Appendix I

Search strategies[1]
PubMed: (((hormonal AND contracepti*) OR ("hormonal methods")) OR ((progestin* OR progestins[MeSH] OR Progesterone[MeSH] OR progestogen* OR progestagen*) AND contracept*) OR (oral contracept*) OR ((((depo OR depot) AND medroxyprogesterone) OR depomedroxyprogesterone OR depo OR depot OR dmpa OR "net en" OR net-en OR "norethisterone enanthate" OR norethisterone-enanthate OR Medroxyprogesterone 17-Acetate[MeSH]) AND (contracept* OR inject*)) OR (((levonorgestrel OR etonogestrel) AND implant) OR (uniplant OR jadelle OR implanon OR norplant OR norplant2 OR sino-implant)) OR (contraceptives, postcoital[MeSH] OR (contracept* AND (emergency OR postcoital OR "post coital")) OR "ulipristal acetate" OR "Plan B" OR mifepristone) OR ((levonorgestrel AND (intrauterine devices[MeSH] OR iud OR iucd OR ius OR "intrauterine system" OR "intra-uterine system" OR "intrauterine device" OR "intra-uterine device")) OR mirena) OR ((combin* AND inject* AND contracept*) OR (("once a month" OR monthly) AND inject* AND contracept*) OR (cyclofem OR lunelle OR mesigyna OR "cyclo provera" OR cycloprovera)) OR ((((contraceptive devices[MeSH] OR contraceptive agents[MeSH]) AND ring) OR nuvaring OR "nuva ring")) OR ((((contraceptive devices[MeSH] OR contraceptive agents[MeSH]) AND patch) OR "ortho evra" OR orthoevra)) AND ("HIV Seropositivity"[MeSH] OR "HIV"[MeSH] OR "HIV Infections"[MeSH] OR "Acquired Immunodeficiency Syndrome"[MeSH] OR "HIV progression" OR "HIV disease progression" OR "HIV shedding" OR "viral shedding" OR "HIV transmission" OR "Virus Shedding"[MeSH]) AND Humans[MeSH]).

Embase: ("Hormonal contraception") AND HIV.

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[1] Although our search strategy was designed to identify studies relevant to the relationship between hormonal contraception and HIV acquisition, HIV progression, or HIV transmission to a male partner, this review includes only articles relevant to the relationship between hormonal contraception and HIV progression.

Appendix II: Mortality or progression to AIDS

Primary author, year, funding	Study design, Location	Study population	Contraceptive method/ Comparison group/ Outcome	Results [Adj HR (95% CI) unless otherwise noted]	Strengths	Weaknesses	Quality
Stringer 2007 [21], 2009 [23] Elizabeth Glaser Pediatric AIDS Foundation, USAID, NICHD	RCT, 2 years follow-up Prevalent cases Zambia	599 postpartum women living with HIV Excluded WHO stage III or IV ART became available during study	OCs or DMPA (n=303) Copper IUD (n=296) CD4 count <200 or ART initiation Death (all cause)	**CD4<200 or initiate ART** *Intent-to-treat* – crude HR (95% CI) OC vs IUD 1.54 (0.98-2.42); DMPA vs IUD 1.81 (1.26-2.6) *Actual use* – OC vs IUD 1.67 (1.10-2.51); DMPA vs IUD 1.62 (1.16-2.28) **Mortality (all cause)** *Intent-to-treat* – crude HR (95% CI) OC vs IUD 1.06 (0.38-2.97); DMPA vs IUD 1.39 (0.63-3.06) *Actual use* – OC vs IUD 1.24 (0.42-3.63); DMPA vs IUD 1.83 (0.82-4.08) **Mortality (all cause), CD4<200, or initiate ART** *Intent-to-treat* – crude HR (95% CI) OC vs IUD 1.52 (1.00-2.32); DMPA vs IUD 1.81 (1.30-2.53) *Actual use* – OC vs IUD 1.67 (1.10-2.51); DMPA vs IUD 1.62 (1.16-	-Randomization with adequate concealment and equal distribution of potential confounders among groups -Intent-to-treat and actual use analysis performed -Relatively long follow-up (2 years) -Controlled for baseline characteristics in multivariate analysis	-Groups became non-comparable over time due to loss to follow-up, method switching (31% discontinued initially assigned contraceptive) -High and differential loss to follow-up (23% in IUD group, 32% in HC group over 2 years)	I, fair

Primary author, year, funding	Study design, Location	Study population	Contraceptive method/ Comparison group/ Outcome	Results [Adj HR (95% CI) unless otherwise noted]	Strengths	Weaknesses	Quality
				2.28)			
MRC collaborative study [24] 1999 Medical Research Council	Prospective cohort, up to 4 years follow-up Prevalent cases Britain and Ireland	505 women recruited from HIV/GU clinics; multiple ethnic groups from multiple sites	OCs (n=73) Other or no contraception (n=432) Development of AIDS (clinical definition) Death (all cause)	**Progression to AIDS:** OC vs non-OC users 0.84 (0.42-1.66) **Mortality (All cause):** OC vs non-OC users 1.01 (0.56-1.85)	-Long follow-up (up to 4 years, although no info on mean follow-up time) -ART use included as time-dependent variable, though unclear whether this was included in the OC model	-No time-varying analysis of HC use -Prevalent cases with no clear control for baseline characteristics -Comparison group may be using hormonal methods	II-2, Poor
Kilmarx [16] 2000 CDC	Prospective cohort, median 81 months follow-up Mix of prevalent and incident cases Thailand	160 sex workers living with HIV at baseline, 34 additional seroconverters	OCs (n=112) DMPA (n=55) Other or no contraception (n=27) CD4 count <200 Death (all cause)	**Time to CD4 cell count <200:** OCs vs non-OC users 1.3 (0.7-2.3); DMPA vs non-DMPA 0.7 (0.3-1.2); **Mortality (All cause):** OCs vs non-OC users 1.1 (0.6-2.0); DMPA vs non-DMPA 1.0 (0.5-1.9); when non-OC, non-DMPA group analyzed, did not find a difference	-Left -censored prevalent cases at enrollment and controlled for initial viral load -Multivariate analysis -Long follow-up (median 81 months)	-No time-varying analysis of HC use -Comparison group does not exclude HC users	II-2, Poor
Allen [13] 2007 NIH	Prospective cohort, 6 years follow-up Prevalent cases Rwanda	460 women living with HIV age 15-35, recruited from prenatal and pediatric clinics	OCs(n=55) injectables (n=51) Never used OC (n=342) Never used injectables (n=350) Death (HIV-	**Mortality (HIV-related):** OC vs never-OC users 0.28 (0.07-1.15, p=0.0786); Injectable vs never-injectable users 0.41 (0.15-1.13, p=0.0857)	-Low loss to follow-up (10% over 6 years)and long-follow up (6 years); time-varying analysis of HC method use -Prevalent cases controlled for baseline disease stage		II-2, Fair

Primary author, year, funding	Study design, Location	Study population	Contraceptive method/ Comparison group/ Outcome	Results [Adj HR (95% CI) unless otherwise noted]	Strengths	Weaknesses	Quality
			related)				
Stringer [22] 2009 Gates, Hewlett, David & Lucille Packard, Robert Wood Johnson, Henry J. Kaiser Family, John D. and Catherine T. MacArthur, Rockefeller, & Starr Foundations ; USAID	Prospective cohort, median 1 year follow-up Prevalent cases 12 African countries & 1 Asian country	7846 post-partum women living with HIV not on or eligible for ART at beginning of study	OCs (n=222) implants/injectables (n=823) No method or no hormonal method (n=3064) Eligible for or initiation of ART (as defined by program) Death (all cause) Composite: ART eligibility, initiation, or death	**ART eligible:** OC vs no HC exposure 0.9 (0.7-1.2); implant/ injectable vs no HC exposure 1.0 (0.8-1.1) **Mortality (All cause):** OC vs no HC exposure; 0.0 (0.0-inf); implant/injectable vs no HC exposure 0.7 (0.3-1.3) **Composite ART or death** OC vs no HC exposure 0.8 (0.6-1.1); implant/injectable vs no HC exposure 1.0 (0.8-1.1);	-Largest sample size -Prevalent cases with control for baseline CD4 count and disease stage -Time-varying analysis of HC method use -Multivariate analysis -Censored at initiation of ART	-No differentiation between injectables (DMPA/NET-EN)/implants -Methods of contraceptives used varied significantly among sites -Short follow-up time (median 379 days)	II-2, Fair

Primary author, year, funding	Study design, Location	Study population	Contraceptive method/ Comparison group/ Outcome	Results [Adj HR (95% CI) unless otherwise noted]	Strengths	Weaknesses	Quality
Polis [19] 2010 UNDP; UNFPA; WHO; World Bank; NIAID; Fogarty Foundation	Retrospective cohort, mean 4 year follow-up Incident cases Uganda	625 newly seroconverted women from a community cohort	OCs [61/1294 (4.7%) of time intervals] Injectables [197/1294 (15.2%)] Norplant [15/1294(1.2%)] No method or no hormonal method (79%) Onset of AIDS (CD4 <250 or clinically WHO stage 3 or 4 if no CD4 available) or death (all cause, composite outcome) Death (all cause)	**Composite: Time to AIDS or death**: OC vs no HC exposure 0.65 (0.33-1.28); Injectable vs no HC exposure 0.72 (0.50-1.05) **Mortality (all cause):** OC vs no HC exposure 0.73 (0.23-2.37); Injectable vs no HC exposure 0.93 (0.46-1.86)	-Large sample size (n=625) -Community-based cohort -Long follow-up (mean 4 years) -Incident cases -Time-varying analysis of HC use -Multivariate analysis - Analysis of treatment-naïve population	-Infrequent data collection (yearly)	II-2, Good

Primary author, year, funding	Study design, Location	Study population	Contraceptive method/ Comparison group/ Outcome	Results [Adj HR (95% CI) unless otherwise noted]	Strengths	Weaknesses	Quality
Morrison [18] 2011 NICHD; NIH; DHHS; FHI	Prospective cohort, median 58 months follow-up Incident cases Uganda and Zimbabwe	306 newly sero-converted women from family planning clinics	OCs (n=108) DMPA (n=70) No method or no hormonal method (n=128) Onset of AIDS (CD4<200 or WHO Stage 4 or severe stage 3) Onset of AIDS, initiation of ART, or death (all cause, composite outcome)	**Time to AIDS:** DMPA vs no HC exposure 0.9 (0.76-1.08) OC vs no HC exposure 1.07 (0.89-1.29) **Time to AIDS, death, or ART initiation:** DMPA vs no HC exposure 0.9 (0.77-1.06) OC vs no HC exposure 1.02 (0.86-1.22)	-Incident cases -Time-varying analysis of HC use -Multivariate analysis -Censored at initiation of ART use -Long follow-up (median 58 months) -Low loss to follow-up (5%) and frequent follow-up visits (every 3 months)		II-2, Good
Heikinheimo [15] 2011 Helsinki University Central Hospital Research Fund	Retrospective cohort, 5 year follow-up Prevalent cases Finland	40 women living with HIV	LNG-IUD (n=15) No method or no hormonal method (n=25, included 1 implant user) Initiation of ART	**ART initiation:** No difference in ART initiation between groups (p=0.91)	-Long follow up (5 yrs) -Only published evidence for LNG-IUD including a comparison group -Accounted for ART use in analysis	-Prevalent cases, no adjustment for baseline disease -No multivariate analysis -Comparison group includes users of other HC methods -Small sample size, retrospective	II-2, Poor

Appendix III: Change in viral load, CD4

Primary author, year, funding	Study design, Location	Study population	Contraceptive method/ Comparison group/ Outcome	Results	Strengths	Weaknesses	Quality
Kilmarx [16] 2000 CDC	Prospective cohort (median 81 months follow-up) Mix of prevalent and incident cases Thailand	160 sex workers living with HIV at baseline, 34 additional seroconverters	OCs (n=112) DMPA (n=55) Other or no contraception (n=27) rapid decline in CD4 (defined by 50th percentile within study group, faster than median of 3.9 cells/mcl/mo)	**Rapid rate of decline** (faster than median of 3.9 cells/mcl/mo); RR (95% CI): OCs vs non-OCs 1.14 (0.73-1.77); DMPA vs non-DMPA 1.23 (0.84-1.80); when non OC, non-DMPA group analyzed, did not find a difference	-Left-censored prevalent cases at enrolment and controlled for initial viral load -Multivariate analysis -Long follow-up (median 81 months)	-No time-varying analysis of HC use -Comparison group did not exclude HC users	Poor, II-2,
Cejtin [14] 2003 NIH; AHRQ; CDC	Prospective cohort (1-2 years follow-up) Prevalent cases US	1721 women living with HIV	OCs (n=87) DMPA (n=77) implant (n=13) Non-hormonal or no contraception (n=1544) plasma HIV-1 RNA CD4 cell count	**Change in viral load**: HC use not associated with viral load changes (p=0.526) **Change in CD4**: CD4 increased over time among HC users, mean increase 27.6 cells/mcl; p=0.01	-Time-varying analysis of HC use -Prevalent cases with control for baseline characteristics -Multivariate analysis done -Low loss to follow-up (10%) -Use of ART controlled for	-No separate analysis of different types of HC (though did report no difference when progestin-only compared with OCPs) -Small percentage of HC users (10%) -Mean follow-up not stated	Fair, II-2,

Primary author, year, funding	Study design, Location	Study population	Contraceptive method/ Comparison group/ Outcome	Results	Strengths	Weaknesses	Quality
Lavreys [17] 2004 NIH	Prospective cohort (median 34 months follow-up) Incident cases Kenya	161 sex workers, newly seroconverted	OCs (n=34) DMPA (n=50) implant (n=2) No contraception (n=75) Rate of change of viral load	**Change in viral load** not different in HC users vs non-HC users (univariate model); (log copies/mL/month; 95% CI) DMPA: -0.0021 (-0.0110 - +0.0067) OCs: -0.0071 (-0.0166- +0.0024) implant: 0.0034 (-0.0346- +0.0287); Multivariate model incorporating time-varying use of DMPA reported as no difference, estimate not reported	-Frequent follow-up (monthly) -Incident cases -Different HC methods examined separately (but only in univariate analysis)	-Multivariate analysis done only on those using DMPA at time of infection -Time-varying analysis done only on DMPA use; -Loss to follow-up not specified -Differences between HC/non-HC groups not reported -Covariates not clearly controlled for	Poor, II-2,

Primary author, year, funding	Study design, Location	Study population	Contraceptive method/ Comparison group/ Outcome	Results	Strengths	Weaknesses	Quality
Richardson [20] 2007 NIH	Prospective cohort (24 months follow-up) Prevalent cases Rwanda	283 women living with HIV, post-partum	OCs (n=41) DMPA (n=43) Non-hormonal or no contraception (n=109) Change in plasma HIV RNA; change in CD4 cell count; examined both "immediate" (pre- and post-initiation) and "longer-term" (up to 24 months)	**Immediate effect**: *change in log HIV RNA*; OCP vs non-HC no difference (p=0.2); DMPA vs non-HC no difference (p=0.9) *CD4 count* ;OCP vs non-HC no difference p=1.0, DMPA vs non-HC no difference (p=0.3) **Longer-term effect** *change in log HIV RNA*; OCP vs non-HC non-sig trend for faster increase for OC users (p=0.08, 0.1 in multivariate model), DMPA vs non-HC no difference (p=0.7, 1.0 multivariate) *CD4 count* OCP vs non-HC no difference (p=0.9), DMPA vs non-HC non-significant trend for slower decrease in DMPA users (p=0.08 in multivariate model)	-Prevalent cases with control for baseline health status -Multivariate analysis -Censored on initiation of ART -Time-varying analysis of HC use -HC methods analyzed separately -Frequent follow-up (every 3 months) -Relatively long follow-up (2 years)	-Loss to follow-up not reported -Difficult to interpret "immediate effect" in light of recent post-partum status of participants	Fair, II-2,

Primary author, year, funding	Study design, Location	Study population	Contraceptive method/ Comparison group/ Outcome	Results	Strengths	Weaknesses	Quality
Heikinheimo [15] 2011 Helsinki University Central Hospital Research Fund	Retrospective cohort Prevalent cases Finland	40 women living with HIV	LNG-IUD (n=15) No method or no hormonal method (n=25, included 1 implant user) CD4 count 5 years after IUD placement; plasma viral load	CD4 counts not different between groups after 5 years (p=0.97); increase in viral load among non-ART users comparable between the groups in year 1, not significant	-Long follow up (5 yrs) -Only published evidence for LNG-IUD including a comparison group -Accounted for ART use in analysis	-Prevalent cases, no adj. for baseline characteristics -No multivariate analysis -Comparison group does not exclude users of other HC -Small sample size -Retrospective	II-2, Poor