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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)

	Model (Median, 90% range)	Examples of observed data
Proportion of new infection from new partners	52% (41% - 68%)	
HIV prevalence:		
age 15-49	26% (25% - 29%)	28% (2012) ⁱ
age 15-19 men / women	2.2% / 7.7%	2.2% / 8.5% (2012) ⁱ
age 20-24 men / women	8.7% / 24.6%	10.0% / 26.0% (2012) ⁱ
HIV incidence age 15-49 (/100 person years)	2.5 (1.9 - 3.3)	3.3 (2012) ⁱ
HIV incidence age 15-24 women (/100 person years)	3.6 (2.1 - 5.2)	
Proportion of HIV positive people diagnosed	84% (75% - 88%)	
Proportion of diagnosed people on ART	76% (67% - 83%)	
Number of adults on ART	1,163,000	1,059,193 ⁱⁱ
Of people on ART, proportion with VL < 1000 cps/mL	83% (80% - 90%)	85% ⁱⁱⁱ
Of people on ART with VL > 1000 cps/mL, proportion with:		
K65R	60% (45% - 78%)	56% (southern Africa) ^{iv}
M184V	90% (84% - 95%)	59% (southern Africa) ^{iv}
in majority virus		
Proportion of women who are FSW (have ≥ 5 condomless sex partners in a 3 month period in past yr)	2.8% (0.8% - 4.7%)	0.4% - 4.3% urban areas in sub Saharan Africa ^v
Proportion of new infections with NNRTI resistance	7% (3% - 14%)	

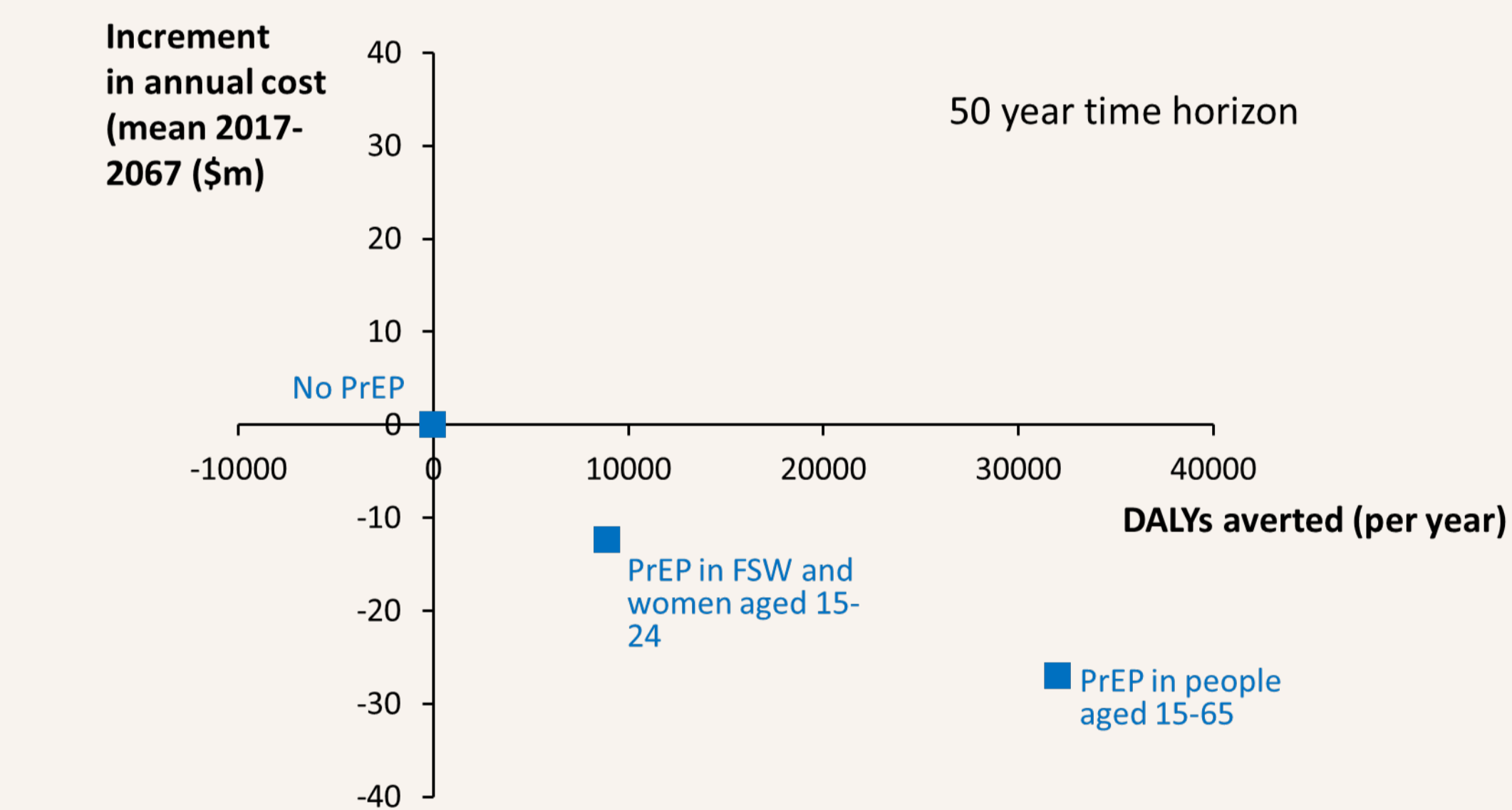
People age 15-64 unless stated. ⁱHSRC Survey 2012 (T Rehle S Moyo, HSRC); ⁱⁱSouth African DoH annual report 2015; ⁱⁱⁱWorld Bank, South Africa national viral load report 2015; ^{iv}TenoRes Study Group, Lancet ID 2016; ^vVandepitte STIs 2006.

Predicted effects of PrEP policies on use and intermediate health outcomes

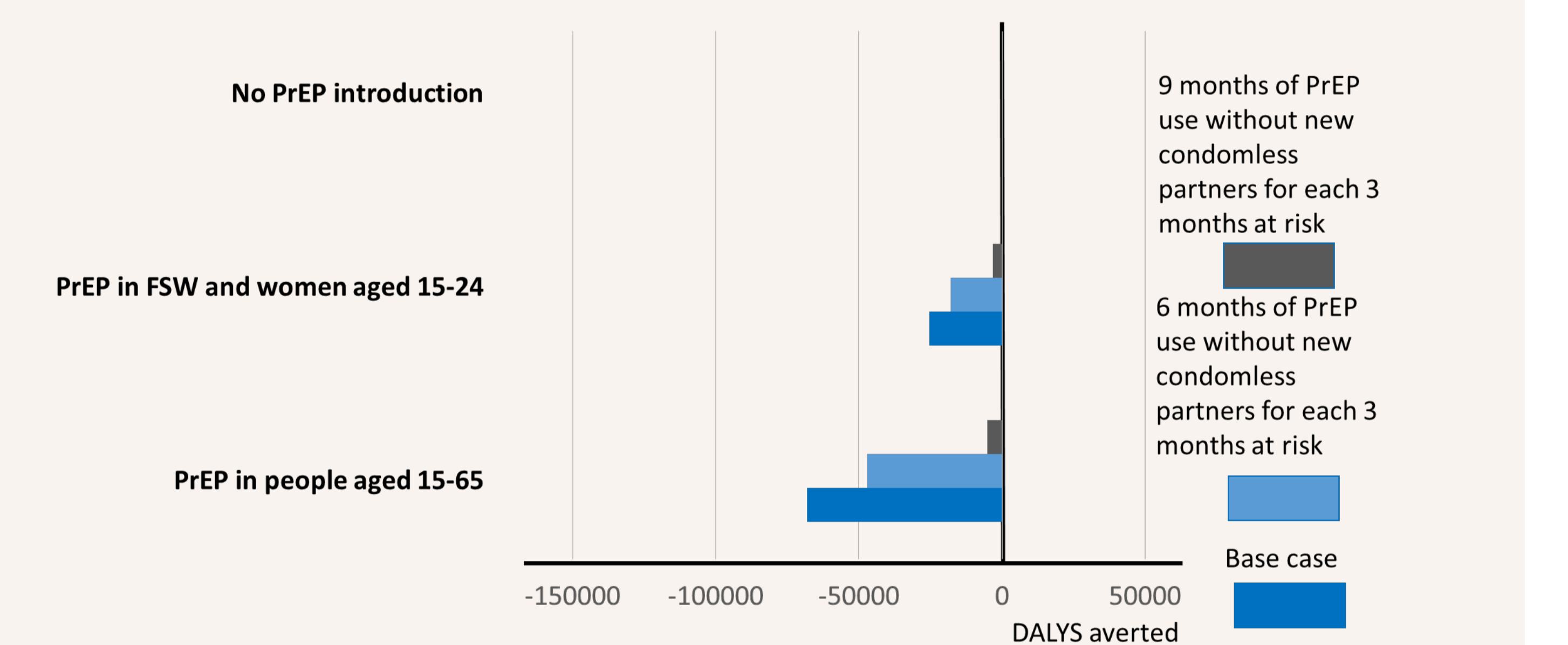
Outcome mean over 20 years 2017 - 2037 except where stated; (90% uncertainty range)	No PrEP	PrEP in FSW and women aged 15-24	PrEP in people aged 15-65
Proportion of women age 15-25 on PrEP	0%	7.4% (2.9% - 12.7%)	7.6% (3.1% - 12.9%)
Proportion of people age 15-65 on PrEP	0%	1.2% (0.5% - 2.0%)	3.4% (1.9% - 5.4%)
Of women age 15-25 who have ≥ 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)]

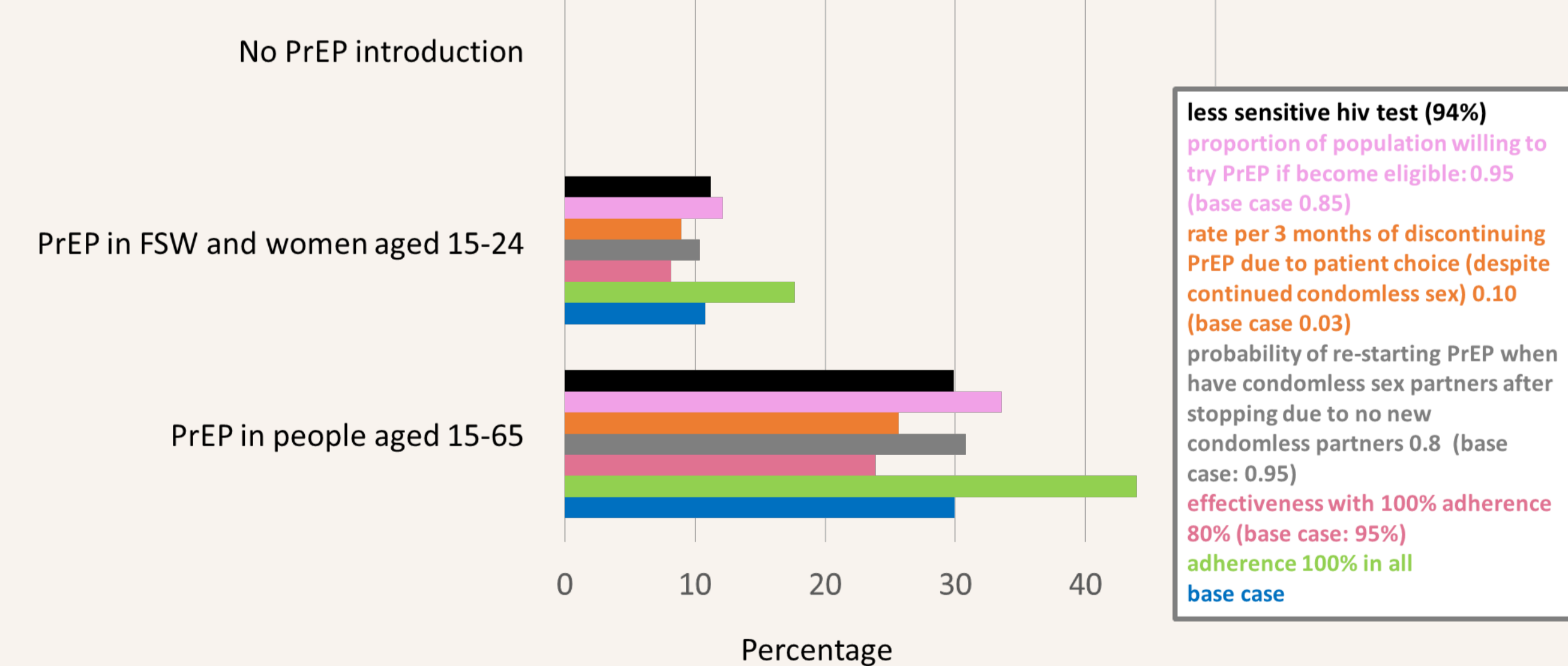
Increment in DALYs and costs (mean over 50 years)



Difference in net DALYs per year (50 year time horizon) compared with no PrEP according to ratio of time on PrEP when at risk compared to when not at risk

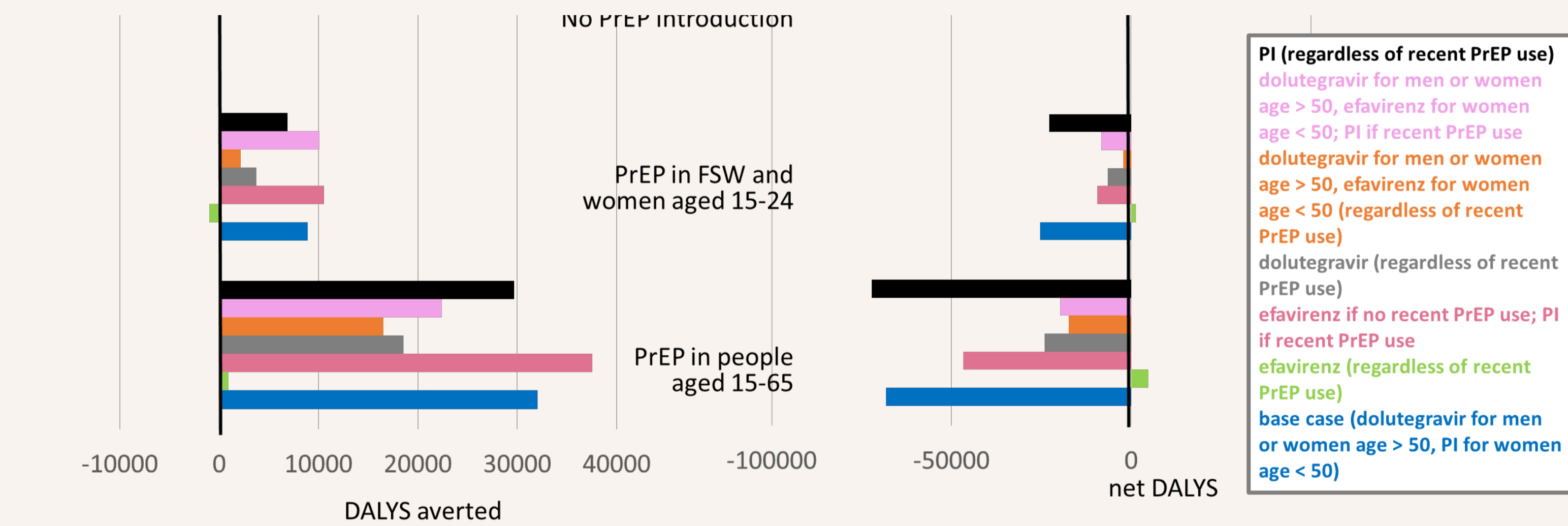


Percentage reduction in incidence (mean over 20 years)



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 effects of ART



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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