

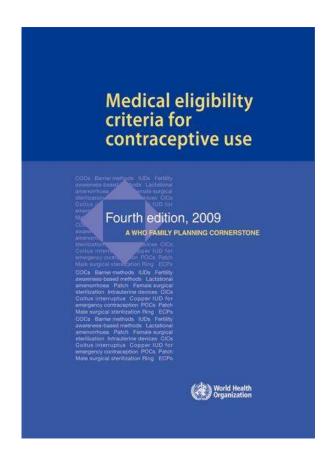
HIV and contraception – the latest recommendations

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Medical eligibility criteria for contraceptive use (MEC)



1996, 2000, 2004, 2009

<u>Purpose</u>: Who can safely use contraceptive methods?

- Women at high risk of HIV
- Women living with HIV
 - asymptomatic or mild HIV clinical disease
 - severe or advanced HIV clinical disease
- Women living with HIV and using antiretroviral therapy



MEC Categories

1	A condition for which there is no restriction for the use of the contraceptive method
2	A condition where the advantages of using the method generally outweigh the theoretical or proven risks
3	A condition where the theoretical or proven risks usually outweigh the advantages of using the method
4	A condition which represents an unacceptable health risk if the contraceptive method is used

Where warranted, recommendations will differ if a woman is starting a method (I = initiation) or continuing a method (C = continuation)

CATEGORY	WITH CLINICAL JUDGEMENT	WITH LIMITED CLINICAL JUDGEMENT			
1	Use method in any circumstances	Yes			
2	Generally use the method	(Use the method)			
3	Use of method not usually recommended unless other more appropriate methods are not available or not acceptable	No (Do not use the method)			
4	Method not to be used				



Methods

- Followed WHO requirements for guideline development
- 4 systematic reviews of epidemiological and pharmacological evidence
 - Does the use of hormonal contraception (HC) increase the risk of HIV acquisition ?
 - Does the use of HC accelerate HIV disease progression ?
 - Does the use of HC increase the risk of female-to-male HIV sexual transmission?
 - Are there any possible interactions between HC and ARV medications?
- GRADE evidence profiles to assess quality of evidence



Evidence: hormonal contraception and high risk of HIV acquisition

- Outcomes: laboratory-confirmed HIV infection
- Injectable hormonal contraceptive use vs. non-use
 - 9 cohort studies (N=28,219), HR range 0.94-2.0, 4 studies show significant increased risk, low quality
 - DMPA: HR range 0.46–2.0 in 6 studies: 4 studies reporting increased risk, significant in 1 study, NET-EN: HR range 0.87–2.5 in 5 studies: 4 studies with increased risk, 1 study significant
- Oral hormonal contraceptive use vs. non-use
 - 8 cohort studies, HR range 0.66-1.8, 1 study reported significant increased risk, 5 studies no effect, low quality
- *Implant use vs. non-use*
 - 1 cohort (N=1272), HR=1.6 (0.5-5.7), very low



Recommendations: High risk of HIV

CONDITION	CATEGORY									
	Combined oral pills	Patch, Vaginal ring	Combined injectable	Progestogen- only pills	DMPA	NET-EN	LNG/ETG implants	LNG-IUD		
HIGH RISK OF HIV	1	1	1	1	1 ^a	1 ^a	1	1		

^a Available studies on the association between progestogen-only injectable contraception and HIV acquisition have important methodological limitations hindering their interpretation. Some studies suggest that women using progestogenonly injectable contraception may be at increased risk of HIV acquisition; other studies have not found this association. The public health impact of any such association would depend upon the local context, including rates of injectable contraceptive use, maternal mortality, and HIV prevalence. This must be considered when adapting guidelines to local contexts. WHO expert groups continue to actively monitor any emerging evidence. At the meeting in 2014, as at the 2012 technical consultation, it was agreed that the epidemiological data did not warrant a change to the MEC. Given the importance of this issue, women at high risk of HIV infection should be informed that progestogen-only injectables may or may not increase their risk of HIV acquisition. Women and couples at high risk of HIV acquisition considering progestogen-only injectables should also be informed about and have access to HIV preventive measures, including male and female condoms.

Evidence: hormonal contraception and HIV disease progression

- Outcomes: mortality; progression to CD4 < 200 or AIDS or ART initiation; composite of all three
- □ Hormonal contraception (oral or injectable) vs. copper IUD
 - 1 RCT (N=599), NS for mortality, increased risk for progression and composite measure, low quality
- □ Injectable hormonal contraceptive use vs. non-use
 - 4-5 cohort studies (N=6851 7136), majority NS, low- moderate quality
- □ Oral hormonal contraceptive use vs. non-use
 - 4-6 cohort studies (N=6059 6864), NS, low-moderate quality
- □ Levonorgestrel IUD vs. no hormonal contraception
 - Initiation of ART 1 study (n=40), NS, very low quality



Evidence: hormonal contraception and female to male transmission

 Outcomes: sero-conversion among previously HIVnegative partner

□ Injectable hormonal contraceptive use vs. non-use

 2 cohort studies (n=2635), significant results reported in one study, very low quality

□ Oral hormonal contraceptive use vs. non-use

 2 cohort studies (n=2635), elevated risk reported in one study (but not significant), very low quality



Recommendations: Living with HIV

HIV-infected → Asymptomatic or mild HIV clinical disease (WHO Stage 1 or 2)

AIDS → Severe or advanced HIV clinical disease (WHO Stage 3 or 4)

CONDITION				CATEGO = initiation, C =		n			
	Combined Patch, Vaginal ring Combined Progestogen DMPA NET-EN				LNG/ETG	LNG-IUD			
	oral pill		injectable	- only pills			Implants	I	С
ASYMPTOMATIC OR MILD HIV CLINICAL DISEASE (WHO STAGE 1 OR 2)	1 ^b	1 ^b	1 ^b	1 ^b	1 ^b	1 ^b	1 ^b	2	2
SEVERE OR ADVANCED HIV CLINICAL DISEASE (WHO STAGE 3 OR 4)	1 ^b	1 ^b	1 ^b	1 ^b	1 ^b	1 ^b	1 ^b	3	2

^b Because there may be drug interactions between hormonal contraceptives and ARV therapy, refer to the section on drug interactions.



Evidence: living with HIV and using antiretroviral therapy

- Outcomes: contraceptive effectiveness (pregnancy, ovulation, ovarian activity, breakthrough bleeding), ARV effectives (disease progression, viral load, CD4 count), adverse events of either HC or ARV)
- Hormonal contraception plus ART vs. HC alone
 - 2 studies (N=336 non-randomized trial, N=4531 cohort), no differences in pregnancy rates for NVP in one good quality study, higher pregnancy rates reported by poor quality study after ART initiation, GRADE: very low quality
- □ EFV vs. other ART in women using HC
 - 2 cohort studies (N=1197), effect on pregnancy mixed, very low quality
- \Box ART + HC vs. ART alone
 - 3 cohort studies (N=679), no effect on ART effectiveness, low quality



Recommendations: living with HIV using antiretroviral therapy

ANTI-RETROVIRAL DRUGS	CATEGORY										
	I = initiation, C = continuation										
	COC	Patch,	CIC	POP	DMPA	NET-EN	LNG/ETG	LNG-IUD			
		ring					Implants				
NUCLEOSIDE REVERSE TRANSCRIPT	ASE INHI	BITORS (N	NRTIs)					I	С		
ABC, TDF, AZT, 3TC, DDI, FTC, D4T	1	1	1	1	1	1	1	2/3 ^c	2 ^c		
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTIs)									С		
EFAVIRENZ (EFV) AND NEVIRAPINE (NVP)	2 ^d	2 ^d	2 ^d	2 ^d	1	2 ^d	2 ^d	2/3 ^c	2 ^c		
ETRAVIRINE (ETR) AND RILPIVIRINE (RPV)	1	1	1	1	1	1	1	2/3 ^c	2 ^c		
PROTEASE INHIBITORS (PIs)								I	С		
ATV/r, LPV/r, DRV/r, RTV	2 ^d	2 ^d	2 ^d	2 ^d	1	2 ^d	2 ^d	2/3 ^c	2 ^c		
INTEGRASE INHIBITORS							I	С			
RALTEGRAVIR (RAL)	1	1	1	1	1	1	1	2/3 ^c	2 ^c		

d Antiretroviral drugs have the potential to either decrease or increase the levels of steroid hormones in women using hormonal contraceptives. Pharmacokinetic data suggest potential drug interactions between some antiretroviral drugs (particularly some NNRTIs and ritonavir-boosted protease inhibitors) and some hormonal contraceptives. These interactions may reduce the effectiveness of the hormonal contraceptive.

Conclusion

- For women at high risk of HIV or living with HIV, WHO recommends no restrictions for:
 - Combined hormonal contraceptives or progestogen-only contraceptives
 - Women and couples at high risk of HIV infection & using POIs should be informed about (and have access to) HIV preventative measures, including male and female condoms.
 - LNG –IUDs can generally be used; however, initiation should be generally avoided if advanced/severe disease
- □ For women taking ART, WHO recommends they *are generally eligible* to use hormonal contraception:
 - Special consideration for efavirenz or neviripine & some protease inhibitors may be warranted.
- Consistent and correct use of condoms, male or female, is critical to protect against STIs/HIV and for prevention of HIV transmission



WHO's commitment



- To continually review
 MEC recommendations
- Strongly supports the need for further research to identify definitive answers that address concerns around increased biological vulnerability to HIV and understanding of possible drug interactions