Sex hormone binding globulin and type 2 diabetes risk in middle-aged Black South African women living with and without HIV

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Background

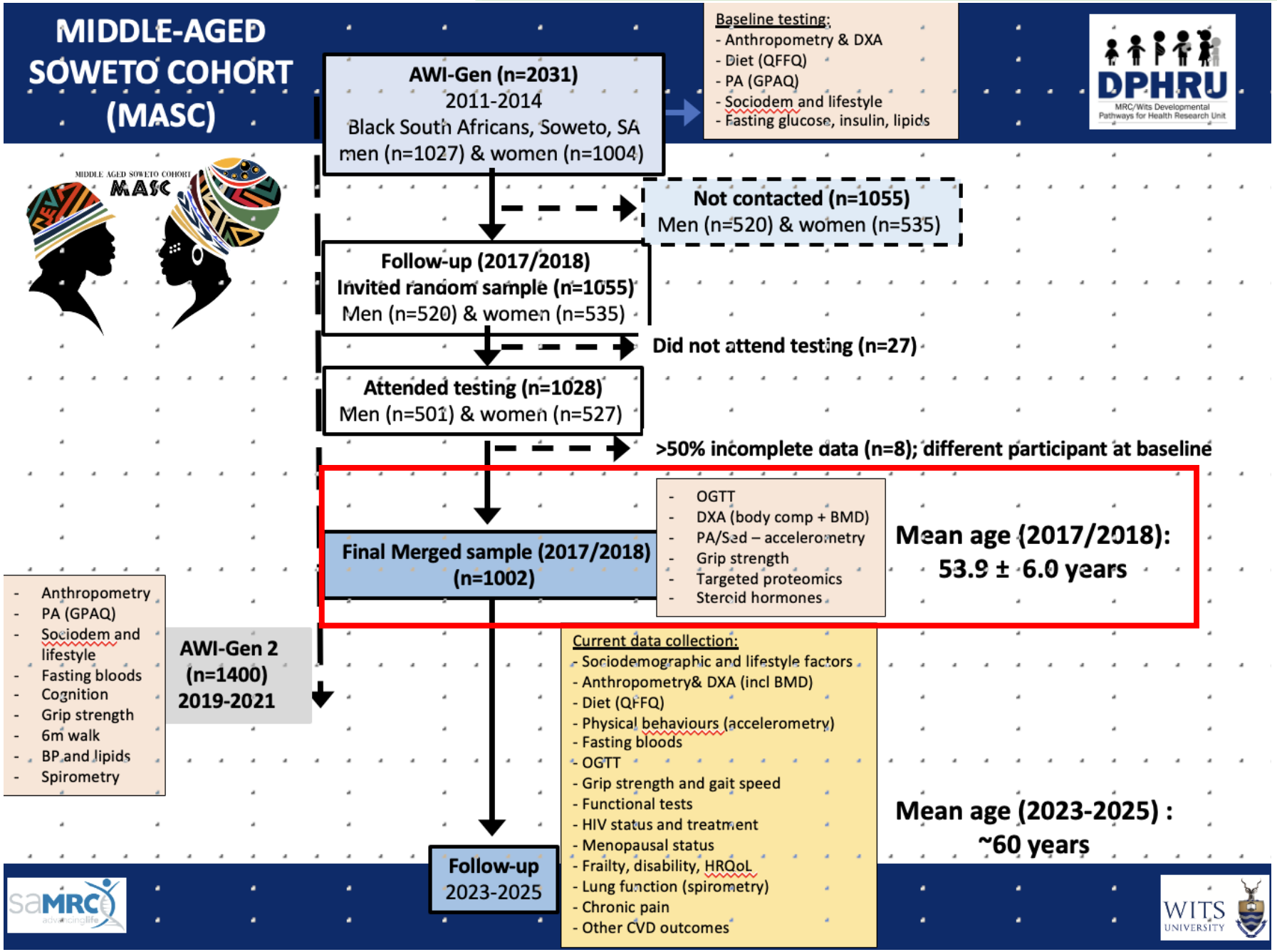
- Type 2 diabetes (T2D) has reached epidemic proportions globally and is associated with obesity and ageing.
- South Africa has the highest number of people living with T2D in SSA
- Women are disproportionately affected by T2D in SA – main drivers being HIV and menopause
- Sex hormones play a critical role in the development and progression of T2D, and are influenced by HIV

Background

- Sex hormone binding globulin (SHBG) is a glycoprotein that regulates sex hormones
- Higher SHBG levels are associated with lower risk for T2D
- US studies have shown that women living with HIV have higher SHBG levels compared to women living without HIV

Aim

To investigate the association between SHBG and T2D in middle-aged Black South African WLWH and WLWOH.



- WLWH and WLWOH
- Dual-energy X-ray absorptiometry was used to determine fat mass
- Fasting bloods and a 2 hour oral glucose tolerance test (OGTT).
- SHBG and sex hormones

- WHO criteria were used to classify participants with normal glucose tolerance (NGT), impaired fasting glucose and impaired glucose tolerance (impaired glucose metabolism, IGM), and T2D.

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Results

	Premenopausal			Postmenopausal		
	WLWOH (n=57)	WLWH (n=24)	P value	WLWOH (n=236)	WLWH (n=44)	P Value
Sociodemographic and lifestyle factors						
Age (years)	48 (46-51)	46 (45-49)	0.065	58 (54-61)	54 (50-59)	<0.001
Housing density (people per room)	1.2 (0.9-1.5)	1.0 (0.8-1.3)	0.271	1.2 (0.8-1.6)	1.1 (0.6-1.6)	0.447
Asset index (% of 12)	75.0 (66.7-83.3)	75.0 (58.3-91.6)	0.664	75.0 (58.3-83.3)	75.0 (58.3-83.3)	0.871
Current smoker (n (%))	7 (12.3)	0	0.079	10 (4.2)	2 (4.5)	0.931
Current alcohol consumer (n(%))	24 (42.1)	13 (54.2)	0.320	53 (22.5)	11 (25.0)	0.712

Results

	Premenopausal			Postmenopausal		
	WLWOH (n=57)	WLWH (n=24)	P value	WLWOH (n=236)	WLWH (n=44)	P value
Body composition						
BMI (kg/m^2)	33.3 (29.4-37.7)	31.6 (26.8-35.7)	0.121	33.1 (29.1-37.8)	33.1 (26.6-36.5)	0.184
Waist (cm)	95.5 (89.6-103.0)	95.5 (77.5-106.0)	0.432	96.5 (89.6-105.6)	96.6 (85.1-103.8)	0.384
Fat mass (%)	43.8 (41.8-46.7)	43.8 (39.0-45.6)	0.364	46.2 (42.2-49.0)	44.3 (38.6-49.3)	0.170
FMI (kg/m^2)	14.2±3.5	12.5±3.7	0.059	14.5±4.3	13.5±4.8	0.151
Leg %FM	44.7±7.1	43.9±7.2	0.681	44.2±6.4	44.1±7.2	0.972
Trunk %FM	42.7±6.3	42.8±6.1	0.924	43.2±6.0	43.2±6.3	0.973

Results

	Premenopausal			Postmenopausal		
	WLWOH (n=52)	WLWH (n=21)	P value	WLWOH (n=225)	WLWH (n=41)	P value
SHBG (nmol/l)	55.4 (43.4-81.7)	64.2 (51.3-111.3)	0.176	50.6 (37.8-65.2)	72.1 (54.2-103.0)	<0.001
Total testosterone (nmol/l)	0.45 (0.25-0.56)	0.24 (0.18-0.34)	0.008	0.35 (0.21-0.57)	0.25 (0.09-0.48)	0.023
Free testosterone (pmol/l)	5.4 (3.5-6.9)	2.5 (1.3-4.3)	0.012	4.8 (2.5-8.0)	2.0 (1.0-3.6)	<0.001
Glycaemic status						
NGT	46 (80.7)	19 (86.4)	0.703	154 (65.8)	34 (77.3)	0.065
IGM	5 (8.8)	2 (9.1)		44 (18.8)	2 (4.5)	
T2D	6 (10.5)	1 (4.5)		36 (15.4)	8 (18.2)	
Dysglycaemia	11 (19.3)	3 (13.6)	0.555	80 (34.2)	10 (22.7)	0.136

Results

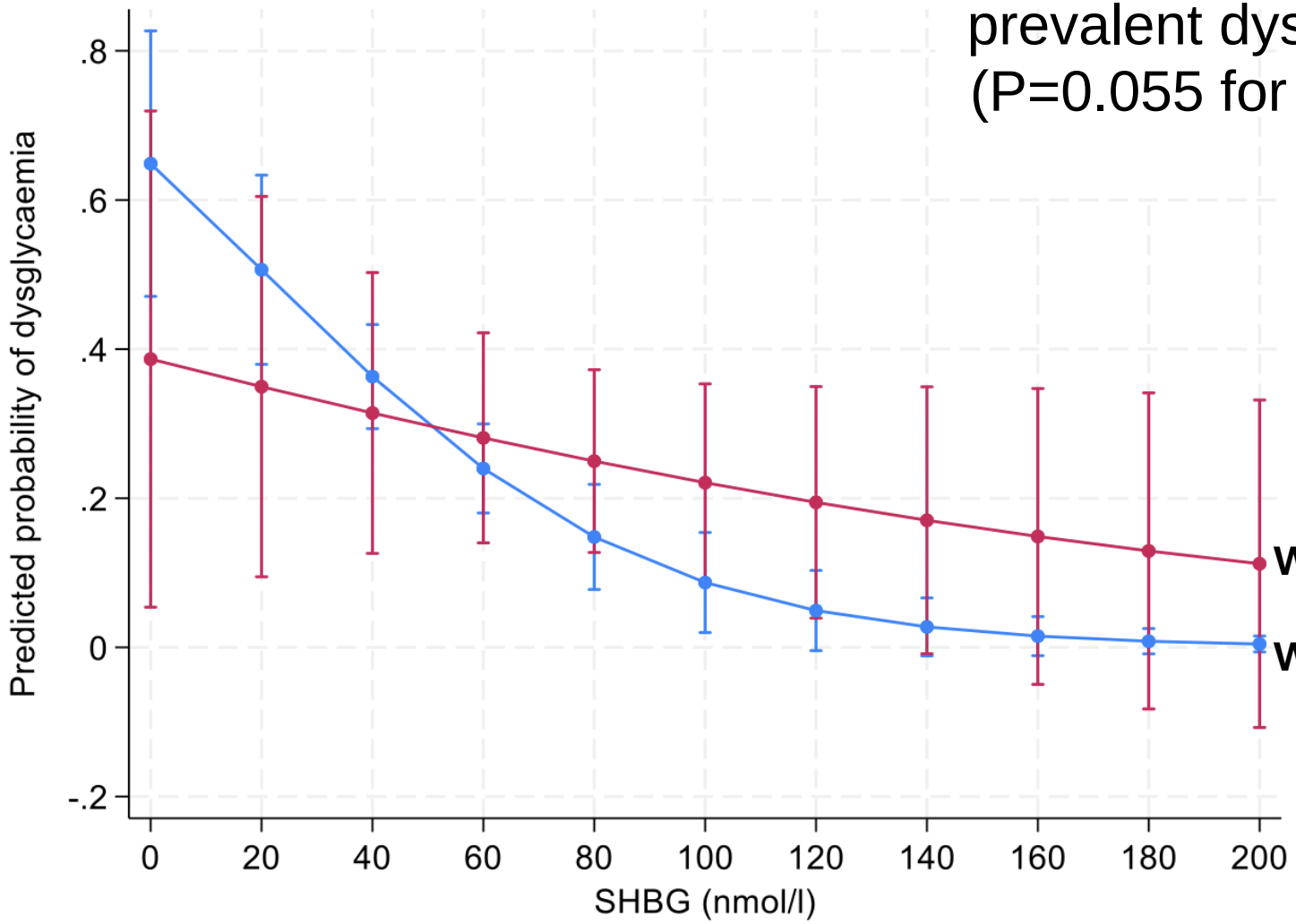
Parameter	SHBG (SD)		Total testosterone (SD)		Free testosterone (SD)	
	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Dysglycaemia	0.44 (0.28 – 0.69)#	<0.001	0.91 (0.66 – 1.24)	0.540	1.02 (0.79 – 1.32)	0.876

Models adjusted for age, fat mass index and HIV status. # SHBG x HIV interaction

Every 1SD higher SHBG was associated with 66% lower odds of presenting with dysglycaemia

Results

The association between SHBG and prevalent dysglycaemia by HIV status (P=0.055 for SHBG x HIV interaction)



WLWH; OR (95% CI): 0.85 (0.46 – 1.55)

WLWOH; OR (95% CI): 0.33 (0.19 – 0.57)

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Conclusion

- This is the first study to report sex hormones in African women over the menopausal transition, how these differ by HIV, and how they associate with prevalent dysglycaemia.
- Although SHBG is higher in WLWH the prevalence of dysglycaemia is not different between HIV groups, and the association between SHBG and dysglycaemia is only significant in WLWOH – so may not confer reduced risk for T2D.
- Further longitudinal research is required to unpack these complex associations and their clinical implications.

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