| **Author,Year** | **Type of study** | **Location/setting/****high or low prevalence population (based on 0.1%** **prevalence rate)** | **Study duration/****followup** | **Treatment groups (or comparision groups if observational study)** | **Demographics/ baseline disease** | **Eligibility criteria** | **Exclusion criteria** | **Number screened/eligible/enrolled/withdrawals/****% analyzed** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Cohen et al, 2011109 | RCT | Botswana, Kenya, Malawi, South Africa, Zimbabwe, India, Brazil, Thailand, and United States | Median followup, 42 months | Treatment: immediate ARTComparison: delayed ART initiated after decline in CD4 count to ≤250 x 109 cells/mL or onset of AIDS-related illness | 61% of participants ages 26 to 40 years Median CD4 count: 0.442 x 109 cells/L for early-therapy group, 0.428 x 109 cells/L for delayed therapy group | Couples in which 1 partner was HIV-1 positive and the other negative; CD4 counts 0.350–0.550 x 109 cells/L; in a stable relationship for ≥3 months; reported ≥3 instances of vaginal or anal intercourse; willing to disclose serostatus to partner | HIV-positive participants who had previously received ART (with exception of short-term prevention of mother-to-child transmission) | 10,838 screened; 1763 couples enrolled |
| Del Romero et al, 201093 | Prospective cohort | Madrid, Spain; HIV clinic; high prevalence (no ART: 9.2%, ART: 8.7%) | 1355 couple-years | ART vs. no ART | Index cases 83% male; women median age, 29 years; men median age, 32 years;, median CD4 count, 0.500 x 109 cells/L (IQR, 0.295–0.700 x 109); median pasma HIV RNA, 200 copies/mL (IQR, ND to 8876); 54% detectable viral load | All heterosexual couples who had an ongoing sexual relationship over preceding 6 months, were serodiscordant for HIV, and returned for ≥1 followup visit | Nonindex partner with previous HIV diagnosis or known risk exposures other than relationship with index partner | 648 eligible; 602 serodiscordant at first visit; 424 with followup |
| Donnell et al, 2010110 | Pre-post analysis of prospective cohort data | 14 sites in 7 African countries (Botswana, Kenya, Rwanda, South Africa, Tanzania, Uganda, and Zambia) | Median study duration at ART initiation, 13 months | PreART transmission vs. postART transmission | HIV-infected partner vs. HIV-susceptible partnerMean age: 32 vs. 33 yearsFemale sex: 68% vs. 32%HSV-2 positive: 100% vs. 68% | HIV-1 and HSV-2 serodiscordant couples reporting ≥3 episodes of vaginal intercourse during previous 3 months, with seropositive partner ages ≥18 years, CD4 count ≥0.250 x 109 cells/L  | History of AIDS-defining condition, receiving ART | 3408 enrolled; 3381 analyzedNote: 27 couples' baseline serology did not confirm HIV-1 and HSV-2 |
| Goncalves Melo et al, 2008111 | Retrospective cohort | Urban HIV/AIDS referral center in Porto Alegre, Brazil; assumed high prevalence | Median followuptransmitters: 25.5 monthsnontransmitters: 22.3 months | Transmitters vs. nontransmitters | 72% women (index cases); 57.7% IDUs; 91% unprotected sex; 23.6% STD diagnosis | ART-naive HIV-1 infected people with uninfected, steady, opposite-sex partners | None | 4500 screened retrospectively; 56 enrolled retrospectively and 37 enrolled prospectively (93 total enrolled) |
| Musicco et al, 1994107 | Prospective cohort | Multicenter; Italy; assumed high prevalence (high risk) | Mean followup, 2 years (740 person-years) | Zidovudine vs. no zidovudine | Mean age, 26 years; 100% female; median duration of relationship with HIV-positive partner, 3 years; 56% consistent condom use; 53% regular sexual intercourse; 15% anal sex; 48% oral sex | Serodiscordant women identifyed through partner's attendance at specialty clinic with ≥1 followup visit | None | Not reported; 525 eligible; 436 enrolled; unclear; unclearData from 103 person-years excluded |
| Reynolds et al, 2011112 | Retrospective cohort | Multicenter; Rakai, Uganda; high prevalence | Median followupBefore ART initiation: 1.57 yearsAfter ART initiation: 1.54 years | PreART transmission vs. postART transmission | Male index partner: 58% (142/250) Consistent condom use: 4%Polygamous husbands: 20% | HIV-1 discordant married couples | None | 15,000 screened; 250 eligible; 250 enrolled |
| Sullivan et al, 2009113 | Retrospective cohort | Rwanda and Zambia | Median followup, 512 days (1.4 years) | ART vs. no ART | Not reported | HIV-serodiscordant couples | Not reported | 2993 enrolled |
| Wang et al, 2010114 | Retrospective cohort | Multicenter, community-based in Henan Province, China; assumed high prevalence (high risk) | Median followup, 2.8 years | ART vs. no ART | Mean age, 44 years; 43% female; 84% regular sexual intercourse; 78% condom use; 99% monogamous | Serodiscordant couples; stable marriage with no separation or divorce; voluntary participation and provided informed consent | None | 4348 screened; 4301 eligible; 1927 enrolled; no withdrawals; 100% analyzed |

| **Author,Year** | **Virologic response** | **CD4 count response** | **Outcomes** | **Adverse events** | **Funding sourceand role** | **Quality rating** |
| --- | --- | --- | --- | --- | --- | --- |
| Cohen et al, 2011109 | Virologic failure, treatment vs. comparison45/886 (5%) vs. 5/184 (3%); p=0.23 | Treatment: 0.442 x 109 cells/L at enrollment to 0.603 x 109 cells/L at 12 monthsComparison: 0.428 x 109 cells/L at enrollment to 0.399 x 109 cells/L at 12 months | Transmission events, treatment vs. comparison4 events (IR, 0.3 per 100 person-years [95% CI, 0.1–0.6]) vs. 35 events (IR, 2.2 per 100 person-years [95% CI, 1.6–3.1]); HR, 0.11 (95% CI, 0.04–0.32); p<0.001Total clinical events, treatment vs. comparisonHR, 0.59 (95% CI, 0.40–0.88)Linked transmission, treatment vs. comparisonHR, 0.04 (95% CI, 0.01–0.28); p<0.001 | Severe or life-threatening adverse events, treatment vs. comparison127/886 (14%) vs. 119/877 (14%); NSMost frequent adverse events: infections, psychiatric and nervous system disorders, and gastrointestinal disordersGrade 3 or 4 laboratory abnormalities, treatment vs. comparison242/886 (27%) vs. 161/877 (18%); p<0.001Most frequent laboratory abnormalities: neutropenia, abnormal phosphate levels, bilirubin elevations | National Institute of Allergy and Infectious Diseases | Good |
| Del Romero et al, 201093 | Detectable viral load in 111/120 (93%) not taking ART vs. 30/145 (21%) on ART; p<0.001 | Not reported | Proportion engaging in unprotected sexual intercourse, no ART vs. ART 273/476 (57%) vs. 69/149 (46%); p=0.019 Proportion of couples with previous pregnancies, no ART vs. ART 226/476 (47%) vs. 53/149 (36%); p=0.011 Transmission, no ART vs. ART5 instances vs. 0 instancesRate per 100 couple-years, no ART vs. ART0.4 (95% CI, 0.2–1.4) vs. 0 (95% CI, 0–1.1) | Not reported | Grant from FIPSE (foundation formed by Spanish Ministry of Health and Consumer Affairs and multiple pharmaceutical companies) and Spanish Network for Research on AIDS | Fair |
| Donnell et al, 2010110 | Not reported | Not reported | PreART vs. postART transmissionOverall: 102/4558 person-years (IR, 2.24 [95% CI, 1.84–2.72]) vs. 1/273 person-years (IR, 0.37 [95% CI, 0.09–2.04])Overall adjusted incidence RR: 0.08 (95% CI, 0.00–0.57); p=0.004 | Not reported | Bill & Melinda Gates Foundation; University of Washington Center for AIDS Research; University of Washington AIDS Clinical Trials Group Virology Support Laboratory; US National Institutes of Health | Good |
| Goncalves Melo et al, 2008111 | Not reported | Not reported | Transmissions, ART vs. no ART 0/41 vs. 6/52 Median viral load, transmitters vs. nontransmitters 24,082 (range, 1479–100,539) vs. 4583 (range, 78–47,974); p=0.042 | Not reported | Not reported | Fair |
| Musicco et al, 1994107 | Not reported | Not reported | Seroconversions, zidovudine vs. no zidovudine6/64 (3.8/100 person-years) vs. 21/? (4.4/100 person-years); adjusted RR, 0.5 (95% CI, 0.1–0.9) | Not reported | Ministry of Health, Italy; National Research Council of Italy | Fair |
| Reynolds et al, 2011112 | 6 months: 71.4% (20/28) below detectable limit and remaining 28.6% (8/28) below 2000 copies/mL12 months: 85.2% (23/27) below 400 copies/mL, 14.8% (4/27) ranging from 2293 to 672,513 copies/mlL24 months: 100% (28/28) below 400 copies/mL | Not reported | TransmissionPreART: 9.2/100 person-years (95% CI, 6.59–12.36)PostART: 0/53.6 person-years (95% CI, -1.91 to 16.38); p=0.0097 | Not reported | Division of Intramural Research, National Instutute of Allergy and Infectious Diseases; Eunice Kennedy Shriver National Instutute of Child Health and Human Development | Fair |
| Sullivan et al, 2009113 | Not reported | Not reported | Transmissions, ART vs. no ART4/175 vs. 171/175Incidence density, ART vs. no ART0.7%/100 person-years vs. 3.4%/100 person-years (RR, 0.21 [95% CI, 0.08–0.59])Hazard of infection, ART vs. no ARTHR, 0.21 (95% CI, 0.09–0.52) | Not reported | Not reported | NA |
| Wang et al, 2010114 | Not reported | Not reported | Seroconversions, ART vs. no ART66/1369 (4.8%) vs 18/558 (3.2%); univariate RR, 0.76 (95% CI, 0.45–1.28) | Not reported | China and Fogarty International Center; National Institutes of Health, Office of the Director, Office of AIDS Research; National Cancer Center; National Eye Institute; National Heart, Blood, and Lung Institute; National Institute of Dental and Craniofacial Research; National Institute on Drug Abuse; National Institute of Mental Health; National Institute of Allergy and Infectious Diseases Health | Fair |

ART = antiretroviral therapy; CI = confidence interval; HR = hazard rate; HSV-2 = herpes simplex virus 2; IDU = injection drug user; IR = incidence rate; IQR = interquartile range; NA = not applicable; RCT = randomized, controlled trial; RR = relative risk; STD = sexually transmitted disease.