

TABLE 1 Baseline Characteristics of Study Population by HIV and ART status

	HIV ⁻ (N=807)	HIV ⁺ , ART-naïve (N=125)	HIV ⁺ , first-line ART (N=385)	HIV ⁺ , second-line (N=47)
SOCIO-DEMOGRAPHIC CHARACTERISTICS				
Age in years, median (IQR)	34.0 [24.0, 49.0]	36.0 [30.0, 47.0]	41.0 [36.0, 49.0]	44.0 [39.5, 50.0]
Women	402 (49.8%)	81 (64.8%)	255 (66.2%)	26 (55.3%)
<i>Highest level of education</i>				
None	31 (3.8%)	4 (3.2%)	14 (3.6%)	1 (2.1%)
Primary	137 (17.0%)	33 (26.4%)	87 (22.6%)	14 (29.8%)
Secondary and Matric	555 (68.8%)	78 (62.4%)	262 (68.1%)	27 (57.4%)
College and University	84 (10.4%)	10 (8.0%)	22 (5.7%)	5 (10.6%)
Stable relationship (married, life-partner, cohabiting)	493 (61.1%)	54 (43.2%)	211 (54.8%)	25 (53.2%)
<i>Employment</i>				
Employed	131 (16.2%)	24 (19.2%)	108 (28.1%)	14 (29.8%)
Unemployed	538 (66.7%)	96 (76.8%)	262 (68.1%)	31 (66.0%)
Other (student, disabled, retired, volunteer)	138 (17.1%)	5 (4.0%)	15 (3.9%)	2 (4.3%)
<i>Income per person per month (ZAR) (n=1300)^a</i>				
<648	482 (59.7%)	82 (65.6%)	228 (59.2%)	28 (59.6%)
648-992	65 (8.1%)	10 (8.0%)	35 (9.1%)	3 (6.4%)
>992	221 (27.4%)	27 (21.6%)	105 (27.3%)	14 (29.8%)
BEHAVIOURAL CHARACTERISTICS				
Alcohol use, ever	601 (74.5%)	95 (76.0%)	241 (62.6%)	30 (63.8%)
Alcohol use, past 30 days	319 (39.5%)	43 (34.4%)	101 (26.2%)	16 (34.0%)
<i>Smoking</i>				
Ever	360 (44.6%)	57 (45.6%)	129 (33.5%)	18 (38.3%)
Current	263 (32.6%)	40 (32.0%)	82 (21.3%)	13 (27.7%)
<i>Physical activity, MET-min/week^b</i>				
Low	265 (32.8%)	48 (38.4%)	167 (43.4%)	20 (42.6%)
Moderate	319 (39.5%)	45 (36.0%)	139 (36.1%)	15 (31.9%)
High	223 (27.6%)	32 (25.6%)	79 (20.5%)	12 (25.5%)
CLINICAL CHARACTERISTICS (n=1363)				
BMI, kg/m ² , median (IQR)	23.4 [19.8, 28.7]	22.6 [19.7, 27.3]	23.2 [19.7, 27.3]	22.3 [19.1, 27.2]
Waist circumference, cm	83.1 (13.7)	83.1 (13.4)	85.8 (12.5)	84.0 (12.3)
Waist-to-hip ratio	0.84 (0.09)	0.83 (0.10)	0.86 (0.08)	0.847 (0.10)
Total cholesterol, mmol/L (n=1351)	4.22 (1.03)	3.92 (0.92)	4.43 (0.98)	4.32 (1.09)
HDL-C, mmol/L (n=1351)	1.38 (0.34)	1.28 (0.36)	1.51 (0.41)	1.50 (0.59)
Triglycerides, mmol/L, median (IQR) (n=1351)	0.90 [0.60, 1.33]	0.90 [0.70, 1.20]	1.00 [0.80, 1.50]	1.05 [0.73, 1.48]
Diabetes Mellitus	48 (5.9%)	0 (0%)	15 (3.9%)	3 (6.4%)
Average systolic BP, mmHg ^{c*}	119 (20.8)	117 (18.3)	114 (16.4)	118 (15.0)
Average diastolic BP, mmHg ^{d*}	74.8 (12.4)	75.5 (11.1)	74.4 (10.5)	73.8 (10.9)
Elevated BP ^{e*}	198 (24.5%)	35 (28.0%)	94 (24.4%)	14 (29.8%)
Hypertensive ^{e*}	165 (20.4%)	17 (13.6%)	39 (10.1%)	5 (10.6%)
Family history of hypertension	129 (16.0%)	11 (8.8%)	46 (11.9%)	4 (8.5%)
Use of BP medication	75 (9.3%)	7 (5.6%)	13 (3.4%)	4 (8.5%)

^aLower bound poverty line: <648 ZAR, upper bound poverty line: >992 ZAR

^bModerate: 1-149 MET minutes per week of combined activity, High: ≥150 MET mins/week

^cElevated BP defined as an average systolic and diastolic BP between 120/80 mmHg and 140/90 mmHg

^dHypertension defined as a systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg or self-reported use of antihypertensives.

Abbreviations: IQR; inter quartile range, HIV; human immunodeficiency virus, ART; antiretroviral therapy, ZAR; South African Rand, MET; metabolic equivalent task, BMI; body mass index, HDL-C; high-density lipoprotein-cholesterol, BP; blood pressure.

Data are expressed as mean (standard deviation) or count (%) unless otherwise specified.

*Indicates imputed values

TABLE 2 HIV-Related Characteristics

	ART-naïve (N=125)	First-line ART (N=385)	Second-line ART (N=47)
Newly Diagnosed (0-8 weeks before enrolment) (n=553)	83 (66.4%)	0	0
Time since HIV diagnosis (months) (n=553)	0 [0, 14.0]	73.0 [36.8, 106]	106 [73.0, 129]
Time on ART at enrolment (months)	-	60.0 [23.0, 98.0]	103 [58.5, 123]
Of which time on second-line ART	-	-	35.0 [19.5, 49.0]
CD4+ cell count, cells/mm³ (n=547)			
<200	21 (16.8%)	22 (5.7%)	4 (8.5%)
200-350	28 (22.4%)	61 (15.8%)	7 (14.9%)
>350	73 (58.4%)	296 (76.9%)	35 (74.5%)
Viral Load, cp/mL (n=548)			
<50	23 (18.4%)	310 (80.5%)	26 (55.3%)
50-1000	18 (14.4%)	32 (8.3%)	10 (21.3%)
>1000	81 (64.8%)	38 (9.9%)	10 (21.3%)

Data are expressed as median (interquartile range) or count (percentage).

Abbreviations: HIV; human immunodeficiency virus, ART; antiretroviral therapy.

TABLE 3 Estimates of Fixed Effects for the Association of Mean Systolic and Diastolic BP and HIV Status

		Systolic BP		Diastolic BP	
		β (95% CI)	P Value	β (95% CI)	P Value
Model 1: Unadjusted Crude Model					
Clinic Visit	Baseline	REF	REF	REF	REF
	24 Months	7.00 [5.23—8.78]	<0.001	5.87 [4.67—7.08]	<0.001
	36 Months	7.21 [6.07—8.36]	<0.001	7.11 [6.32—7.90]	<0.001
HIV Positive		-6.92 [-8.97—-4.88]	<0.001	-2.17 [-3.41—-0.92]	<0.001
Model 2: Model 1 + age and sex					
Clinic Visit	Baseline	REF	REF	REF	REF
	24 Months	5.52 [3.76—7.28]	<0.001	5.22 [4.03—6.41]	<0.001
	36 Months	5.31 [4.15—6.47]	<0.001	6.12 [5.33—6.93]	<0.001
HIV Positive		-8.85 [-10.77—-6.92]	<0.001	-3.27 [-4.47—-2.07]	<0.001
Age		0.61 [0.54—0.69]	<0.001	0.33 [0.29—0.38]	<0.001
Male		3.45 [1.51—5.38]	<0.001	1.24 [0.04—2.43]	0.043
Model 3					
Clinic Visit	Baseline	REF	REF	REF	REF
	24 Months	6.75 [4.42—9.08]	<0.001	6.09 [4.51—7.68]	<0.001
	36 Months	6.27 [4.87—7.68]	<0.001	6.48 [5.50—7.45]	<0.001
HIV Positive		-4.26 [-6.71—-1.80]	<0.001	-0.91 [-2.51—0.70]	0.269
Age		0.52 [0.45—0.59]	<0.001	0.28 [0.24—0.33]	<0.001
Male		8.38 [6.31—10.46]	<0.001	3.74 [2.44—5.04]	<0.001
BMI (kg/m²)		1.01 [0.87—1.56]	<0.001	0.58 [0.48—0.67]	<0.001
Consumed alcohol in the last 30 days		2.82 [1.21—4.43]	<0.001	2.31 [1.25—3.38]	<0.001
Use of BP medication		3.03 [0.59—5.48]	0.015	1.64 [0.03—3.26]	0.046
HIV Positive * Baseline		REF		REF	
HIV Positive * 24 Months		-4.40 [-7.87—-0.93]	0.013	-2.50 [-4.86—-0.14]	0.038
HIV Positive * 36 Months		-3.84 [-6.22—-1.46]	0.002	-1.58 [-3.23—0.07]	0.061

Mixed model with random intercept and uncorrelated residuals based on an available case analysis.

Model 3 adjusted for BMI, clinic visit, HIV status, sex, age, alcohol, and self-reported use of hypertension medication, and an interaction between HIV status and time.

Reference category: HIV uninfected women who have not consumed alcohol in the past 30 day nor are taking medication to treat hypertension.

Abbreviations: CI; confidence interval, HIV; human immunodeficiency virus, BMI; body mass index, BP; blood pressure.

TABLE 4 Estimates of Fixed Effects for the Association of Mean Systolic and Diastolic BP and ART Status

		Systolic BP		Diastolic BP	
		β (95% CI)	P Value	β (95% CI)	P Value
Model 1: Unadjusted Crude Model					
Clinic Visit	Baseline	REF	REF	REF	REF
	24 Months	7.46 [5.64–9.28]	<0.001	6.13 [4.90–7.37]	<0.001
	36 Months	7.43 [6.27–8.59]	<0.001	7.16 [6.36–7.96]	<0.001
ART Status	HIV Negative	REF	REF	REF	REF
	HIV-Positive ART-Naive	-2.17 [-5.74–1.40]	0.233	-0.70 [-2.98–1.57]	0.545
	HIV-Positive on ART	-7.96 [-10.18–-5.75]	<0.001	-2.48 [-3.83–-1.13]	<0.001
Model 2: Model 1 + age and sex					
Clinic Visit	Baseline	REF	REF	REF	REF
	24 Months	6.10 [4.30–7.90]	<0.001	5.57 [4.34–6.78]	<0.001
	36 Months	5.53 [4.36–6.71]	<0.001	6.20 [5.39–7.01]	<0.001
ART Status	HIV Negative	REF	REF	REF	REF
	HIV-Positive ART-Naive	-2.31 [-5.68–1.06]	0.179	-0.66 [-2.83–1.51]	0.549
	HIV-Positive on ART	-10.51 [-12.60–-8.43]	<0.001	-3.95 [-5.25–-2.65]	<0.001
Age		0.63 [0.55–0.70]	<0.001	0.34 [0.29–0.38]	<0.001
Male		3.37 [1.42–5.32]	<0.001	1.17 [0.04–2.39]	0.057
Model 3					
Clinic Visit	Baseline	REF	REF	REF	REF
	24 Months	5.66 [3.90–7.43]	<0.001	5.39 [4.19–6.59]	<0.001
	36 Months	5.20 [4.04–6.36]	<0.001	6.01 [5.21–6.82]	<0.001
ART Status	HIV Negative	REF	REF	REF	REF
	HIV-Positive ART Naive	-1.17 [-4.40–2.06]	0.478	0.02 [-2.06–2.11]	0.427
	HIV-Positive on ART	-8.41 [-10.40–-6.42]	<0.001	-2.71 [-3.96–-1.46]	<0.001
Age		0.53 [0.46–0.61]	<0.001	0.29 [0.24–0.33]	<0.001
Male		8.15 [6.05–10.26]	<0.001	3.67 [2.35–4.99]	<0.001
BMI (kg/m²)		0.99 [0.84–1.14]	<0.001	0.57 [0.48–0.67]	<0.001
Consumed alcohol in the last 30 days		2.92 [1.29–4.56]	<0.001	2.33 [1.25–3.41]	<0.001
Use of BP medication		3.08 [0.59–5.57]	0.016	1.66 [0.02–3.30]	0.048

Mixed model with random intercept and uncorrelated residuals based on an available case analysis.

Model 3 adjusted for BMI, clinic visit, HIV and ART status, sex, age, alcohol, and self-reported use of antihypertensives.

Reference category: HIV uninfected women who have not consumed alcohol in the past 30 day nor are taking medication to treat hypertension.

Abbreviations: ART; antiretroviral therapy, CI; confidence interval, HIV; human immunodeficiency virus, BMI; body mass index, BP; blood pressure.

TABLE 5 Estimates of Fixed Effects for the Association of Mean Systolic and Diastolic Blood Pressure and ART status for Men and Women Separately

		Women				Men			
		Systolic BP		Diastolic BP		Systolic BP		Diastolic BP	
		β (95% CI)	<i>P</i> Value	β (95% CI)	<i>P</i> Value	β (95% CI)	<i>P</i> Value	β (95% CI)	<i>P</i> Value
Clinic Visit	Baseline	REF	REF	REF	REF	REF	REF	REF	REF
	24 Months	4.40 [1.82—6.99]	<0.001	4.82 [3.09—6.55]	<0.001	6.83 [4.37—9.29]	<0.001	6.44 [4.73—8.15]	<0.001
	36 Months	4.58 [3.09—6.07]	<0.001	5.10 [4.09—6.11]	<0.001	6.40 [4.57—8.24]	<0.001	7.66 [6.36—8.96]	<0.001
ART Status	HIV Negative	REF	REF	REF	REF	REF	REF	REF	REF
	HIV-Positive ART Naive	0.44 [-3.57—4.45]	0.829	0.79 [-1.79—3.37]	0.549	-3.31 [-8.78—2.15]	0.236	-1.02 [-4.60—2.56]	0.578
	HIV-Positive on ART	-8.65 [-11.2—-6.08]	<0.001	-3.39 [-5.01—-1.77]	<0.001	-7.27 [-10.37—-4.17]	<0.001	-1.55 [-3.51—0.41]	0.123
Age	0.68 [0.58—0.78]	<0.001	0.31 [0.25—0.38]	<0.001	0.36 [0.26—0.47]	<0.001	0.24 [0.17—0.31]	<0.001	
BMI	0.82 [0.65—0.99]	<0.001	0.51 [0.40—0.62]	<0.001	1.56 [1.26—1.85]	<0.001	0.83 [0.64—1.02]	<0.001	
Consumed alcohol in the last 30 days					4.08 [1.95—6.21]	<0.001	3.00 [1.58—4.43]	<0.001	
Use of BP medication					5.07 [0.53—9.61]	0.029	3.53 [0.50—6.56]	0.023	

Mixed model with random intercept and uncorrelated residuals based on an available case analysis.

Model 3 adjusted for BMI, clinic visit, HIV status, sex, age, alcohol, and self-reported use of hypertension medication, and an interaction between HIV status and time.

Abbreviations: CI; confidence interval, HIV; human immunodeficiency virus, BMI; body mass index, BP; blood pressure.

FIGURE 1 Directed Acyclic Graph for the Relationship between HIV status and Blood Pressure Changes

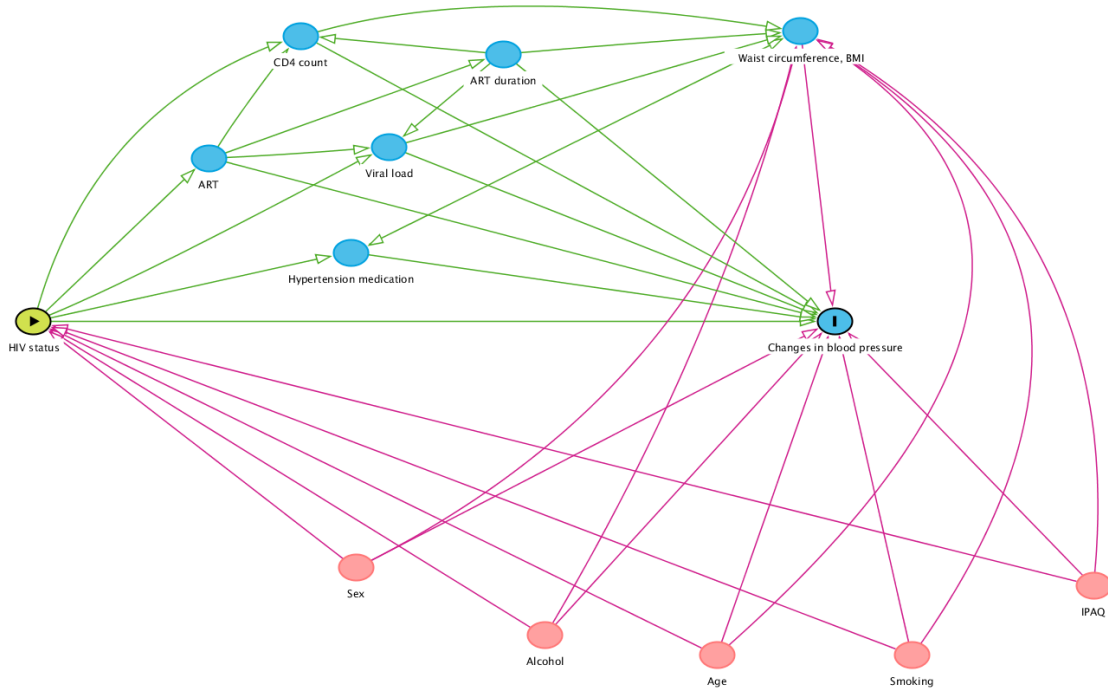


FIGURE 2 Flow Chart for HIV-Positive and HIV-Negative Participant Selection

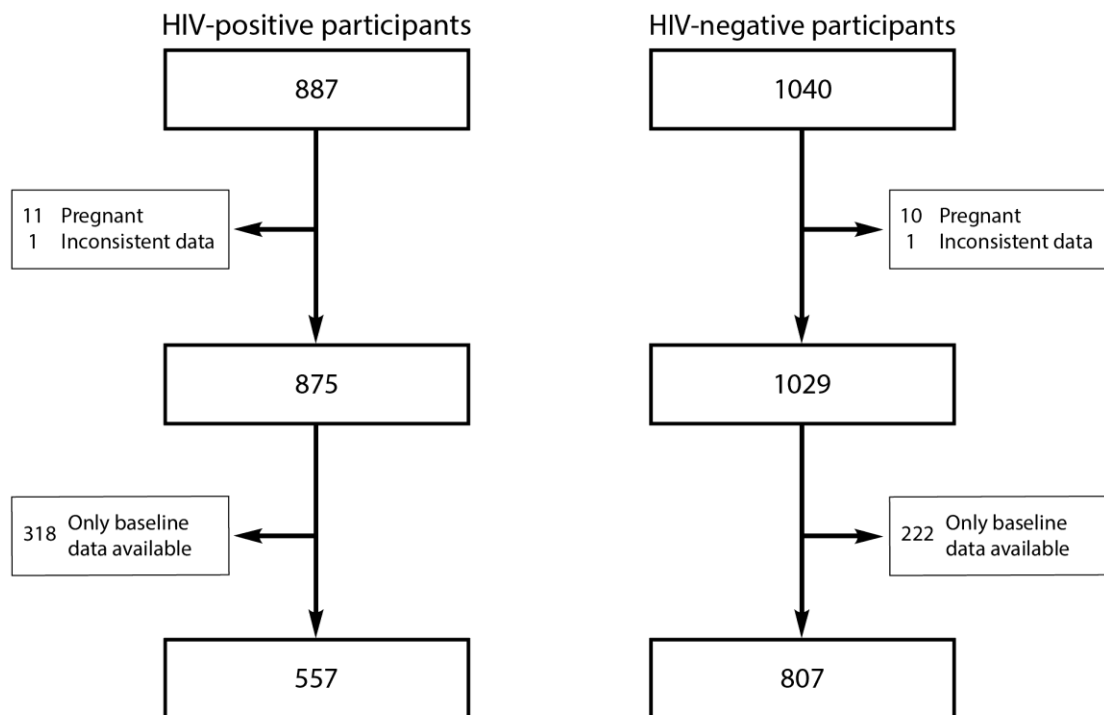
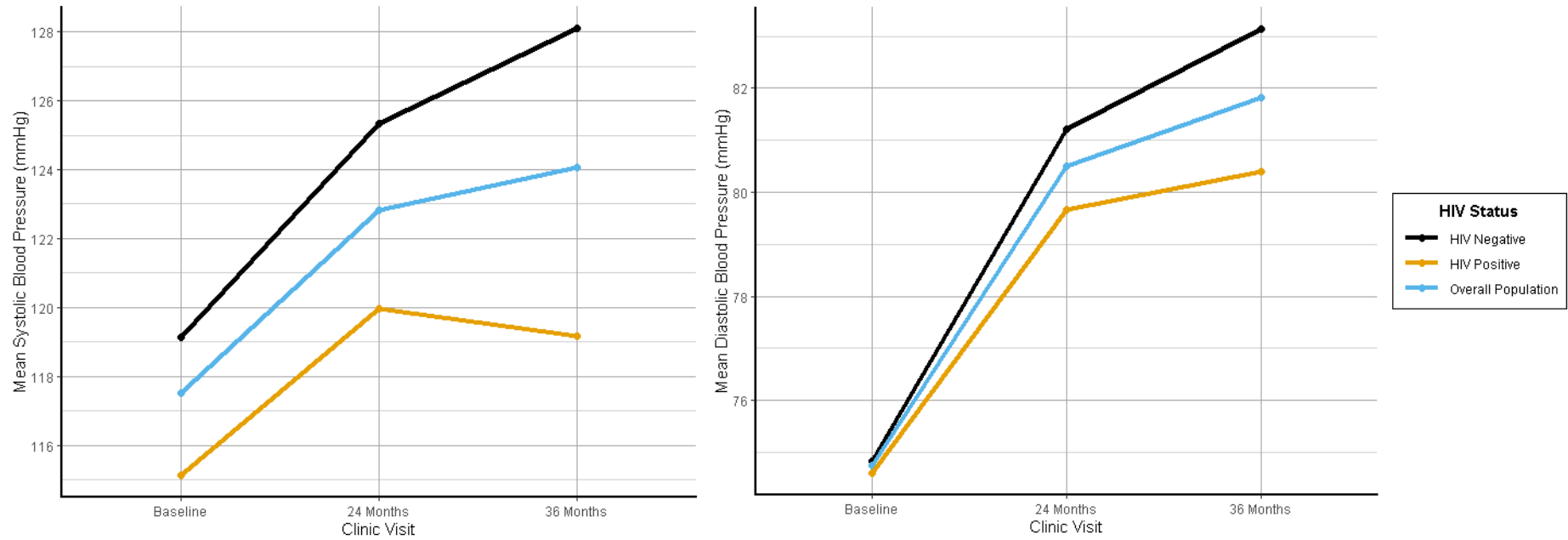


FIGURE 3 Trajectories of Mean Systolic and Diastolic Blood Pressure over 36-Months Follow-up by HIV Status



Abbreviation: HIV; human immunodeficiency virus.

FIGURE 4 Relative percentages of BP categories according to clinic visit

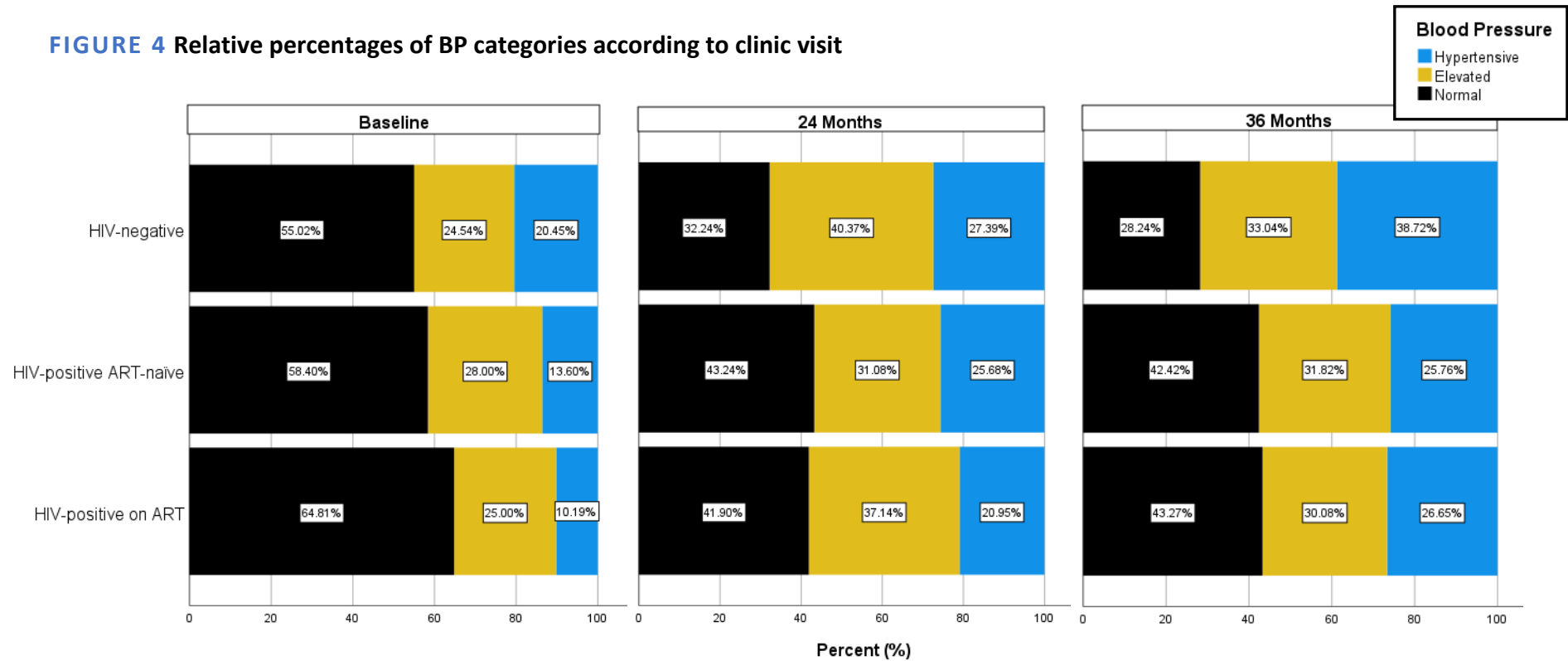


Figure illustrates relative percentages of participants having normal, elevated or hypertensive blood pressure (BP) across 36-months follow-up.

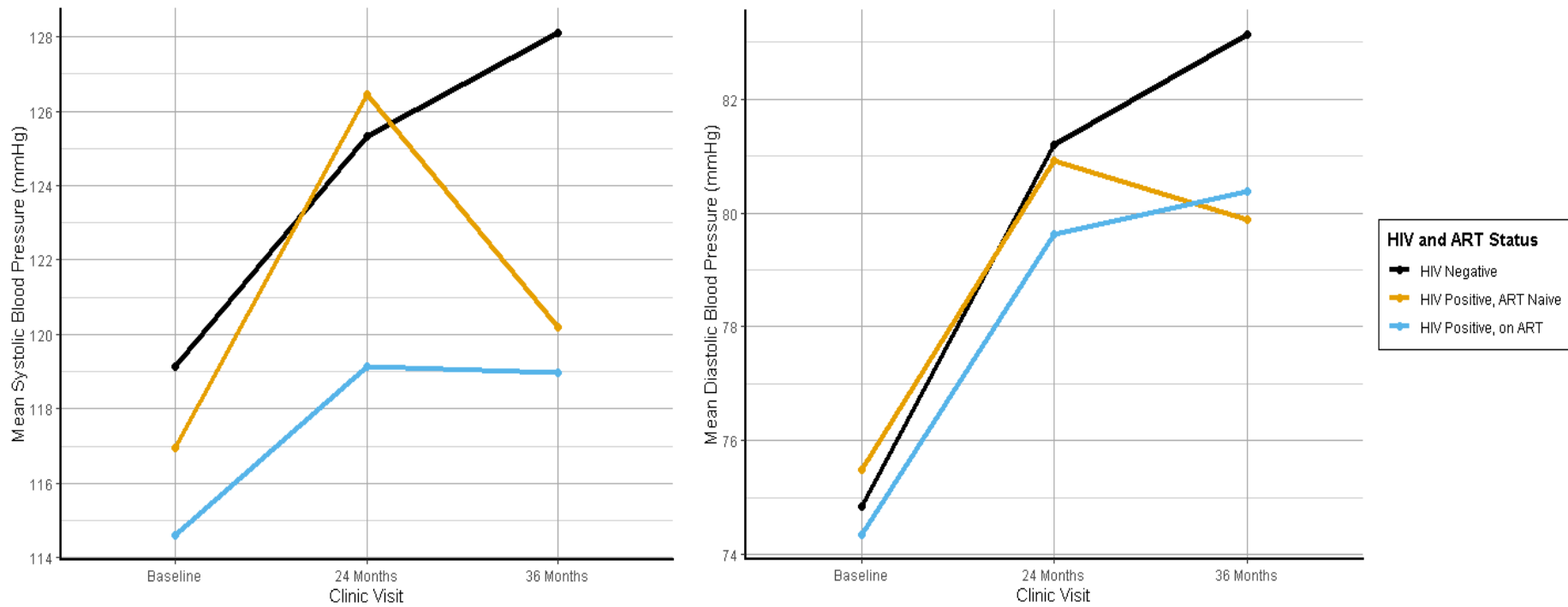
Abbreviations: BP; blood pressure, ART; antiretroviral therapy.

Normal BP was defined as systolic BP <120 mmHg and diastolic BP <80 mmHg. Elevated BP defined as an average systolic and diastolic BP between 120/80 mmHg and 140/90 mmHg.

Hypertension defined as a systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg or self-reported use of hypertension medication.

Based on imputed datasets

FIGURE 5 Mean Systolic and Diastolic Blood Pressure over time by HIV and ART Status



Abbreviations: HIV; human immunodeficiency virus, ART; antiretroviral therapy.

Supplementary Tables and Figures

SUPPLEMENTARY TABLE 1 Comparison of Fixed Effects Estimates for the Association of Mean Systolic and Diastolic Blood Pressure and ART Status: Available Case Analysis vs Pooled Estimates from an Analysis with Multiple Imputation for Missing BP Values

		Available Case Analysis				Analysis with Multiple Imputation (N=20)			
		Systolic BP		Diastolic BP		Systolic BP		Diastolic BP	
		β (95% CI)	SE	β (95% CI)	SE	β (95% CI)	SE	β (95% CI)	SE
Clinic Visit	Baseline	REF	REF	REF	REF	REF	REF	REF	REF
	24 Months	5.66 [3.90—7.43]	0.902***	5.39 [4.19—6.59]	0.613***	3.96 [2.61—5.32]	0.684***	4.99 [4.14—5.83]	0.429***
	36 Months	5.20 [4.04—6.36]	0.594***	6.01 [5.21—6.82]	0.411***	4.38 [3.11—5.64]	0.642***	5.82 [5.02—6.63]	0.409***
ART Status	HIV Negative	REF	REF	REF	REF	REF	REF	REF	REF
	HIV-Positive ART Naive	-1.17 [-4.40—2.06]	1.648	0.02 [-2.06—2.11]	1.065	-0.19 [-3.18—2.80]	1.560	0.71 [-1.30—2.73]	1.018
	HIV-Positive on ART	-8.41 [-10.40—-6.42]	1.016***	-2.71 [-3.96—-1.46]	0.638***	-6.40 [-8.19—-4.60]	0.913***	-1.60 [-2.79—-0.41]	0.603**
Age	0.53 [0.46—0.61]	0.038***	0.29 [0.24—0.33]	0.024***	0.50 [0.43—0.57]	0.035***	0.27 [0.23—0.31]	0.022***	
Male	8.15 [6.05—10.26]	1.075***	3.67 [2.35—4.99]	0.675***	8.48 [6.74—10.21]	0.885***	3.95 [2.79—5.10]	0.587***	
BMI	0.99 [0.84—1.14]	0.076***	0.57 [0.48—0.67]	0.048***	0.88 [0.75—1.02]	0.069***	0.52 [0.43—0.61]	0.045***	
Consumed alcohol in the last 30 days	2.92 [1.29—4.56]	0.836***	2.33 [1.25—3.41]	0.553***	2.49 [1.06—3.93]	0.729***	2.01 [1.02—2.99]	0.499***	
Use of BP medication	3.08 [0.59—5.57]	1.271**	1.66 [0.02—3.30]	0.839*	3.99 [1.59—6.40]	1.221**	1.76 [0.27—3.24]	0.757*	

Abbreviations: CI; confidence interval, SE; standard error, HIV; human immunodeficiency virus, ART; antiretroviral therapy, BMI; body mass index, BP; blood pressure. Reference category: HIV uninfected women who have not consumed alcohol in the past 30 day nor are taking medication to treat hypertension. P-value: statistical significance (0.049–0.01)*; 0.009–0.001**; less than 0.001***

SUPPLEMENTARY TABLE 2 Stepwise Model Selection Comparing Waist Circumference and BMI

	Systolic Blood Pressure		Diastolic Blood Pressure	
	Test Statistic	<i>P</i> Value	Test Statistic	<i>P</i> Value
Model 1	115.82	9.08 x 10 ⁻¹⁴	56.82	3.27 x 10 ⁻¹⁶
Model 2	123.37	8.36 x 10 ⁻¹⁸	33.08	1.94 x 10 ⁻¹¹

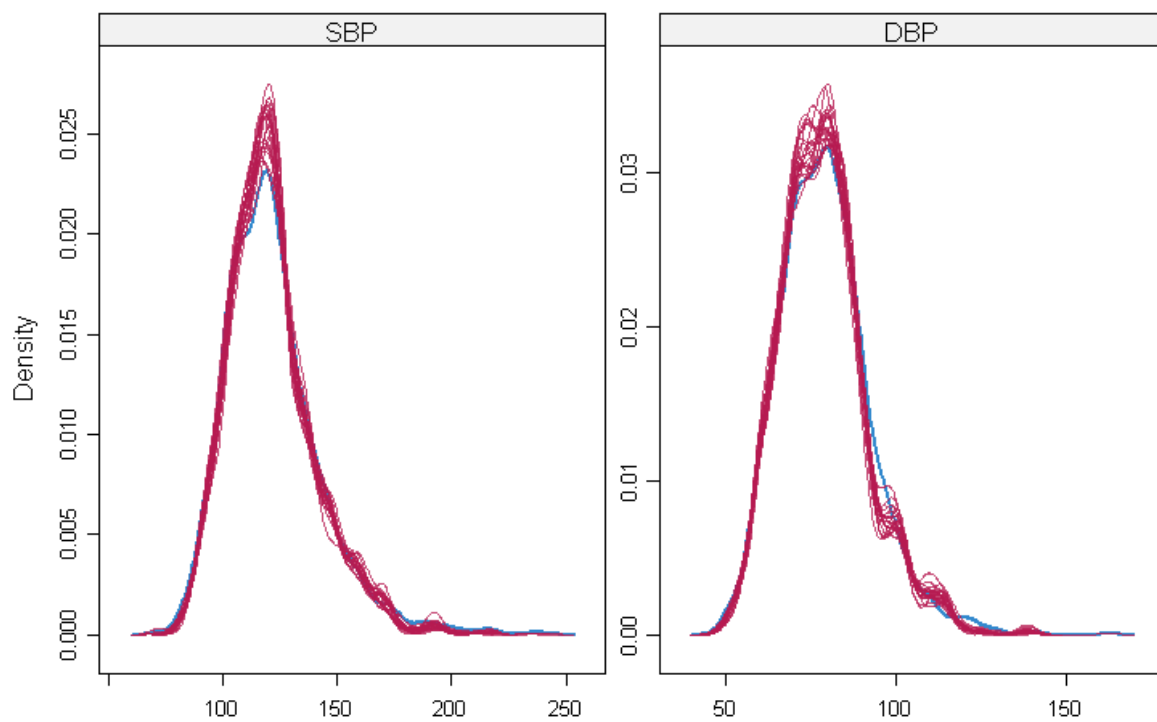
Model 1 adjusted for waist circumference, clinic visit, ART status, sex, age, alcohol and use of antihypertensive medication. Model 2 adjusted for BMI, clinic visit, ART status, sex, age, alcohol and self-reported use of hypertension medication. Both compared to a model adjusted for clinic visit, ART status, sex, age, alcohol and self-reported use of hypertension medication.

Abbreviations: ART; antiretroviral therapy, BMI; body mass index.

SUPPLEMENTARY TABLE 3 Stepwise Model Selection for Systolic BP Comparing Spline term for age

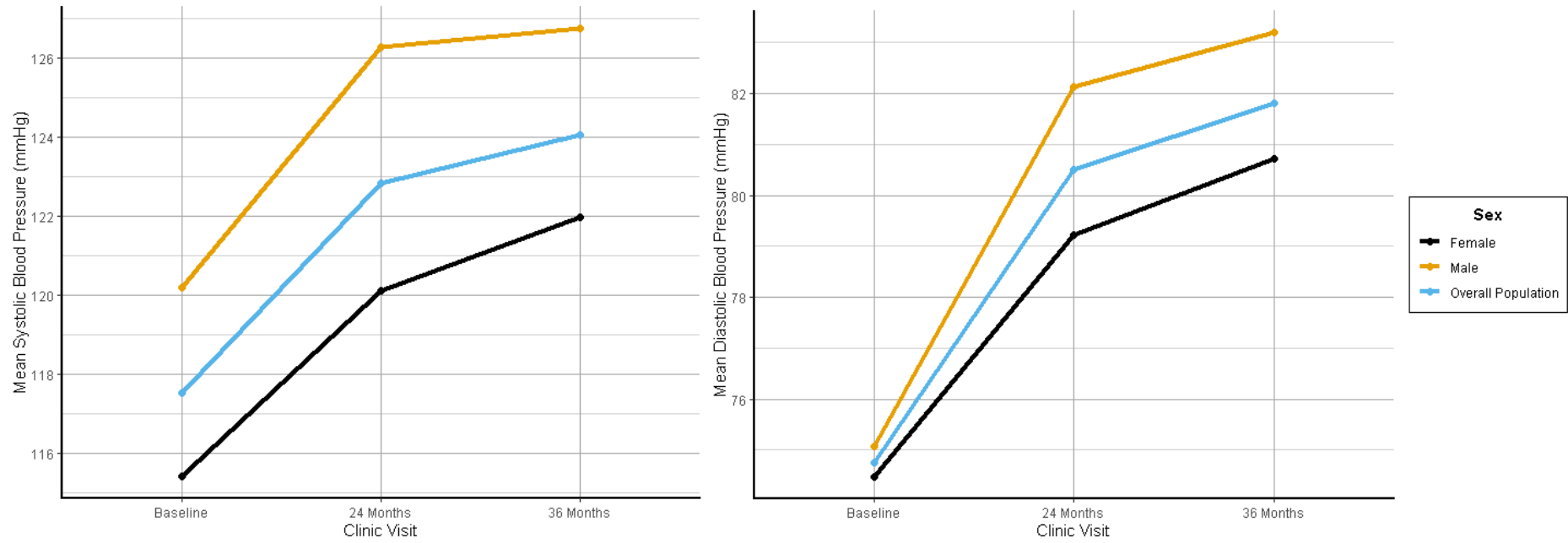
	Likelihood Ratio Test	<i>P</i> Value
Model without spline vs model with spline	20.80	<0.001

SUPPLEMENTARY FIGURE 1 Density plot of 20 Multiple Imputed Datasets for Systolic and Diastolic Blood Pressure



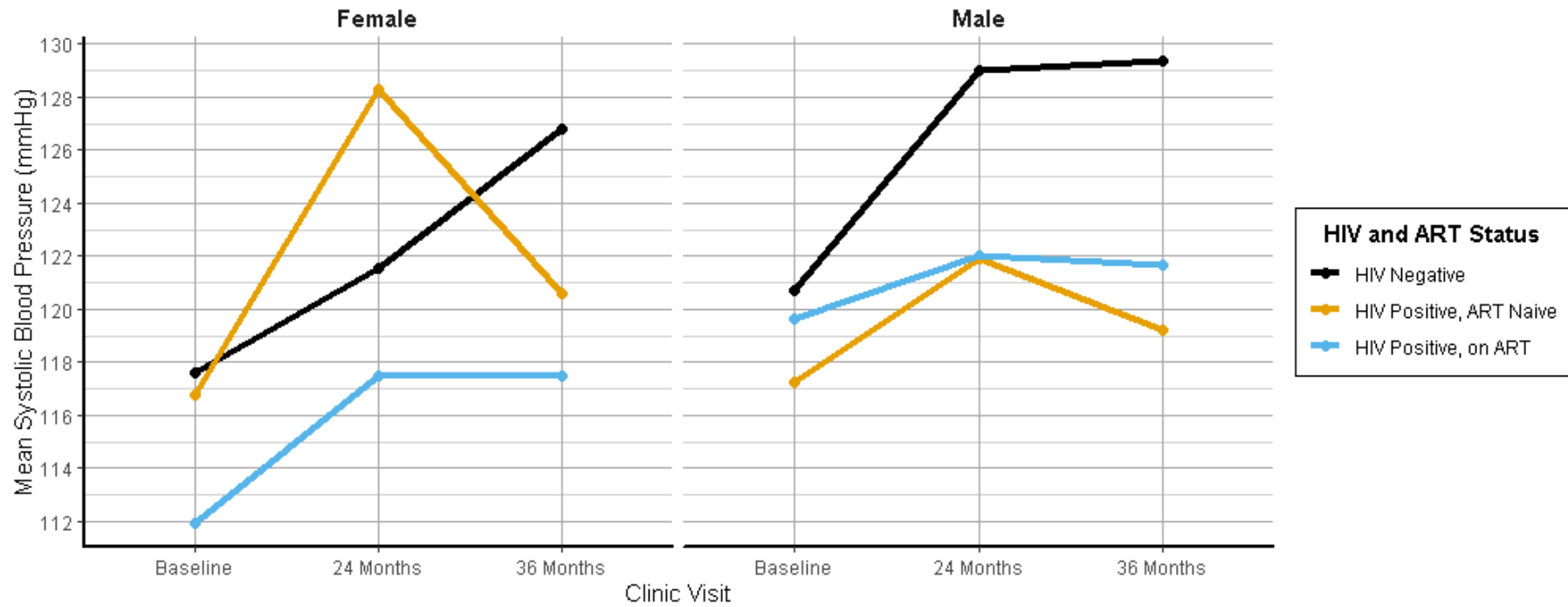
Abbreviations: SBP; systolic blood pressure, DBP; diastolic blood pressure.

SUPPLEMENTARY FIGURE 2 Trajectories of Mean Systolic and Diastolic Blood Pressure over 36 Months Follow-up by Sex



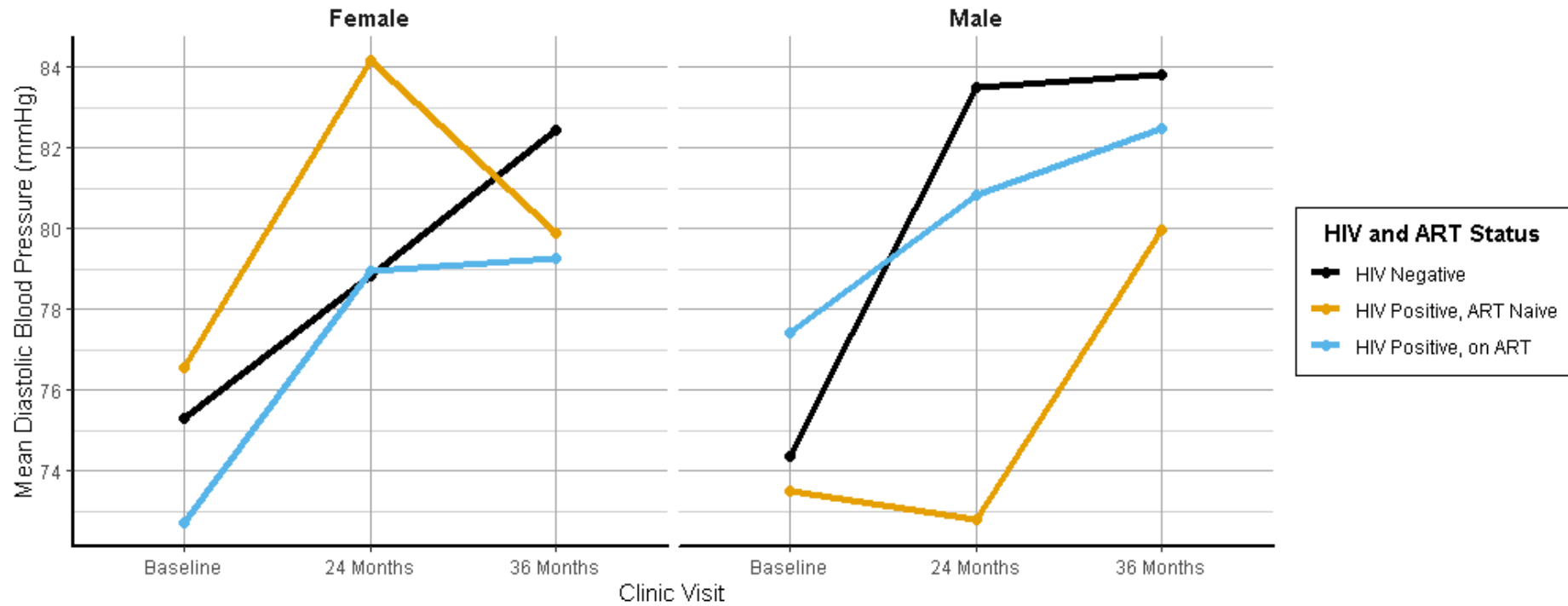
Based on imputed datasets

SUPPLEMENTARY FIGURE 3 Mean Systolic Blood Pressure over time by HIV and ART Status, Stratified by Sex



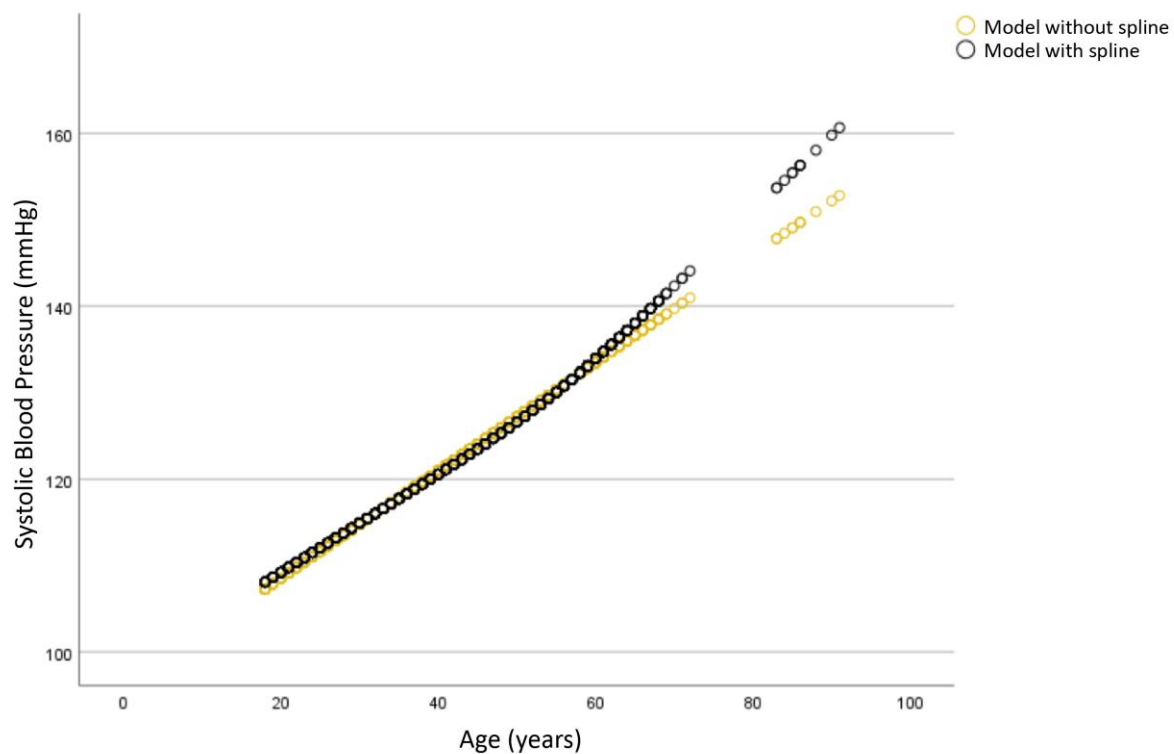
Abbreviations: HIV; human immunodeficiency virus, ART; antiretroviral therapy.
Based on imputed datasets

SUPPLEMENTARY FIGURE 4 Mean Diastolic Blood Pressure over time by HIV and ART Status, Stratified by Sex



Abbreviations: HIV; human immunodeficiency virus, ART; antiretroviral therapy.
Based on imputed datasets

SUPPLEMENTARY FIGURE 5 Comparison of observed vs predicted values for model with and without natural cubic spline for age.



Model with spline shows predicted values of fixed effects for age with 3 knot natural cubic plotted against observed values. Model without spline shows predicted values of fixed effects for age plotted against observed values.