provided blood: 91% urine: 94% vag swabs: 93%

Accepted treatment: 95%





STD Trial Main Results

- 6602 intervention and 6124 control arm participants
- Significant reductions in vaginal STDs and syphilis
- HIV incidence 1.5/100 py in both arms (RR=0.97, CI 0.81-1.16)
- Conclusion: STD mass treatment had no effect on HIV incidence at the community level



Rakai Program Tour of 1999

Geneva audience takes in the Rakai STD results





Mother Infant Supplementary Study (MISS)

- Nested in the adult STD Control Trial
- Pregnant women: n=2070 intervention arm n=1963 control arm



- Intervention arm received mass presumptive STD treatment with oral antibiotics once during pregnancy .
- Control arm received standard of care
- <u>All pregnant women with positive syphilis serology</u> received IM Benzathine penicillin in both arms

Gray et al. Amer J Obstet Gynecol 2001 Kigozi et al. Amer J Obstet Gynecol 2003



Maternal Infections Postpartum

Infections	Intervention	Control	RR (95%CI)
Syphilis	3.4%	3.3%	1.18 (0.94-1.47)
Trichomonas	4.7%	15.9%	0.28 (0.18-0.49)
BV	36.3%	48.5%	0.78 (0.69-0.87)
Gonorrhea/ Chlamydia	1.9%	4.3%	0.43 (0.27-068)
HIV Incidence	3.4/100 py	2.3/100 py	1.44 (0.64-3.25)



Infant Infections and Birth Outcomes

Outcome	Intervention	Control	IRR (95%CI)
Ocular Gonorrhea	0.6%	1.7%	0.35 (0.18-0.67)
Ocular Chlamydia	0.6%	1.1%	0.44 (0.19-0.98)
Low Birth Weight	9.1%	11.0%	0.70 (0.51-0.96)
Preterm Birth	9.8%	11.8%	0.73 (0.54-0.99)
Neonatal Death	25.4/1000	29.1/1000	0.83 (0.71-0.97)
MTCT of HIV	18.9%	22.3%	0.92 (0.29-2.91)



MISS Trial, Conclusion

Bacterial STD control during pregnancy

- reduced maternal and infant STD infections
- improved pregnancy outcomes

However, no effect on

- maternal HIV incidence
- mother-to-child transmission

HIV Incidence in Trials of Bacterial STD Control for HIV Prevention





Trials of STD Control for HIV Prevention

- WHY did STD control not have the hypothesized effect?
- To explain the largely negative trials we analyzed Rakai trial data to assess factors associated with HIV acquisition

Population attributable risk of HIV acquisition associated with STDs in Rakai



Even if <u>all</u> bacterial STDs could be eliminated, this would reduce HIV incidence by only ~17%

Gray et al. AIDS 2005

Proportion of HIV Incidence (%)



HIV viral load and infectivity in HIV discordant couples nested in the trial population cohort



HIV <u>transmission</u> per coital act by stage of infection. Retrospective analysis, Rakai HIV discordant couples nested in STD trial cohort Wawer et al, JID 2005



ORIGINAL ARTICLE

Viral Load and Heterosexual Transmission of Human Immunodeficiency Virus Type 1

Thomas C. Quinn, M.D., Maria J. Wawer, M.D., Nelson Sewankambo, M.B., David Serwadda, M.B., Chuanjun Li, M.D., Fred Wabwire-Mangen, Ph.D., Mary O. Meehan, B.S., Thomas Lutalo, M.A., and Ronald H. Gray, M.D., for the Rakai Project Study Group

N Engl J Med 2000; 342:921-929 March 30, 2000 DOI: 10.1056/NEJM200003303421303



Rates of HIV-1 Transmission per Coital Act, by Stage of HIV-1 Infection, in Rakai, Uganda 🚥

Maria J. Wawer ➡; Ronald H. Gray; Nelson K. Sewankambo; David Serwadda; Xianbin Li; Oliver Laeyendecker; Noah Kiwanuka; Godfrey Kigozi; Mohammed Kiddugavu; Thomas Lutalo; ... Show more

J Infect Dis (2005) 191 (9): 1403-1409. DOI: https://doi.org/10.1086/429411

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Male Circumcision and HIV Transmission in HIV Discordant Couples Nested in STD Trial Cohort Gray et al, AIDS 2000



Findings led to the Rakai trials of voluntary male circumcision for HIV prevention in men and women



Conclusion

- Rakai STD control trials had negative outcomes with respect to HIV control
- However, they informed multiple future studies on determinants of HIV transmission and HIV prevention strategies