

# testing frequency

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### Background & Research Questions

PrEP is being rolled out in South Africa in female sex workers and young people as well as serodiscordant couples and MSM. It would be useful to identify conditions under which such programmes are likely to be most impactful on an on-going basis while remaining cost effective. Since PrEP drugs are also used as part of 1st line ART regimens, issues of drug resistance should continue to be considered. This is particularly the case when considering whether the frequency of PrEP follow-up visits / HIV testing for people on PrEP could safely be reduced from 3 monthly if necessary, as this could significantly reduce costs and reduce barriers to uptake and continuation of PrEP.

### **Research Questions**

What is the impact and cost-effectiveness of PrEP use during condomless sex with new partners and how does drug resistance 1st line regimen choice, and sensitive nucleic based HIV testing change impact and cost-effectiveness. To address this in the context of Kwa Zulu Natal (KZN) province taking into account the potential consequences for drug resistance, and in consideration of future 1st line ART regimen choice and frequency of HIV testing. Could PrEP introduction could be cost effective in groups beyond adolescent girls and young women and sex workers?

### Methods - 1

We used an individual-based model of heterosexual transmission and progression of HIV and the effect of ART. Each time the model is run it creates data set of outputs on a population of adults from 1989 to 2067 - with updates every 3 month period on variables including the following: Entire adult population - age, gender, # condomless sex partners, circumcision status, current STI, use of PrEP; HIV positive people - time from infection, CD4 count, viral load, currently on ART, drug regimen, current adherence level, drug resistance mutations.

### Results

### HIV epidemic and programmatic characteristics in 2017 (KZN, South Africa)



Africa national viral load report 2015; <sup>iv</sup> TenoRes Study Group, Lancet ID 2016; <sup>v</sup> Vandepitte STIs 2006.







### Potential effectiveness and cost effectiveness of condomless sex targeted PrEP in KZN, South Africa: considerations of drug resistance, ART regimen and HIV

### Methods - 2

### Policy Options Compared

**Option 1: No PrEP** Option 2: PrEP available for women aged 15-24 and female sex workers Option 3: PrEP available all adults age 15-65

### **Criteria for advising to start and continue PrEP**

> 1 new condomless sex partners in past 3 months or on-going condomless sex partner diagnosed with HIV but off ART

### Assumptions related to PrEP

PrEP is only initiated if the individual presents for care and tests negative for HIV at the time PrEP offered. After stopping, PrEP can be restarted if tested HIV negative and again fulfils the above criteria (95% chance if stopped PrEP due to no condomless sex, 20% chance if stopped PrEP despite condomless sex).

Distribution of adherence: 11% of people have an average adherence < 50%, 35% 50-80% and 54% >80% adherence (adherence varies within person; i.e. is randomly assigned in each 3 month period given their own distribution)

Efficacy of PrEP: 95% against non resistant virus: If partner has non resistant HIV: effectiveness is 0.95 times the adherence. Average effectiveness as implemented (accounting for adherence) was 0.70 (i.e. average 70% protection from each infected condomless parter in a 3 month period)

PrEP is assumed only partially effective (50% efficacy) against a virus containing both M184V and K65R mutation but fully effective otherwise

15% of people will not consider starting PrEP even if eligible; no increases in condomless sex in the population as a result of PrEP being introduced.

### Predicted effects of PrEP policies on use and intermediate health outcomes

Outcome mean over 20 years 2017 - 2037 except where stated; (90% uncertainty range)	No PrEP	PrEP in FSW and women aged 15-24	PrEP in people aged 15-65
Proportion of women age 15-25 on PrEP	0%	<b>7.4%</b> (2.9% - 12.7%)	7.6% (3.1% - 12.9%)
Proportion of people age 15-65 on PrEP	0%	1.2% (0.5% - 2.0%)	3.4% (1.9% - 5.4%)
Of women age 15-25 who have $\geq$ 1 new condomless sex partner in a 3 month period, proportion on PrEP	0%	36% (21% - 43%)	37% (22% - 43%)
Percent reduction in HIV incidence in women aged 15-25 compared with no PrEP introduction		24% (11% - 35%)	32% (17% - 42%)
Percent reduction in HIV incidence in people age 15-65 compared with no PrEP introduction		11% (4% - 18%)	30% (19% - 42%)
Number of people on ART	1,590,000	1,539, 000	1,468,000
Number of people on PrEP	0	100,000	275,000
Of people on PrEP, percent with (undetected) HIV		3.0% (1.2% - 6.5%)	2.3% (0.8% - 3.7%)
Of people starting ART, proportion with resistance to at least one 1st line drug	3% (2% -5%)	6% (4% - 9%)	15% (10% - 21%)
HIV prevalence age 15-49 in 20 years time	23% (20% - 27%)	21% (17% - 24%)	18% (13% - 21%)
*(90% uncertainty range represent variability across scenarios that are consistent with observed data used in calibration (likely largely due to different sexual behaviour patterns in different scenarios - they do not include uncertainty over uptake and persistence of use))			

effects of ART

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### Methods - 3

People can receive PrEP while living with HIV either because a person uses PrEP when already infected with HIV (due to < 100% sensitivity of the test or because they are in primary infection (test window period)) or because they get infected despite being on PrEP (due to sub-optimal adherence, less than 100% PrEP efficacy (against non-resistant virus or presence of PrEP drug resistance in infecting source partner) Model output of resistance emergence for persons taking PrEP having been infected with (non-resistant) HIV\*: mean (90% range) proportion with M184V by 3 months of infection 11% (0% - 30%). For K65R 4% (0% - 17%)

### Assumption on 1st line ART regimen

Dolutegravir / 3TC / TDF will be the first line ART regimen in SA from 2019 in men and women aged > 50. In women age < 50, a boosted PI / 3TC / TDF / regimen will be used in new ART initiators.

### Assumption on other interventions

We assume that VMMC, HIV testing and ART initiation given HIV diagnosis all remain constant at the 2017 rate into the future

### **Economic analysis**

Cost per year for a person on PrEP (\$36 for 4 HIV tests, \$40 for 4 clinic visits, \$60 for PrEP drug): \$136; Mean cost of clinical care per year per person with HIV under care (in 2017): \$362. Cost-effectiveness analysis conducted from a healthcare perspective. Costs and health outcomes both discounted to present \$ values at 3% per annum. Costeffectiveness threshold of \$750 in base case for South Africa. Net DALYs are DALYs adjusted for the opportunity cost of resources consumed.



### DALYs and net DALYs averted (mean over 50 years): base case and sensitivity analysis

around 1st line ART regimen The impact and cost effectiveness of PrEP is dependent on avoidance of use of efavirenz in 1st regimens of people who have recently used PrEP, to avoid increases in NNRTI resistance which would undermine the



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### Conclusions

PrEP use concentrated amongst people and periods of risky condomless sex has the potential to be substantially impactful on HIV incidence and is likely to be cost-effective in KZN over a long time horizon.

The challenge for programmes is to achieve such concentrated PrEP use.

The impact and cost effectiveness of PrEP is dependent on avoidance of use of efavirenz in 1st regimens of people who have recently used PrEP, to avoid increases in NNRTI resistance which would undermine the effects of ART.

In this context, less frequent than 3 monthly testing is predicted to be marginally more cost effective than 3 monthly testing (data not shown).



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