Exploring menopausal care integration for older women living with HIV in southwestern Uganda

1. Background: In 2022, Africa had over 11 million women living with HIV(WLH).¹ Of these, 23% (2.53 million) were aged 50 or older² and experiencing menopause, a natural menstrual cessation, typically between 45 and 55 years.³⁻⁶ Most women, 80%, experience disruptive menopausal symptoms, such as hot flashes⁷⁻⁹, but about 15% receive crucial treatment like hormonal- or psycho-therapy.¹⁰ Evidence suggests that WLH experience menopause earlier^{11,12} with more frequent symptoms than peers without HIV.¹²⁻¹⁴ Stigma, limited awareness, and communication gaps between clinicians and WLH hinder menopausal care access,¹⁵⁻¹⁹ yet severe symptoms can lower retention in HIV care and medication adherence.²⁰⁻²⁴

African descent is linked to longer menopausal transition (median 10.1 vs. 4.5 years).^{12,25,26} <u>However,</u> in Africa, including Uganda, menopausal care is understudied and suboptimal despite a growing aging WLH population and the potential for severe symptoms to disrupt HIV care. ^{6,21,27} Thus, there is a critical need to train local researchers to bridge this gap. As HIV programs integrate the reproductive health care of younger women, such as contraceptives and prenatal care²⁸, <u>the unmet needs of older women</u>, including menopausal <u>care, persist.</u> ^{6,10,16} Addressing these critical research and practice gaps can significantly improve the lives of older WLH in Africa by enhancing HIV treatment outcomes, integrating culturally appropriate menopausal care, and informing future research across the lifespan of WLH.

2. Aims and approach: I propose an innovative mixed-methods study to explore menopausal care integration for <u>older WLH aged 45-60 years</u> attending high-volume HIV clinics at Masaka and Mbarara regional referral hospitals in Uganda. I will describe menopause symptoms and care and use the comprehensive "PRECEDE" framework²⁹ to map <u>predisposing</u>, reinforcing, and enabling factors influencing menopausal care integration into HIV services (excluding WLH on hormonal therapy or had oophorectomy or currently pregnant). I will then use a <u>human-centered design (HCD)</u> approach³⁰ to develop and refine an integrated menopausal care model that is contextually fit while meeting the WLH's needs and preferences.

<u>Aim 1. To determine the proportion of older WLH with severe menopausal symptoms and those treated</u>. Using an interviewer-administered questionnaire and medical records³¹, I will collect cross-sectional data on clinical, sociodemographic, and treatment outcomes on a clustered random sample of WLH(N=428). I will use self-reported menstrual patterns to determine and stage menopausal status per the standard "stages of reproductive aging workshop (STRAW+10)" criteria^{7,32} and the menopausal rating scale³³ to assess and categorize menopausal symptoms. Self-reported symptom treatment will be considered. I will first calculate the percentages of WLH with severe menopausal symptoms and those treated and then use logistic regression to identify sociodemographic and clinical factors associated with severe symptoms.

<u>Aim 2.</u> To explore WLH and clinicians' perspectives on menopausal care integration into HIV services. Using purposive sampling, I will conduct i) four focus group discussions (2 per site) with mixed pre-, peri- and postmenopausal WLH^{7,32}, ii) in-depth interviews with HIV clinicians (n=6) balanced by cadre, and iii) key informant interviews with gynecologists (n=2) and clinic managers (n=2). Semi-structured interview guides will follow "PRECEDE" model constructs. I will use Atlas ti software to code and analyze data using thematic analysis. <u>Aim 3: To develop a culturally relevant menopausal care integration model using the HCD approach.</u> Building on the results of Aim 2, I will conduct four multiday HCD workshops to brainstorm and develop innovative solutions for the integrated model. Each site group will comprise purposively sampled gynecologists (n=2), WLH(n=10), and HIV clinicians(n=8) balanced by cadre. We will create prototypes outlining potential care pathways and iteratively refine prototypes using feedback from WLH and providers.

3. Study team: <u>Ugandan mentor Prof Moses Kamya</u> is a respected HIV researcher with 25+ years of experience, 400+ publications, and 50+ supervised graduates. He heads the host institution whose resources and partnerships will support this project. <u>US-based mentor</u>, <u>Prof Alison El Ayadi</u>, is an expert in HIV and women's health. <u>The trainee</u>, <u>Dr Owaraganise</u>, will leverage 10+ years of HIV research expertise and gynecology training to implement this study. <u>Mentorship plan</u>: I will meet mentors at least biweekly in person and virtually to set goals, address challenges, and track progress from study design and implementation to results dissemination. Attend short mixed methods course, University of Antwerp. Details are in bio-sketches.

4. Future directions: Ultimately, findings will inform a future K43 grant proposal to test menopausal care integration strategies within HIV differentiated care for the expanding population of older WLH in Africa.

5. Significance: This study will bridge critical data and practice gaps on menopausal care for older WLH in Uganda and strengthen local research capacity to improve their health outcomes.

6. Work plan: Year 1: Engage stakeholders, prepare study sites, secure protocol approvals, implement Aims 1 and 2, attend a six-week Fall 2025 mixed methods course, and submit a progress report and year two requisition. Year 2: Implement Aim 3, analyze data and disseminate results, develop a K43 proposal, submit manuscripts, and final report.

References:

1. UNAIDS. Fact Sheet UNAIDS Global HIV Statistics. 2023.

https://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf (accessed May 23 2024).

2. Barr E, Marshall LJ, Collins LF, et al. Centering the health of women across the HIV research continuum. *The Lancet HIV* 2024; **11**(3): e186-e94.

3. UNAIDS. The Gap Report 2014: People aged 50 years and older. 2014.

https://www.unaids.org/sites/default/files/media_asset/12_Peopleaged50yearsandolder.pdf (accessed 31 May 2024).

4. WHO. Menopause Key Facts. 2022. https://www.who.int/news-room/fact-

<u>sheets/detail/menopause#:~:text=Most%20women%20experience%20menopause%20between,changes%20in%20t</u> <u>he%20menstrual%20cycle</u>.

5. WHO. Research on the menopause in the 1990s: report of a WHO scientific group: World Health Organization; 1996.

6. NIH. Health of Women of Understudied, Underrepresented, and Underreported (U3) Populations Data Book. Fifth Edition ed: Office of Research on Women's Health Office of the Director; 2024.

7. Harlow S, Gass M, Hall J, et al. TJ De Villiers Executive summary of the Stages of Reproductive Aging Workshop+ 10: Addressing the unfinished agenda of staging reproductive aging., 2012, 19. DOI: <u>https://doi</u> org/101097/gme 0b013e31824d8f40 PMID: <u>https://www</u> ncbi nlm nih gov/pubmed/22343510: 387-95.

8. Minkin MJ, Reiter S, Maamari R. Prevalence of postmenopausal symptoms in North America and Europe. *Menopause* 2015; **22**(11): 1231-8.

9. Okhai H, Sabin C, Haag K, et al. The prevalence and patterns of menopausal symptoms in women living with HIV. *AIDS and Behavior* 2022; **26**(11): 3679-87.

10. Davis SR, Pinkerton J, Santoro N, Simoncini T. Menopause—Biology, consequences, supportive care, and therapeutic options. *Cell* 2023; **186**(19): 4038-58.

11. Conde DM, Pinto-Neto AM, Costa-Paiva L. Age at menopause of HIV-infected women: a review. *Gynecological Endocrinology* 2008; **24**(2): 84-6.

12. Hachfeld A, Atkinson A, Stute P, et al. Women with HIV transitioning through menopause: Insights from the Swiss HIV Cohort Study (SHCS). *HIV medicine* 2022; **23**(4): 417-25.

13. Ferreira CE, Pinto-Neto AM, Conde DM, Costa-Paiva L, Morais SS, Magalhães J. Menopause symptoms in women infected with HIV: prevalence and associated factors. *Gynecological Endocrinology* 2007; **23**(4): 198-205.

14. Gold EB. The timing of the age at which natural menopause occurs. *Obstetrics and Gynecology Clinics* 2011; **38**(3): 425-40.

15. Kingsberg SA, Schaffir J, Faught BM, et al. Female sexual health: Barriers to optimal outcomes and a roadmap for improved patient–clinician communications. *Journal of women's health* 2019; **28**(4): 432-43.

16. Caixas U, Tariq S, Morello J, et al. Comorbidities and menopause assessment in women living with HIV: a survey of healthcare providers across the WHO European region. *AIDS care* 2024; **36**(1): 107-14.

17. Nappi RE, Kokot-Kierepa M. Women's voices in the menopause: results from an international survey on vaginal atrophy. *Maturitas* 2010; **67**(3): 233-8.

18. Reynolds Z, Gilbert R, Sentongo R, et al. Priorities for health and wellbeing for older people with and without HIV in Uganda: a qualitative methods study. *Journal of the International AIDS Society* 2022; **25**: e26000.

19. Swaminathan A, Lepping P, Kumar G. Menopause and mental health. *The Obstetrician & Gynaecologist* 2023; **25**(3): 229-38.

20. Dragovic B, Rymer J, Nwokolo N. Menopause care in women living with HIV in the UK-A review. *Journal of Virus Eradication* 2022; **8**(1): 100064.

21. Cutimanco-Pacheco V, Arriola-Montenegro J, Mezones-Holguin E, et al. Menopausal symptoms are associated with non-adherence to highly active antiretroviral therapy in human immunodeficiency virus-infected middle-aged women. *Climacteric* 2020; **23**(3): 229-36.

Nudy M, Aragaki AK, Jiang X, et al. The severity of individual menopausal symptoms, cardiovascular disease, and all-cause mortality in the Women's Health Initiative Observational Cohort. *Menopause* 2022; 29(12): 1365-74.
Maki PM, Springer G, Anastos K, et al. Cognitive changes during the menopausal transition: a longitudinal study in women with and without HIV. *Menopause* 2021; 28(4): 360-8.

24. Solomon D, Sabin CA, Burns F, et al. The association between severe menopausal symptoms and engagement with HIV care and treatment in women living with HIV. *AIDS care* 2021; **33**(1): 101-8.

25. Avis NE, Crawford SL, Greendale G, et al. Duration of menopausal vasomotor symptoms over the menopause transition. *JAMA internal medicine* 2015; **175**(4): 531-9.

26. Lewis Johnson T, Rowland LM, Ashraf MS, et al. Key Findings from Mental Health Research During the Menopause Transition for Racially and Ethnically Minoritized Women Living in the United States: A Scoping Review. *Journal of Women's Health* 2024; **33**(2): 113-31.

27. Abelman R, Tien PC. The reproductive transition: effects on viral replication, immune activation, and metabolism in women with HIV infection. *Current HIV/AIDS Reports* 2022: 1-7.

28. Kangudie DM, Guidigbi H, Mensah S, Bala AA, Delate R. Effective integration of sexual reproductive health and HIV prevention, treatment, and care services across sub-Saharan Africa: where is the evidence for program implementation? *Reproductive health* 2019; **16**(Suppl 1): 56.

29. Aboumatar H, Ristaino P, Davis RO, et al. Infection prevention promotion program based on the PRECEDE model: improving hand hygiene behaviors among healthcare personnel. *Infection Control & Hospital Epidemiology* 2012; **33**(2): 144-51.

30. Mukherjee TI, Zerbe A, Falcao J, et al. Human-centered design for public health innovation: Codesigning a multicomponent intervention to support youth across the HIV Care Continuum in Mozambique. *Global Health: Science and Practice* 2022; **10**(2).

31. Uganda M. CONSOLIDATED GUIDELINES FOR THE PREVENTION AND TREATMENT OF HIV AND AIDS IN UGANDA. 2022; **November 2022**: 380.

32. Ambikairajah A, Walsh E, Cherbuin N. A review of menopause nomenclature. *Reproductive health* 2022; **19**(1): 29.

33. Heinemann K, Ruebig A, Potthoff P, et al. The Menopause Rating Scale (MRS) scale: a methodological review. *Health and Quality of life Outcomes* 2004; **2**: 1-8.