Menopause is Associated with Faster Increases in Insulin Resistance in Women with HIV

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BACKGROUND

- Women with HIV (WWH) are at increased risk for developing diabetes compared to women without HIV (WWOH).
- Menopause in WWOH is associated with metabolic changes that increase diabetes risk.
- We previously found that switching to an integrase strand transfer inhibitor (INSTI) during late perimenopause and menopause is associated with faster increases in waist circumference and BMI when compared to WWOH and WWH who did not switch.
- Objective: Determine whether HIV and menopause are associated with faster increases in insulin resistance and whether switching to an INSTI modifies this association.

METHODS

- **Study population:** 389 non-pregnant WWH with viral suppression and 334 WWOH from the Women's Interagency HIV Study between 2006-2019.
- Participants were WWH who switched to an INSTI (INSTI+), WWH who did not switch (INSTI-), and WWOH from a similar time window, or index visit.
- **Exclusion criteria:** 1) Women with a history of diabetes 2) Women with hepatitis C virus
- **Statistical analysis:** Linear mixed effect models were used to evaluate the change in insulin resistance using log HOMA-IR across five years of follow-up by group and time-varying menopausal phase.
- We then compared trajectories by menopausal phase.
- Menopausal phase (premenopause, early and late perimenopause, and menopause) was determined using anti-Müllerian hormone (AMH), a biomarker of ovarian reserve.

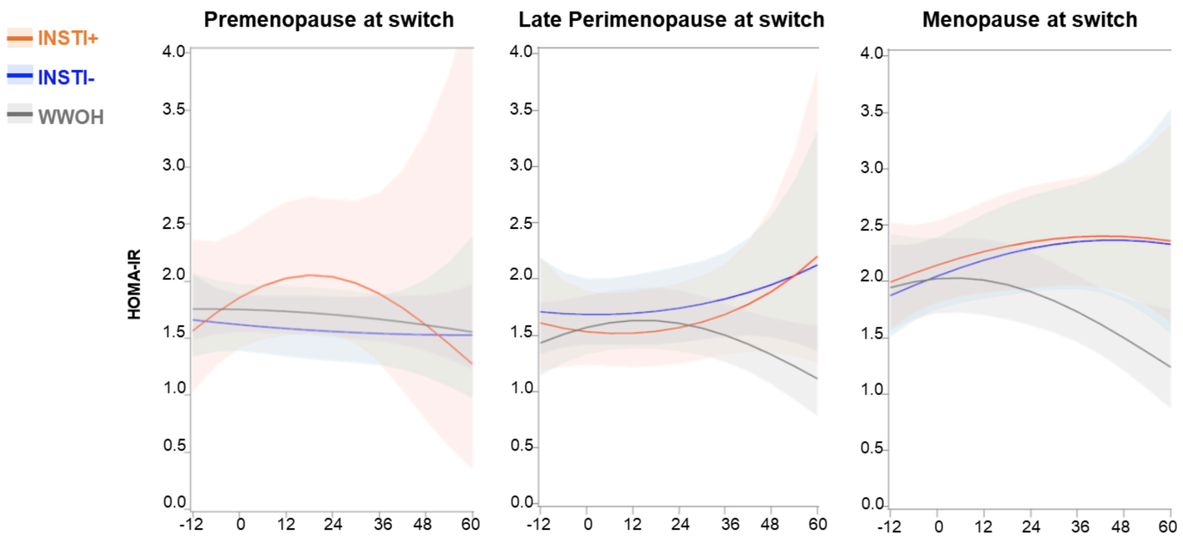
RESULTS

Clinical and demographic characteristics

N (%) or Median (IQR)	INSTI+ (N=133)	INSTI- (N=334)	WWOH (N=256)
Age (y)	50 (43-56)	47 (40-53)	44 (36-51)
Race/Ethnicity			
White	20%	24%	17%
Black	67%	59%	71%
Other	14%	17%	13%
Hispanic	20%	29%	21%
Menopausal status			
Premenopause	23%	37%	49%
Early Perimenopause	6.8%	11%	11%
Late Perimenopause	27%	24%	20%
Menopause	43%	28%	20%
HOMA IR (mg/dL)			
Current Smoking	32%	31%	45%
Chronic Kidney disease	19%	9.9%	7.4%
HIV-related factors	2.05 (1.32-3.68)	1.83 (1.09-3.09)	1.68 (0.96-2.81)
CD4 (cells/mm^3)	715 (554-853)	617 (450-832)	-
Tenofovir disoproxil fumarate (TDF) use	28%	84%	-
Efavirenz use	3%	27%	-

- At the index visit, 40% of the women were premenopausal, 10% were in early perimenopause, 23% were in late perimenopause, and 27% were menopausal.
- WWH were older (48 vs 44) and had a higher median HOMA-IR (2.67 mg/dL vs 2.41 mg/dL) than WWOH.
- Compared to WWOH, WWH in premenopause had a 0.58% faster annual increase in HOMA-IR (95% CI: -5.39, 6.92).
- In contrast, WWH in late perimenopause and menopause had a 4.57% (95% CI: -1.91, 11.47) and 10.16% (95% CI: 3.60, 17.13%) faster annual increase in HOMA-IR, respectively.

HOMA-IR trajectories with 95% confidence intervals by menopausal phase at index visit by INSTI status*



	Premenopause		Late Perimenopause		Menopause	
	% change/yr (95% CI)	p-value	% change/yr (95% CI)	p-value	% change/yr (95% CI)	p-value
INSTI+*year	7.03% (-4.99%, 20.58%)	0.263	4.87% (-3.59%, 14.06%)	0.267	9.18% (1.6%, 17.33%)	**0.017**
INSTI-*year	-1.01% (-7.34%, 5.75%)	0.762	4.38% (-3.1%, 12.44%)	0.258	11.28% (3.27%, 19.91%)	**0.005**
INSTI+ vs INSTI-*year	8.13% (-4.78%, 22.79%)	0.228	0.47% (-8.39%, 10.18%)	0.921	-1.89% (-9.42%, 6.28%)	0.640

**Based on linear mixed effect model adjusted for waist circumference, age, race, site, smoking, drinking, Center for Epidemiologic Studies Depression Scale, chronic kidney disease, and hypertension.*

Women with HIV in late perimenopause and menopause have faster increases in insulin resistance when compared to women without HIV.

CONCLUSIONS

- WWH in late perimenopause and menopause have faster increases in insulin resistance when compared to WWOH, even after adjustment for waist circumference.
- Switching to an INSTI did not further accelerate increases in insulin resistance.
- This suggests there may be an additional mechanism driving insulin resistance in WWH beyond visceral adiposity.
- Our findings support that diabetes screening and prevention in midlife WWH is imperative.

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