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Updates on HIV and the menopause plus contraception for transgender people and people living with HIV

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A reproductive health update

People living with HIV on ART
• Menopause management
• Contraceptive options

Contraception for transgender and non binary people
Menopause and HIV: key considerations

- Women with HIV are living longer & we will encounter more peri/post menopausal women in our practices
- Diagnosing menopause; effect of HIV on menopause
  
  **May have earlier menopause and more severe symptoms**

  **Women living with HIV may be ‘untreated’ for their symptoms**

- Management options for symptomatic women
- Effect of menopausal hormone therapy (MHT) on disease progression
- Effect of MHT on ART and vice versa (evidence sparse)

Menopause and HIV: diagnosing menopause

- Possible earlier menopause - annual menstrual cycle review & assessment of menopausal symptoms from 45
  
  **Average age 51 (range 40 – 55); Premature Ovarian Insufficiency < 40**

- Perimenopause: hormonal fluctuations months to years
- Heavy, light, irregular bleeding patterns

**A clinical diagnosis; blood tests not routinely indicated**
- 12 m + amenorrhea (if 50+) & not on hormonal contraception (or by menopausal symptoms after hysterectomy)
- Hot flushes - also caused by HIV, ART, other medications and medical conditions......

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Menopause and HIV: symptoms and long term health effects

**Perimenopause into menopause**
- Vasomotor symptoms (hot flushes and night sweats)
- Genitourinary symptoms – vaginal atrophy & dyspareunia
- Sexual dysfunction; Sleep disturbance
- Mood changes, poor concentration (mood disorders)

**Postmenopause**
- Cardiovascular disease; osteopaenia and osteoporosis
  
  *Risks also increased by HIV, treatment and ageing***
Menopause and HIV

- Prioritise concerns
- Assess contraceptive needs
- Information on menopause & treatment options
- Information on lifestyle modification for symptoms and long term health (exercise, diet, alcohol, smoking, sleep hygiene)
- 3-yearly assessment of fracture risk; baseline bone density screening
- 2-yearly mammograms 50 to 74 years
- Cervical screening every 3 years

Menopause and HIV: sexual function

- Sexual desire, arousal, orgasm and sexual pain disorders (includes urogenital atrophy)
- Poorer sexual functioning associated with menopause, low CD4 count, low mood and poor body image
- Complications of infection & treatment (neuropathy, endocrine disturbances, atherosclerosis) may cause or contribute to sexual difficulties
**Menopause and HIV: genitourinary health**

- Vaginal lubricants
- Vaginal moisturisers
- **Vaginal oestrogens**
  
  *no VTE or cardiovascular risks; no need to monitor endometrial thickness unless any postmenopausal bleeding*
- Vaginal laser?

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**Menopause and HIV – management of vasomotor symptoms**

**Menopausal hormone therapy – the most effective approach**

- Not CI in women living with HIV
- Evidence lacking for optimal management
- No known effect on disease progression or ART therapeutic effect
- Increases QoL (reduces fragility fractures)

Menopausal hormone therapy

- Oestrogen (E) for symptom management
- Progestogen (P) to protect endometrium for women with a uterus
- Sequential or continuous P (sequential if within 12m of last menses)

**Initiate within 10 years of menopause or before 60 years**

- Use minimal hormonal dose to manage symptoms (drug interactions likely to be similar to hormonal contraception but consequences differ)
- Continue beyond 60 years case by case; wean off vs immediate stop


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Menopause and HIV: MHT

**Contraindications**

- Breast cancer, VTE, arterial vascular disease, active liver disease,
- Caution with multiple cardiovascular risk factors

**Risks (lack of evidence in women with HIV)**

- Addition of P ↓ endometrial CA; ↑ breast CA after 5 years (approx. 9 extra cases per 10,000 women per year)
- ↑ risk VTE with oral but not transdermal MHT delivery
- Some evidence of CHD protection if started within 10 years of menopause
MHT options from AMS equivalent doses factsheet

**Combined E+ P products with intact uterus:**

- Combined sequential or continuous E+P tablets
  
  *Femoston sequi/conti (PBS)*

- Tibolone (synthetic E+P+T qualities) (*Livial*)

- **Combined E+P patches *Estalis (PBS)***

  Transdermal recommended 1st line by NICE (minimise VTE and stroke)

**E-only products:**

- E-only tablets, patches, gel
- Low, medium, high dose

  ➢ Women without a uterus can use E products alone

  ➢ Women with a uterus must use a compatible P dose

**P-only products:**

- Synthetic P tablets
- Micronised progesterone tablets
- Levonorgestrel IUS (*Mirena*)
Menopause and HIV: alternatives to MHT

AVOID bioidentical hormones
• Lack of safety data with known cases of endometrial cancer

Non-hormonal prescribed options
• Low dose SNRI venlafaxine 75mg SR (off label)
• Gabapentin, clonidine

Over the counter and lifestyle approaches
• Black cohosh (remifemin; rare cases liver failure)
• No evidence for red clover, evening primrose oil
• Soy products
• Acupuncture, meditation, cognitive behavioural therapy

Mananging menopause – go to websites

www.menopause.org.au

www.jeanhailes.org.au
Contraception and women living with HIV on ART

Key issues

• Effect of contraceptive on disease progression and response to ART (evidence limited; systematic review of 11 studies, 10 showed no effect of hormonal contraception)
• Effects on bone loss
• Effect of ART on contraceptive effectiveness

What methods are available in 2018?

Contraceptive efficacy: perfect & typical use rates

<table>
<thead>
<tr>
<th>method</th>
<th>Perfect use effectiveness %</th>
<th>Typical use effectiveness %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contraceptive implant</td>
<td>&gt; 99.9</td>
<td>99.9</td>
</tr>
<tr>
<td>Hormonal IUD</td>
<td>99.8</td>
<td>99.8</td>
</tr>
<tr>
<td>Copper IUD</td>
<td>99.4</td>
<td>99.2</td>
</tr>
<tr>
<td>Depot injection</td>
<td>99.8</td>
<td>94</td>
</tr>
<tr>
<td>Pills &amp; ring</td>
<td>99.7</td>
<td>91</td>
</tr>
<tr>
<td>Diaphragm</td>
<td>94</td>
<td>88</td>
</tr>
<tr>
<td>Male condom</td>
<td>98</td>
<td>82</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>96</td>
<td>78</td>
</tr>
</tbody>
</table>

Adapted Trussel J. contraception 2011; 83 (5)
Contraception: women living with HIV on ART

• Consider all options……
• **Choice depends on** medical eligibility, SEs including bone density, drug interactions, non-contraceptive benefits, underlying fertility, discretion, access to services, cost, pregnancy plans, personal preference
• Consistent **condoms encouraged** with additional contraception (depends on history, HIV status of partner and whether on suppressive therapy)

www.fsrh.org/documents/ukmec-2016

Drug interactions: hormonal contraception and ART

• ARV may decrease or increase bioavailability of contraceptive steroids (quality of evidence low to very low)
• Hormonal contraceptives metabolised by cytochrome P450 isoenzyme system and glucuronidation pathway

**Affected methods: combined and PO pills, vaginal ring, implant, ECPs**

• Unaffected methods: DMPA (clearance approximates hepatic blood flow), LNG-IUD (mainly acts locally) and non-hormonal methods

University of Liverpool [https://www.hiv-druginteractions.org/](https://www.hiv-druginteractions.org/)
Drugs interactions: hormonal contraception and ART

- NRTIs - renally eliminated & not metabolised by CYP450 or glucuronidation pathways - all methods can be used
- NNRTIs, protease inhibitors and integrase inhibitors including those boosted with cobicistat may interact as several are inducers and/or inhibitors of either or both pathways
- Efavirenz can inhibit & induce pathways involved in metabolising EE & significantly lowers P levels – not recommended except with hormonal IUS and injection

Women living with HIV on ART – what are the options? advice evolving.....

Most effective way to prevent pregnancy and reduce transmission is a condom + an IUD (a barrier may not be required in context of suppressive ART)

- IUDs: safe with no evidence of increased post-insertion infection risk; theoretical risk if CD4 count < 200 (MEC 3)
- No evidence of increased viral shedding or transmission
- No effect on BMD
- HIV diagnosed with IUD in situ – continue to use
  ✔ Hormonal IUS – light or no menstrual bleeding
  ✔ Copper IUD – heavier prolonged menstrual bleeding (can be used as emergency contraception)
Women living with HIV on ART – alternative options

- Consider permanent methods
- Condoms can be used alone but less effective than other methods
- Diaphragms are relatively ineffective

**Advice on optimising effectiveness of combined pill (tricycle 50-70mcg EE dose with a 4 day break + condoms; effect unpredictable)**

- Data lacking for vaginal ring; case reports of implant failure
- Remember EC (double dose of LNG-EC; copper IUD most effective)

- DMPA - small loss of BMD (HIV infection may also ↓BMD; ART initiation associated with initial loss); evaluate osteoporosis risks and benefits every 2 years; no robust evidence for routine DEXA

DMPA & HIV acquisition

- Biological plausibility for increased risk (vaginal atrophy)
- Significant global implications for sub-Saharan countries
- Large RCT (ECHO trial) underway following several systematic reviews of the effect of DMPA on HIV risk with mixed results
  

**Current WHO advice:**

*A woman at high risk of HIV should be made aware that some studies have found that users of PO injectables have an ↑risk of HIV acquisition but it is not known whether this is due to the injection itself or confounding factors eg non use of condoms. All women at high risk should be advised to use effective contraception to reduce the risk of unplanned pregnancy and to use condoms reliably.*
Transgender and non-binary people: contraceptive considerations

- Consider if engaging in vaginal sex with risk of unintended pregnancy
- No restriction on any method for people on account of their current gender identity
- Appropriate and acceptability of different methods will vary; consider personal characteristics, existing medical conditions or drug therapies, body dysmorphia

New guidance:
Contraception for transgender people assigned female at birth

- T therapy can cause amenorrhoea but does not provide adequate contraception (GnRH analogues suppress ovarian function but cannot be relied on for contraception)
- Misperceptions and misinformation documented amongst transmen
- Pregnancy is an absolute CI to T therapy

**T treatment in current regimens can be associated with teratogenicity i.e. masculinisation of a female fetus**

- Condoms provide additional STI protection but contraceptive failure rates can be high (2% in perfect use up to 18% in typical use)
- Permanent contraception (sterility) if required in either partner can be achieved with tubal occlusion or vasectomy

*Light et al. Contraception 2018*

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Contraception for transgender people assigned female at birth

- Cu-IUDs – safe, no effect on hormone regimens; may cause unacceptable unpredictable vaginal spotting and bleeding
- Hormonal IUD, injections, implant, PO pills- not thought to interfere with hormone regimens
  - **P-only injections and hormonal IUD may reduce/stop vaginal bleeding**
  - **Consider effect of T on comfort of IUD insertion**

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Contraception for transgender people assigned female at birth

- Combined pills & ring (E + P) not recommended for transgender men and non-binary people undergoing T treatment as E counteracts the masculinising effects of T
- **Offer EC after unprotected vaginal intercourse**
  UPA (EllaOne), LNG ECP and the Cu-IUD can be used with no interference on hormone treatment
- T not thought to reduce efficacy of EC pills

Contraception for transgender people assigned male at birth

- Transgender women and non-binary (assigned male) people who have not undergone orchidectomy or vasectomy require effective contraception if having vaginal sex & their partner does not wish to conceive
  **Although estradiol treatment impairs spermatogenesis it does not provide adequate contraception**
  - Hormonal therapy (e.g. GnRH analogues, finasteride or cyproterone acetate can’t be relied on to reduce or block sperm production)
  - Condoms can be used (consider failure rate)
  - Permanent contraception (sterility) can be achieved with vasectomy
Any questions?