Healthy LIVing
Quality of life with HIV webinar series

Women Living with HIV: Midlife and the Menopause

This meeting has been organised and funded by MSD

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Quality of life with HIV webinar series

Reproductive health in women over the age of 40

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What happens in midlife?

- Language:
  - Premenopause: everything up until the beginning of the menopausal transition (not a useful term) [1]
  - Perimenopause / menopausal transition / climacteric: from the beginning of symptoms to postmenopause[1]
  - Menopause: the last menstrual period[1]
  - Postmenopause: from 12 months after last period[2]

  - Premature menopause: menopause before the age of 40 years[3]
  - Early menopause: menopause before the age of 45 years[3]

1. Healthline. Premenopause, Perimenopause, and Menopause. August 2020. Available online at: https://www.healthline.com/health/menopause/difference-perimenopause [Accessed online 08.03.22]
2. Post Menopause. Available online at https://menopausetreatment.co.uk/what-is-menopause/post-menopause/ [Accessed online 08.03.22]
3. Cleveland Clinic. Premature and Early Menopause. October 2019. Available online at https://my.clevelandclinic.org/health/diseases/21138-premature-and-early-menopause#:~:text=The%20difference%20between%20premature%20menopause%20and%20early%20menopause%20is%20when,undergoes%20menopause%20before%20age%2045. [Accessed online 08.03.22]

But for the woman…

- Changes to periods
- Symptoms (physical and emotional)
- Effect on sex life
- Effect of social situations
- Effect on fertility and contraception
- Uncertainty, stigma, shame, silence

What is normal?

- Symptoms usually start whilst still menstruating – will vary month to month and premenstrual syndrome (PMS) may worsen
- Periods usually become irregular, with runs of regular periods and then months without
- Periods often become lighter but may be more painful

NHS UK. Menopause. August 2018. Available online at https://www.nhs.uk/conditions/menopause/symptoms/ [Accessed online 08.03.22]

Symptoms: climacteric vs ageing

- Hot flushes
- Night sweats and poor sleep
- Tiredness, brain fog
- Mood changes, anxiety
- Palpitations
- Joint aches
- Headaches
- Restless legs
- Reduced libido, vaginal and urinary symptoms
- Weight gain
- Skin itching and dryness
- Loss of confidence

NHS UK. Menopause. August 2018. Available online at https://www.nhs.uk/conditions/menopause/symptoms/ [Accessed online 08.03.22]

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What is abnormal? Red flags

- Periods becoming heavier or lasting longer (perimenopausal menorrhagia, endometrial hyperplasia, endometrial cancer)
- Night sweats as the only symptom
- Bloating (exclude ovarian cancer)
- Consider other causes, especially in younger women
  - Pituitary tumours
  - Hyperprolactinaemia
  - Polycystic Ovary Syndrome (PCOS)
  - Pregnancy
  - Thyroid disease

What can we offer?

- Lifestyle advice
- HRT
- Non-HRT medications
- Psychological support / Cognitive behavioural therapy (CBT)
- Contraception
- Support in the workplace
- General awareness

Personalised care

- **LISTEN!**

- What are the most distressing symptoms?
- Fertility
- Hopes and fears
- What is her knowledge like so far? Plans for the menopause?
- Medical and family history
- Lifestyle
- What does she want from the consultation?

Lifestyle

- Diet
- Exercise
- Social support
- Relationships

CBT / psychological support

- Management of symptoms
- Increase confidence
- Help others to support
- Relationships
- Talk about sex
- Group work

HRT: the issues

- The risk:benefit analysis
- For how long?
- How to help the woman whose risk outweighs the benefit?

Multiple Options

Oestrogen

- Transdermal
- Patches
- Gel
- Spray
- Oral
- Vaginal

Progestogen

- Transdermal patches
- Oral
- Vaginal
- Intrauterine

Regimens

- Oestrogen alone (only if no uterus)
- Sequential
- Continuous combined

- Vaginal oestrogen

The risk:benefit analysis

- Symptoms
- Quality of life
- Bone protection
- Colon cancer
- Cognitive function?

- Breast cancer

Cardiovascular Disease
Venous Thromboembolism (VTE)

Quality of life

- Continuous combined hormone replacement therapy (CCHRT) resulted in improved quality of life after 6 and 9 years of treatment, even after dose reduction
- Quality of life declined in those who stopped HRT after end of study period

Ylikangas S et al. 2005. Decade-long use of continuous combined hormone replacement therapy is associated with better health-related quality of life in postmenopausal women, as measured by the generic 15D instrument. Journal of BMS Vol 11 No 4.

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Bone

- Oestrogen can reduce the incidence of vertebral and non-vertebral fracture[1,2]
- The Million Women Study suggests that current use of any HRT preparation reduces fracture risk[3]
- Oestrogen is not the first-line therapy for osteoprotection in the asymptomatic woman (since Million Women Study)[4]

1. M.H. Komulainen et al.HRT and Vit D in prevention of non-vertebral fractures in postmenopausal women; a 5 year randomized trial. . Maturitas 31 (1998) 45–54.
2. Lufkin EG et al. Treatment of postmenopausal osteoporosis with transdermal estrogen. Ann Intern Med 1992;117:1–9.
3. Banks E et al.. Million Women Study C. Fracture incidence in relation to the pattern of use of hormone therapy in postmenopausal women. JAMA. 2004;291(18):2212–20
4. Gambacciani et al. Hormone replacement therapy and the prevention of postmenopausal osteoporosis. Prz Menopauzalny 2014; 13(4): 213-220

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Breast cancer

- Risk relates to duration of use (background of 45/1,000 cases):[1]
  - 5-year use: 2/1,000 attributable cases
  - 10-year use: 6/1,000 attributable cases
  - 15-year use: 12/1,000 attributable cases

- Similar to effect of obesity / alcohol intake[2]
- Oestrogen alone does not increase risk. Type of progestogen may have an effect[3]

1. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormone replacement therapy: collaborative reanalysis of data from 51 epidemiological studies of 52 705 women with breast cancer and 108 411 women without breast cancer. Lancet 1997; 350: 1047–59
2. British Menopause society Tool for clinicians. Fast Facts: HRT and breast cancer risk. November 2020.
3. British Menopause Society. Joint RCOG & BMS statement in response to the Lancet study on HRT use and breast cancer risk. August 2019.

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Venous Thromboembolism (VTE) risk - incl. stroke

- 16 per 10 000 women years (unexposed population)
- Risk increased by increasing age, obesity, immobility
- Number of extra VTE cases was nine per 10 000 women years (overall oral HRT use)
- Transdermal oestrogen is thought to not increase risk of VTE
- Most occur in first year

Vinogradova Y et al. Use of hormone replacement therapy and risk of venous thromboembolism: nested case-control studies using the QResearch and CPRD databases. BMJ 2019;364:k4810 [2018]

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Cardiovascular Disease (CVD)

- Risk of CVD increases with time after menopause[1]
- NICE: HRT started before the age of 60 years does not increase the risk of CVD and does not affect the risk of dying from CVD[2]
- Lifestyle factors that aim to reduce CVD risk are of prime importance[2]

1. British Heart Foundation, Menopause and heart disease. [Accessed online 08.03.2022]
2. Menopause: diagnosis and management. NICE guideline [NG23]. 12TH November 2015.

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Cognitive function

- Oestrogen replacement may reduce cognitive decline in some women
- Oestrogen replacement may delay the onset of Alzheimer's Disease in some women, or may increase risk in older women
- Women are more likely to benefit if oestrogen replacement is started at menopause onset rather than later
- Research to date is insufficient to allow HRT to be recommended for this purpose

British Menopause Society. Possible link between hormones and Alzheimer's Dementia. July 2020. Accessed online: https://thebms.org.uk/2020/07/possible-link-between-hormones-and-alzheimers-dementia/ [Accessed on 08.03.22]

For how long?

- Depends on indication
- Agree plan
- Change preparation over time
- Yearly risk:benefit review
- Premature menopause: offer HRT until average age of menopause (50–52 years)
- Arbitrary limits should not be placed on the duration of usage of HRT; if symptoms persist, the benefits of hormone therapy usually outweigh the risks

Contraception

- HRT regimens are not contraceptive unless progestogen is intrauterine
- Need contraception until age 55 unless:
  - 12 months of amenorrhoea without hormone treatment
  - 2 raised Follicle Stimulating Hormone (FSH) levels > 12 months ago

- Can add progestogen-only contraception to HRT regimen
- Combined Oral Contraceptive can be used up to age 50 as HRT, but probably less good for osteoprotection
- Do not rely on ‘safe period’

The Faculty of Sexual and Reproductive Healthcare. FSRH Guideline: Contraception for Women aged over 40 years. August 2017 (Amended September 2019)

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As well as caring for the individual, we should improve…

- Public awareness (should be culturally sensitive)
- Support in the workplace
- Better education for healthcare professionals

Considerations for women living with HIV

Outline

- Review the epidemiology of Women With HIV (WWH) in the UK
- HIV and menopause: what's different in WWH?
- WWH and comorbidities
- Guidelines

Women living with HIV (WWH) in the UK

- 1/3 of PWH in the UK are women (29,500 in 2018) with a median age of 45 years[1]
- Of these, 1/3 are aged ≥ 50
- 2/3 are Black African, 1/5 are White
- 23% of new HIV diagnoses in 2018 were in women > 50 years and more likely diagnosed late[2]
- Life expectancy in women with CD4 > 350 cells/mm^3 mirrors that of the general population[3,4]

Women diagnosed with HIV receiving HIV specialist care: 2008–2017, by age group[1]

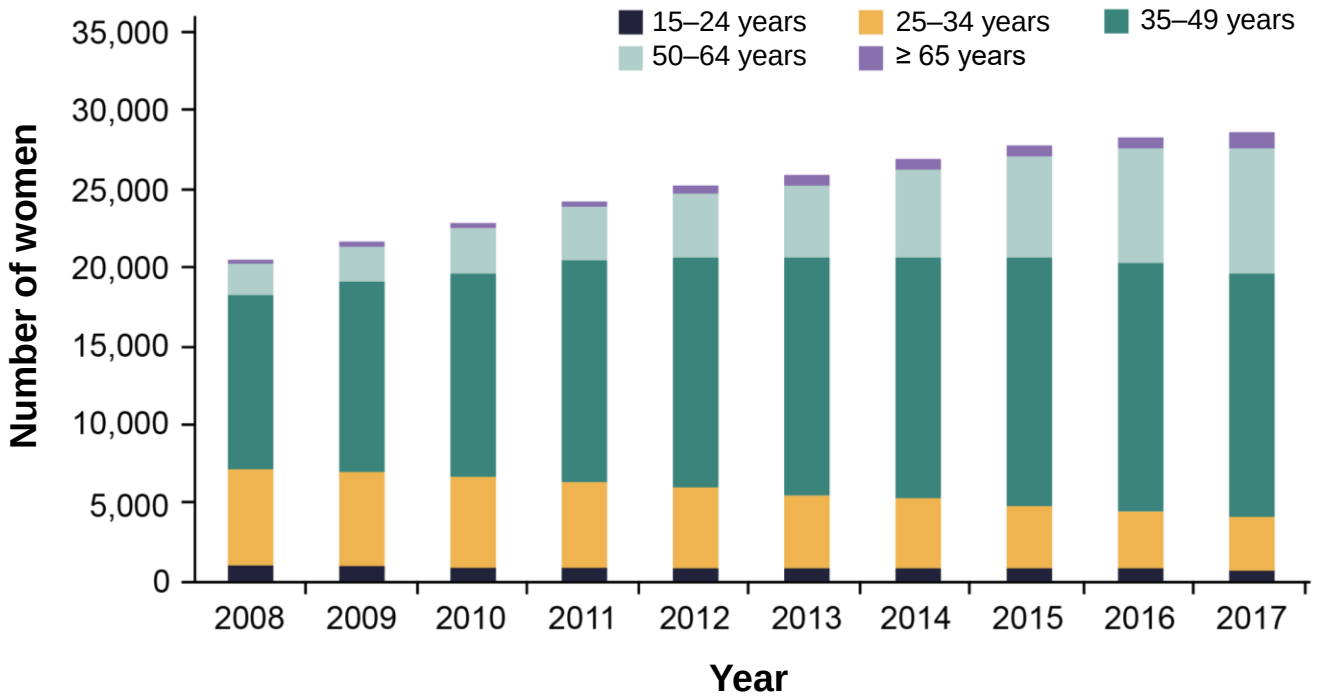

Figure adapted from Public Health England. 2019[1].

1. Brown A et al. October 2019. Women and HIV in the UK. Public Health England, London.
2. O'Halloran C et al. 2011. HIV in the United Kingdom. Towards zero HIV transmissions by 2030. Public Health England, London.
3. May M et al. 2011. Impact of late diagnosis and treatment on life expectancy in people with HIV-1: UK Collaborative HIV Cohort (UK CHIC) Study. BMJ 343:d6016
4. Marcus J et al. 2020. Comparison of Overall and Comorbidity-Free Life Expectancy Between Insured Adults With and Without HIV Infection, 2000-2016. JAMA Netw Open.3(6):e207954.

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Menopause and HIV

- Most WWH reach menopause between 46 and 50 years[1,2]
- Conflicting evidence as to whether WWH are more likely to have earlier menopause than those without HIV[2,3]
- Higher rates of early menopause and premature ovarian insufficiency in some cohorts, but higher rates of other factors associated with early menopause (e.g. substance misuse, smoking)[4–6]
- WWH more likely to have amenorrhoea without biochemical evidence of menopause[3]

1. Tariq S et al. 2016. The impact of the menopause transition on the health and wellbeing of women living with HIV: A narrative review. Maturitas. 88:76-83.
2. Imai K et al. 2013. HIV and Menopause: A Systematic Review of the Effects of HIV Infection on Age at Menopause and the Effects of Menopause on Response to Antiretroviral Therapy. Obstetrics and Gynecology International. Volume 2013, Article ID 340309,11pages.
3. Cejtin H et al. 2012. Care of the Human Immunodeficiency Virus-Infected Menopausal Woman. Am J Obstet Gynecol. 2012 August ; 207(2): 87–93.
4. Schoenbaum E et al. 2005. HIV Infection, Drug Use, and Onset of Natural Menopause. Clinical Infectious Diseases. 41:1517–24
5. Fantry L et al. 2005. Age of Menopause and Menopausal Symptoms in HIV-Infected Women. AIDS Patient Care STDS. 19 (11):703-711
6. Calvert GA et al. 2015. Predictors of early menopause in HIV-infected women: a prospective cohort study. Am J Obstet Gynecol. 212:765.e1-13.

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Age at menopause for WWH

Author	Country	Study	Control	Number	Post menopause (%)	Definition	Age at menopause (median)	% early menopause	POI
Clark RA et al[1]	US	XS	N	52 > 40 years	50	Self-report FSH > 35 Investigator diagnosis > 6/12 amen age > 55	47 (mean)	-	-
Schoenbaum EE et al[2]	US	XS	Y	571 (53% HIV+) > 40 years	17.8	Self-report	46 HIV+ 47 HIV–	26 HIV+ 10 HIV-	-
Calvert GA et al[3]	Brazil	Prosp. cohort	N	667 > 30 years	-	Self-report	48	27	2.3
Boonyanurak P et al[4]	Thailand	XS	N	268	20.5	Self-report	47.3 (mean)	-	-
Fantry LE et al[5]	US	XS	N	120 > 40 years	25	Self-report	50	20	35
Cejtin HE[6]	US	XS WIHS	Y	1139 HIV+ 292 HIV– > 55 years	-	Self-report no period × 2 visits FSH > 25	47 HIV+ 47 HIV–	-	-
de Pommerol M et al[7]	France	Prosp. cohort	N	404	24.3	Self-report	49	22	12

1. Clark RA , Cohn SE, Jarek C. Perimenopausal symptomatology among HIV infected women at least 40.J Acquir Immune Defit Syndr 2000 23(1):99-100
2. Schoenbaum E et al. 2005. HIV Infection, Drug Use, and Onset of Natural Menopause. Clinical Infectious Diseases. 41:1517–24
3. Calvert GA et al. 2015. Predictors of early menopause in HIV-infected women: a prospective cohort study. Am J Obstet Gynecol.212:765.e1-13.
4. Boonyanurak P et al. 2012,. Age at menopause and menopause-related symptoms in humanimmunodeficiency virus infected Thai women. Menopause: The Journal of The North American Menopause SocietyV ol. 19, No. 7, pp. 820/824.
5. Fantry L et al. 2005. Age of Menopause and Menopausal Symptoms in HIV-Infected Women. AIDS Patient Care STDS. 19 (11):703-711
6. Cejtin H et al. 2012. Care of the Human Immunodeficiency Virus-Infected Menopausal Woman. Am J Obstet Gynecol. 2012 August ; 207(2): 87–93.
7. Pommerol M D et al. 2011. Menopause and HIV infection: age at onset and associatedfactors, ANRS CO3 Aquitaine cohort. Int J STD AIDS 2011;22(2):67-72

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HIV and menopause: the Prime Study (Positive Transitions Through the Menopause)[1,2]

- Cross-sectional, mixed methods study of 900 HIV+ women in the UK aged 45–60 years
- Demographics:
  - Median age of cohort 49 years
  - 81% Black African or Black other, 85% not born in the UK
  - 88% completed some sort of education, 66% employed, 53% in a relationship
  - 98% on ART, 88% undetectable viral load
  - 43% perimenopausal, 34% postmenopausal, 9.5% early menopause
  - **Median age at menopause 53 years**
  - 12% of those postmenopausal had 2 or more comorbidities (hypertension, type 2 diabetes Mellitus)

1. Tariq S et al. 2018. Menopause in women living with HIV in England: findings from the PRIME Study.
2. Okhai H et al. 2021. Menopausal status, age and management among women living with HIV in the UK HIV Medicine. 2021;22:834–842

Are WWH more likely to have symptoms related to menopause?[1]

- In some XS studies with a control group, HIV has been shown to be independently associated with increased symptoms[1]
- Others have shown that severity of symptoms, such as vasomotor, is greater in WWH[2]
- Several studies showed no difference in vasomotor symptoms or vaginal dryness in WWH compared to HIV negative women[3]
- Conflicting findings regarding CD4 count and impact on menopausal symptoms
- Conflicting findings may be due to the study of different populations and differences in socioeconomic factors[3]

1. Ferreira C et al. 2007. Menopause symptoms in women infected with HIV: Prevalence and associated factors. Gynecol Endocrinol.23(4):198-205
2. Looby S et al. 2014. Increased Hot Flash Severity and Related Interference inPerimenopausal HIV-infected Women. Menopause. 21(4):403-409
3. Andany N et al. 2016. Perspectives on menopause and women with HIV. Int Jnl Womens Health. 8:1-22

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HIV and menopause: the Prime Study[1]

- 70% reported menopausal symptoms, 27% severe

Prevalence of any menopausal symptoms by symptom domain

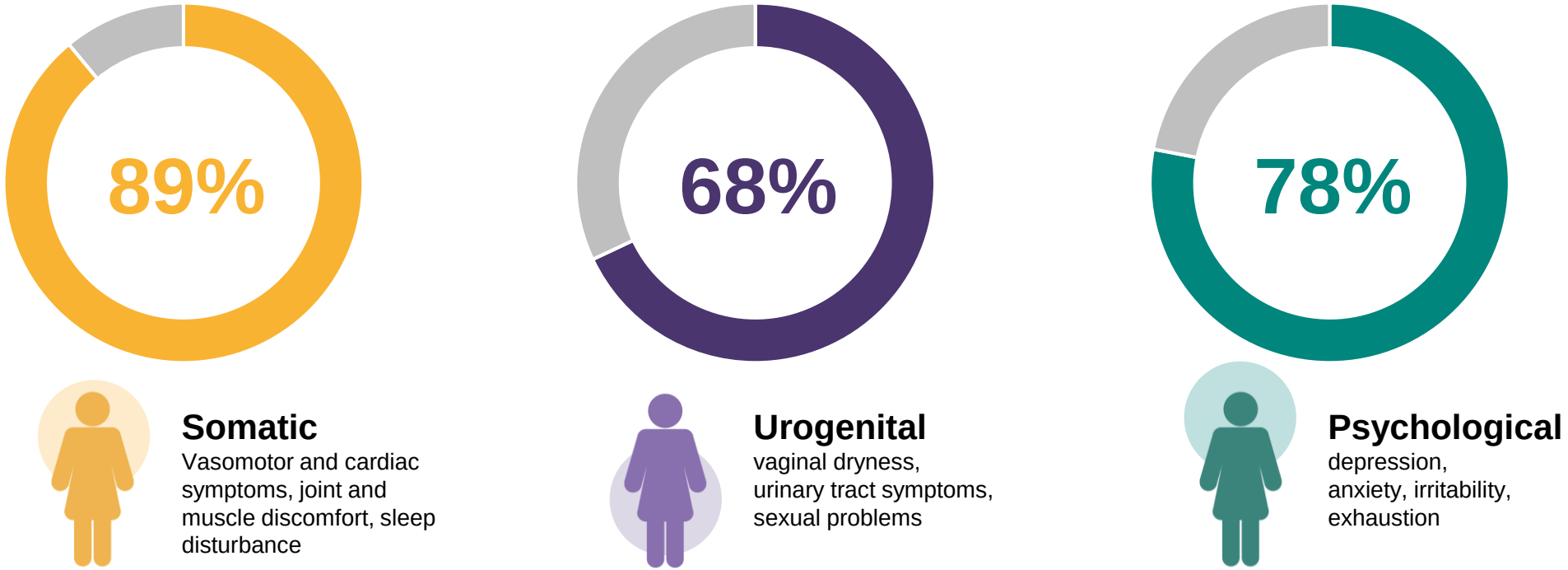

Figure adapted from Tariq S. 2018[1].

- Psychosocial problems, including unemployment, poverty, social isolation and depression are common[2]

1. Tariq S et al. 2018. Menopause in women living with HIV in England: findings from the PRIME Study.
2. Solomon D et al. 2021. Ethnic inequalities in mental health and socioeconomic status among older women living with HIV: results from the PRIME Study. Sex Trans Infect 2021:0:1-4

Association of HIV status with sexual function in women aged 45–60 in England: results from two national surveys

- Analysis of cross-sectional data from sexually active women aged 45–60 comparing PRIME study and NATSAL 3 data
- Sexual problems were more common in WWH (69%) compared with HIV negative women from the same age group (54%) and were more pronounced in postmenopausal women

Prevalence and odds ratios of reporting sexual function problems by sexually active participants in Natsal-3 and PRIME*

Sexual problems	Natsal-3 (HIV–) N = 1228†, 1677** % (95% CI)	PRIME (HIV+) N = 386 % (95% CI)	p value‡	Crude OR (95% CI)	AOR§ (95% CI)
Lacked interest in sex	38.3 (36.1–40.5)	48.4 (41.4–56.6)	0.007	1.51 (1.12–2.04)	2.30 (1.30–4.07)
Lacked enjoyment in sex	13.1 (11.6–14.8)	31.6 (27.4–36.1)	< 0.001	3.06 (2.39–3.91)	3.50 (1.94–6.30)
Felt anxious during sex	3.5 (2.6–4.6)	16.1 (12.6–20.3)	< 0.001	5.34 (3.56–8.00)	4.01 (2.24–7.16)
Physical pain as a result of sex	7.5 (6.3–8.9)	15.3 (12.8–18.2)	< 0.001	2.23 (1.69–2.95)	2.71 (1.83–4.01)
No excitement / arousal during sex	8.7 (7.5–10.1)	28.8 (23.2–33.3)	< 0.001	4.07 (3.02–5.49)	3.17 (1.84–5.44)
No orgasm / took a long time to reach orgasm despite arousal	14.9 (13.2–16.6)	31.1 (26.7–35.8)	< 0.001	2.59 (2.01–3.32)	2.82 (1.86–4.28)
Reached orgasm too quickly	2.4 (1.8–3.3)	7.4 (4.6–11.2)	< 0.001	3.15 (1.79–5.54)	2.20 (0.67–7.26)
Vaginal dryness	17.2 (15.5–19.1)	28.5 (24.4–33.0)	< 0.001	1.91 (1.50–2.45)	2.44 (1.47–4.06)
Experienced at least one problem	54.3 (52.1–56.5)	68.7 (63.8–73.1)	< 0.001	1.84 (1.46–2.33)	2.44 (1.49–4.00)
Overall sexual function¶ low sexual function	22.9 (21.0-25.0)	44.6 (37.3–52.2)	< 0.001	2.71 (1.96–3.75)	3.75 (2.15-6.56)

* Sexually active participants were those who reported having sex in the past 1 year. Sexual problems were reported from the past year and lasted ≥ 3 months.
† Unweighted denominator. ** Weighted denominator. ‡ Chi-squared p value for associations between HIV status and sexual problems variables. § Adjusted for age, ethnicity, ongoing relationship status, depression and number of chronic conditions. ¶ Score ≥ 13.44 indicated low sexual function.

AOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio

Torabally N et al. 2020. Association of HIV status with sexual function in women aged 45–60 in England:results from two national surveys. AIDS Care. 32(3):286-295

HIV and menopause: the Prime Study

- Many participants reported that talking about periods and menopause was taboo in their culture
- 47% had insufficient information about menopause, felt underprepared and requested more information
- Difficult to distinguish between HIV and menopause-related symptoms
- 40% of postmenopausal women were aware of HRT but only 8% were currently using HRT (3% topical oestrogen)
- Women described being caught between HIV specialist and GP

[The HIV doctors] are telling us to take everything to the GP… the GP then tells you to take it back to your HIV consultant. It's very frustrating if you're suffering all these things, and you keep going backwards and forwards.

1. Tariq S et al. 2018. Menopause in women living with HIV in England: findings from the PRIME Study.

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Managing menopause in WWH: a survey of primary care practitioners

- Questionnaire-based study of primary care practitioners attending SRH conference
- 19% response rate (95/500 questionnaires)
- Respondents were mainly female, 99% confident in managing menopause
- 2/3 had seen WWH for general consultations
- 47% felt confident managing menopause in WWH
- 50% thought menopause in WWH should be managed by primary care, 22% by specialist menopause services, 24% by HIV services
- 75% stated they would benefit from further training in menopause and HIV

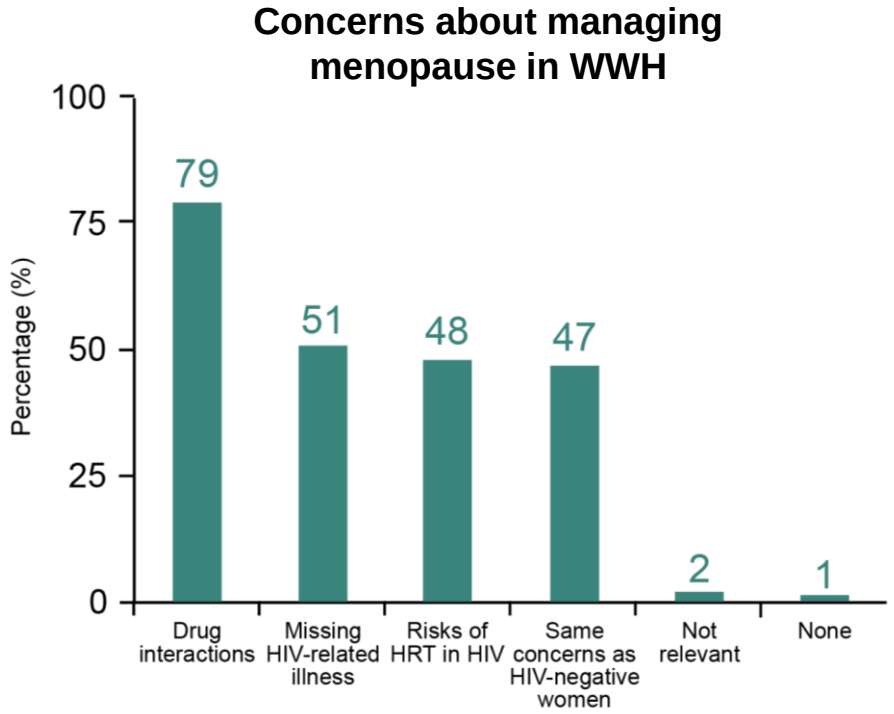

Figure adapted from Chirwa M et al. 2017

Chirwa M et al. 2017. Managing menopause in women living with HIV: A survey of primary care practitioners Post Reprod Health. 23:111-115

Impact of menopause on HIV

- Untreated postmenopausal WWH have lower CD4 counts compared with premenopausal WWH[1]
- No difference in pharmacokinetic or virological / immunological responses to ART
- Menopause diagnosis may be delayed as symptoms are misattributed to HIV by patients[2,3] and not questioned or considered by HIV clinicians[4]

1. Andany N et al. 2016. Perspectives on menopause and women with HIV. Int Jnl Womens Health. 8:1-22
2. Schnall R et al. 2018. People Living with HIV (PLWH), Menopause (natural or surgical) Contributes to the Greater Symptom Burden in Women: results from an online US survey. Menopause.5(7):744-752.
3. Johnson M et al. 2008. Attribution of menopause symptoms in human immunodeficiency virus-infected or at-risk drug-using women. Menopause.15(3):551-7
4. Munatsi S et al. 2019. The menopause experience: A quality improvement project. BHIVA. P151

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Association between severe menopausal symptoms and engagement with HIV care and treatment in WWH

- Analysis of women from Prime study N = 701
- Adherence and clinic attendance evaluated from validated questionnaires
- Women with severe menopausal symptoms more likely to have suboptimal adherence (OR 3.44, AOR 2.22)
- Women with severe menopausal symptoms were more likely to have suboptimal clinic attendance (AOR 1.52)
- Severe psychological and somatic symptoms associated with suboptimal attendance but not severe urogenital symptoms

Univariable and multivariable logistic regression analyses of the association between menopausal symptoms and suboptimal adherence to ART		Suboptimal adherence to ART	
		OR	95% CI
All menopausal symptoms	None/mild/moderate (MRS < 17)	**Ref**	
Multivariable analysis (all symptoms)*	Severe (MRS ≥ 17) Non/mild/moderate	**3.44** **Ref**	**2.04–5.79**
Somatic menopausal symptoms	Severe None/mild/moderate	**2.22** Ref	**1.13–4.35**
Multivariable analysis (somatic)*	Severe None/mild/moderate	1.50 Ref	0.80–2.83
Psychological menopausal symptoms	Severe None/mild/moderate	0.59 **Ref**	0.27–1.28
Multivariable analysis (psychological)*	Severe None/mild/moderate	**2.62** Ref	**1.56–4.40**
Urogenital menopausal symptoms	Severe None/mild/moderate	1.36 Ref	0.71–2.64
Multivariable analysis (urogenital)*	Severe None/mild/moderate	1.54 Ref	0.91–2.62
Number of severe symptoms	Severe 0/1	0.96 Ref	0.51–1.81
Multivariable analysis (number of severe symptoms)*	2/3 0/1	**2.01** Ref	**1.16–3.49**
Menopausal status	2/3 Premenopausal Perimenopausal Postmenopausal	0.90 Ref 0.98 1.12	0.45–1.79 0.50–1.92 0.55–2.25

*Adjusted for ethnicity, employment, high-risk alcohol use, current smoking, basic needs met and years since diagnosis.

Univariable and multivariable logistic regression analyses of the association between menopausal symptoms and suboptimal HIV clinic attendance		Suboptimal HIV clinic attendance	
		OR	95% CI
All menopausal symptoms	None/mild/moderate (MRS < 17) Severe (MRS ≥ 17)	Ref 1.35	0.91–2.01
Multivariable analysis (all symptoms)*	None/mild/moderate	Ref	
Somatic menopausal symptoms	Severe None/mild/moderate	1.52 **Ref**	1.01–2.29
Multivariable analysis (somatic)*	Severe None/mild/moderate	**1.81** **Ref**	**1.15–2.86**
Psychological menopausal symptoms	Severe None/mild/moderate	**1.98** **Ref**	**1.24–3.16**
Multivariable analysis (psychological)*	Severe None/mild/moderate	**1.62** **Ref**	**1.09–2.40**
Urogenital menopausal symptoms	Severe None/mild/moderate	**1.76** Ref	**1.17–2.65**
Multivariable analysis (urogenital)*	Severe None/mild/moderate	1.01 Ref	0.67–1.51
Number of severe symptoms	Severe 0/1	1.06 Ref	0.70–1.61
Multivariable analysis (number of severe symptoms)*	2/3 0/1	1.48 **Ref**	0.96–2.26
Menopausal status	2/3 Premenopausal Perimenopausal Postmenopausal	**1.59** Ref 1.03 0.87	**1.03–2.46** 0.64–1.66 0.52–1.45

* Adjusted for age and ethnicity.

AOR, adjusted odds ratio; CI, confidence interval; MRS, Menopause Rating Scale; OR, odds ratio

Solomon D et al. 2021. The association between severe menopausal symptoms and engagement with HIV care and treatment in women living with HIV. AIDS Care. 33 (1):101-108

HIV and non-AIDS comorbidity(NACM)

- PWH with virological control have increased rates of NACM and mortality, and these occur at an earlier age[1,2]
- WWH are likely to have more comorbidities compared to HIV negative controls[3]

1. Guaraldi G et al. 2011. Premature Age-Related Comorbidities Among HIV-Infected Persons Compared With the General Population Clin. Infect. Dis. 53:1120–1126.
2. McGettrick P et al. 2018. Ageing with HIV. Healthcare (Basel). 6(1): 17
3. Collins L et al.2021. The Prevalence and Burden of Non-AIDS Comorbidities Among Women Living With or at Risk for Human Immunodeficiency Virus Infection in the United States. Clin Infect Dis. 72(8):1301-1311

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The prevalence and burden of NACM in women living with, or at risk of, HIV in the US

- Analysis of Women's Interagency HIV Study, 2009–2018
- Examined number of NACM per participant and prevalence of NACM

Demographics

- 2,309 HIV+, 923 HIV-, median age 50, 65% Black
- WWH 81% virological suppression, CD4 615 cells/mm^3, median time since cART initiation 12.5 years

Results

- NACM burden and prevalence increased with each age group
- WWH had a higher mean NACM burden than HIV negative ($p < 0.0001$)
- WWH had higher prevalence of psychiatric illness, liver disease, dyslipidaemia, bone disease, Chronic Kidney Disease, non-AIDS cancer
- No difference in hypertension, diabetes mellitus, lung disease, CVD

Distribution of prevalent NACM burden by HIV serostatus and age group

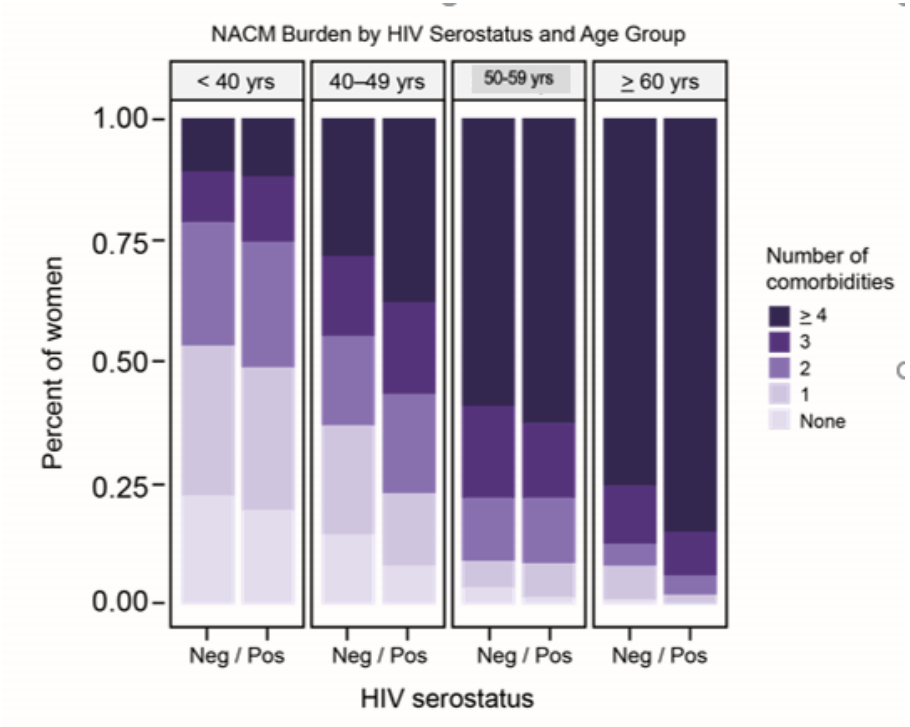

Figure adapted from Collins L et al.2021

Collins L et al.2021. The Prevalence and Burden of Non-AIDS Comorbidities Among Women Living With or at Risk for Human Immunodeficiency Virus Infection in the United States. Clin Infect Dis. 72(8):1301-1311

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HIV and non-AIDS comorbidity

- PWH with virological control have increased rates of NACM and mortality, and these occur at an earlier age[1,2]
- WWH are likely to have more comorbidities compared to HIV negative controls[3]
- Chronic, increased levels of inflammatory markers despite virological control and long-term effects of some ART are contributors[4,5]
- Prevalence of CVD, osteoporosis, impaired cognitive function,[3] metabolic syndrome, liver and kidney disease, non-AIDS cancer all increased
- Increased risk of VTE (× 2–10), initial and recurrent VTE[6]

1. Guaraldi G et al. 2011. Premature Age-Related Comorbidities Among HIV-Infected Persons Compared With the General Population Clin. Infect. Dis. 53:1120–1126.
2. McGettrick P et al. 2018. Ageing with HIV. Healthcare (Basel). 6(1): 17
3. Collins L et al.2021. The Prevalence and Burden of Non-AIDS Comorbidities Among Women Living With or at Risk for Human Immunodeficiency Virus Infection in the United States. Clin Infect Dis. 72(8):1301-1311
4. Raghavan A et al. 2017. Sex-Differences in Select Non-communicable HIV-Associated Comorbidities: Exploring the Role of Systemic Immune Activation/Inflammation. Curr HIV/AIDS Rep. 14, 220-228
5. Alcaide M et al. 2013. Immune Activation in HIV-Infected Aging Women o nAntiretrovirals—Implications for Age-Associated Comorbidities: A Cross-Sectional Pilot Study. PLoS ONE 8(5): e63804
6. Rokx C et al. 2020. Risk of recurrent venousthromboembolism in patients with HIV infection: A nationwide cohort study. PLoSMed 17(5):e100310

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HIV and non-AIDS comorbidity

- HIV associated with increased Cardiovascular disease risk (× 2)[1] and is the leading cause of non-AIDS mortality in PWH
- WWH have higher rates of cardiovascular disease (CVD), which happens earlier, and a higher rate of CV mortality compared with men with HIV (MWH) [2–4]
- WWH more likely to form non-calcified plaques compared with MWH and HIV– controls, which is thought to be associated with greater levels of immune activation[4]
- HIV significantly associated with increased risk of stroke in WWH, and at a younger age[4]
- WWH more likely to have other risk factors for CVD such as metabolic syndrome, high BMI and be under- or untreated for hypertension and dyslipidaemia[4–6]
- BHIVA recommends annual screening for CVD risk in those > 50 years and/or in those with high BP, diabetes or other risks[7]

1. Vachiat A et al. 2017. HIV and Ischemic Heart Disease J. Am. Coll. Cardiol. 69 73-82
2. Womack J et al. 2014. HIV Infection and Cardiovascular Disease in Women J. Am. Heart Assoc. 3 e1001035.
3. Hanna D et al. 2020. Sex- and Poverty-Specific Patterns in Cardiovascular Disease Mortality Associated With Human Immunodeficiency Virus, New York City, 2007–2017 Clin Infect Dis. 71(3):491-498
4. Pond R et al.2021. Sex Differences in Non-AIDS Comorbidities Among People With Human Immunodeficiency Virus. Open Forum Infect Dis. 8(12) ofab558
5. Solomon D et al. 2018. Cardiovascular disease in women living with HIV: A narrative review. Maturitas. 108; 58-70T
6. Tariq S et al. BHIVA 2017 P91
7. BHIVA guidelines on the routine investigation and monitoring of HIV-1 positive adults 2019. Available at https://www.bhiva.org/monitoring-guidelines. Accessed online 08.03.22

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Bone disease and WWH

- HIV is an independent risk factor for osteopaenia and osteoporosis with higher rates of osteoporosis (7.3–84%) and fractures (× 1.5) reported compared with uninfected controls[1,2]
- Postmenopausal WWH have accelerated bone loss and increased risk of osteoporosis compared with MWH and HIV– controls[1]
- Specific ARTs associated with 7 times increased risk of osteoporosis in WWH compared with MWH[3]
- Low vitamin D more common in PWH[4]
- BHIVA recommends screening for bone disease using 3-yearly FRAX for all patients > 50, postmenopausal women and others at risk[4]

1. Cortes YI et al. 2015. Bone Density and Fractures in HIV-infected Postmenopausal Women: A Systematic Review J Assoc Nurses AIDS Care. 26(4): 387–398
2. Yin MT, et al. 2010. Short term bone loss in HIV infected premenopausal women. J Endocrinol Metab. 95:620–9.
3. Negredo E et al. 2018. High risk and probability of progression to osteoporosis at 10 years inHIV-infected individualsJ Antimicrob Chemother 2018; 73:2452–9.
4. BHIVA guidelines on the routine investigation and monitoring of HIV-1 positive adults 2019. Available at https://www.bhiva.org/monitoring-guidelines. Accessed online 08.03.22

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Current guidelines

- Current BHIVA[1], EACS[2] and DHSS[3] guidelines now have menopause sections
- British Menopause Society (BMS) [4] fact sheet
- BHIVA recommendations
  - Baseline and thereafter annual assessment of menstrual pattern
  - Proactive questions around menopausal symptoms in women > 45 years
  - Screening for bone health
  - Use of HRT and vaginal oestrogen for symptoms as recommended by NICE
  - Recommended use of transdermal HRT
  - Caution with ART drug interactions
  - Signposting to information about menopause for patients

1. BHIVA guidelines for the treatment of HIV-1-positive adults with antiretroviral therapy 2015 (2016 interim update). Available online at https://www.bhiva.org/file/RVYKzFwyxpgiI/treatment-guidelines-2016-interim-update.pdf. Accessed 08.03.22.
2. EACS guidelines Version 11.0 October 2021. Available online at https://www.eacsociety.org/media/final2021eacsguidelinesv11.0_oct2021.pdf. Accessed 08.03.22.
3. DHSS guidelines for the use of Antiretroviral agents in adults and adolescents living with HIV. Available online at https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/women-hiv. Accessed 08.03.22.
4. British menopause society factsheet. HIV and the menopause [2018]. Available online at https://thebms.org.uk/wp-content/uploads/2018/10/BMS-TfC-HIV-and-the-menopause-01B.pdf. Accessed 08.03.22.

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HRT for WWH

- No studies evaluating use of HRT in WWH
- Low usage compared with general population[1]
- Concerns about increased pill burden and side effects[2]
- Lack of knowledge about menopause and HRT[1]
- Stigma of menopause and HRT rarely discussed in non-white communities[2]
- Drug interactions and impact on hormone levels
- Implications of changing ART regimen

I don't want to take anything else [menopausal hormone therapy].
I don't want to be a slave to something else.

1. Okhai H et al. 2021. Menopausal status, age and management among women living with HIV in the UK HIV Medicine. 2021;22:834–842
2. Tariq S et al. 2018. Menopause in women living with HIV in England: findings from the PRIME Study.

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Approach to managing menopause in WWH

- Ask about menstrual pattern and any menopausal symptoms
- Assess risk of other comorbidities (QRISK, FRAX, BP, BMI, smoking, alcohol use)
- Assess ART (reduction in risk of CVD, bone disease, drug interactions)
- Inform about menopause
- Discuss different management options
- Signpost to information:
  - www.womens-health-concern.org
  - Balance app
  - https://www.newsonhealth.co.uk/resources/#factsheets
  - Shades of menopause (Instagram)

Summary

- WWH are ageing with > 1/3 over 50 years
- Possibly earlier menopause in WWH and higher rates of early and premature menopause
- Increased risk of other comorbidities associated with ageing
- Limited research investigating WWH with menopause, including use of HRT with many unknowns
- Don’t forget to ask about menstrual pattern and menopausal symptoms
- Think about comorbidities and need to modify ART or reduce drug–drug interactions
- Signpost to information

Healthy LIVing
Quality of life with HIV webinar series

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