HIV Drug Resistance among virally unsuppressed respondents in the 5th South African National HIV Prevalence, Incidence, Behaviour and Communication Survey, 2017

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Background

- Conducted as part of the 5th South African National HIV Prevalence, Incidence, Behaviour and Communication Survey, 2017
  - Cross-sectional, population-based household survey conducted using a multi-stage stratified cluster random sampling approach
  - Persons of all ages in selected household eligible to participate
  - Questionnaire data
  - Dried blood spot samples

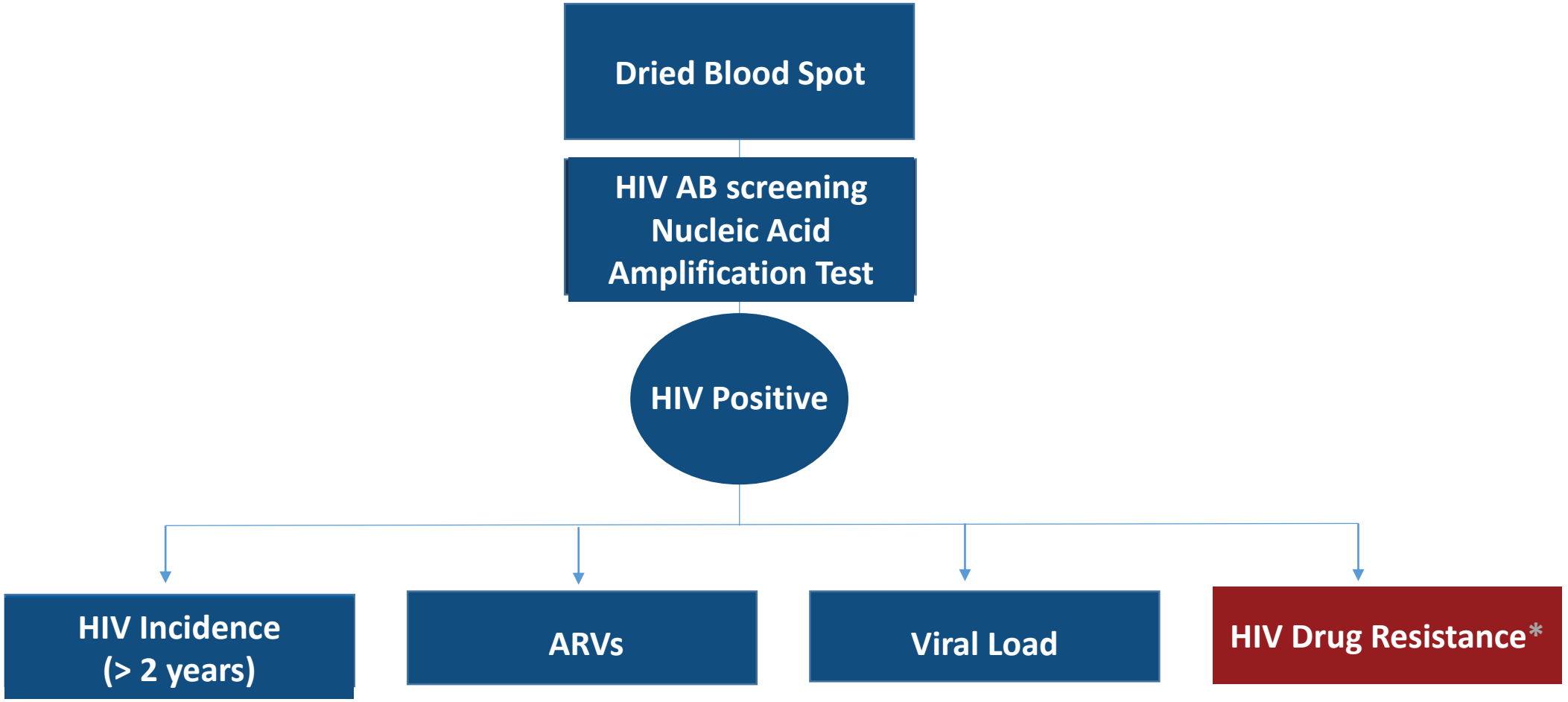
- HIV drug resistance (HIVDR) testing was included in the 2017 survey for the first time in the survey series
- Over 7 million people living with HIV in South Africa
- Large ART programme, expanding further in 2016 with the implementation of 'universal test and treat' policy **(4.4 million people on ART in 2017, HSRC, 2018**)

Including HIV drug resistance testing in the survey

- To understand the levels of HIVDR in a large and expanding ART programme

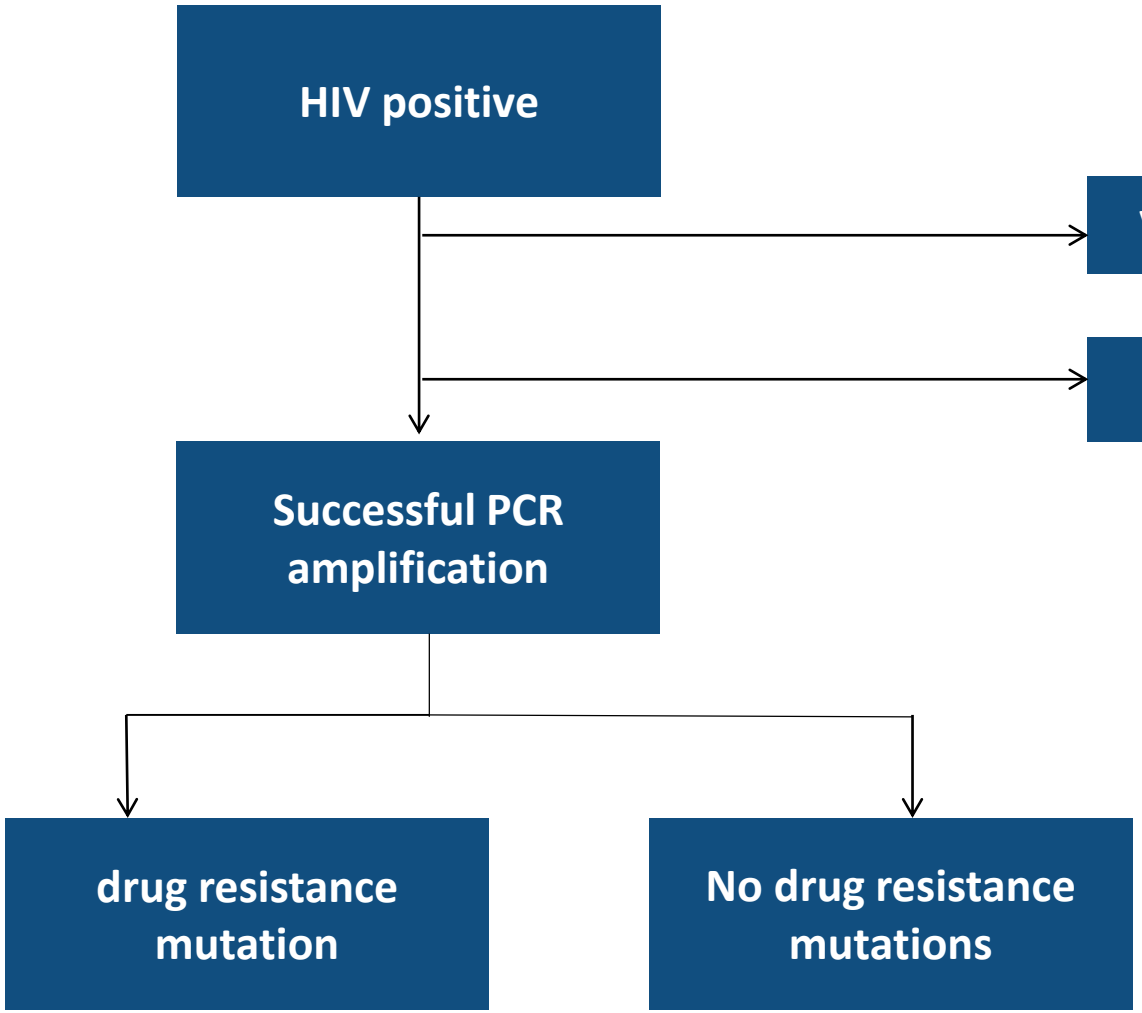
- The HIVDR estimates from this survey are unique
  - based on household population level data
  - include people who are not accessing care, disengaged from care and those accessing private care

Laboratory Testing



*Results presented today

HIV drug resistance testing



- DBS spots excised
- TNA extracted
- Amplification of a 1,084bp PCR fragment
- PCR products sequenced
- Stanford v8.0 algorithm
- All specimens with a sequence similarity of <1.0% were repeated from extraction for confirmatory purposes

Adult antiretroviral therapy guidelines, 2017

TABLE 2: Dosage and common adverse drug reactions of antiretroviral drugs available in southern Africa.

Generic name	Class of drug‡	Recommended dosage	Common or severe ADR§
Tenofovir (TDF)¶	NtRTI	300 mg daily	**Renal failure**, tubular wasting syndrome, reduced bone mineral density, nausea
Lamivudine (3TC)	NRTI	150 mg 12-hourly or 300 mg daily	**Anaemia (pure red cell aplasia)** (rare)
Emtricitabine (FTC)†	NRTI	200 mg daily	Palmar hyperpi
Abacavir (ABC)	NRTI	300 mg 12-hourly or 600 mg daily	**Hypersensitivi**
Zidovudine (AZT)¶	NRTI	300 mg 12-hourly	**Anaemia, neu** hyperlactataer
Stavudine (d4T)¶	NRTI	30 mg 12-hourly	Peripheral neu steatohepatitis
Didanosine (ddI)¶	NRTI	400 mg daily (250 mg daily if < 60 kg) taken on an empty stomach (only enteric-coated formulation available)	Peripheral neu **hyperlactataer**
Efavirenz (EFV)	NNRTI	600 mg at night (400 mg at night if < 40 kg)	Central nervou concentration, **rash, hepatitis**
Nevirapine (NVP)	NNRTI	200 mg daily for 14 days, then 200 mg 12-hourly	**Rash,** hepatitis
Rilpivirine (RPV)	NNRTI	25 mg daily with food	**Rash, hepatitis**
Etravirine (ETR)	NNRTI	200 mg 12-hourly	Rash, hepatitis
Atazanavir (ATV)	PI	400 mg daily (only if ART-naive) or 300 mg with ritonavir 100 mg daily (preferable) with TDF, always 300/100 mg daily and with EFV 400/100 mg daily	Unconjugated patients), dysli hepatitis (unco
Lopinavir/ritonavir (LPV/r)	Boosted PI	400/100 mg 12-hourly or 800/200 mg daily (only if PI-naive)	GI upset, dyslipidaemia, hepatitis
Darunavir (DRV)	PI	600 mg 12-hourly with 100 mg ritonavir 12-hourly or 800/100 mg daily (only if PI-naive)	GI upset, rash, dyslipidaemia, hepatitis (uncommon). Contains sulphonamide moiety (use with caution in patients with sulpha allergy)
Saquinavir (SQV) (rarely used)††	PI	1000 mg with 100 mg ritonavir; 12-hourly, or 1600 mg with 100 mg ritonavir daily (only if PI-naive); Take with a fatty meal, or up to 2 h after meal	GI disturbance (mild), hepatitis, hyperglycaemia, dyslipidaemia
Raltegravir (RAL)	InSTI	400 mg 12-hourly	Headache and other CNS side effects, GI u (rare), rhabdomyolysis (rare)
Dolutegravir (DTG)	InSTI	50 mg daily	Insomnia, headache and other CNS side ef and rash (rare)
Maraviroc (MVC)	CCR5 blocker	150 mg, 300 mg or 600 mg 12-hourly (doses depend on concomitant medication and interactions)	Rash, hepatitis, fever, abdominal pain, cough, dizziness, musculoskeletal symptoms (all rare)

TABLE 4: Preferred first-line regimen options.

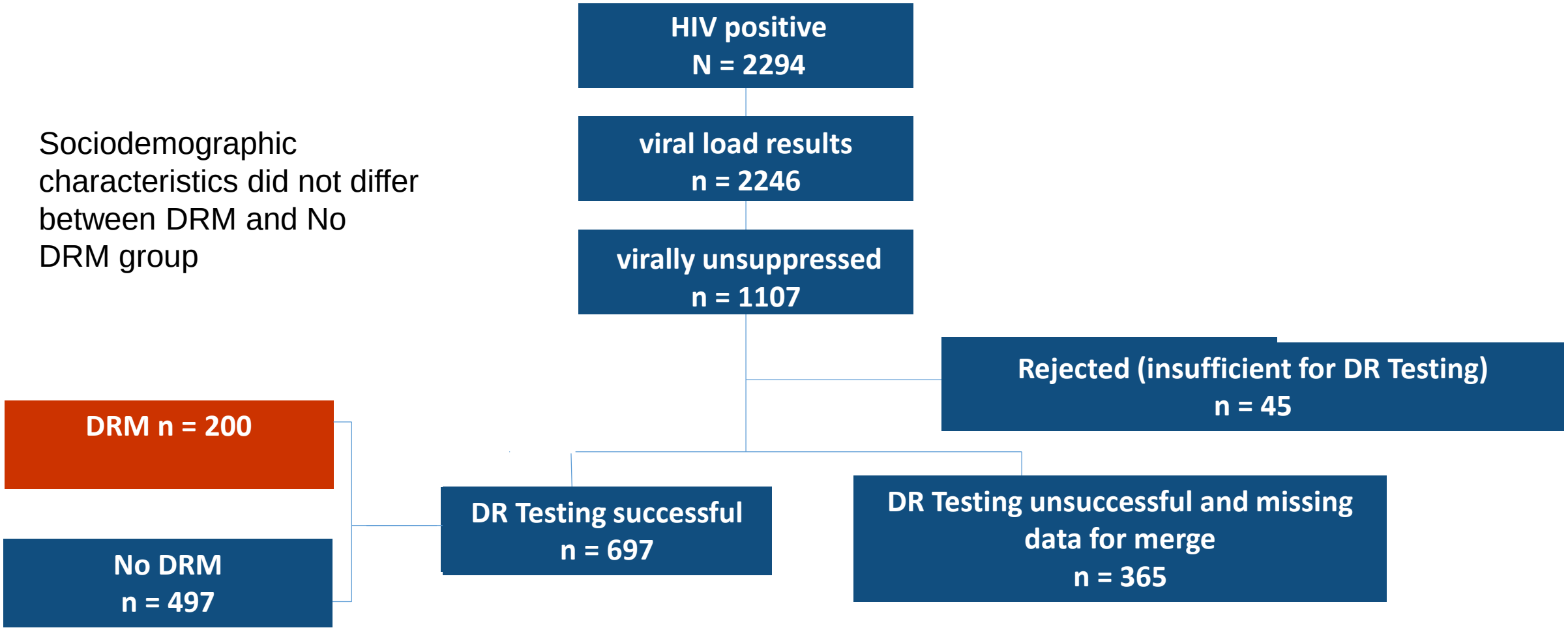
Options	Preferred	Alternative	One of
NRTI backbone	TDF + FTC/3TC	ABC† + 3TC	–
	–	AZT‡ + 3TC	–
	–	d4T§ + 3TC	–
Third drug	–	–	EFV
	–	–	DTG
	–	–	RPV¶

Adult antiretroviral therapy guidelines, 2017
Meintjes G. *et al*, 2017

Results (weighted %)

Testing Flow diagram: results

Sociodemographic characteristics did not differ between DRM and No DRM group



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HIV drug resistance by drug class

	% weighed	95% CI
Total (any resistance)	27.4	22.8-32.6
Drug type/class		
NNRTI	18.9	14.8-23.8
NNRTI+NRTI	7.8	5.6-10.9
PI+NNRTI+NRTI	0.5	0.1-2.1

HIV drug resistance by ARV status

Variable	Any DRM % (95% CI)	p value	NNRTI-only resistance % (95% CI)	p value	Dual NNRTI & NRTI Resistance % (95%CI)	p value
ARV status						
ARV+ve	55.7 (42.6-67.9)	<0.001	14.3 (7.5-25.6)	0.311	40.4 (29.6-52.2)	<0.001
ARV –ve	22.8 (17.7-28.7)		20.0 (15.4-25.7)		2.1 (0.6-6.8)	
ARV defaulters**	75.9 (59.2-87.3)		56.4 (34.4-76.2)		14.3 (2.5-52.1)	
ARV naïve***	15.3 (6.3-32.8)		15.3 (6.3-32.8)		0	

**ARV defaulters - self-reported daily ARV use but tested ARV -ve

***ARV naïve- self reported not taking ART and tested ARV –ve

HIV drug resistance by sex and age

Variable	Any DRM % (95% CI)	p value	NNRTI-only resistance % (95% CI)	p value	Dual NNRTI & NRTI Resistance % (95%CI)	p value
Sex						
Male	29.4 (22.5-37.4)	0.473	19.6 (13.5-27.7)	0.772	9.7 (5.8-15.7)	0.202
Female	25.8 (19.8-32.8)		18.3 (13.2-24.8)		6.3 (4.2-9.5)	
Age (years)						
0-14	33.7 (17.6-54.7)	0.803	17.7 (7.2-37.4)	0.883	14.9 (5.3-35.2)	0.527
15-24	30.5 (18.7-45.5)		22.1 (12.6-35.9)		5.7 (1.7-16.8)	
25-49	26.6 (21.7-32.2)		18.6 (13.8-24.8)		8.2 (5.4-12.2)	
50+	24.1 (14.8-36.7)		17.0 (8.9-30.0)		5.7 (2.5-12.8)	

HIV drug resistance by sex -youth & reproductive age group

Variable	Any DRM %* (95% CI)	p value	NNRTI-only resistance %* (95% CI)	p value	Dual NNRTI & NRTI Resistance %*(95%CI)	p value
15-24 years	30.5 (18.7-45.5)		22.1 (12.6-35.9)		5.7 (1.7-16.8)	
Males	48.7 (26.7-71.2)	0.067	36.7 (17.8-60.7)	0.063		
Females	22.6 (11.4-39.7)		15.8 (7.4-30.7)			
15-49 years	27.5 (22.5-33.2)		19.2 (14.8-24.4)		7.8 (5.3-11.3)	
Males	28.8 (21.4-37.6)	0.676	19.7 (13.2-28.2)	0.857	9.1 (5.1-15.9)	0.392
Females	26.4 (19.7-34.4]		18.7 (13.0-26.2)		6.6 (4.1-10.4)	

Conclusions

- First HIVDR dataset from nationally representative household survey in South Africa
- Drug resistant mutations >25% of HIV-infected persons
- Drug resistant mutations >50% of those on treatment
- Drug resistant mutations >20% of those not on treatment
  - Very high proportions in HIV-infected persons no longer in care
  - High proportion in ART naïve HIV-infected persons
- No significant differences by sex, age (high across all age groups)
  - High level of DRMs among male youth
- Low levels of resistance among those on second line drugs

Programmatic implications

- Stronger adherence support to reduce defaulting from ARVs
- Strengthened first line ART regimens by including integrase strand transfer inhibitors (INSTIs) as a part of first line treatment
- Switching of failing patients to alternative regimens more quickly
- Continued monitoring of HIVDR levels

Limitations and further analyses

Limitations

- Cross-sectional design & survey data
- No data on duration of treatment
- Limited data on recent infections no analysis for objective asses included

Further analysis

- Investigate associations with behavioral data to further understand some of estimates

Collaborators

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- HSRC Survey team
- All partners/ collaborators
- Survey respondents

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