Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Health technology assessment of a PrEP programme for populations at substantial risk of sexual acquisition of HIV

Appendices

14 June 2019

CONTENTS

Health Information and Quality Authority

About the Health Information and Quality Authority

The Health Information and Quality Authority (HIQA) is an independent statutory authority established to promote safety and quality in the provision of health and social care services for the benefit of the health and welfare of the public.

HIQA's mandate to date extends across a wide range of public, private and voluntary sector services. Reporting to the Minister for Health and engaging with the Minister for Children and Youth Affairs, HIQA has responsibility for the following:

- **Setting standards for health and social care services** — Developing person-centred standards and guidance, based on evidence and international best practice, for health and social care services in Ireland.

- **Regulating social care services** — The Office of the Chief Inspector within HIQA is responsible for registering and inspecting residential services for older people and people with a disability, and children's special care units.

- **Regulating health services —** Regulating medical exposure to ionising radiation.

- **Monitoring services** — Monitoring the safety and quality of health services and children's social services, and investigating as necessary serious concerns about the health and welfare of people who use these services.

- **Health technology assessment** — Evaluating the clinical and cost-effectiveness of health programmes, policies, medicines, medical equipment, diagnostic and surgical techniques, health promotion and protection activities, and providing advice to enable the best use of resources and the best outcomes for people who use our health service.

- **Health information** — Advising on the efficient and secure collection and sharing of health information, setting standards, evaluating information resources and publishing information on the delivery and performance of Ireland's health and social care services.

- **National Care Experience Programme** — Carrying out national service-user experience surveys across a range of health services, in conjunction with the Department of Health and the HSE.

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The membership of the EAG was as follows:

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Members of the Evaluation Team

Members of HIQA's Evaluation Team were Dr Éamon Ó Murchú (project lead), Dr Patricia Harrington, Mr Liam Marshall, Ms Debra Spillane, Dr Conor Teljeur and Dr Máirín Ryan

Conflicts of interest

None

Appendix 1

1.1 Full list of countries with ongoing or planned PrEP programmes*

Country	Ongoing Programmes	Planned Programmes	Target Populations	Service Delivery Settings	Truvada Registration	Generic Registration	PrEP indicated in Guideline	Policy Framework
Australia	Demonstration projects (3)	Demonstration project (1)	• MSM • Men • Transgender women • Transgender men • Serodifferent couples • N-PEP users • High-risk individuals • Women	• Private sector • Public sector • Pharmacies • Hospitals • Testing centers • Primary/general health clinics • NGOs	Approved	No	Yes	
Belgium	**National Level (1)**		• MSM	Testing centers, Primary/general health clinics	Approved	Approved	Yes	HIV plan 2014-2019 Belgium
Benin	Demonstration project (1) (completed, still providing PrEP)		• FSW	Primary/general health Clinics	No	No	No	

Botswana	Implementation project (1)	**National level (1)**	Not available	Not available	Approved	Planned	Yes	
Brazil	Demonstration projects (5) **National level (1)**	Demonstration project (1) Implementation project (1)	• MSM • MSW • AGYW • CSW • FSW • Adolescent men • Transgender women • Transgender men • Serodifferent couples	• Public sector • Hospitals • Testing centers • Primary/general health clinics • NGOs	Approved	No	Yes	
Burkina Faso	Demonstration project (1)		• MSM • MSW	• Public sector • NGOs	No	No	No	
Canada	**National level (1)**		• MSM • Transgender women	• Public sector • Hospitals	Approved	Approved	Yes	Guidance for the use of PrEP in British Columbia (2016) Canadian guideline on HIV pre-exposure prophylaxis and nonoccupatio

							nal postexposure prophylaxis
China	Demonstration project (1) Implementation project (1)	Not available	Not available	No	No	No	
Cote d'Ivoire	Demonstration project (1) Implementation project (1)	• MSM • MSW	• Public sector • NGOs	No	Planned	No	
Democrati Republic o the Congo	Implementation project (1)	Not available	Not available	No	No	No	
Dominican Republic	Implementation project (1)	Not available	Not available	No	No	No	

England	Implementation project (1)	Not available	• MSM • Transgender women • Highrisk individuals	Not available	Approved	Approved	Yes	British HIV Association/British Association for Sexual Health and HIV (2012) BHIVA/BASHH guidelines on the use of HIV pre-exposure prophylaxis -- Version for Public Consultatoin
Ethiopia	Implementation project (1)		Not available	Not available	No	No	No	
France	Implementation project (1) **National Level (1)**		• MSM • Men • Transgender women • Women	• Public sector • Hospitals	Approved	Approved	Yes	ANSM Pre-exposure Prophylaxis Guidelines (2017)

Georgia	Demonstration project (1)	• MSM • Transgender women	Not available	No	No	No	THE GEORGIAN NATIONAL HIV/AIDS STRATEGIC PLAN FOR 2016–2018
Germany	Implementation project (1)	Not available	Not available	Approved	Approved	No	Integrated Strategy for HIV, Hepatitis B and C and Other Sexually Transmitted Infections
Greece	Demonstration project (1)	• MSM	Not available	Approved	Approved	No	
Haiti	Implementation project (1)	Not available	Not available	No	No	Yes	
India	Demonstration projects (2)	• FSW	• Public sector • NGOs	No	Approved	No	
Israel	**National level (1)**	Not available	Not available	Approved	Approved	No	
Japan	Demonstration project (1)	• MSM • Men	Not available	No	No	No	

Kenya	Demonstration project (1) (Completed, still providing PrEP) Ongoing demonstration projects (3) Implementation projects (5) Product introduction and support project (1)	Clinical trial (1) Demonstration project (1)	• MSM • MSW • AGYW • FSW • Adolescent Men • Men • Serodifferent couples • High-risk individuals • Women • Injecting drug users	• Private sector • Public sector • Hospitals • Testing centres • Primary/general health clinics • Research clinics • Family planning clinics • NGOs • Mobile clinics	Approved	Approved	Yes	Framework for the Implementation of Pre-Exposure Prophylaxis in Kenya (2017) Guidelines on use of ARV drugs for treating and preventing HIV infections (2016)
Laos	Implementation project (1)		Not available	Not available	No	No	No	
Lesotho	Implementation projects (2)		AGYW	Not available	Approved	Approved	Yes	National Guidelines on the Use of Antiretroviral Therapy For HIV Prevention and Treatment

								(2016)
Malawi	Implementation project (1)	Clinical trial (1)	• MSM • AGYW • FSW • Pregnant women	Research clinics	Approved	Planned	No	The National HIV Prevention Strategy (2015-2020) Malawi Guidelines for Clinical Management of HIV in Children and Adults (2016)
Malaysia		Demonstration projects (2)	• MSM • Transgender women	• Private sector • Public sector • Hospitals • Family planning clinics • NGOs	No	No	No	
Mali	Demonstration project (1)	Not available	• MSM • MSW	• Public sector • NGOs	No	No	No	
Mexico	Demonstration project (1)	Implementation project (1)	• MSM • Transgender women • Transgender men	• Public sector • Hospitals • Testing centres •	Planned/in progress	No	No	

				Primary/general health clinics • NGOs				
Morocco	Implementation project (1)		• MSM • FSW	• NGOs	No	No	No	
Mozambique	Demonstration project (1) Implementation project (1)		• MSM • FSW • Women	Private sector	Planned/in progress	Pending	No	
Namibia	Demonstration project (1) Implementation projects (2)	**National level (1)**	• AGYW • Pregnant women	Not available	Approved	No	Yes	National Guidelines For Antiretroviral Therapy (2016)
Netherlands	Demonstration project (1)		• MSM • Transgender women	• Public sector • Primary/general health clinics	Approved	Approved	Yes	HIV Pre-exposure Prophylaxis (PrEP) Guideline for the Netherlands (2017)
New	Demonstration	Not available	• MSM	• Public sector	Approved	No	Yes	Australasian

Zealand	project (1) **National level (1)**	• Transgender women • High-risk individuals	• Pharmacies • Hospitals • Primary/general health clinics				Society for HIV, Viral Hepatitis and Sexual Health Medicine HIV pre-exposure prophylaxis: clinical guidelines
Norway	**National level (1)**						
Nigeria	Demonstration project (1)	• Men • Serodifferent couples • Women	• Private sector • Public sector • Hospitals	Approved	Approved	No	NATIONAL GUIDELINES FOR HIV PREVENTION TREATMENT AND CARE (2016) National Strategic Framework on HIV and AIDS: 2017-2021

Peru	Demonstration projects (3)	Implementation project (1)	• MSM • Transgender women • Transgender men	• Public sector • Hospitals • Testing centres • Primary/general health clinics • NGOs	Approved	No	No	
Philippines	Demonstration project (1)		• MSM • Transgender women	Not available	No	No	No	
Portugal	**National level (1)**		Not available	Not available	Approved	Approved	No	
Scotland	**National level (1)**		Not available	Not available	Approved	Approved	Yes	Scottish Medicines Consortium Truvada Assessment (2017)
Slovenia		Demonstration project (1)	• MSM • Transgender women • Serodifferent couples • Pregnant women	Not available	Approved	Approved	No	
South Africa	Demonstration project (1)	• Clinical trials (2) •	• MSM • AGYW • CSW	• Private sector • Public sector • Testing	Approved	Approved	Yes	

	(completed and still providing PrEP) Clinical trial (1) Demonstration projects (4) Implementation projects (4) Open label extension (1) Product introduction and supports (2)	Demonstration projects (2) • Implementation project (1)	• FSW • Adolescent men • Men • Transgender women • Women • Pregnant women	centres • Primary/general health clinics • Research clinics • Family planning clinics • NGOs			
Spain	Implementation projects (3) Demonstration project (1)		• MSM • Transgender women	• Hospitals • NGOs	Approved	Approved	Yes	Documento de consenso de GESIDA sobre control y monitorización de la infección por

								el VIH (2018)
Swaziland	Implementation projects (2) Demonstration projects (3)	Not available	• MSM • MSW • AGYW • FSW • Adolescent men • Men • Transgender women • Transgender men • Serodifferent couples • High-risk individuals • Women	• Private sector • Public sector • Hospitals • Primary/general health clinics • Family planning clinics	Approved	Approved	No	
Taiwan	Demonstration project (1)	**National level (1)** Demonstration project (1)	Not available	Not available	Approved	No	Yes	Taiwan National Pre-Exposure Prophylaxis Guidelines (2016)

Tanzania	Implementation projects (1) Demonstration project (1)		• AGYW	Not available	Approved	Pending	No	
Thailand	**National level (1)** Demonstration projects (4) Implementation projects (4)	Demonstration project (1)	• MSM • AGYW • FSW • Adolescent men • Men • Transgender women • Transgender men • Serodifferent couples • Women • Injecting drug users	• Public sector • Testing centres • NGOs	Approved	Approved	Yes	Thailand National Guidelines on HIV/AIDS Treatment and Prevention 2017
Togo	Demonstration project (1)		• MSM • MSW	• Public sector • NGOs	No	No	No	
Uganda	**National level (1)** Demonstration project (1) Implementation projects	Clinical trial (1) Product Introduction and Support (1)	• AGYW • Men • Serodifferent couples • High-risk individuals • Women • Pregnant women	• Private sector • Public sector • Testing centres • Research clinics	Planned/in progress	Approved	Yes	National HIV AND AIDS Strategic Plan 2015/2016 - 2019/2020 Consolidated Guidelines

								for Prevention and Treatment of HIV in Uganda (2016)
Ukraine	Implementation project (1) Demonstration project (1)		• MSM • Men	Not available	Submitted/ awaiting approval	Planned	No	
USA	Clinical trial (1) Demonstration projects (3) Implementation project(1) **National level (1)**	Demonstration project (1)	• MSM • FSW • Men • Transgender women • Transgender men • High-risk individuals • Women • Injecting drug users	• Private sector • Public sector • Primary/General health clinics • Family planning clinics • Home	Approved	Approved	Yes	National HIV/AIDS Strategy for the United States: Updated to 2020 CDC Clinical Practice Guidelines (2014)
Vietnam	Implementation projects (4)		Not available	• Private sector • Public sector • Primary/general health clinics	No	No	No	

Wales	**National level (1)**		Not available	Not available	Approved	Approved	Yes	
Zambia	Implementation projects (2)		• AGYW	Not available	Approved	Planned	Yes	
Zimbabwe	Product introduction and support (1) Implementation projects (2) Open label extension (1)	Clinical trials (2)	• MSM • MSW • AGYW • FSW • Transgender women • Transgender men • Serodifferent couples • Women • Pregnant women	• Public sector • Research clinics	Approved	Approved	Yes	Guidelines for Antiretroviral Therapy for the Prevention and Treatment of HIV in Zimbabwe

*Source: PrEPWatch/AVAC (Global Advocacy for HIV Prevention) 2018. Accessed September 2018. PrEP Watch was created and is maintained by AVAC, a non-profit organization based in New York that uses education, policy analysis, advocacy and a network of global collaborations to accelerate the ethical development and global delivery of new and emerging HIV prevention options as part of a comprehensive response to the HIV/AIDS pandemic.
Abbreviations: MSM=men who have sex with men; MSW=men who have sex with women; AGYW=adolescent girls and young women; CSW=commercial sex worker; FSW=female sex worker; N-PEP=nonoccupational post-exposure prophylaxis; NGO=nongovernmental organisation

Appendix 2

2.1 Characteristics of HIV notifications in 2017

		Number	%
Number of HIV Diagnosis		492	-
Rate of diagnoses (per 100,000 population)		10.3	-
Sex	Male (%)	376	76.4
	Female (%)	116	23.6
	Male to Female ratio	3.2	-
Age	Median age of adult cases (years)	35	-
	Age range of adult cases (years)	18-75	-
	Young people aged 15-24 years (%)	41	8.3
	Aged 50 and older (%)	69	14.0
Probable Route of Transmission	MSM (%)	262	53.3
	Heterosexual (%)	163	33.1
	Infecting Drug Use (%)	17	3.5
	Mother to Child Transmission (%)	0	0.0
	Other (%)	7	1.4
	Unknown (%)	43	8.7
Region of Birth	Born in Ireland (%)	130	26.4
	Born Abroad (%)	308	62.6
	Unknown (%)	54	11.0
Co-infection	Acute STI (%)	67	13.6
	TB (%)	17	3.5
Previous history of testing	Previously tested positive abroad (%)	190	8.5
	Transfer of care (% among those previously positive abroad) (%)	16	87.9

Source: HPSC HIV in Ireland 2017 Report.

2.2 Additional characteristics of HIV notifications in 2017 by risk group

1. MSM

		All Diagnoses	New diagnoses (not previously positive)	Previously positive
Total (n)		262	151	111
Age	Median Age (years)	32	34	30
	Range (years)	18-71	18-71	21-63
	Young people aged 15-24 years %	11.5	13.2	9.0
	Aged 50 and older %	9.9	12.6	6.3
Region of Birth	Ireland (%)	32.1	45.7	13.5
	Latin America (%)	33.6	17.9	55.0
	Europe (%)	17.9	18.5	17.1
	Other (%)	9.9	7.3	13.5
	Unknown (%)	6.5	10.6	1.0
Co-infections	Acute STI (%)	22.5	17.2	29.7

Source: HPSC HIV in Ireland 2017 Report

2. Heterosexuals

		Male	Female	Total
Total (n)		63	100	163
Age	Median Age (years)	38	36	37
	Range (years)	24-75	19-72	19-75
	Young people aged 15-24 years (%)	4.8	4.0	4.3
	Aged 50 and older (%)	30.2	10.0	17.8
Region of Birth	Ireland (%)	42.9	6.0	20.2
	Latin America (%)	39.7	74.0	60.7
	Europe (%)	6.3	10.0	8.6
	Other (%)	9.5	7.0	8.0
	Unknown (%)	1.6	3.0	2.5
Co-infections	Acute STI (%)	6.3	1.0	3.1
	TB (%)	4.8	8.0	6.7
Previous history of testing	Previously tested positive abroad (%)	41.3	43.0	42.3
	Transfer of care (among those previously positive)	84.6	86.1	85.5

Source: HPSC HIV in Ireland 2017 Report

Appendix 3

3.1 Clinical effectiveness search strategy

Table 3.1. Search strategy: PubMed

Search	Most Recent Queries
#6	Search #1 AND #2 AND #5
#5	Search #3 OR #4
#4	Search tenofovir OR TNF OR tenofovir OR PMPA OR viread OR emtricitabine OR EMC OR truvada OR emtriva OR coviracil
#3	Search pre-exposure prophylaxis[tiab] OR preexposure prophylaxis[tiab] OR PREP[tiab] OR anti-retroviral chemoprophylaxis[tiab] OR antiretroviral chemoprophylaxis[tiab] OR chemoprevention[mh] OR chemoprevention[tiab] OR HIV prophylaxis[tiab]
#2	Search (randomised controlled trial [pt] OR controlled clinical trial [pt] OR randomised [tiab] OR placebo [tiab] OR drug therapy [sh] OR randomly [tiab] OR trial [tiab] OR groups [tiab]) NOT (animals [mh] NOT humans [mh])
#1	Search HIV Infections[MeSH] OR HIV[MeSH] OR HIV[tw] OR hiv-1*[tw] OR hiv-2*[tw] OR hiv1[tw] OR hiv2[tw] OR HIV infect*[tw] OR human immunodeficiency virus[tw] OR human immunedeficiency virus[tw] OR human immuno-deficiency virus[tw] OR human immune-deficiency virus[tw] OR ((human immun*) AND (deficiency virus[tw])) OR acquired immunodeficiency syndrome[tw] OR acquired immunedeficiency syndrome[tw] OR acquired immuno-deficiency syndrome[tw] OR acquired immune-deficiency syndrome[tw] OR ((acquired immun*) AND (deficiency syndrome[tw])) OR "sexually transmitted diseases, viral"[MESH:NoExp]

Table 3.2. Search strategy: Cochrane Central register

ID	Search
#1	MeSH descriptor HIV Infections explode all trees
#2	MeSH descriptor HIV explode all trees
#3	hiv OR hiv-1* OR hiv-2* OR hiv1 OR hiv2 OR HIV INFECT* OR HUMAN IMMUNODEFICIENCY VIRUS OR HUMAN IMMUNEDEFICIENCY VIRUS OR HUMAN IMMUNE-DEFICIENCY VIRUS OR HUMAN IMMUNO-DEFICIENCY VIRUS OR HUMAN IMMUN* DEFICIENCY VIRUS OR ACQUIRED IMMUNODEFICIENCY SYNDROME
#5	MeSH descriptor Sexually Transmitted Diseases, Viral, this term only
#6	(#1 OR #2 OR #3 OR #4 OR #5)
#7	MeSH descriptor Chemoprevention explode all trees
#8	pre-exposure prophylaxis:ti,ab,kw OR preexposure prophylaxis:ti,ab,w OR PREP:ti,ab,kw OR anti-retroviral chemoprophylaxis:ti,ab,kw OR antiretroviral chemoprophylaxis:ti,ab,kw OR hiv prophylaxis:ti,ab,kw
#9	(#7 OR #8)
#10	tenofovir OR TNF OR tenofovir OR PMPA OR viread OR emtricitabine OR EMC OR truvada OR emtriva OR coviracil
#11	(#9 OR #10)
#12	(#6 AND #11)

Table 3.3. Search strategy: EMBASE

No.	Query
#6	#1 AND #2 AND #5
#5	#3 OR #4
#4	'tenofovir'/syn OR tnf OR Tenofovir OR 'pmpa'/syn OR 'viread'/syn OR

	'emtricitabine'/syn OR emc OR 'truvada'/syn OR 'emtriva'/syn OR 'coviracil'/syn
#3	'pre-exposure prophylaxis' OR 'preexposure prophylaxis' OR prep OR 'anti-retroviral chemoprophylaxis' OR 'antiretroviral chemoprophylaxis' OR 'chemoprevention'/syn OR 'hiv prophylaxis' OR 'chemoprophylaxis'/syn
#2	random*:ti OR random*:ab OR factorial*:ti OR factorial*:ab OR cross?over*:ti OR cross?over:ab OR crossover*:ti OR crossover*:ab OR placebo*:ti OR placebo*:ab OR (doubl*:ti AND blind*:ti) OR (doubl*:ab AND blind*:ab) OR (singl*:ti AND blind*:ti) OR (singl*:ab AND blind*:ab) OR assign*:ti OR assign*:ab OR volunteer*:ti OR volunteer*:ab OR 'crossover procedure'/de OR 'crossover procedure' OR 'double-blind procedure'/de OR 'double-blind procedure' OR 'single-blind procedure'/de OR 'single-blind procedure' OR 'randomised controlled trial'/de OR 'randomised controlled trial' OR allocat*:ti OR allocat*:ab
#1	'human immunodeficiency virus infection'/exp OR 'human immunodeficiency virus infection'/de OR 'human immunodeficiency virus infection' OR 'human immunodeficiency virus'/exp OR 'human immunodeficiency virus'/de OR 'human immunodeficiency virus' OR hiv:ti OR hiv:ab OR 'hiv-1':ti OR 'hiv-1':ab OR 'hiv-2':ti OR 'hiv-2':ab OR 'human immunodeficiency virus':ti OR 'human immunodeficiency virus':ab OR 'human immuno-deficiency virus':ti OR 'human immuno-deficiency virus':ab OR 'human immunedeficiency virus':ti OR 'human immunedeficiency virus':ab OR 'human immune-deficiency virus':ti OR 'human immune-deficiency virus':ab OR 'acquired immune-deficiency syndrome':ti OR 'acquired immune-deficiency syndrome':ab OR 'acquired immunedeficiency syndrome':ti OR 'acquired immunedeficiency syndrome':ab OR 'acquired immunodeficiency syndrome':ti OR 'acquired immunodeficiency syndrome':ab OR 'acquired immuno-deficiency syndrome':ti OR 'acquired immuno-deficiency syndrome':ab

3.2 Data collection, management and analysis

Data collection and management	
Selection of studies	Citations will be screened by one reviewer to eliminate clearly irrelevant studies. Two people will independently review the remaining citations per the inclusion criteria. Any disagreements will be resolved by discussion or, if necessary, a third reviewer.
Data extraction and management	Data extraction will be performed independently onto a data extraction pro forma by two people. Any disagreements will be resolved by discussion or a third reviewer. RevMan software will be used to record extracted data.
Assessment of risk of bias in included studies	Risk of bias will be assessed using the Cochrane Risk of Bias Tool for randomised control trails (RCTs). This will be performed by two people independently, with any disagreement being resolved by discussion or a third party. Small study bias will be assessed using a funnel plot and Egger's test. An overall assessment of the quality of the evidence will be assessed using the GRADE approach.†
Measures of treatment effect and data synthesis	Effect sizes will be expressed as the reduction in relative risk (RR) of HIV infection in the treatment group compared to control. A meta-analysis will be performed to provide a pooled risk if there is sufficient homogeneity across studies (all statistical analysis will be performed in Review Manager 5.3 software). If significant heterogeneity is observed, a narrative metasynthesis will be performed.
Assessment of heterogeneity	Clinical heterogeneity will be assessed by the reviewers based on the description of the interventions in the RCTs. Statistical heterogeneity will be examined using the I^2 statistic. I^2 values above 50–70% will be deemed heterogenous.

†The Cochrane Handbook. Section 12.2.1: The GRADE approach. Available at: http://handbook.cochrane.org/chapter_12/12_2_1_the_grade_approach.htm. Accessed May 2017.

3.3 List of studies included in review of clinical effectiveness

1. Baeten JM, Donnell D, Ndase P, Mugo NR, Campbell JD, Wangisi J, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. New England journal of medicine [Internet]. 2012; 367(5):[399-410 pp.]. Available from: http://cochranelibrary-wiley.com/o/cochrane/clcentral/articles/266/CN-00840266/frame.html https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3770474/pdf/nihms493581.pdf.

2. Baeten JM, Heffron R, Kidoguchi L, Mugo NR, Katabira E, Bukusi EA, et al. Integrated Delivery of Antiretroviral Treatment and Pre-exposure Prophylaxis to HIV-1–serodiscordant Couples: A Prospective Implementation Study in Kenya and Uganda. PLOS Medicine. 2016;13(8):e1002099.

3. Bekker LG, Roux S, Sebastien E, Yola N, Amico KR, Hughes JP, et al. Daily and non-daily pre-exposure prophylaxis in African women (HPTN 067/ADAPT Cape Town Trial): a randomised, open-label, phase 2 trial. The lancet HIV. 2018;5(2):e68-e78.

4. Choopanya K, Martin M, Suntharasamai P, Sangkum U, Mock PA, Leethochawalit M, et al. Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomised, double-blind, placebo-controlled phase 3 trial. Lancet (London, England). 2013;381(9883):2083-90.

5. Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. New England journal of medicine [Internet]. 2010; 363(27):[2587-99 pp.]. Available from: http://cochranelibrary-wiley.com/o/cochrane/clcentral/articles/306/CN-00771306/frame.html https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3079639/pdf/nihms264954.pdf.

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7. Hosek SG, Siberry G, Bell M, Lally M, Kapogiannis B, Green K, et al. The acceptability and feasibility of an HIV preexposure prophylaxis (PrEP) trial with young men who have sex with men. Journal of acquired immune deficiency syndromes (1999). 2013;62(4):447-56.

8. Kibengo FM, Ruzagira E, Katende D, Bwanika AN, Bahemuka U, Haberer JE, et

al. Safety, adherence and acceptability of intermittent tenofovir/emtricitabine as HIV pre-exposure prophylaxis (PrEP) among HIV-uninfected Ugandan volunteers living in HIV-serodiscordant relationships: a randomized, clinical trial. PLoS One. 2013;8(9):e74314.

9. Marrazzo JM, Ramjee G, Richardson BA, Gomez K, Mgodi N, Nair G, et al. Tenofovir-based preexposure prophylaxis for HIV infection among African women. The New England journal of medicine. 2015;372(6):509-18.

10. McCormack S, Dunn DT, Desai M, Dolling DI, Gafos M, Gilson R, et al. Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. Lancet (London, England). 2016;387(10013):53-60.

11. Molina JM, Capitant C, Spire B, Pialoux G, Cotte L, Charreau I, et al. On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection. The New England journal of medicine. 2015;373(23):2237-46.

12. Mutua G, Sanders E, Mugo P, Anzala O, Haberer JE, Bangsberg D, et al. Safety and adherence to intermittent pre-exposure prophylaxis (PrEP) for HIV-1 in African men who have sex with men and female sex workers. Plos one [Internet]. 2012; 7(4):[e33103 p.]. Available from: http://cochranelibrary-wiley.com/o/cochrane/clcentral/articles/614/CN-00848614/frame.html https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3325227/pdf/pone.0033103.pdf.

13. Peterson L, Taylor D, Roddy R, Belai G, Phillips P, Nanda K, et al. Tenofovir Disoproxil Fumarate for Prevention of HIV Infection in Women: A Phase 2, Double-Blind, Randomized, Placebo-Controlled Trial. PLoS Clinical Trials. 2007;2(5):e27.

14. Thigpen MC, Kebaabetswe PM, Paxton LA, Smith DK, Rose CE, Segolodi TM, et al. Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. New England journal of medicine [Internet]. 2012; 367(5):[423-34 pp.]. Available from: http://cochranelibrary-wiley.com/o/cochrane/clcentral/articles/265/CN-00840265/frame.html.

15. Van Damme L, Corneli A, Ahmed K, Agot K, Lombaard J, Kapiga S, et al. Preexposure prophylaxis for HIV infection among African women. The New England journal of medicine. 2012;367(5):411-22.

3.4 List of studies excluded from review of clinical effectiveness

1. Agot K, Taylor D, Corneli AL, Wang M, Ambia J, Kashuba AD, et al. Accuracy of Self-Report and Pill-Count Measures of Adherence in the FEM-PrEP Clinical Trial: Implications for Future HIV-Prevention Trials. AIDS and behavior. 2015;19(5):743-51. [reason: secondary analysis of FEM-PrEP]

2. Anderson PL, Glidden DV, Liu A, Buchbinder S, Lama JR, Guanira JV, et al. Emtricitabine-tenofovir concentrations and pre-exposure prophylaxis efficacy in men who have sex with men. Science translational medicine. 2012;4(151):151ra25. [reason: secondary analysis of iPrEX]

3. Baeten JM, Donnell D, Mugo NR, Ndase P, Thomas KK, Campbell JD, et al. Single-agent tenofovir versus combination emtricitabine plus tenofovir for pre-exposure prophylaxis for HIV-1 acquisition: an update of data from a randomised, double-blind, phase 3 trial. The lancet Infectious diseases [Internet]. 2014; 14(11):[1055-64 pp.]. Available from: http://cochranelibrary-wiley.com/o/cochrane/clcentral/articles/639/CN-01053639/frame.html https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4252589/pdf/nihms635147.pdf. [reason: duplicate]

6. Buchbinder SP, Glidden DV, Liu AY, McMahan V, Guanira JV, Mayer KH, et al. HIV pre-exposure prophylaxis in men who have sex with men and transgender women: a secondary analysis of a phase 3 randomised controlled efficacy trial. The Lancet Infectious diseases. 2014;14(6):468-75. [reason: secondary analysis of iPrEX]

7. Buchbinder SP, Liu AY. CROI 2014: New tools to track the epidemic and prevent HIV infections. Topics in Antiviral Medicine. 2014;22(2):579-93. [reason: review; not a RCT]

8. Campbell JD, Herbst JH, Koppenhaver RT, Smith DK. Antiretroviral prophylaxis for sexual and injection drug use acquisition of HIV. American Journal of Preventive Medicine. 2013;44(1 SUPPL. 2):S63-S9. [reason: review, not a RCT]

9. Celum C, Baeten JM. Antiretroviral-based HIV-1 prevention: Antiretroviral treatment and pre-exposure prophylaxis. Antiviral Therapy. 2012;17(8):1483-93. [reason: review/not a RCT]

11. Corneli AL, Deese J, Wang M, Taylor D, Ahmed K, Agot K, et al. FEM-PrEP: adherence patterns and factors associated with adherence to a daily oral study product for pre-exposure prophylaxis. Journal of acquired immune deficiency

syndromes (1999). 2014;66(3):324-31. [reason: secondary analysis of FEM-PrEP]

12. Corneli AL, McKenna K, Headley J, Ahmed K, Odhiambo J, Skhosana J, et al. A descriptive analysis of perceptions of HIV risk and worry about acquiring HIV among FEM-PrEP participants who seroconverted in Bondo, Kenya, and Pretoria, South Africa. Journal of the International AIDS Society. 2014;17(3). [reason: secondary analysis of FEM-PrEP]

14. Deutsch MB, Glidden DV, Sevelius J, Keatley J, McMahan V, Guanira J, et al. HIV pre-exposure prophylaxis in transgender women: a subgroup analysis of the iPrEx trial. The lancet HIV. 2015;2(12):e512-9. [reason: secondary analysis of iPrEX]

15. Dolling DI, Desai M, McOwan A, Gilson R, Clarke A, Fisher M, et al. An analysis of baseline data from the PROUD study: An open-label randomised trial of pre-exposure prophylaxis. Trials. 2016;17(1). [reason: secondary analysis of PROUD]

16. Dunn DT, Glidden DV. Statistical issues in trials of preexposure prophylaxis. Current Opinion in HIV and AIDS. 2016;11(1):116-21. [reason: review/not a RCT]

17. Elbirt D, Mahlab-Guri K, Bezalel-Rosenberg S, Asher I, Sthoeger Z. Pre-exposure prophylaxis as a method for prevention of human immunodeficiency virus infection. Israel Medical Association Journal. 2016;18(5):294-8. [reason: review, not a RCT]

18. Fidler S, Bock P. Prophylactic antiretroviral HIV therapy prevents infection in heterosexual men and women. Evidence-Based Medicine. 2013;18(5):184-5. [Reason: not a RCT, review of Baeten et al.]

19. Gilmore HJ, Liu A, Koester KA, Amico KR, McMahan V, Goicochea P, et al. Participant experiences and facilitators and barriers to pill use among men who have sex with men in the iPrEx pre-exposure prophylaxis trial in San Francisco. AIDS patient care and stds [Internet]. 2013; 27(10):[560-6 pp.]. Available from: http://cochranelibrary-wiley.com/o/cochrane/clcentral/articles/551/CN-00962551/frame.html. [reason: secondary analysis of iPrEX]

20. Grangeiro A, Couto MT, Peres MF, Luiz O, Zucchi EM, de Castilho EA, et al. Pre-exposure and postexposure prophylaxes and the combination HIV prevention methods (The Combine! Study): protocol for a pragmatic clinical trial at public healthcare clinics in Brazil. BMJ open. 2015;5(8):e009021. [reason: protocol]

22. Grant RM, Liegler T, Defechereux P, Kashuba AD, Taylor D, Abdel-Mohsen M, et al. Drug resistance and plasma viral RNA level after ineffective use of oral pre-

exposure prophylaxis in women. AIDS (London, England). 2015;29(3):331-7. [reason: not an efficacy RCT; further analysis of FEM-PrEP]

23. Gray RH, Wawer MJ. Infection in 2012: Mixed results of pre-exposure prophylaxis for HIV prevention. Nature Reviews Urology. 2013;10(2):74-5. [reason: review]

25. Gulick RM, Wilkin TJ, Chen YQ, Landovitz RJ, Amico KR, Young AM, et al. Phase 2 Study of the Safety and Tolerability of Maraviroc-Containing Regimens to Prevent HIV Infection in Men Who Have Sex With Men (HPTN 069/ACTG A5305). The Journal of infectious diseases. 2017;215(2):238-46. [reason: different intervention (maraviroc)]

26. Gulick RM, Wilkin TJ, Chen YQ, Landovitz RJ, Amico KR, Young AM, et al. Safety and Tolerability of Maraviroc-Containing Regimens to Prevent HIV Infection in Women: A Phase 2 Randomized Trial. Annals of internal medicine. 2017;167(6):384-93. [reason: different intervention (maraviroc)]

27. Gust DA, Soud F, Hardnett FP, Malotte CK, Rose C, Kebaabetswe P, et al. Evaluation of Sexual Risk Behavior Among Study Participants in the TENOFOVIR2 PrEP Study Among Heterosexual Adults in Botswana. Journal of acquired immune deficiency syndromes (1999). 2016;73(5):556-63. [reason: secondary analysis of TD2 trial]

28. Haberer JE, Baeten JM, Campbell J, Wangisi J, Katabira E, Ronald A, et al. Adherence to Antiretroviral Prophylaxis for HIV Prevention: A Substudy Cohort within a Clinical Trial of serodiscordant Couples in East Africa. PLoS Medicine. 2013;10(9). [reason: secondary analysis of Partners PrEP]

29. Hanscom B, Janes HE, Guarino PD, Huang Y, Brown ER, Chen YQ, et al. Brief report: Preventing HIV-1 infection in women using oral preexposure prophylaxis: A meta-analysis of current evidence. Journal of Acquired Immune Deficiency Syndromes. 2016;73(5):606-8. [reason: meta-analysis of RCTs]

31. Jiang J, Yang X, Ye L, Zhou B, Ning C, Huang J, et al. Pre-exposure prophylaxis for the prevention of HIV infection in high risk populations: A meta-analysis of randomized controlled trials. PLoS ONE. 2014;9(2). [reason: meta-analysis of existing RCTs]

32. K RA, McMahan V, Goicochea P, Vargas L, Marcus JL, Grant RM, et al. Supporting study product use and accuracy in self-report in the iPrEx study: next step counseling and neutral assessment. AIDS and behavior. 2012;16(5):1243-59. [reason: secondary analysis of iPrEX]

34. Koester KA, Liu A, Eden C, Amico KR, McMahan V, Goicochea P, et al. Acceptability of drug detection monitoring among participants in an open-label pre-exposure prophylaxis study. AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV. 2015;27(10):1199-204. [reason: observational study on subset of iPrEX OLE study]

35. Koss CA, Bacchetti P, Hillier SL, Livant E, Horng H, Mgodi N, et al. Differences in Cumulative Exposure and Adherence to Tenofovir in the VOICE, iPrEx OLE, and PrEP Demo Studies as Determined via Hair Concentrations. AIDS Research and Human Retroviruses. 2017;33(8):778-83. [reason: secondary analysis of 3 studies]

36. Lehman DA, Baeten JM, McCoy CO, Weis JF, Peterson D, Mbara G, et al. Risk of drug resistance among persons acquiring HIV within a randomized clinical trial of single-or dual-agent preexposure prophylaxis. Journal of Infectious Diseases. 2015;211(8):1211-8. [reason: secondary analysis of Partners PrEP study]

37. Liu A, Glidden DV, Anderson PL, Amico KR, McMahan V, Mehrotra M, et al. Patterns and correlates of PrEP drug detection among MSM and transgender women in the global iPrEx study. Journal of Acquired Immune Deficiency Syndromes. 2014;67(5):528-37. [reason: secondary analysis of iPrEX]

38. Liu AY, Vittinghoff E, Chillag K, Mayer K, Thompson M, Grohskopf L, et al. Sexual risk behavior among HIV-uninfected men who have sex with men participating in a tenofovir preexposure prophylaxis randomized trial in the United States. Journal of acquired immune deficiency syndromes (1999). 2013;64(1):87-94. [reason: secondary analysis of US CDC Safety Study]

39. Lorente N, Fugon L, Carrieri MP, Andreo C, Le Gall JM, Cook E, et al. Acceptability of an on-demand pre-exposure HIV prophylaxis trial among men who have sex with men living in France. AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV. 2012;24(4):468-77. [reason: acceptability study prior to RCT]

40. Markowitz M, Frank I, Grant RM, Mayer KH, Elion R, Goldstein D, et al. Safety and tolerability of long-acting cabotegravir injections in HIV-uninfected men (ECLAIR): a multicentre, double-blind, randomised, placebo-controlled, phase 2a trial. The lancet HIV. 2017;4(8):e331-e40. [reason: intervention different (cabotegravir)]

42. Martin M, Vanichseni S, Suntharasamai P, Sangkum U, Chuachoowong R, Mock PA, et al. Enrollment characteristics and risk behaviors of injection drug users participating in the Bangkok Tenofovir Study, Thailand. PLoS One.

2011;6(9):e25127. [reason: secondary analysis of Bangkok tenofovir study enrolment characteristics]

43. Martin M, Vanichseni S, Suntharasamai P, Sangkum U, Mock PA, Leethochawalit M, et al. Risk behaviors and risk factors for HIV infection among participants in the Bangkok tenofovir study, an HIV pre-exposure prophylaxis trial among people who inject drugs. PLoS One. 2014;9(3):e92809. [reason: secondary analysis of Bangkok tenofovir study enrolment characteristics]

45. McCormack SM, Noseda V, Molina JM. PrEP in Europe - Expectations, opportunities and barriers. Journal of the International AIDS Society. 2016;19. [reason: not a RCT; review article]

47. Mugwanya KK, Donnell D, Celum C, Thomas KK, Ndase P, Mugo N, et al. Sexual behaviour of heterosexual men and women receiving antiretroviral pre-exposure prophylaxis for HIV prevention: a longitudinal analysis. The lancet Infectious diseases [Internet]. 2013; 13(12):[1021-8 pp.]. Available from: http://cochranelibrary-wiley.com/o/cochrane/clcentral/articles/297/CN-00915297/frame.html. [reason: longitudinal analysis of Partners PrEP]

48. Mujugira A, Baeten JM, Donnell D, Ndase P, Mugo NR, Barnes L, et al. Characteristics of HIV-1 serodiscordant couples enrolled in a clinical trial of antiretroviral pre-exposure prophylaxis for HIV-1 prevention. Plos one [Internet]. 2011; 6(10):[e25828 p.]. Available from: http://cochranelibrary-wiley.com/o/cochrane/clcentral/articles/232/CN-00805232/frame.html. [reason: secondary analysis Partners PrEP]

49. Murnane PM, Brown ER, Donnell D, Coley RY, Mugo N, Mujugira A, et al. Estimating Efficacy in a Randomized Trial With Product Nonadherence: Application of Multiple Methods to a Trial of Preexposure Prophylaxis for HIV Prevention. American Journal of Epidemiology. 2015;182(10):848-56. [reason: secondary analysis Partners PrEP]

50. Murnane PM, Celum C, Mugo N, Campbell JD, Donnell D, Bukusi E, et al. Efficacy of preexposure prophylaxis for HIV-1 prevention among high-risk heterosexuals: subgroup analyses from a randomized trial. AIDS (london, england) [Internet]. 2013; 27(13):[2155-60 pp.]. Available from: http://cochranelibrary-wiley.com/o/cochrane/clcentral/articles/174/CN-01000174/frame.html. [reason: secondary analysis Partners PrEP]

52. Ndase P, Celum C, Campbell J, Bukusi E, Kiarie J, Katabira E, et al. Successful discontinuation of the placebo arm and provision of an effective HIV prevention product after a positive interim efficacy result: the partners PrEP study experience. Journal of acquired immune deficiency syndromes (1999) [Internet].

2014; 66(2):[206-12 pp.]. Available from: http://cochranelibrary-wiley.com/o/cochrane/clcentral/articles/717/CN-00992717/frame.html. [reason: review of Partners PrEP]

53. Page K, Tsui J, Maher L, Choopanya K, Vanichseni S, Philip Mock M, et al. Biomedical HIV prevention including pre-exposure prophylaxis and opiate agonist therapy for women who inject drugs: State of research and future directions. Journal of Acquired Immune Deficiency Syndromes. 2015;69:S169-S75. [reason: review; not a RCT]

55. Sacks HS. Preexposure tenofovir-emtricitabine reduced HIV infection in men who have unprotected anal sex with men. Annals of Internal Medicine. 2016;164(2):JC3. [reason: review of PROUD]

57. Thomson KA, Baeten JM, Mugo NR, Bekker LG, Celum CL, Heffron R. Tenofovir-based oral preexposure prophylaxis prevents HIV infection among women. Current Opinion in HIV and AIDS. 2016;11(1):18-26. [reason: review; not a RCT]

59. Vermund SH. Safety and tolerability of tenofovir for preexposure prophylaxis among men who have sex with men. Journal of Acquired Immune Deficiency Syndromes. 2013;64(1):3-6. [reason: review; not a RCT]

60. Yacoub R, Nadkarni GN, Weikum D, Konstantinidis I, Boueilh A, Grant RM, et al. Elevations in serum creatinine with tenofovir-based HIV pre-exposure prophylaxis: A meta-analysis of randomized placebo-controlled trials. Journal of Acquired Immune Deficiency Syndromes. 2016;71(4):e115-e8. [reason: meta-analysis of RCTs]

3.5 Additional efficacy results

Results from Thigpen 2012 (by gender)

	Tenofovir-emtricitabine group	Placebo group	Efficacy	95% CI	95% CI
Female	7	14	49.4	-21.5, 80.8	0.11
Male	2	10	80.1	24.6, 96.9	0.03

This is the protective efficacy by gender; modified intention-to-treat cohort

Appendix 4

4.1 Cost-effectiveness review search results

Pubmed

Search	Query	Results
#33	#5 AND #16 AND #32	585
#32	ICER OR QALY OR "incremental cost effectiveness ratio" OR "quality adjusted life year" OR "economic model" OR "cost benefit analysis" OR pharmacoeconomics OR "budget impact analysis" OR budget OR cost OR CUA OR "cost utility analysis" OR CEA OR "cost effectiveness analysis"	843854
#31	"cost effectiveness analysis"	9065
#30	ICER	3448
#29	QALY	16054
#28	"incremental cost effectiveness ratio"	4543
#27	"quality adjusted life year"	4581
#26	"economic model"	1962
#25	"cost benefit analysis"	76864
#24	pharmacoeconomics	22922
#23	"budget impact analysis"	536
#22	budget	33596
#21	cost	790000
#20	CUA	1977
#19	"cost utility analysis"	2200
#18	CEA	35309
#17	“cost effectiveness analysis”	9065
#16	TDF OR FTC-TDF OR TDF-FTC OR pre-exposure prophylaxis OR prep OR truvada OR emtricitabine OR tenofovir disoproxil fumarate OR tenofovir OR "antiretroviral agent”	15896
#15	TDF	2767
#14	FTC-TDF	204
#13	TDF-FTC	353
#12	pre-exposure prophylaxis	2959
#11	prep	7033
#10	truvada	632
#9	emtricitabine	2517
#8	tenofovir disoproxil fumarate	6458
#7	tenofovir	6458
#6	"antiretroviral agent”	287
#5	human immunodeficiency virus 1 OR acquired immune deficiency syndrome OR human immunodeficiency virus OR HIV	391648
#4	human immunodeficiency virus 1	97378
#3	acquired immune deficiency syndrome	91178
2	human immunodeficiency virus	354100
#1	HIV	341670

Embase

Search	Query	Results
#4	#1 AND #2 AND #3	1204
#3	47'cost effectiveness analysis' OR 'cost utility analysis' OR costing OR budget OR 'budget impact analysis' OR pharmacoeconomics OR 'cost benefit analysis' OR 'economic model' OR 'quality adjusted life year' OR 'incremental cost effectiveness ratio' OR 'cea' OR 'cua' OR 'markov model' OR 'decision tree	380862
2	46'antiretroviral agent' OR tenofovir OR 'tenofovir disoproxil' OR emtricitabine OR 'emtricitabine plus tenofovir disoproxil' OR truvada OR tdf OR 'tdf-ftc' OR 'ftc-tdf' OR 'tdf' OR 'prep' OR 'pre-exposure prophylaxis	37468
#1	hiv OR aids OR 'human immunodeficiency virus infection' OR 'acquired immune deficiency syndrome' OR 'human immunodeficiency virus 1@	555785

EbscoHost

Search	Query	Results
#4	**#1 AND #2 AND #3**	**54**
#3	**"antiretroviral agent" OR tenofovir OR tenofovir disoproxil OR emtricitabine OR truvada OR prep OR pre-exposure prophylaxis OR TDF-FTC OR FTC-TDF**	**3,496**
#2	**hiv OR aids OR human immunodeficiency virus OR acquired immunodeficiency syndrome OR HIV1**	**125,464**
#1	**cost effectiveness analysis OR cost utility analysis OR costing OR budget OR budget impact analysis OR pharmacoeconomics OR cost benefit analysis OR economic model OR quality adjusted life year OR incremental cost effectiveness analysis OR cea OR cua**	**50,584**

4.2 Included studies

Bernard CL, Owens DK, Goldhaber-Fiebert JD, Brandeau ML. Estimation of the cost-effectiveness of HIV prevention portfolios for people who inject drugs in the United States: A model-based analysis. PLoS Medicine. 2017;14(5)
Cambiano V, Miners A, Dunn D, McCormack S, Ong KJ, Gill ON, et al. Cost-effectiveness of pre-exposure prophylaxis for HIV prevention in men who have sex with men in the UK: a modelling study and health economic evaluation. The Lancet Infectious Diseases. 2018;18(1):85-94.
Desai K, Sansom SL, Ackers ML, Stewart SR, Hall HI, Hu DJ, et al. Modeling the impact of HIV chemoprophylaxis strategies among men who have sex with men in the United States: HIV infections prevented and cost-effectiveness. AIDS. 2008;12(22(14)):1829-39.
Durand-Zaleski I, Mutuon P, Charreau I, Temblay C, Rojas D, Chas J, et al. Cost effectiveness of on demand PrEP in men who have sex with men (MSM) in the ANRS IPERGAY study. Journal of the International AIDS Society. 2016;19:97.
Gray RG, A. Discussion paper: Estimates of the number of people eligible for PrEP in Australia, and related cost-effectiveness. Kirby Institute & CSRH. 2017.
Gomez GB, Borquez A, Caceres CF, Segura ER, Grant RM, Garnett GP, et al. The Potential Impact of Pre-Exposure Prophylaxis for HIV Prevention among Men Who Have Sex with Men and Transwomen in Lima, Peru: A Mathematical Modelling Study. PLoS Medicine. 2012;9(10).
Juusola JL, Brandeau ML, Owens DK, Bendavid E. The cost-effectiveness of preexposure

prophylaxis for HIV prevention in the united states in men who have sex with men. Annals of Internal Medicine. 2012;156(8):541-50.

Lin F, Farnham PG, Shrestha RK, Mermin J, Sansom SL. Cost Effectiveness of HIV Prevention Interventions in the U.S. American Journal of Preventive Medicine. 2016;50(6):699-708.

Luz PM, Osher B, Grinsztejn B, Maclean RL, Losina E, Stern ME, et al. The cost-effectiveness of HIV pre-exposure prophylaxis in men who have sex with men and transgender women at high risk of HIV infection in Brazil. J Int AIDS Soc. 2018;21(3):e25096.

MacFadden DR, Tan DH, Mishra S. Optimizing HIV pre-exposure prophylaxis implementation among men who have sex with men in a large urban centre: A dynamic modelling study. Journal of the International AIDS Society. 2016;19(1).

McKenney J, Chen A, Hoover KW, Kelly J, Dowdy D, Sharifi P, et al. Optimal costs of HIV pre-exposure prophylaxis for men who have sex with men. PLoS ONE. 2017;12(6).

Nichols BE, Boucher CAB, van der Valk M, Rijnders BJA, van de Vijver DAMC. Cost-effectiveness analysis of pre-exposure prophylaxis for HIV-1 prevention in the Netherlands: a mathematical modelling study. The Lancet Infectious Diseases. 2016;16(12):1423-9.

Ong KJ, Desai S, Field N, Desai M, Nardone A, van Hoek AJ, et al. Economic evaluation of HIV pre-exposure prophylaxis among men-who-have-sex-with-men in England in 2016. Euro Surveillance: Bulletin Europeen sur les Maladies Transmissibles = European Communicable Disease Bulletin. 2017;22(42).

Ouellet E, Durand M, Guertin JR, LeLorier J, Tremblay CL. Cost effectiveness of 'on demand' Hiv pre-exposure prophylaxis for non-injection drug-using men who have sex with men in Canada. Canadian Journal of Infectious Diseases and Medical Microbiology. 2015;26(1):23-9.

Paltiel AD, Freedberg KA, Scott CA, Schackman BR, Losina E, Wang B, et al. HIV preexposure prophylaxis in the United States: impact on lifetime infection risk, clinical outcomes, and cost-effectiveness. Clinical Infectious Diseases. 2009;48(6):806-15.

Reyes-Urueña J, Campbell C, Diez E, Ortún V, Casabona J. Can we afford to offer pre-exposure prophylaxis to MSM in Catalonia? Cost-effectiveness analysis and budget impact assessment. AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV. 2018;30(6):784-92.

Schneider K, Gray RT, Wilson DP. A cost-effectiveness analysis of HIV preexposure prophylaxis for men who have sex with men in Australia. Clinical Infectious Diseases. 2014;58(7):1027-34.

Suraratdecha C, Stuart RM, Manopaiboon C, Green D, Lertpiriyasuwat C, Wilson DP, et al. Cost and cost-effectiveness analysis of pre-exposure prophylaxis among men who have sex with men in two hospitals in Thailand. J Int AIDS Soc. 2018;21 Suppl 5:e25129.

4.3 Excluded studies from review of cost-effectiveness

Reason for exclusion	Study
Non-oral PrEP (n=5)	Adamson 2017[1], Glaubius 2016[2], Moodley 2016[3],Walensky 2012[4]
Conference abstract (n=19)	Anderson 2009[5], Bely 2009[6], Bernard 2016[7], Bórquez 2015[8], Cambiano 2015[9], Cambiano 2016[10], Damm 2016[11], Durand-Zaleski 2016[12], Garnett 2016[13], Kenyon 2015[14], Koppenhaver 2011[15], Musenge 2016[16], Nichols 2014[17], Nichols 2016[18], Obiero 2013[19], Pilkington 2018[20], Quaife 2018[21], Vaidya 2015[22], Ying 2015[23]
Systematic review (n=10)	Cambiano 2016[24], Gomez 2013[25], Gordon 2013[26], Hankins 2014[27], Hellinger 2013[28], Kahn 2011[29], Mugo 2016[30],

	Schackman 2012[31]
Generalised population epidemic studies (n=6)	Abbas 2007[32], Alistar 2014[33], Cremin 2013[34], Hallett 2011[35], Long 2013[36], Pretorius 2010[37],
Inappropriate intervention (n=9)	Chen 2014[38], Cremin 2017[39], Drabo 2016[40], Price 2016[41], Punyacharoensin 2016[42], Ross 2016[43], Shen 2018[44], Jewell 2015[45], Mitchell 2015[46]

1. Adamson BJS, Carlson JJ, Kublin JG, Garrison LP. The potential cost-effectiveness of pre-exposure prophylaxis combined with HIV vaccines in the united states. Vaccines. 2017;5(2).
2. Glaubius RL, Hood G, Penrose KJ, Parikh UM, Mellors JW, Bendavid E, et al. Cost-effectiveness of injectable preexposure prophylaxis for HIV prevention in South Africa. Clinical Infectious Diseases. 2016;63(4):539-47.
3. Moodley N, Gray G, Bertram M. The Price of Prevention: Cost Effectiveness of Biomedical HIV Prevention Strategies in South Africa. Clinical research in HIV/AIDS. 2016;3(1).
4. Walensky RP, Park JE, Wood R, Freedberg KA, Scott CA, Bekker LG, et al. The cost-effectiveness of pre-exposure prophylaxis for HIV infection in South African women. Clinical Infectious Diseases. 2012;54(10):1504-13.
5. Anderson J, Cooper D. Cost-effectiveness of pre-exposure prophylaxis for HIV in an MSM population. HIV Medicine. 2009;10:39.
6. Bely K, Pierre KA, Salinas EG. The cost-effectiveness of truvada, kivexa and combivir in the treatment of antiretroviral naïve HIV-1 infected patients in Mexico. Value in Health. 2009;12(3):A112.
7. Bernard CL, Brandeau ML, Humphreys K, Bendavid E, Holodniy M, Weyant C, et al. Cost-effectiveness of HIV preexposure prophylaxis for people who inject drugs in the United States. Annals of Internal Medicine. 2016;165(1):10-9.
8. Bórquez A, Silva-Santisteban A, Guanira J, Salazar X, Caballero P, Nunes-Curto A, et al. Impact and cost-effectiveness of HIV prevention interventions among transgender women sex-workers in Lima, Peru using mathematical modelling informed by stakeholder analysis and health system capacity evaluation. Sexually Transmitted Infections. 2015;91:A52.
9. Cambiano V, Miners A, Dunn D, McCormack S, Gill N, Nardone A, et al. Is pre-exposure prophylaxis for HIV prevention cost-effective in men who have sex with men who engage in condomless sex in the UK? Sexually Transmitted Infections. 2015;91:A1.
10. Cambiano V. Brief overview of cost-effectiveness of PrEP. Journal of the International AIDS Society. 2016;19:14.
11. Damm O, Scholz S, Greiner W. Systematic review of studies estimating the cost-effectiveness of HIV pre-exposure prophylaxis (PREP) in men who have sex with men (MSM). Value in Health. 2016;19(7):A417.
12. Durand-Zaleski I, Mutuon P, Charreau I, Temblay C, Rojas D, Chas J, et al. Cost effectiveness of on demand PrEP in men who have sex with men (MSM) in the ANRS IPERGAY study. Journal of the International AIDS Society. 2016;19:97.
13. Garnett GP, Krishnaratne S, Rush SH, Hallett TB, Hargreaves JR. The cost-effectiveness, affordability and impact of HIV Prevention: Concepts and Reviews. AIDS Research and Human Retroviruses. 2016;32:299.
14. Kenyon CR, Osbak K. How many MSM in Europe could benefit from PrEP – a 9 billion Euro question? International Journal of STD and AIDS. 2015;26(13):988-90.

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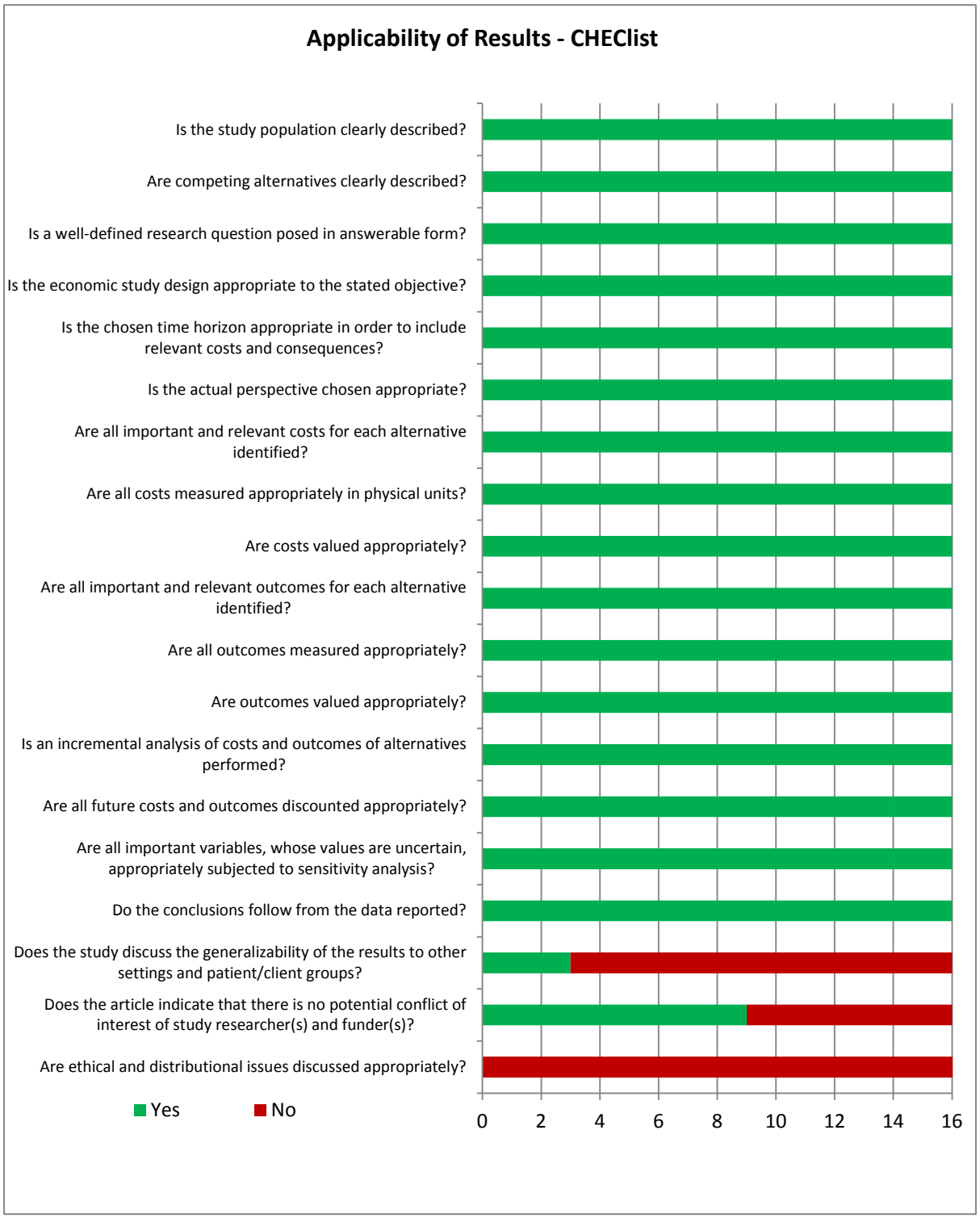
4.4 Quality and applicability of studies

CHEC-list evaluation of the quality of included studies

CHEC-list items
1. Is the study population clearly described?
2. Are competing alternatives clearly described?
3. Is a well-defined research question posed in answerable form?
4. Is the economic study design appropriate to the stated objective?
5. Is the chosen time horizon appropriate to include relevant costs and consequences?
6. Is the actual perspective chosen appropriate?
7. Are all important and relevant costs for each alternative identified?
8. Are all costs measured appropriately in physical units?
9. Are costs valued appropriately?
10. Are all important and relevant outcomes for each alternative identified?
11. Are all outcomes measured appropriately?
12. Are outcomes valued appropriately?
13. Is an incremental analysis of costs and outcomes of alternatives performed?
14. Are all future costs and outcomes discounted appropriately?
15. Are all important variables, whose values are uncertain, appropriately subjected to sensitivity analysis?
16. Do the conclusions follow from the data reported?
17. Does the study discuss the generalizability of the results to other settings and patient/ client groups?
18. Does the article indicate that there is no potential conflict of interest of study researcher(s) and funder(s)?
19. Are ethical and distributional issues discussed appropriately?

CHEC-list diagram

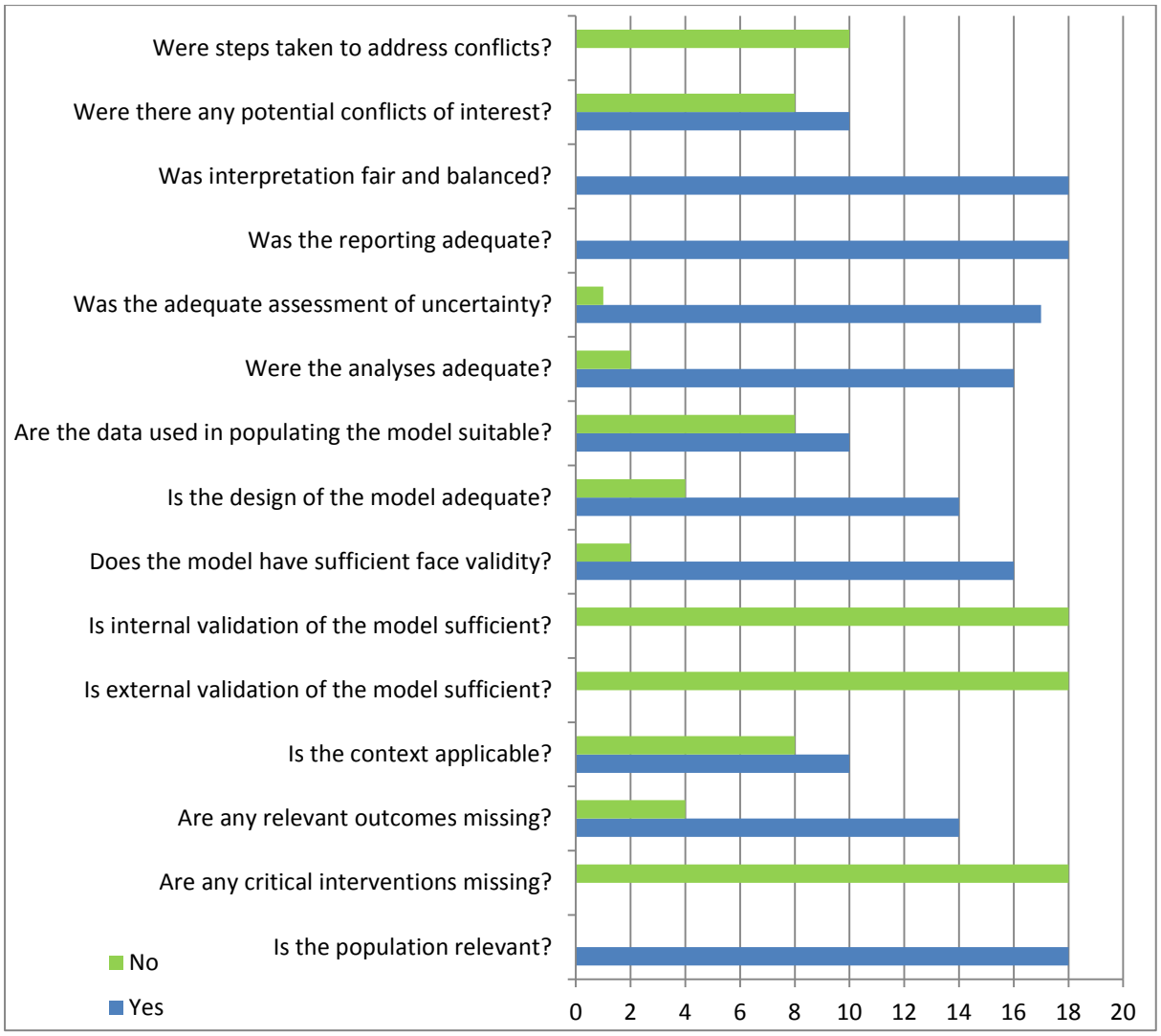


Health Information and Quality Authority

Assessment of applicability — ISPOR

ISPOR items
1. Is the population relevant?
2. Are any critical interventions missing?
3. Are any relevant outcomes missing?
4. Is the context applicable?
5. Is external validation of the model sufficient?
6. Is internal validation of the model sufficient?
7. Does the model have sufficient face validity?
8. Is the design of the model adequate?
9. Are the data used in populating the model suitable?
10. Were the analyses adequate?
11. Was the adequate assessment of uncertainty?
12. Was the reporting adequate?
13. Was interpretation fair and balanced?
14. Were there any potential conflicts of interest?
15. Were steps taken to address conflicts?

ISPOR diagram



4.5 Additional cost-effectiveness study information

Study (Year)	Base case costs and assumptions	Analysis details	Clinical and QALY outcomes	Model costs	Results	Sensitivity analysis
Bernard (2017)[47]	1) Efficacy of PrEP: 49% 2) Dosing regimen: daily 3) Incidence of HIV: n/a 4) Prevalence of HIV: 9.8% 5) Assume 69.9% are aware of their HIV status.	Currency (year): USD (2015) Country: USA Model type: Dynamic transmission Perspective: societal Discount rate: 3% Time horizon: 20 years Utility values: Uninfected: 1 PWDI: 0.9 Asymptomatic HIV: 0.94 Symptomatic HIV: 0.81 Infective AIDS: 0.7	PrEP coverage 36%: Incremental QALYS 220,000 PrEP coverage 40.5%: Incremental QALYS 25,000 PrEP coverage 45%: Incremental QALYS 24,000	PrEP coverage 36%: $69.1 billion PrEP coverage 40.5%: Incremental cost $8.8 Billion PrEP coverage 45%: Incremental cost $8.8Billion Annual costs: PrEP Cost: $10,000 ART HIV cost: $15,000 Asymptomatic HIV: $4,000 Symptomatic HIV: $7,000 Symptomatic HIV (no ART): $6500 AIDS (no ART):$ 20,040 AIDS: $10,000	PrEP coverage 36%: ICER/QALY: $314,000 (162;667) PrEP coverage 40.5%: ICER/QALY: $352,000 (189;713) PrEP coverage 45%: ICER/QALY: $367,000 (196;684)	N/A
Cambiano (2018)[48]	1) Efficacy of PrEP: 86% 2) Dosing regimen: event-based PrEP (mean 5 pills per week) 3) Incidence of HIV: 2.0 per 100 person-years (90%: 0.7–4.3) 4) Prevalence of HIV: n/a 5) 40,000 MSM initiated in Year 1	Currency (year): GBP (No cost year) Country: United Kingdom Model type: dynamic individual-based stochastic model Perspective: health system Discount rate: 3.5%	1) Cumulative mean number of HIV: 134,600 (61,700 to 264,300) 2) Number of HIV infections averted: 44,300 (3,330;97,600) 3) Proportion of HIV infections	Cost (in million £) 56,440 (23,910 to 126,050) Discounted cost (in million £) 19,630 (11,390 to 33,690) Difference in discounted cost (in million £)	Cost saving infections averted: 44,300 (3,300–97,600) Discounted QALY gained: 40,000 (4–70) Discounted cost: -1,000m (-4,900-1,230)	1. 80% probability of cost-effectiveness £20,000 ICER 2. 75% probability of cost-effectiveness £13,000 ICER 3. PrEP cost saving can occur as

	6) Cost of undiagnosed HIV = £0 7) HIV testing, sexual behaviour, probability of initiating ART would remain at current levels. 8) Eligibility criteria similar to PROUD trial. 9) Assumed PrEP stopped if incidence drops below 1 in 1,000. (5,430;7,772) (5,430;7,772)	costs, 3.5% benefits Time horizon: lifetime (80 years old) Utility values: HIV-positive undiagnosed 0 (0; 0) HIV-positive diagnosed with CD4>200 cells/mm3 0.1 (0.08; 0.12) HIV-positive diagnosed with CD4≤200 cells/mm3 0.15 (0.11; 0.19) HIV-positive diagnosed with HIV with WHO4^ 0.55 (0.38; 0.71) HIV-positive diagnosed with HIV with WHO3^ 0.22 (0.15; 0.31) Miners et al. 2014	averted: 25% 4) QALYs (in 1000s) 55,810 (55,290 to 56,120) 5) QALYs gained (in 1,000s) 220 (20 to 430) 6) Discounted QALYs (in 1,000s): 18,450 (18,360 to 18,510) 7) Discounted QALYs gained (in 1,000s): 40 (4 to 70)	-1,000 (–4,900 to 1,230) Net monetary benefit (in million £) 1,490 (–1,360 to 6,580) Annual PrEP ART cost: £4,331 Annual ART cost for HIV+: £6,288 (4,264;9,339) Additional monitoring cost for PrEP Year 1: £82 (47;126) Additional monitoring after Year 1: £94 (56;141) Use of healthcare services: minimum £1,250 (430;2,499) Maximum £6,550	1 billion saved 25% infections averted – 42% directly due to PrEP	early as 20 years with 90% reduction in ART costs. 4. PrEP cost saving for HIV incidence declining and increasing after 40 years. 5. Indicates cost saving will occur between 20–40 years. 6. 21 scenarios were cost saving these scenarios included: (i) Daily PrEP (ii) Efficacy of PrEP (iii) Uptake rates (iv) Cost of PrEP (v) Indefinite continuation of PrEP programme
Desai (2008)[49]	1) Efficacy of PrEP: 50% 2) Dosing regimen: daily 3) Incidence of HIV:1.35% 4) Prevalence of HIV: 14.6 (90%CI:8.1;18.4) 5) Base-case program adherence: 50% 6) Coverage of 15,000 (25%) of high-risk MSM	Currency (year): USD (no cost year) Country: USA Model type: dynamic transmission Perspective: health provider Discount rate: 3% Time horizon: 5 years Utility values: 6.95 per DALY saved	1) Base-case: HIV cases prevented: 1,705 (306;2,947) 2) Base-case percentage of cases prevented: 8.7%	1) Annual PrEP ART cost: $14,235 ($39 by 365)	1) US$/QALY: $31,972 ($17,168;46;775)	1) 36 Scenarios: (i) Efficacy (ii) Mechanism of protection (iii) Coverage (iv) Adherence Latin hypercube sampling 2) At three levels of HIV care cost: low, base-case and high. One scenario across three

						levels reported all three ICERs >$100,000 at when care cost were low and adherence 33%. 3) At base-case and high HIV case costs 39% of scenarios were cost saving. 4) At two levels of case prevented: low and high. Lower case ICER ranged from $3,412 to $2.26 million. High HIV case prevention ICER 70% were cost saving.
Durand (2016)[12]	1) Efficacy of PrEP: 86% 2) Dosing regimen: on demand (15.6 tablets per month) 3) Incidence of HIV: IPERGAY 4) Prevalence of HIV: IPERGAY 5) NNT: 17.2 6) 5.68 infections averted/100 person-years 7) Zero cost for placebo arm	Currency (year): Euro (2016) Country: France Model type: non-mathematical cost benefit model Perspective: health provider Discount rate: none Time horizon: 1 year Utility values: none (CEA)	None	1) Annual PrEP ART Cost: €3,117 2) Annual PrEP Program cost: €4,271 (SD €2,446) 3) Cost of HIV infection averted: €75,258	1) Cost saving for 7.5 years	1) Generic price (€2,771/pp): Cost saving up to 13 years. 2) International market price (€1,517/pp): Cost saving up to 20 years.

Gomez (2012)[50]	1) Efficacy of PrEP: 92% (40;99) 2) Dosing regimen: daily 3) Incidence: (i) MSM 2.0/100PY (ii) High Risk MSM: 3.5/100PY 4) Prevalence:0.2 5) Adherence: good (95%), average (45%), poor (15%) 6) Threshold for Peru: $5,401/DALY averted.	Currency (year): USD Country: Peru Model type: dynamic transmission (mathematical epidemic) Perspective: health provider Discount rate: 3% Time horizon: 10 years Utility values: Fox-Rushby	1) DALY averted per infection undiscounted: 27.12 2) DALY averted per infection discounted: 11.5	1) Annual PrEP ART cost: $420–600 2) PrEP intervention cost: $525–830 3) ART cost: $1,000–3500	N/A	1) Low (5%) and high (20%) coverage scenarios. 2) The three levels of adherence. 3) Across all scenarios highest estimated cost per DALY averted $1,126-$1,780 ($1,036-$4,254). 4) Six main scenarios (coverage & prioritization): $447–$1779/DALY.
Gray (2017)[51]	1) Efficacy of PrEP: 99% 2) Dosing regimen: daily 3) Incidence: n/a 4) Prevalence: n/a 5) High adherence: 90%	Currency (year): AUD (2015) Country: Australia Type: OPTIMA model Perspective: health provider Discount rate: 5% Time Horizon: 15 years (2016–2030) Utility values: Tengs and Lin	1) 30-0-0 scenario. 2) Infections averted: 4,720 (2,510–6,440). 3) QALYs gained: 2,190 (1,160–2,840)	1) Annual PrEP ART cost: $10,249	1) Incremental cost of PrEP programme: $205,242,910 2) Cost per QALY gained: $102,400	1) Eight update scenarios modelled for high/medium/ low risk MSM 2) Infections averted range: 4,720–11,330. 3) QALY gained range: 2,190–6,270.
Juusola (2012)[52]	1) Efficacy of PrEP: 44% 2) Dosing regimen: daily 3) Incidence: 0.8% 4) Prevalence: 12.3% 5) 90% reduction in sexual infectivity due to ART used for treatment of HIV infection.	Currency (year): USD (no cost year) Country: USA Type: deterministic dynamic compartmental Perspective: societal discount rate: 3% Time horizon: 20 Years	All MSM incremental QALYS (i) 100% coverage: 2,217,732 (ii) 50% coverage: 1,263,673 (iii) 20% coverage: 550,166	1) Annual PrEP ART cost: $9,312 2) Annual HIV ART cost: $15,589 3) Annual HIV care cost: $4,130–6,934 4) Annual AIDS care	PrEP in 20% of all MSM: $172,091/QALY PrEP coverage of 100% high-risk MSM: $52,433/QALY $600,000 per	1) PrEP cost, efficacy and quality-of-life impacted cost effectiveness. 2) Sexual disinhibition had no impact.

	6) No change in behavioural disinhibition 7) Discontinuation of PrEP after 20 years or at 65 years of age.	Utility values: HIV positive: 0.94 Tengs and Lin 2002	High-risk MSM incremental QALYS (i) 100% coverage: 1,439,261 (ii) 50% coverage: 817,655 (iii) 20% coverage: 352,840	cost: $6,181–21,863 All MSM incremental costs (billons): (i) 100% coverage: $480 (ii) 50% coverage: $238 (iii) 20% coverage: $95 High-risk MSM costs: (i) 100% coverage: $75 (ii) 50% coverage: $36 (iii) 20% coverage: $14.	infection averted 50% HR MSM: $44,556/QALY 20% HR MSM: $40,279/QALY ($460,000 per infection averted. QALY <$100,000 when targeted at HR MSM and efficacy of 75%.	3) ART cost 75% and efficacy 44% $38,804/QALY gained for high risk MSM. 4) $35,080/QALY gained at efficacy of 73% and full adherence for high-risk MSM.
Lin (2016)[53]	1) Efficacy of PrEP: 44% 2) Dosing regimen: not stated. 3) Incidence of HIV: n/a 4) Prevalence of HIV: 19%	Currency (year): USD (2012) Country: USA Model type: Bernoulli process model Perspective: societal discount rate: n/a Time horizon: n/a Utility values: 4.45 QALY per HIV infection	QALYS per HIV infection prevented: 4.45	1) Annual PrEP ART Cost: $10,338 2) Cost per HIV infection prevented: $679,878.	$58,849/QALY saved	N/R
Luz (2018)[54]	1) Combined point estimates for effectiveness of PrEP: 96% (Efficacy) x 73.9% (Adherence) x 61% (Uptake) = 43.2% 2) Dosing regimen: daily 3) HIV incidence: 4.27 (<40 years old) and 1.0 (>40	Currency (year): USD (2015) Country: Brazil Model Type: CEPAC model-state transition Monte-Carlo Perspective: health provider (Brazil NHS)	Incremental per-person life expectancy for PrEP: 4.2 years Incremental discounted per-person life expectancy: 1.7 years.	1) Annual PrEP ART cost: $272 2) Annual HIV ART cost: $120–6,119 3) Incremental cost of PrEP: $4,320/per person.	ICER (cost/LE): 4320/1.7 = $2,530 Incidence is the major determinant of PrEP CE PrEP remained	1) PrEP remains cost effective in the face of all plausible uncertainty 2) Tornado diagram showed key

	years old) 4) HIV prevalence: 5.2–23.7% 5) PrEP-induced resistance made first and second line ART 10% less effective. 6) Cost effectiveness threshold of $8,540	Discount rate: 3% Time horizon: n/a Lifetime utility values: n/a ICER in dollars per year of life saved (YLS).			cost effective when the cost was less than $100/month PrEP remained cost effective until incidence was reduced to 0.9/100PY	drivers were: (i) Incidence of HIV (ii) PrEP ART cost (iii) PrEP effectiveness. 3) PrEP was cost effective until drug costs were >$100/month. 4) PrEP was cost effective up to incidence of 0.9/100PY
MacFadden (2016)[55]	1) Efficacy of PrEP: 44% 2) Dosing regimen: daily 3) Incidence of HIV:0.62–1.14 per 100PY 4) Prevalence of HIV: n/a 5) No female sexual partners were included 6) Tested PrEP in endemic equilibrium 7) The cost of PrEP remained stable (that is, did not model on-demand dosing) 8) QALY ratio for PrEP users was 1 9) ART adherence for patients with HIV was excellent	Currency (year): CAD (2015) Country: Canada Model type: dynamic transmission perspective: health system Discount rate: 3% Time horizon: 20 years Utility values 1) PrEP: 1 2) Unidentified HIV+ (CD4>200): 0.91 3) Unidentified HIV+ (CD4>200): 0.89 4) Unidentified AIDS: 0.73 5) Identified AIDS: 0.73 6) On ART: 0.83 Tengs and Lin 2002	All MSM incremental QALYS (i) 100% coverage: 5,430 (ii) 75% coverage: 5,363 (iii) 50% coverage: 4,413 (iv) 25% coverage: 2,673 High-risk MSM incremental QALYS (i) 100% coverage: 2,951 (ii) 75% coverage: 3,080 (iii) 50% coverage: 2,321 (iv) 25% coverage: 1,417	All MSM PrEP costs (billions): (i) 100% coverage: $4.37 (ii) 75% coverage: $3.80 (iii) 50% coverage: $2.65 (iv) 25% coverage: $1.36 High-risk MSM PrEP costs (millions) (i) 100% coverage: $269 (ii) 75% coverage: $239 (iii) 50% coverage: $162 (iv) 25% coverage: $79.8 1) Annual PrEP ART Cost:$10,012 2) Initial/Subsequent clinic visits:	*No base-case all scenario analysis.	All MSM cost/QALY gained: (i) 100% coverage: $792,763 (ii) 75% coverage: $696,297 (iii) 50% coverage: $587,050 (iv) 25% coverage: $495,175 High-risk MSM cost/QALY gained: (i) 100% coverage: $68,203 (ii) 75% coverage: $56,084 (iii) 50% coverage: $46,818 (iv) 25% coverage: $34,999 99% efficacy of PrEP cost/QALY: 25-100% Coverage: $15,275–44,427

				\$305/\$100 3) Annual cost HIV+ (on ART) =\$15,264		
McKenney (2017)[56]	1) Efficacy of PrEP: 56% 2) Dosing regimen: daily 3) Incidence of HIV: 0.19 (0.05-0.4) 4) Prevalence of HIV: n/a 5) Base-case Chen et al. 6) Updated the per-act probability of HIV: 0.0138 (0.0102–0.0186)	Currency: USD (no cost year) Country: USA Model type: decision analytic Perspective: societal Ddiscount rate: 3% (Chen et al.) Time horizon: lifetime (1 year of PrEp) Utility values: HIV+ CD4 cell count >350cells/µl: 0.94 HIV+ CD4 cell count 200-350cells/µl: 0.82 Infected AIDS: 0.7 Tengs and Lin 2002	Discounted QALY gained per case of HIV averted: 2.24 QALY loss per additional STI: 0.02	1) Lifetime HIV cost: \$327,503 2) Annual PrEP ART cost: \$10,711 (\$4,772-15,000)	Base-case: \$64,000/QALY gained All scenarios cost saving when the cost of PrEP is reduced by 60% All scenarios are cost saving at high levels of efficacy/adherence	For PrEP to be cost saving at base-case adherence/efficacy levels and at background prevalence of 20%, drug cost would need to be reduced to \$8,021 per year (25% reduction) with no disinhibition and to \$2,548 (76% reduction) with disinhibition.
Nichols (2016)[57]	1) Efficacy of PrEP: 86% 2) Dosing regimen: daily and on-demand 3) Incidence of HIV: n/a 4) Prevalence of HIV: n/a 5) Average of 4,500 MSM on PrEP at full scale-up 6) Daily and on-demand have same effectiveness 7) On-demand costs half as much as daily dosing 8) No change in sexual behaviour	Currency (year): euro (2015) Country: Netherlands Type: mathematical Perspective: third-party payer Discount rate: 3% Time horizon: 40 years Utility values: susceptible/on PrEP: 1 (Assumption) HIV+ CD4 cell count >350cells/µl: 0.94 HIV+ CD4 cell count 200-350cells/µl: 0.82 Infected AIDS: 0.7 Tengs and Lin 2002	N/A	1) Annual PrEP ART cost (Daily): €7,400 2) Annual PrEP ART cost (on-demand): €3,850 3) One time additional costs during first year of treatment: €1,130–3,539 4) Cost of ART for HIV: €12,468–13,505	Daily PrEP Stable HIV epidemic – cost per QALY gained: €7,800 (100% efficacy) to €20,000 (40% efficacy On-demand PrEP Stable HIV epidemic – cost per QALY gained: cost saving (100% efficacy) to €9,100	1) Univariate sensitivity analysis 2) Daily PrEP the discount rate for costs and QALYs had most profound effect 3) ICERs: €5,200–15,000 4) On-demand PrEP the cost of ART had most profound effect 5) ICERs: €700–3,700

		Infected on ART: 0.94 (assumption based on Tengs and Lin)			(40% efficacy At current epidemic all cost per QALY gained <€20,000	6) Efficacy >90% all ICER <€10,000 7) Efficacy >90% and cost of PrEP reduced by 50% intervention is cost saving 8) Daily PrEP declining HIV epidemic – cost per QALY gained: €13,100 (100% efficacy) to €26,000 (40% efficacy) 9) On-demand PrEP declining HIV epidemic – cost per QALY gained: €1,400 (100% efficacy) to €9,100 (40% efficacy)
Ong (2017)[58]	1) Efficacy of PrEP: 86% 2) Dosing regimen: daily and on-demand (4 tablets per week) 3) Incidence of HIV: 3.3/100PY 4) Prevalence of HIV: n/a 5) Risk compensation: 20% 6) Assumption of no disutility between HIV infection and diagnosis. 7) Cumulative lifetime incidence without PrEP:	Currency (year): GBP (2015) Country: United Kingdom Type: decision analytic Perspective: health provider Discount rate: 3.5% Time horizon: lifetime (1 Year PrEP Uutility values: 1) Disutility HIV: 0.11 2) Utility of men >75	1) 118 HIV infections averted 2) 361 (discounted) QALYs saved	Annual PrEP ART Cost: £4,331 PEP: £772 Annual ART HIV cost: £4,741 Annual HIV care >200CD4 cost: £4,734 Annual HIV care <200CD4 cost: £7,479 Annual cost of undiagnosed HIV	Base-case: cost saving -£7,227 (Efficacy 86%, 3.3/100PY, risk compensation 20%) 23 years until years of cumulative saving from HIV care costs averted for the year-1	1) Multivariate sensitivity analysis. (i) Efficacy of PrEP (ii) HIV incidence (iii) Risk compensation (iv) % reduction in HIV ART cost (v) % reduction in PrEP ART cost At 86% efficacy

	16.96% 8) After Year 1 incidence was reduced to 1.35 per 100PY and PrEP was no longer indicated	years old with HIV: 0.75. Tengs and Lin 2002		infection: £0 (£0–2,499) Year 1 program cost: 22.5m.	investment to breakeven.	PrEP scenarios: Cost saving: 75% Cost effective: 18.75% Not cost effective (ICER >£20,000: 6.25%. In both cases when incidence 2.0 per 100 PY No scenarios
Ouellet (2015)[59]	1) Efficacy of PrEP: 44% (grant referenced) 2) Dosing regimen: on demand 3) Incidence of HIV: 7.2/100,000 4) Prevalence of HIV: 212/100,000	Currency (year): CAD (2015) Country: Canada Model type: microcosting Perspective: societal discount rate: 3%/5% Time horizon: n/a Utility values: One year of life for a healthy asymptomatic HIV patient: 0.94 Tengs and Lin 2002	1) Incremental undiscounted QALYS: 16.99 2) Incremental 3% discounted QALYS: 5.53 3) Incremental 5% discounted QALYS: 2.86 4) NNT:51.78	1) HIV costs: $27.695–35,606. 2) Life HIV cost: $1,439,984, $662,295 (3%) $448,901 (5%) 3) Annual PrEP ART cost: $12,001 4) Cost per infection prevented: $621,390	Base-case (undiscounted): Cost saving at high and low cost of HIV	3% discount: Cost saving at high and low cost of HIV Discounted 5%: Low cost of HIV: $47,338 High cost of HIV: $60,223
Paltiel (2009)[60]	1) Efficacy of PrEP: 50% 2) Dosing regimen: daily 3) Incidence of HIV: 1.6% 4) Prevalence of HIV: n/r 5) Highly pessimistic base-case scenario. 6) Assumed annual HIV testing 7) No behavioural disinhibition in base-case scenario.	Currency (year): USD (2006) Country: USA Model type: dynamic transmission (CEPAC) Perspective: societal Discount rate: 3% Time horizon: Lifetime Utility values: n/r	1) Incremental life years: 0.8 2) Incremental QALYS: 0.5 (21.7 increased to 22.2)	1) Annual PrEP ART Cost: $9,036 2) Annual HIV ART Cost: $1,139–3,338 3) Lifetime discounted cost of HIV: $81,100 per person	1) $298,000 QALY life year gained 2) Reduced lifetime risk 44% to 25% 3) Increased LE: 39.9 to 40.7 years	1) PrEP efficacy 90%: $107,000 2) HIV incidence 3.1%: $150,000 3) PrEP cost reduction 50%: $114,000 4) No routine HIV screening in 'No PrEP' scenario: $114,000

Reyes-Uruena (2018)[61]	1) Efficacy of PrEP: 86% 2) Dosing regimen: daily and on-demand 3) Incidence of HIV: 2% 4) Prevalence of HIV 5) MSM willing to take PrEP: 5,989–10,972 (1.86–3.4%) 6) Six outpatient visits per year and incur laboratory costs. 7) Salary losses due to PrEP €536 8) Salary losses due to HIV: €5,661	Currency (year): euro (2016) Country: Spain Model type: n/a Perspective: n/a Discount rate: 3%/5% Time horizon: n/a Utility values: Reduction in QALY in asymptomatic HIV infection: 0.94 Tengs and Lin	Incremental QALYS: (i) Undiscounted: 16.99 (ii) 3% discount: 4.19 (iii) 5% discount: 2.36 Incremental life years: (i) Undiscounted: 14.9 (ii) 3% discount: 3.5 (iii) 5% discount: 1.9	Annual PrEP Program cost (ART Cost): (i) Daily: €7,176.54 (€5,873.90) (ii) On-demand: €7,176.54 (€2,936.90) HIV costs: €13,481.97	ICER daily PrEP: Uundiscounted: €6,281.62 ICER on-demand PrEP: Uundiscounted: -3767.36	ICER Daily PrEP: (i) 3% discount: €57,424.80 (ii) 5% discount: €155,829.82 ICER On-Demand PrEP: (ii) 3% discount: €16,706.73 (ii) 5% discount: €43,329.57
Schneider (2014)[62]	1) Efficacy of PrEP: 95% 2) Dosing regimen: daily and on-demand 3) Incidence of HIV: n/a 4) Prevalence of HIV: n/a Approximately 10% of MSM 5) 60,000 MSM 6) Adherence of 75% 7) No sexual disinhibition in the base-case	Currency (year): AUD (2013) Country: Australia Model type: dynamic transmission Perspective: health provider Discount rate: 3% Time horizon: 10 year Utility values: HIV+ CD4 cell count >350cells/µl (Asymptomatic): 0.94 HIV+ CD4 cell count 200–350cells/µl (Symptomatic): 0.82 Infected AIDS: 0.7 Tengs and Lin 2002	Target group, coverage: QALYG All MSM (i) 10%: 605 (ii) 20%: 1,477 (iii) 30%: 2,142 MSM>10 partners (i) 15%:922 (ii) 30%:1,503 MSM>20 partners (i) 15%: 878 (ii) 30%:1,395 MSM>50 partners (i) 15%: 228 (ii) 30%: 571 MSM SDC: (i) 15%: 527 (ii) 30%: 1,067	Target group, coverage: Incremental cost (billion) All MSM (i) 10%: $3.16 (ii) 20%: $6.31 (iii) 30%: $9.52 MSM>10 partners (i) 15%: $1.66 (ii) 30%: $3.31 MSM>20 partners (i) 15%: $1.28 (ii) 30%: $2.55 MSM>50 partners (i) 15%: $0.31 (ii) 30%: $0.65 MSM SDC (millions): (i) 15%: $4.42 (ii) 30%: $12.35 Annual PrEP ART cost: $9,596.97 PrEP annual	Target Group, Coverage: ICER/QALYG All MSM (i) 10%: $521,848 (ii) 20%: $427,149 (iii) 30%:$180,146	Target group, coverage: ICER/QALYG MSM>10 partners (i) 15%: $180,146 (ii) 30%: $220,252 MSM>20 partners (i) 15%: $145,960 (ii) 30%: $183,195 MSM>50 partners (i) 15%: $134,185 (ii) 30%: $113,673 MSM SDC: (i) 15%: $8,399 (ii) 30%: $11,575

				monitoring cost: $765 Annual HIV ART cost: $10,685–31,411 Annual HIV medical costs: $3,097–7,883		
Suraratdecha (2017)[63]	1) Efficacy of PrEP: 75% 2) Dosing regimen: daily 3) Incidence of HIV: n/a 4) Prevalence of HIV: 11.6% and 5.2% 5) Baseline ART coverage 30% 6) Cost effectiveness threshold: $17,449	Currency (year): USD (No cost year) Country: Thailand Model type: dynamic transmission (OPTIMA) Perspective: health provider Discount rate: 3% Time horizon: 5 years	PrEP to high-risk MSM: (i) DALYs averted: 7,857 (ii) HIV infection averted: 555 PrEP to all MSM: (i) DALYs averted: 19,368 (ii) HIV infection averted: 1,368	Annual PrEP ART costs: $14,106 Total annual PrEP Cost: $17,206 PrEP to high-risk MSM: lifetime treatment cost (millions): $3.99 PrEP to all MSM: lifetime treatment cost (millions): $9.84	PrEP to all MSM: (i) $/DALY averted: $7,089 (ii) $/HIV infection averted: $100,367	80% chance of cost effectiveness in high MSM: $4836 per DALY averted PrEP to high-risk MSM: (i) $/DALY averted: $4,836 (ii) $/HIV infection averted: $68,468

Appendix 5

5.1 Correction factor

Table 5.1. Comparison of self-reported risky behaviour in MSM participating in national versus convenience survey samples

	Natsal-3	EMIS	London-GMSHS	Scotland-GMSHS
Unprotected anal intercourse (with 2+ partners), past year				
%	13.4 (7.4 to 23.1)	25.2	21.6	14.9
Crude OR	1.00	2.18 (1.12 to 4.23)	1.78 (0.90 to 3.54)	1.06 (0.54 to 2.09)
AOR	1.00	2.30 (1.18 to 4.59)	1.61 (0.79 to 3.28)	0.91 (0.44 to 1.89)
Diagnosed with STI, past year				
%	5.0 (2.3 to 10.5)	9.5	11.6	–
Crude OR	1.00	2.01 (0.90 to 4.51)	2.50 (1.08 to 5.76)	
AOR	1.00	1.91 (0.85 to 4.30)	2.43 (0.99 to 5.99)	
Drug use, past year				
%	29.2 (21.1 to 38.9)	60.7	–	–
Crude OR	1.00	3.74 (2.42 to 5.79)		
AOR	1.00	3.62 (2.33 to 5.61)		

Abbreviations: AOR: Adjusted Odds Ratio
Adjusted for age, academic qualification and London residency (EMIS); age, employment and ethnicity (London-GMSHS); age and academic qualification (Scotland-GMSHS).
GMSHS — Gay Men Sexual Health Survey; EMIS — European Men who have sex with men Internet Survey; Natsal — National Survey of Sexual Attitudes and Lifestyles.
Source: Prah et al. 2016.

5.2 Costs

Table 5.2. Cost — first clinical assessment

Staff resource use: first clinical assessment	Time (in minutes)	Cost (2019 €)	Source
Clerical staff	10	4.22	2019 Salary Scales Irish Department of Health & Time in Motion Study (GUIDE - 2013)
Medical review (consultant or specialist registrar)	30	48.74	2019 Salary Scales Irish Department of Health (see below)
Phlebotomy	12	6.00	2019 Salary Scales Irish Department of Health & Time in Motion Study (GUIDE - 2013)
Total staff resource use per visit: €58.96			

Investigations: first clinical assessment	Test	Cost (2018 €)	Source
4th generation venous blood HIV test	HIV Antigen/Antibody (architect)	10.67	National Virus Reference Laboratory
Chlamydia and gonorrhea testing*	GC/CT NAAT	31.74 per site	National Virus Reference Laboratory
Syphilis testing	Syphilis serology	10.05	National Virus Reference Laboratory
HBV testing**	HBV surface antigen (architect)	9.84	National Virus Reference Laboratory
	HBV anti-core antibody (architect)	15.24	National Virus Reference Laboratory
	HBV surface antibody (architect)	12.36	National Virus Reference Laboratory
HCV testing	HCV antibody	13.09	National Virus Reference Laboratory
Serum creatinine and eGFR***	Urea and Electrolytes	12.26	St James's Laboratory
HAV IgG testing if previous vaccination not reported****	HAV IgG	15.86	National Virus Reference Laboratory
Vaccination review******	In line with NIAC recommendations 1. HBV vaccination is recommended for all people attending STI clinics 2. HAV vaccination is recommended for MSM 3. HPV vaccination is recommended for MSM under 45 years of age		
Total Investigations: €128.27			

Total Staff Resource + Investigations €187.23

*Some sites pool samples (rectal, urethral and pharyngeal); assumed 50% pool samples and 50% test sites separately
**It is assumed 50% of attendees will require HBV testing
***eGFR>60 mls/min/1.73m2: Measure creatinine and eGFR three monthly whilst on PrEP. eGFR<60mls/min/1.73m2: At baseline if eGFR is <60mls/min/1.73m2 assess for relevant medical conditions, nephrotoxic drugs and strongly consider renal referral before commencing PrEP. In follow up, if eGFR falls to <60mls/min/1.73m2 whilst on PrEP, continuation is not recommended. Reassess for relevant medical conditions, nephrotoxic drugs and consider renal referral.
For services where eGFR is reported to >90ml/min/1.73m2: if the eGFR falls whilst on PrEP but remains >60ml/min/1.73m2 consideration should be given to discontinuing PrEP.
****Cost of HAV IgG and vaccines not included as many MSM will be up-to-date if already engaged in services, and recommendations do not differ from 'usual care' for MSM so incremental cost will not change
Note: some attendees will also require urinalysis

Table 5.3. Cost — starting visit*

Staff Resource Use: starting visit	Time (in minutes)	Cost (in 2019€)	Source
Clerical staff	10	4.22	2019 Salary Scales Irish Department of Health & Time in Motion Study (GUIDE - 2013)
Medical review (50% performed by clinical nurse specialist and 50% by consultant or specialist registrar)	10	11.90	2019 Salary Scales Irish Department of Health
Total: €16.12			

*Note-only 50% of new patients will require starting visit

Table 5.4. Cost — subsequent visit in Year 1

Staff Resource Use: subsequent visit	Time (in minutes)	Cost (2019 €)	Source
Clerical staff	5–10	2.11	2019 Salary Scales Irish Department of Health & Time in Motion Study (GUIDE - 2013)
Medical review and STI screen (by clinical nurse specialist/advanced nurse practitioner)	15	13.50	2019 Salary Scales Irish Department of Health
Phlebotomy	12	6.00	2019 Salary Scales Irish Department of Health & Time in Motion Study (GUIDE - 2013)

Investigations: subsequent visit	Test	Source	Cost (2019 €)
4th generation venous blood HIV test	HIV antigen/antibody (architect)	National Virus Reference Laboratory	10.67
Chlamydia and gonorrhea testing*	GC/CT NAAT	National Virus Reference Laboratory	31.74 per test
Syphilis testing	Syphilis serology	National Virus Reference Laboratory	10.05

Serum creatinine and eGFR**	Urea and electrolytes	St James's Laboratory	12.26
Total investigations per visit: €96.46			
Total staff resource use + investigations per visit: €118.07			

*Some sites pool samples; assumed 50% pool samples (rectal, pharyngeal and urethral) and 50% test sites separately
**see prior note on eGFR

Table 5.5. Cost – continuing PrEP (additional cost after first year)

Staff Resource Use: subsequent visit			
	Time (in minutes)	**Source**	**Cost (2019 €)**
Medical review (consultant or specialist registrar)*	30*	2019 Salary Scales Irish Department of Health	€48.73
		3-monthly*	*€6.09**

Investigations: costs after first year			
	Test	**Source**	**Cost (2019 €)**
HCV testing – annual	HCV antibody	National Virus Reference Laboratory	€13.09
		3-monthly	*€3.27*
Total cost per visit: €9.36			

*It is assumed 50% of high risk MSM will require a medical review once per year, similar to usual care (see Table 6B6)

Table 5.6. Cost — usual care for high-risk MSM

Staff Resource Use	Time (minutes)	Cost (2019 €)	Source
Clerical staff	10	4.22	2019 Salary Scales Irish Department of Health & Time in Motion Study (GUIDE - 2013)
Medical review (consultant or specialist Registrar)*	30*	6.09*	2019 Salary Scales Irish Department of Health
Phlebotomy	12	6.00	2019 Salary Scales Irish Department of Health & Time in Motion Study (GUIDE - 2013)
Male STI screen (performed by clinical nurse specialist /advanced nurse practitioner)	15	13.50	2019 Salary Scales Irish Department of Health & Time in Motion Study (GUIDE - 2013)
Total staff resource use*: €29.81			

*It is assumed 50% of high risk MSM will require a medical review once per year. One medical review costs €48.73.

Usual Care: Investigations	Test	Cost (2018 €)	Source
4th generation venous blood HIV test	HIV antigen/antibody (architect)	10.67	National Virus Reference Laboratory
Chlamydia and gonorrhea testing*	GC/CT NAAT	31.74 per test	National Virus Reference Laboratory
Syphilis testing	Syphilis serology	10.05	National Virus Reference Laboratory
HBV testing (annual)	HBV surface antigen; anti-core antibody and surface antibody (architect)	37.44	National Virus Reference Laboratory
		3-monthly cost	*9.36*
HCV testing (annual)	HCV antibody	13.09	National Virus Reference Laboratory
		3-monthly cost	*3.27*
HAV IgG testing if previous vaccination not reported**	HAV IgG	15.86	National Virus Reference Laboratory

Vaccination review**	In line with NIAC recommendations 1. HBV vaccination is recommended for all people attending STI clinics 2. HAV vaccination is recommended for MSM 3. HPV vaccination is recommended for MSM under 45 years of age
Total Investigations: €96.83	
Total Staff Resource + Investigations €126.64	

*Some sites pool samples (rectal, urethral and pharyngeal); assumed 50% pool samples and 50% test sites separately

**Cost of HAV IgG and vaccines not included as many MSM will be up-to-date if already engaged in services

Table 5.7. Cost — episode of PEPSE

Staff resource use: first visit

Staff resource use	Time (in minutes)	Cost (2019 €)	Source
Clerical staff	10	4.22	2019 Salary Scales Irish Department of Health & Time in Motion Study (GUIDE - 2013)
Medical review (consultant or specialist registrar)	30	48.73	2019 Salary Scales Irish Department of Health
Phlebotomy	12	6.00	2019 Salary Scales Irish Department of Health & Time in Motion Study (GUIDE - 2013)
Total staff resource use: €58.95			

Staff resource use: second visit

Staff resource use	Time (in minutes)	Cost (2019 €)	Source
Clerical staff	10	4.22	2019 Salary Scales Irish Department of Health & Time in Motion Study (GUIDE - 2013)
Male STI screen (performed by clinical nurse specialist /advanced nurse practitioner)	15	13.50	2019 Salary Scales Irish Department of Health & Time in Motion Study (GUIDE - 2013)
Total staff resource use: €17.72			

Staff resource use: third visit

Staff resource use	Time (in minutes)	Cost (2019 €)	Source
Clerical staff	10	4.22	2019 Salary Scales Irish Department of Health & Time in Motion Study (GUIDE - 2013)
Phlebotomy	12	6.00	2019 Salary Scales Irish Department of Health & Time in Motion Study (GUIDE - 2013)
Total staff resource use: €10.22			

Investigations: first visit

Investigations: First visit			
	Test	Cost	Source

		(2018 €)	
4th generation venous blood HIV test	HIV antigen/antibody (architect)	10.67	National Virus Reference Laboratory
Chlamydia and gonorrhea testing*	GC/CT NAAT	31.74 per site	National Virus Reference Laboratory
Syphilis testing	Syphilis serology	10.05	National Virus Reference Laboratory
HBV testing	HBV surface antigen (architect)	9.84	National Virus Reference Laboratory
	HBV anti-core antibody (architect)	15.24	National Virus Reference Laboratory
	HBV surface antibody (architect)	12.36	National Virus Reference Laboratory
HCV testing	HCV antibody	13.09	National Virus Reference Laboratory
Serum creatinine and eGFR	Urea and Electrolytes	12.26	St James's Laboratory
Urinalysis	Urinary protein	8.16	St James's Laboratory
	Urineary creatinine	8.16	St James's Laboratory
	Urinary electrolytes	8.16	St James's Laboratory
Liver profile	(includes ALT)	12.14	St James's Laboratory
Total Investigations: €183.61			

Investigations: second visit

Investigations: second visit			
	Test	**Cost (2018 €)**	**Source**
Chlamydia and gonorrhea testing*	GC/CT NAAT	31.74 per test	National Virus Reference Laboratory
Syphilis testing	Syphilis serology	10.05	National Virus Reference Laboratory
Total Investigations: €73.53			

*Some sites pool samples (rectal, urethral and pharyngeal); assumed 50% pool samples and 50% test sites separately

Investigations: third visit

Investigations: third visit			
	Test	**Cost (2018 €)**	**Source**
4th generation venous blood HIV test	HIV antigen/antibody (architect)	10.67	National Virus Reference Laboratory
Total Investigations: €10.67			

Table 5.8. Cost — Treating one episode of rectal chlamydia

Staff resource use			
	Time	**Cost (2019 €)**	**Source**
Clerical Staff	10 minutes	4.22	2019 Salary Scales Irish Department of Health & Time in Motion Study
Medical review (Consultant or specialist registrar)	30 minutes	48.73	2019 Salary Scales Irish Department of Health
Cost of treatment/investigations			
Chlamydia testing (GC/CT NAAT)*		31.74 per test	National Virus Reference Laboratory
Cost of medications (doxycycline 100mg twice daily for 7 days)		8.80	
Total Cost		**€125.23**	
Vary by 50% to account for regional differences	*Min*	€62.615	
	Max	€187.845	

*Some sites pool samples (rectal, urethral and pharyngeal); assumed 50% pool samples and 50% test sites separately

5.3 Parameter distributions in probabilistic analysis

Table 5.3.1. Distributions of probabilistic analysis

Name of parameter in model	DESCRIPTION	TYPE	Alpha, Beta, Lambda, mean or SD	Expected Value
Dist_cHIV	Distribution associated with annual cost of HIV	Gamma	alpha: ((10200)^2)/(((10200*1.2-10200*.8)/3.92)^2), lambda: (10200)/(((10200*1.2-10200*.8)/3.92)^2)	10200.0
dist_Chlamydia	Distribution associated with cost of treating chlamydia	Gamma	alpha: ((125)^2)/(((125*1.5-125*.5)/3.92)^2), lambda: (125)/(((125*1.5-125*.5)/3.92)^2)	125.0
dist_cPEPSE	Distribution associated with cost of PEPSE	Gamma	alpha: ((964)^2)/(((964*1.2-964*.8)/3.92)^2), lambda: (964)/(((964*1.2-964*.8)/3.92)^2)	964.0
dist_cPrEP	Distribution incremental cost PrEP prog+drug	Gamma	alpha: ((903)^2)/(((903*1.2-903*0.8)/3.92)^2), lambda: (903)/(((903*1.2-903*0.8)/3.92)^2)	903.0
dist_EMIS2017	Distribution associated with EMIS Ireland 2017 eligible proportion	Beta	subtype: 2, alpha: 647, beta: 2083-647	0.31061
dist_HIV_HIV	Distribution associated with transition probability HIV+ to HIV+	Gamma	alpha: 54375, lambda: 55611	0.97777
dist_mort	Distribution associated with	Normal	mean: 1, stddev: 0.1	1.0

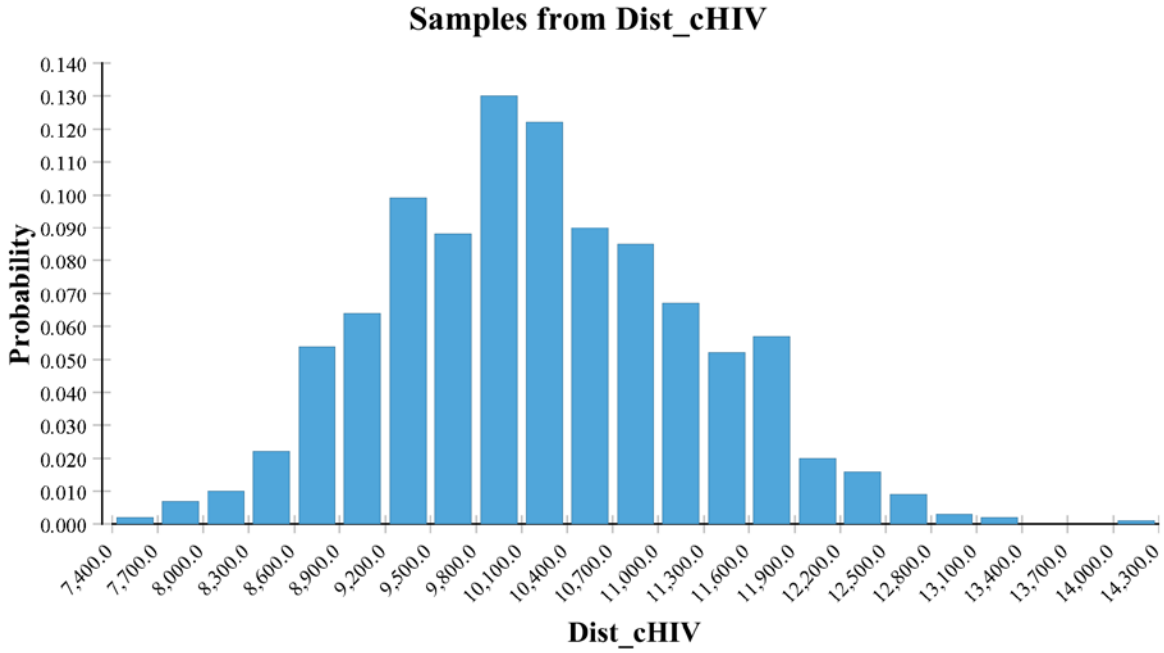
Name of parameter in model	DESCRIPTION	TYPE	Alpha, Beta, Lambda, mean or SD	Expected Value
	age-specific mortality			
dist_NPhigh_HIV	Distribution of transition probability high risk (no PrEP) to HIV	Gamma	alpha: 100, lambda: 3333.3	0.03
dist_NPhigh_NPhigh	Distribution associated with transition probability high risk (no PrEP) to high risk (no PrEP)	Gamma	alpha: 10, lambda: 22.22	0.45005
dist_NPhigh_NPmedlow	Distribution associated with transition probability high risk (no PrEP) to medium/low	Gamma	alpha: 30, lambda: 83.33	0.36001
dist_NPhigh_Phigh	Distribution associated with transition probability high risk (PrEP) to high risk (PrEP)	Gamma	alpha: 10, lambda: 59.52	0.16801
dist_NPmedlow_HIV	Distribution associated with transition probability medium/low risk to HIV+	Gamma	alpha: 100, lambda: 33333.3	0.003
dist_NPmedlow_NPhigh	Distribution associated with transition probability medium/low to high risk (no PrEP)	Gamma	alpha: 6, lambda: 121	0.049587
dist_NPmedlow_NPmedlow	Distribution associated with transition probability medium/low to medium/low	Gamma	alpha: 2224, lambda: 2372	0.93761
dist_Phigh_NPhigh	Distribution associated with transition probability high risk (PrEP) to high risk (no PrEP)	Gamma	alpha: 11, lambda: 113	0.097345
dist_Phigh_NPmedlo	Distribution associated with	Gamma	alpha: 57, lambda: 156	0.36538

Name of parameter in model	DESCRIPTION	TYPE	Alpha, Beta, Lambda, mean or SD	Expected Value
w	transition probability high risk (PrEP) to medium/low			
dist_Phigh_Phigh	Distribution associated with transition probability high risk (PrEP) to high risk (no PrEP)	Gamma	alpha: 112, lambda: 214	0.52336
dist_prop_Chlamydia	Distribution associated with the increased proportion who acquire rectal chlamydia on PrEP	Normal	mean: (0.42+0.24)/2, stddev: (0.42-0.24)/3.92	0.33
dist_PrOP_MSM	Distribution associated with proportion of men who are MSM	Beta	subtype: 2, alpha: 83.3, beta: 1735.8	0.045792
dist_prop_PEPSE	Distribution associated with proportion who obtain PEPSE annually	Normal	mean: (0.03+0.05)/2, stddev: (0.05-0.03)/3.92	0.04
dist_PropHigh	Distribution associated with the proportion of MSM at substantial risk of HIV	Beta	subtype: 2, alpha: 6.48, beta: 45.9	0.12371
Dist_RR	Distribution associated with efficacy of PrEP - meta-analysis of all trials	LogNormal	umeanoflogs: -1.39, sigmastddevoflogs: 0.457	0.27649
Dist_RR_high	Distribution associated with RR of efficacy: PrEP from PROUD and IPERGAY	LogNormal	umeanoflogs: -1.97, sigmastddevoflogs: 0.4	0.15107
dist_sexuallyactive	Distribution associated with sexually active proportoin	Beta	subtype: 2, alpha: 29.4, beta: 18.9	0.6087
dist_SMR_HIV	Distribution associated with Standardised Mortality Ratio	Normal	mean: 4.9, stddev: 0.08	4.9

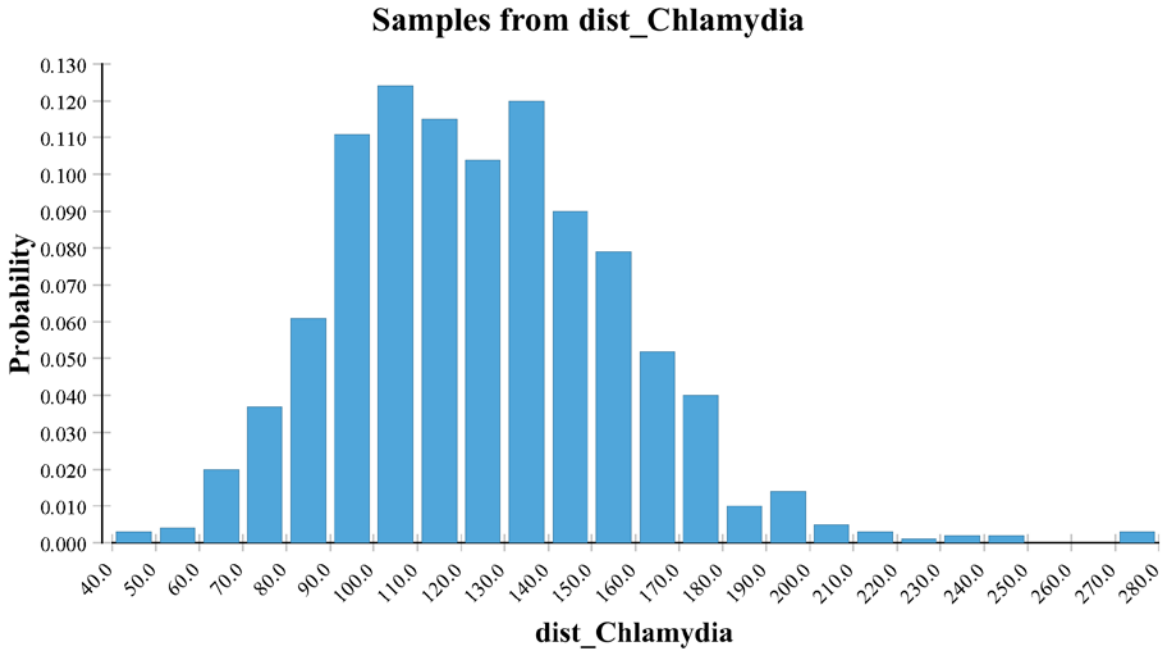
Name of parameter in model	DESCRIPTION	TYPE	Alpha, Beta, Lambda, mean or SD	Expected Value
	for HIV positive			
Dist_uHIV	Distribution associated with utility value for HIV+ individuals	Beta	subtype: 2, alpha: (((0.89)^2)*(1-(0.89))/((0.008)^2)-(0.89)), beta: ((1-(0.89))*(((1-(0.89))*(0.89))/((0.008)^2)-1))	0.89
dist_Uptake	Distribution associated with the uptake rate of PrEP	Beta	subtype: 2, alpha: 31.5, beta: 83.6	0.27368

Figure 5.3.1. Distribution sample histograms (based on 1,000 samples)

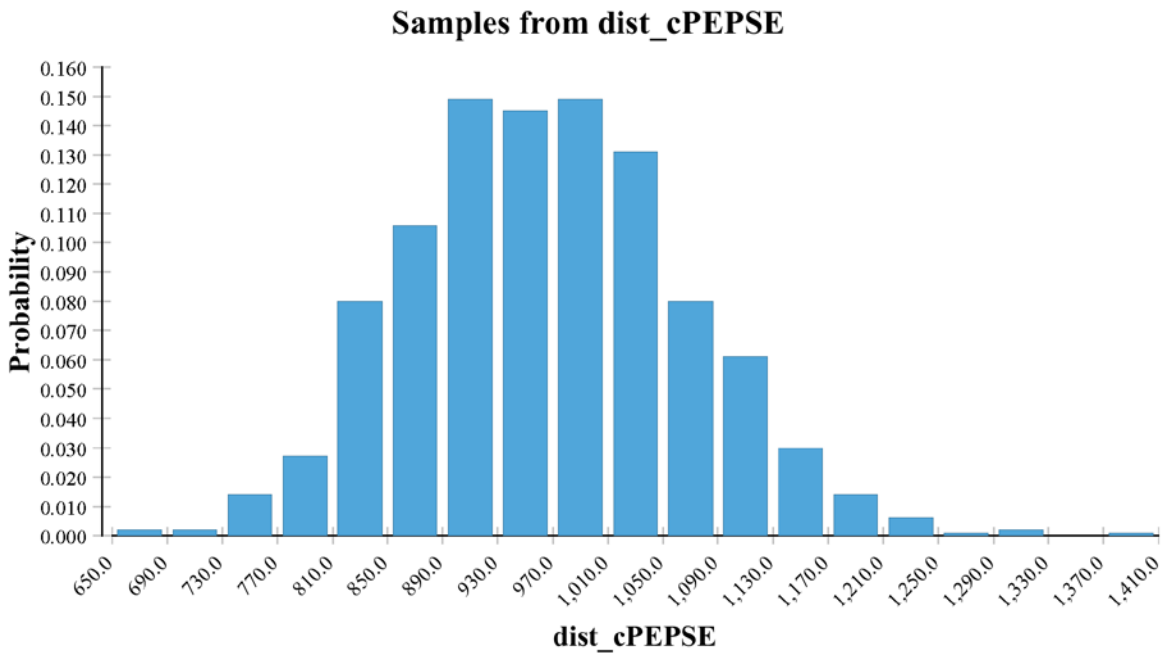
1. Distribution associated with annual cost of HIV



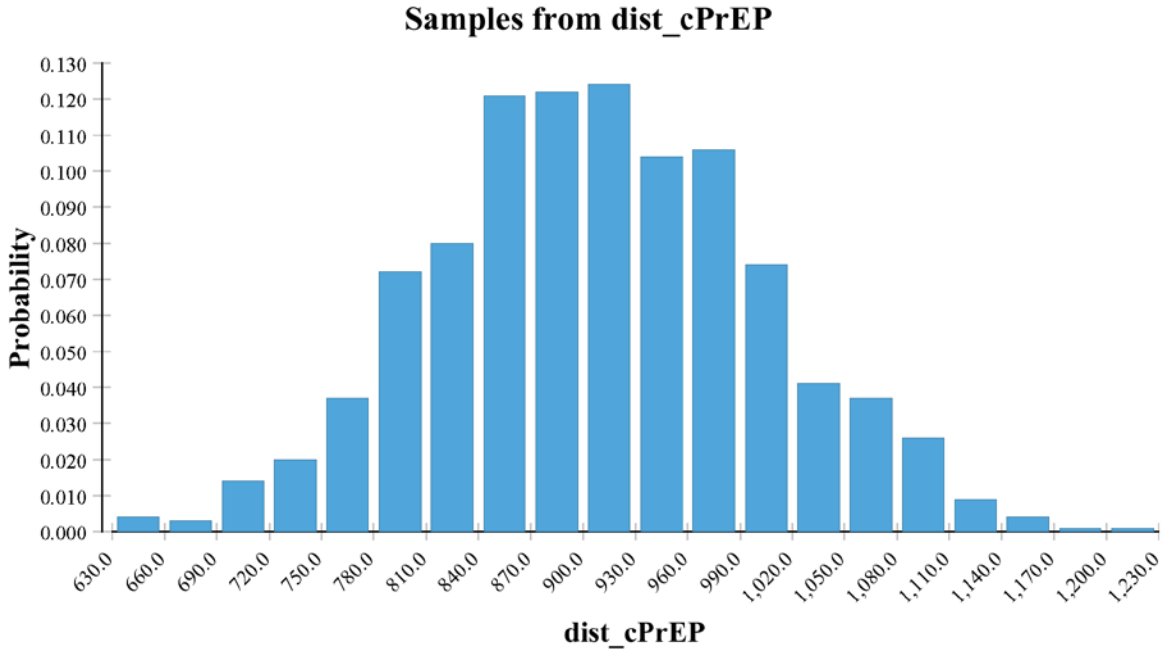
2. Distribution associated with cost of treating chlamydia



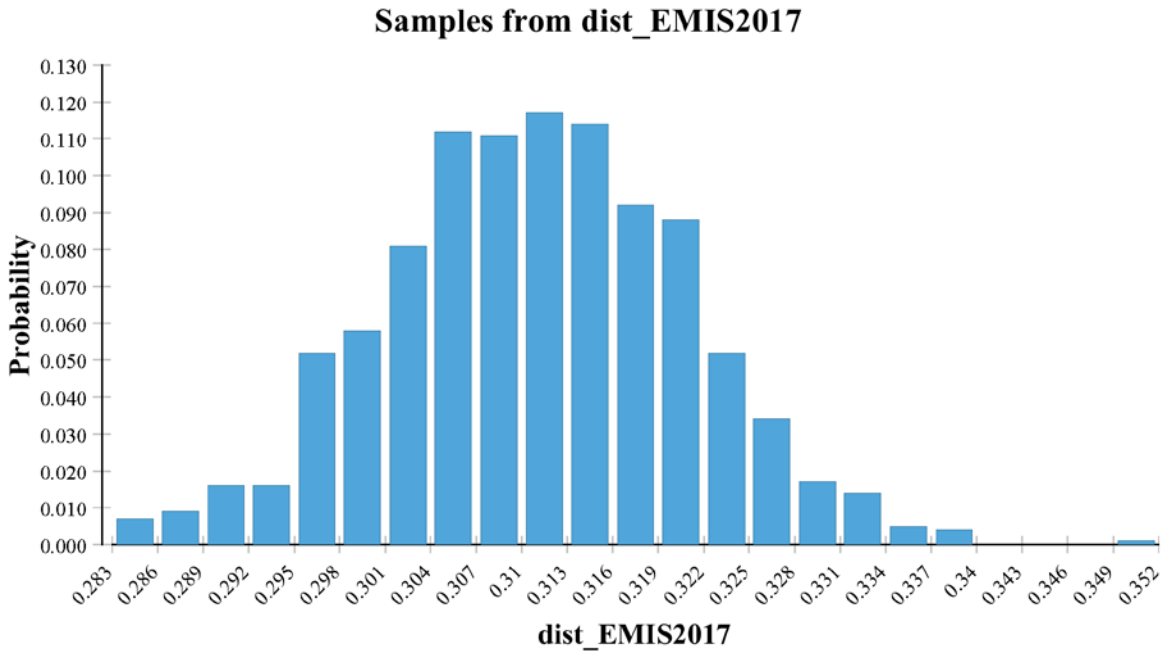
3. Distribution associated with cost of PEPSE



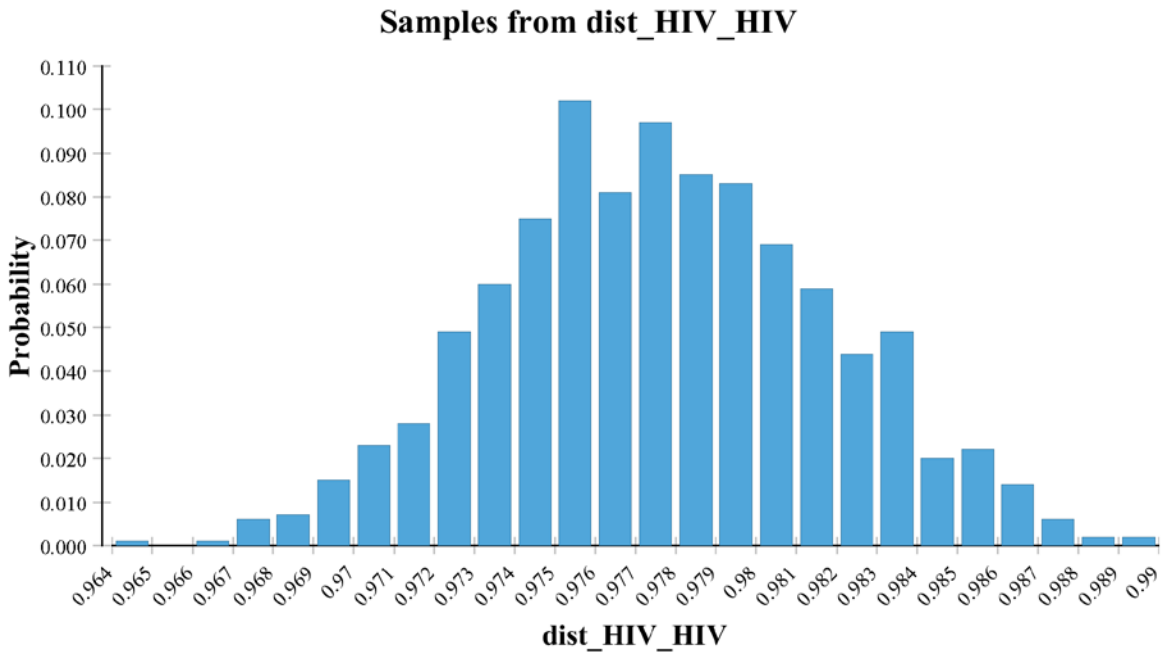
4. Distribution incremental cost PrEP (prog+drug)



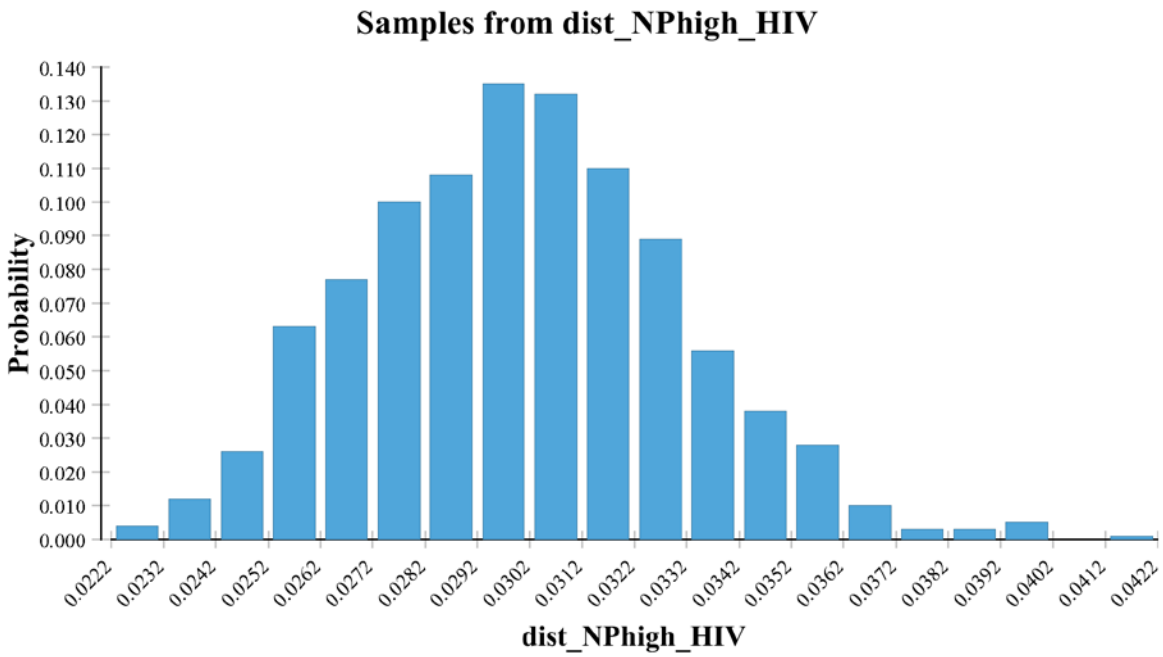
5. Distribution associated with EMIS Ireland 2017 eligible proportion



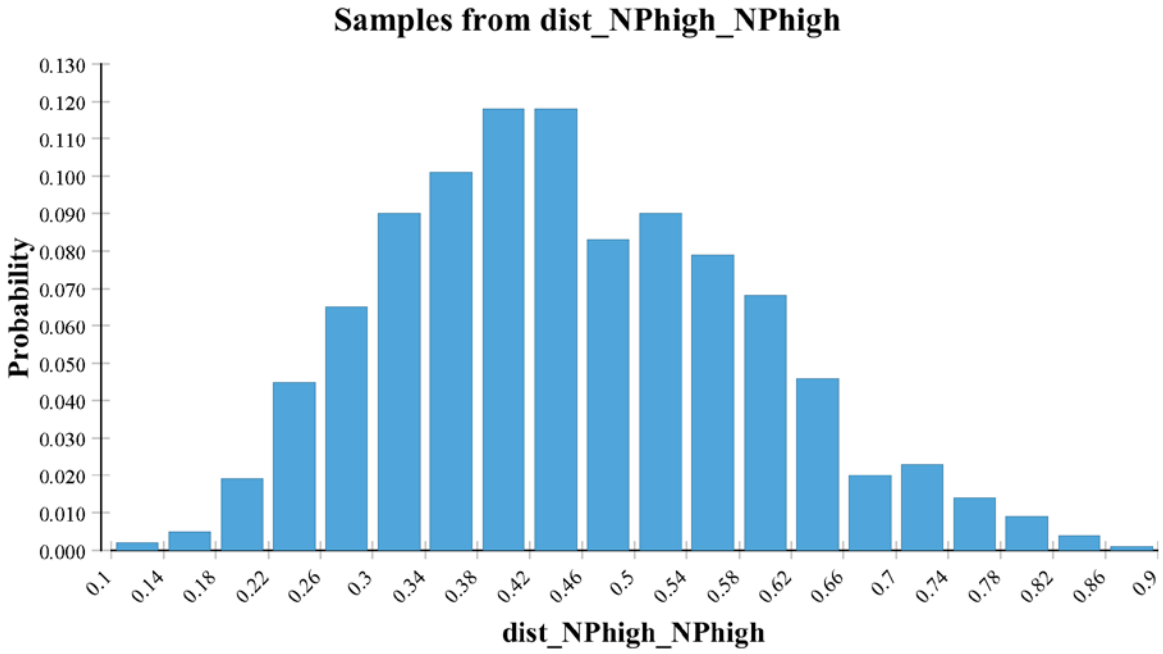
6. Distribution associated with transition probability HIV+ to HIV+



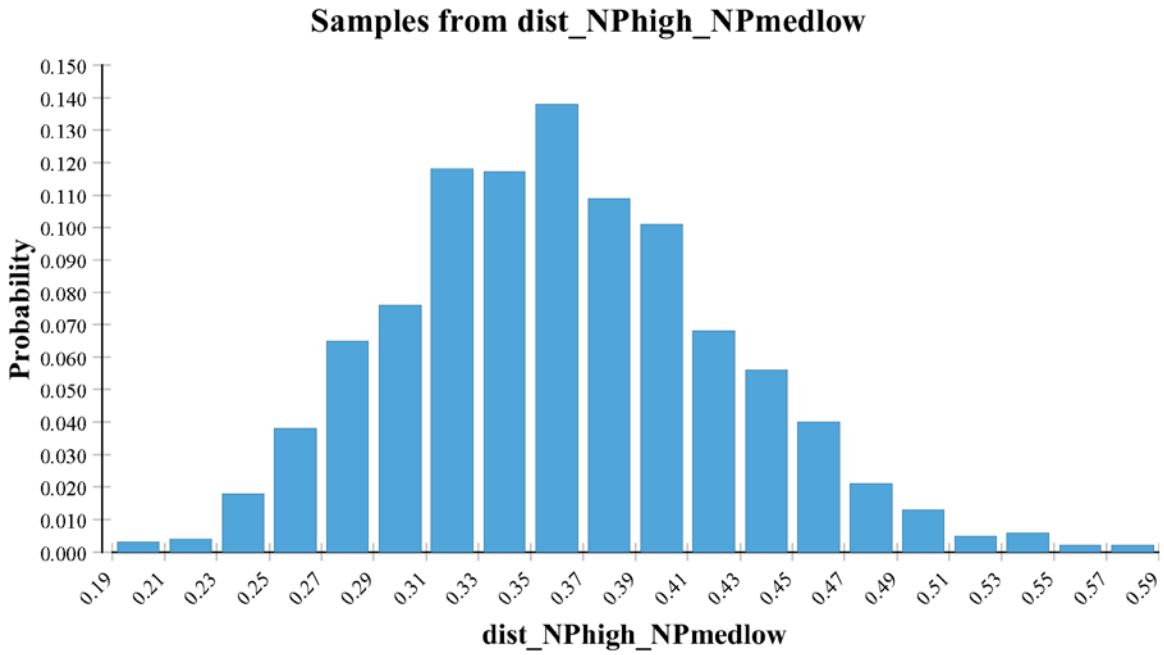
7. Distribution of transition probability high risk (no PrEP) to HIV



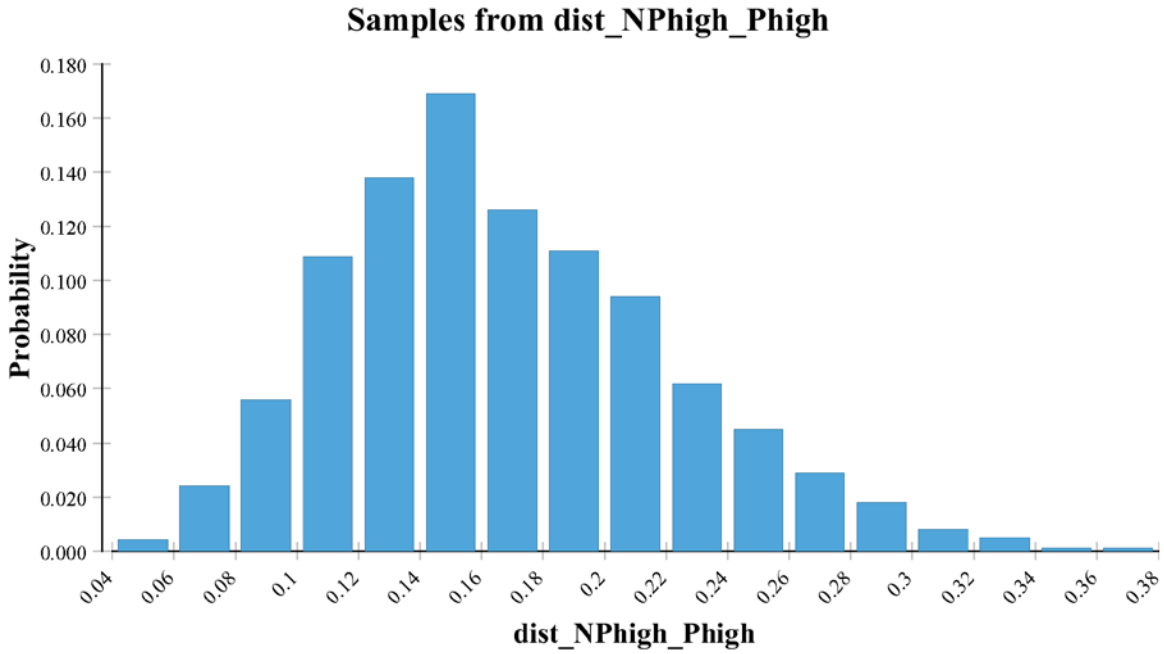
8. Distribution associated with transition probability high risk (no PrEP) to high risk (no PrEP)



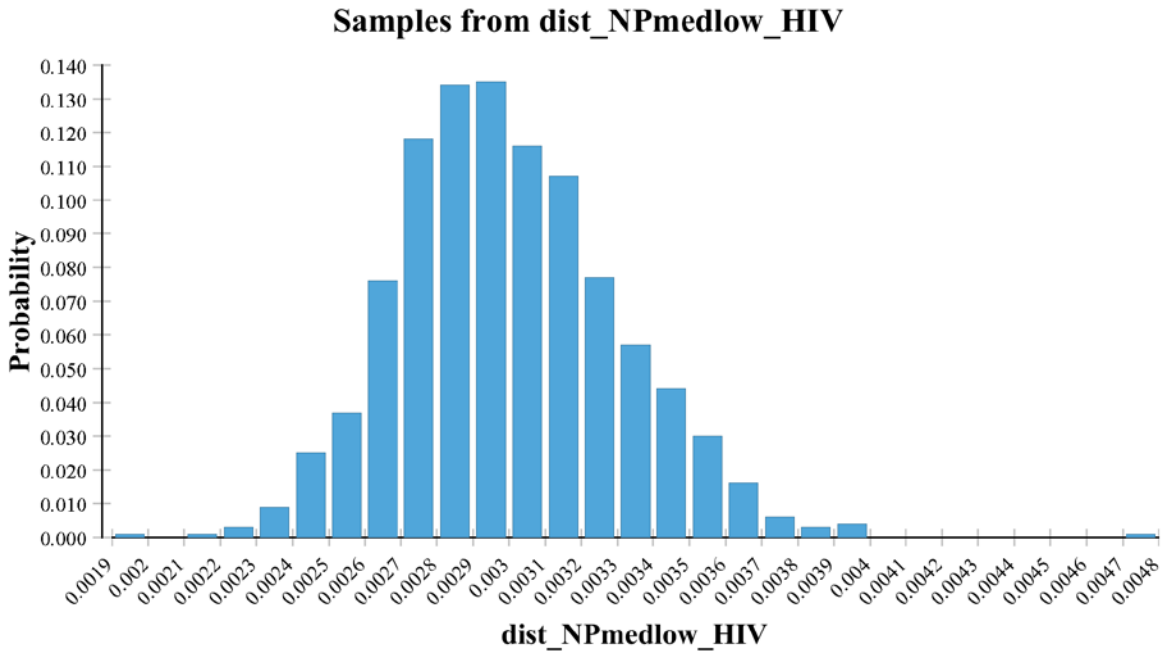
9. Distribution associated with transition probability high risk (no PrEP) to medium/low



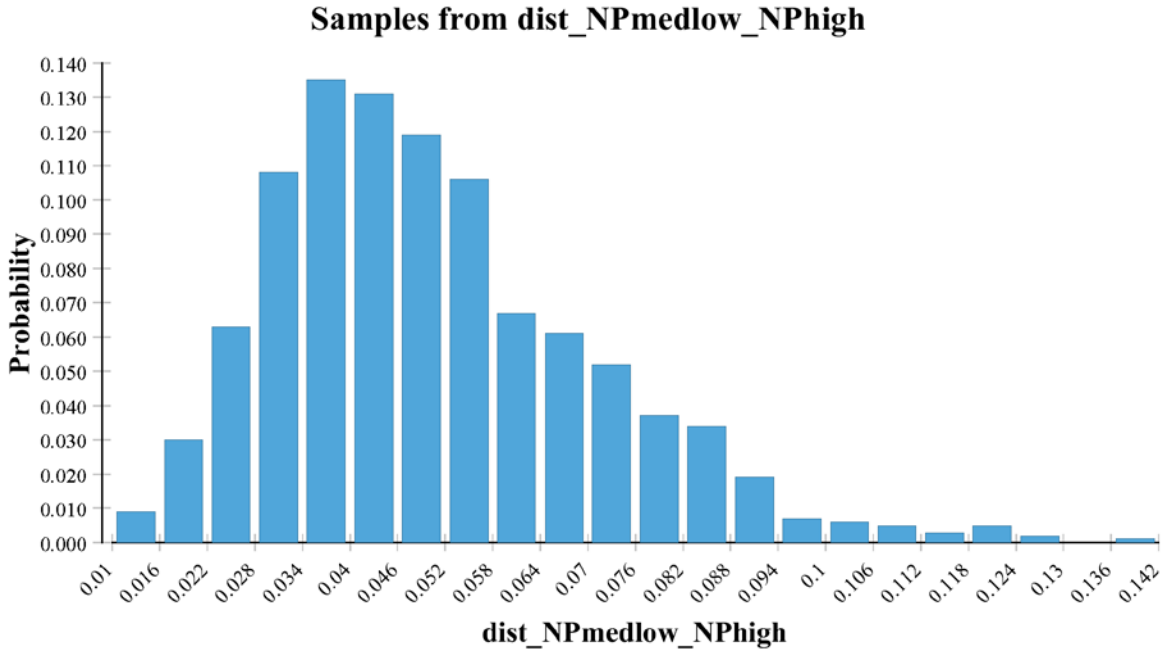
10. Distribution associated with transition probability high risk (PrEP) to high risk (PrEP)



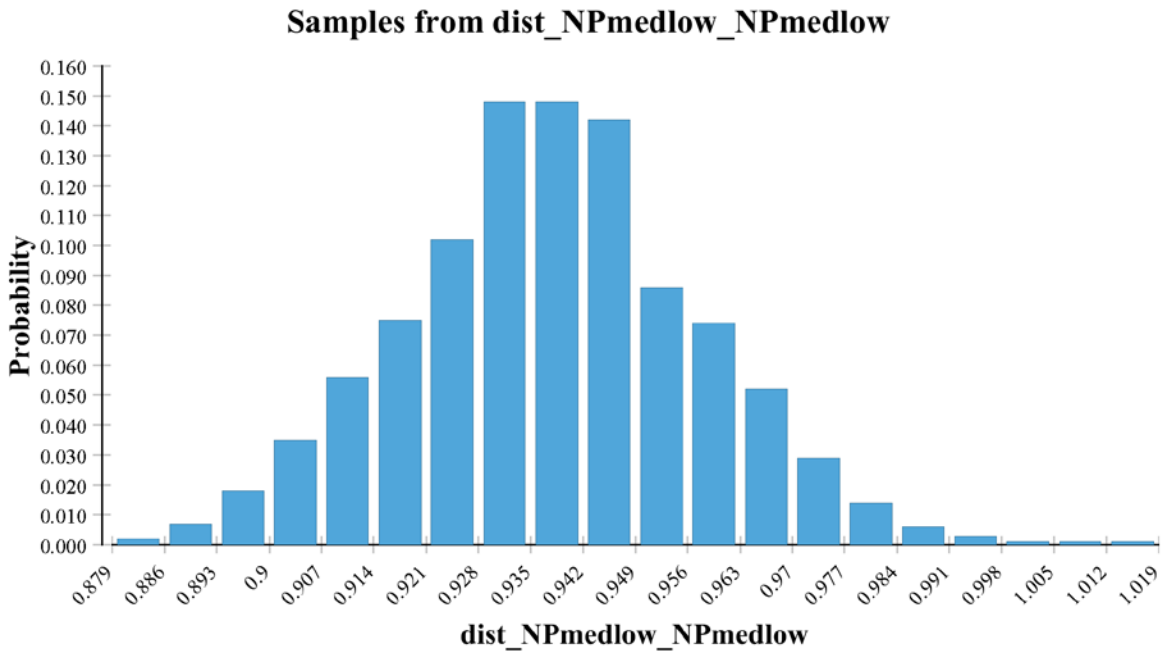
11. Distribution associated with transition probability medium/low risk to HIV+



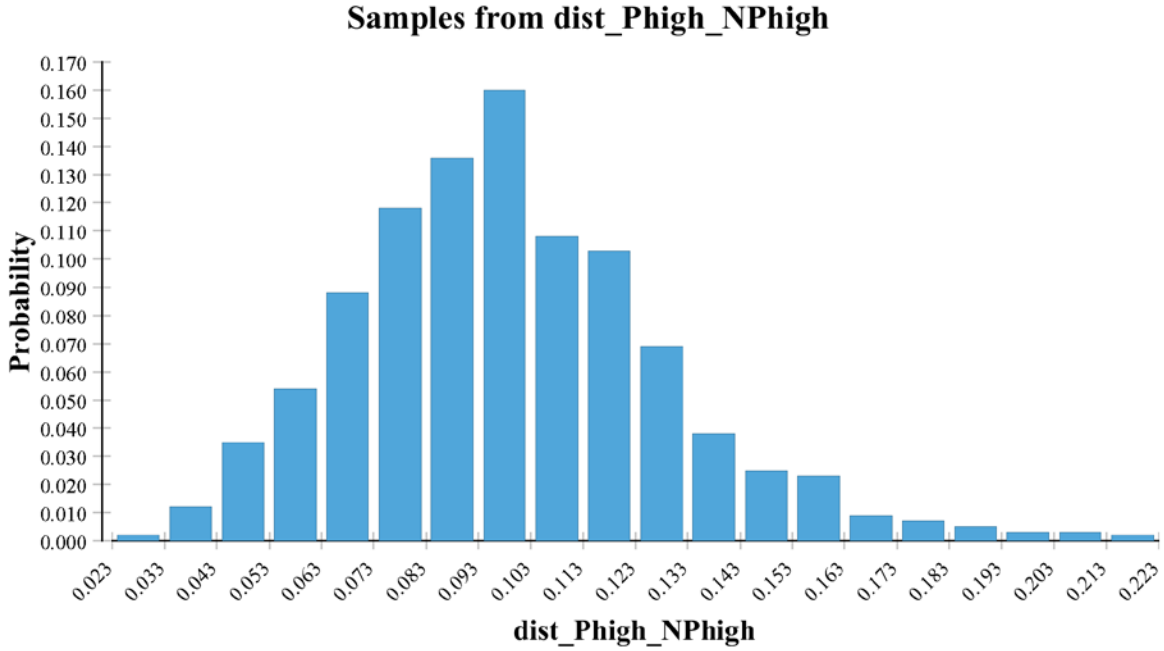
12. Distribution associated with transition probability medium/low to high risk (no PrEP)



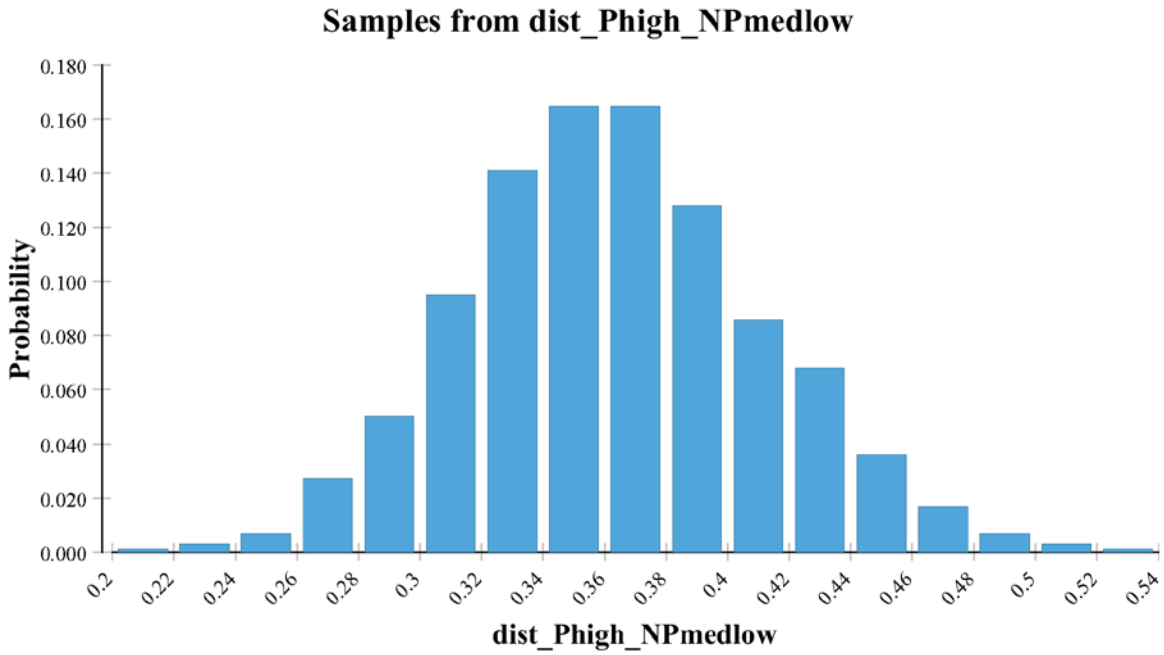
13. Distribution associated with transition probability medium/low to medium/low



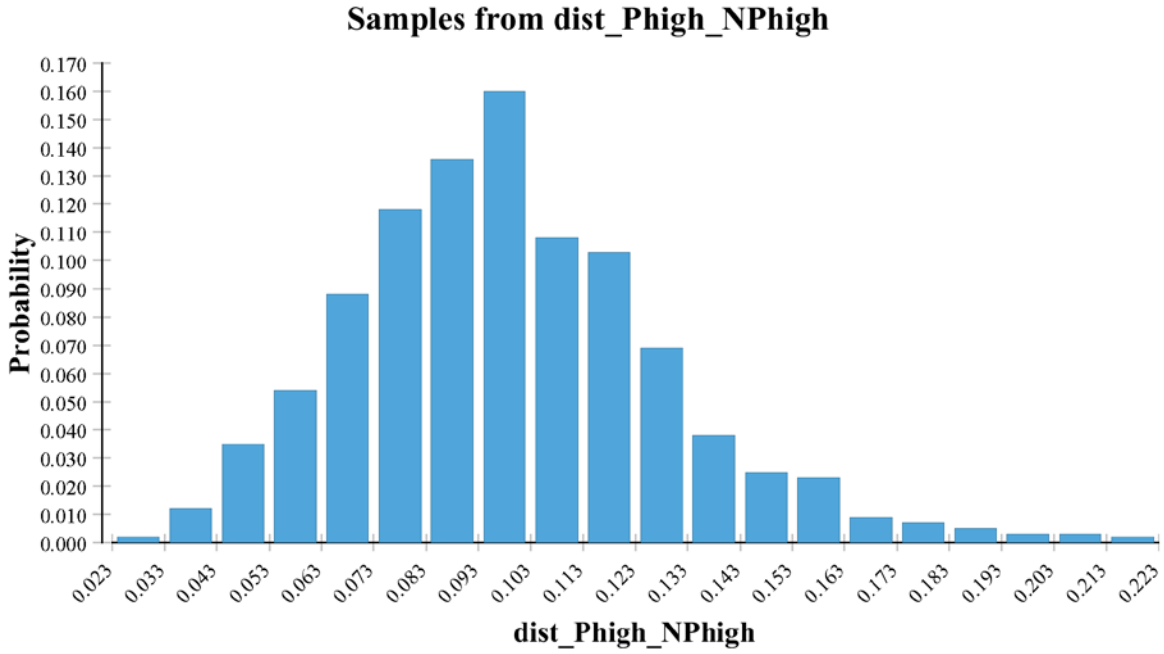
14. Distribution associated with transition probability high risk (PrEP) to high risk (no PrEP)



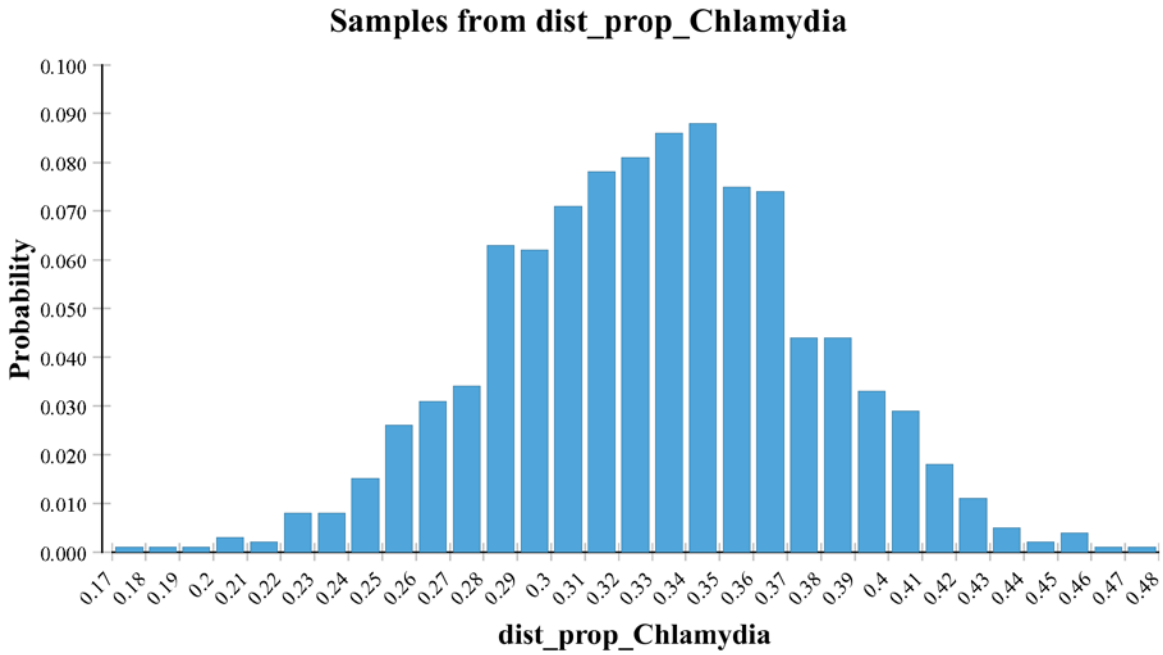
15. Distribution associated with transition probability high risk (PrEP) to medium/low



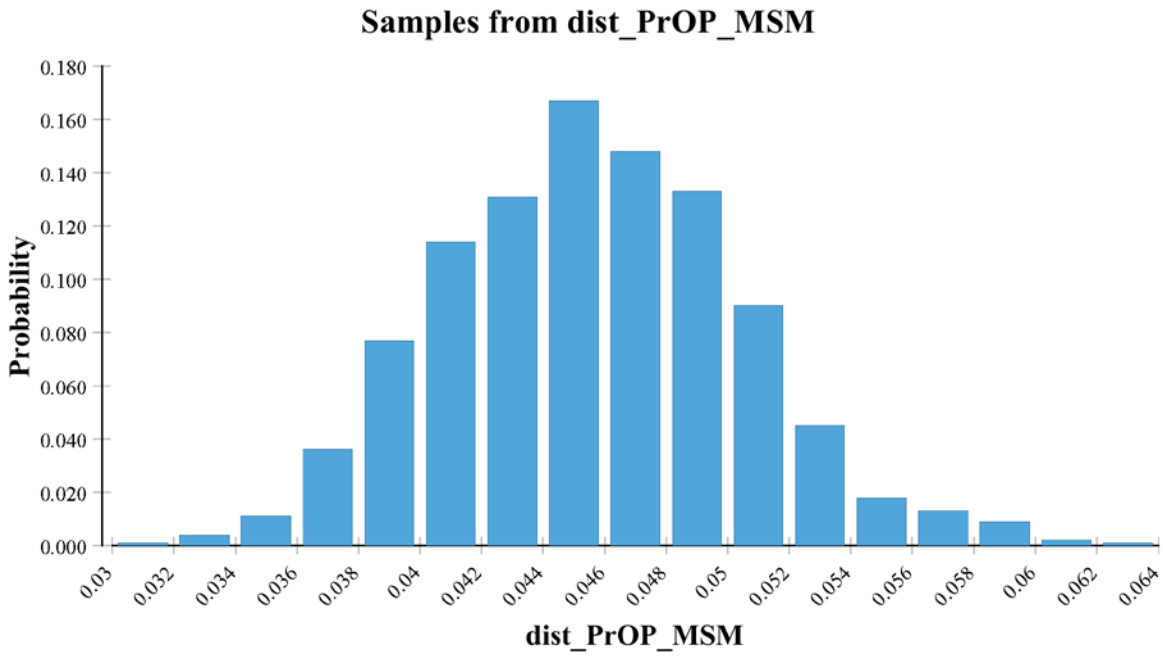
16. Distribution associated with transition probability high risk (PrEP) to high risk (no PrEP)



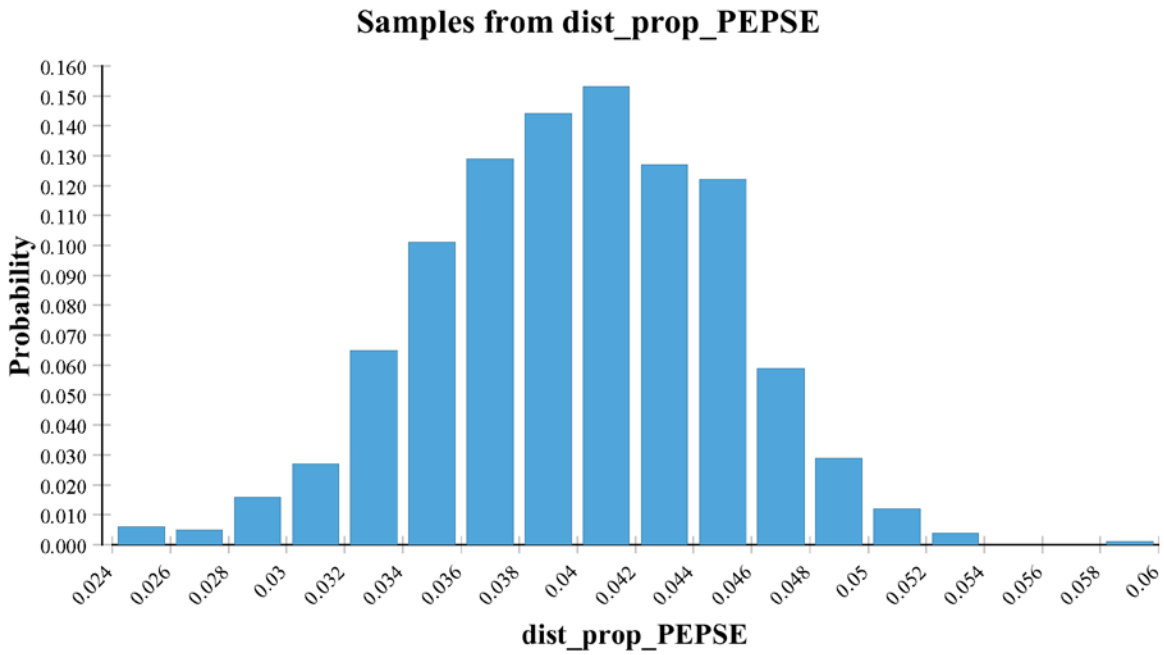
17. Distribution associated with the increased proportion who acquire rectal chlamydia on PrEP



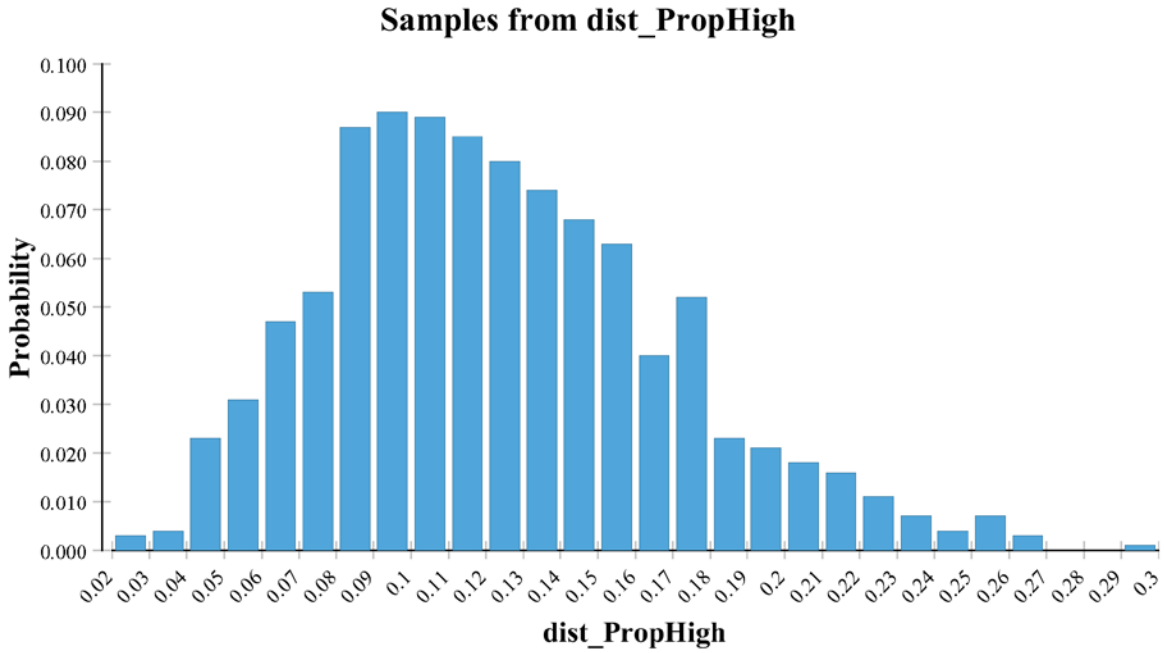
18. Distribution associated with proportion of men who are MSM



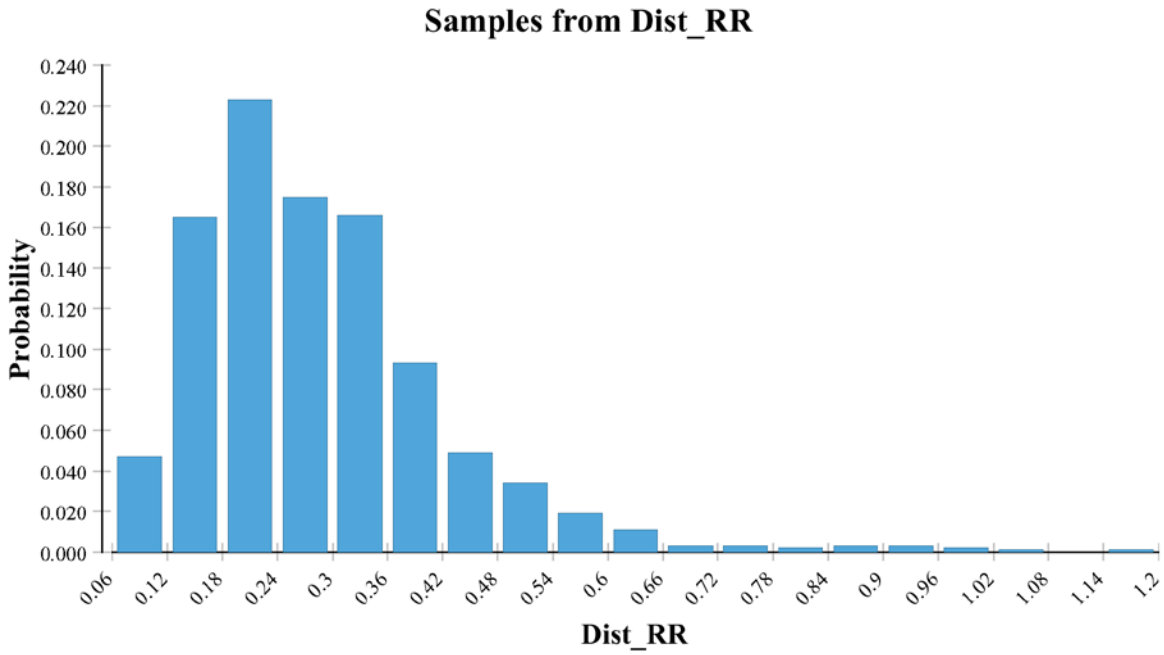
19. Distribution associated with proportion who obtain PEPSE annually



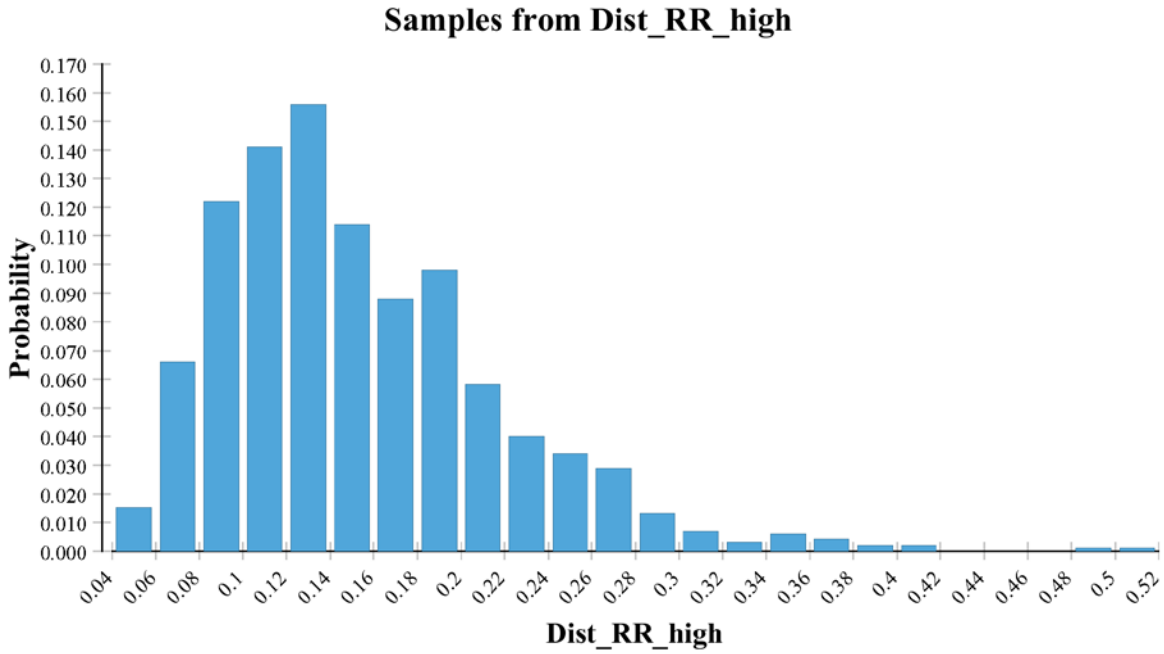
20. Distribution associated with the proportion of MSM at substantial risk of HIV



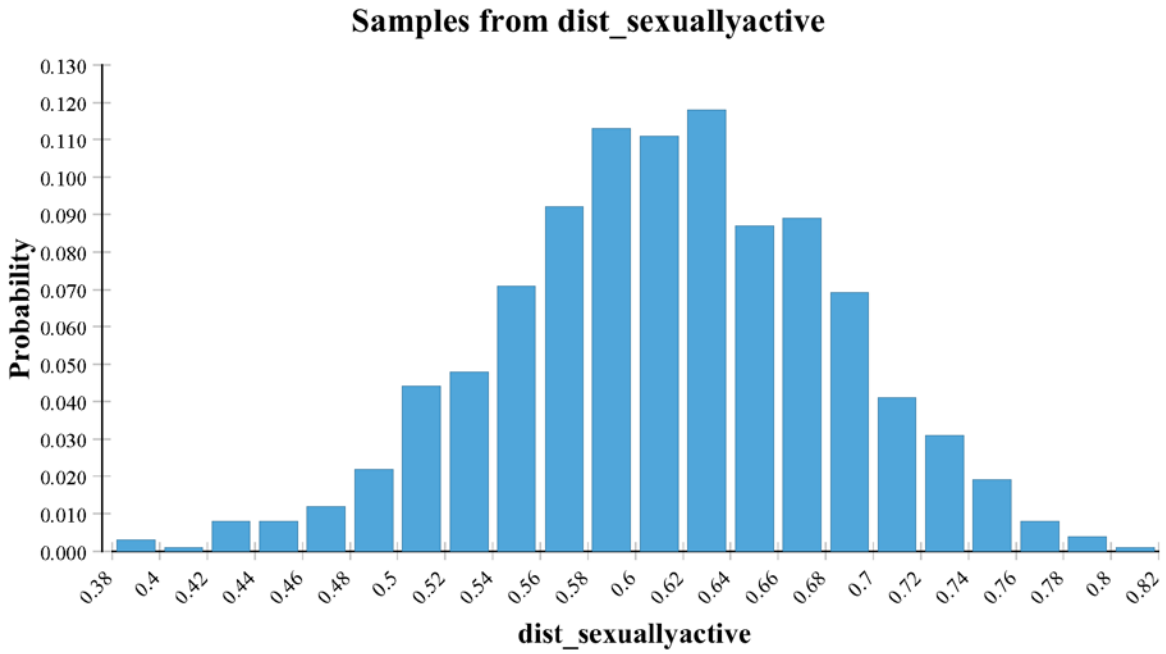
21. Distribution associated with efficacy of PrEP — meta-analysis of all trials



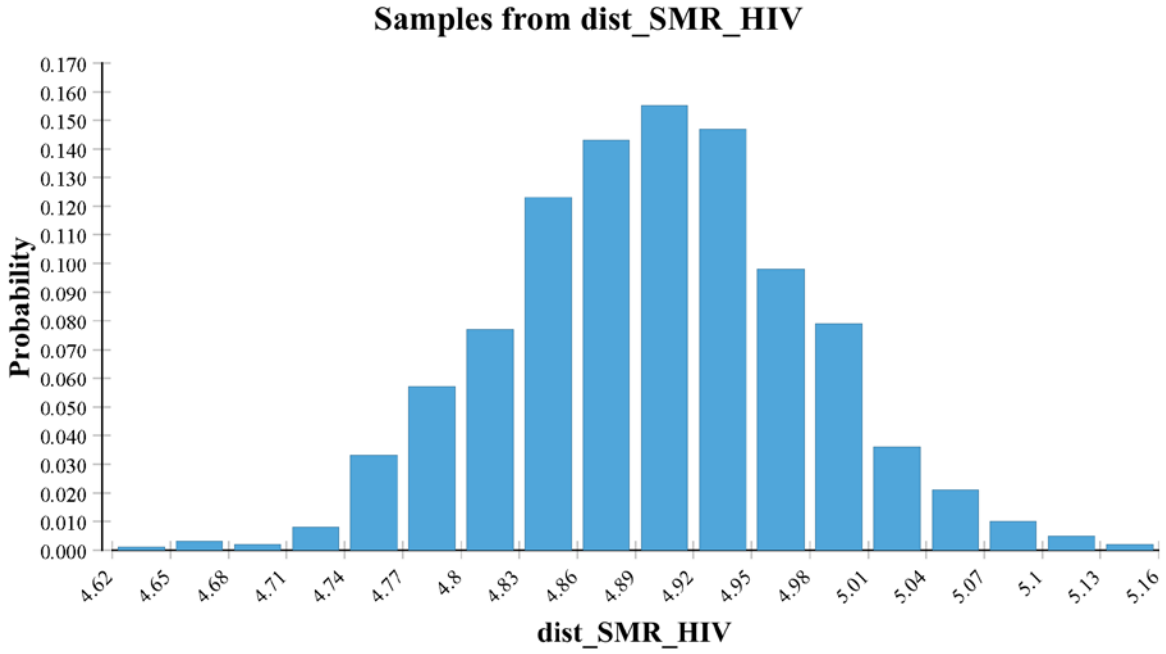
22. Distribution associated with RR of efficacy: PrEP from PROUD and IPERGAY



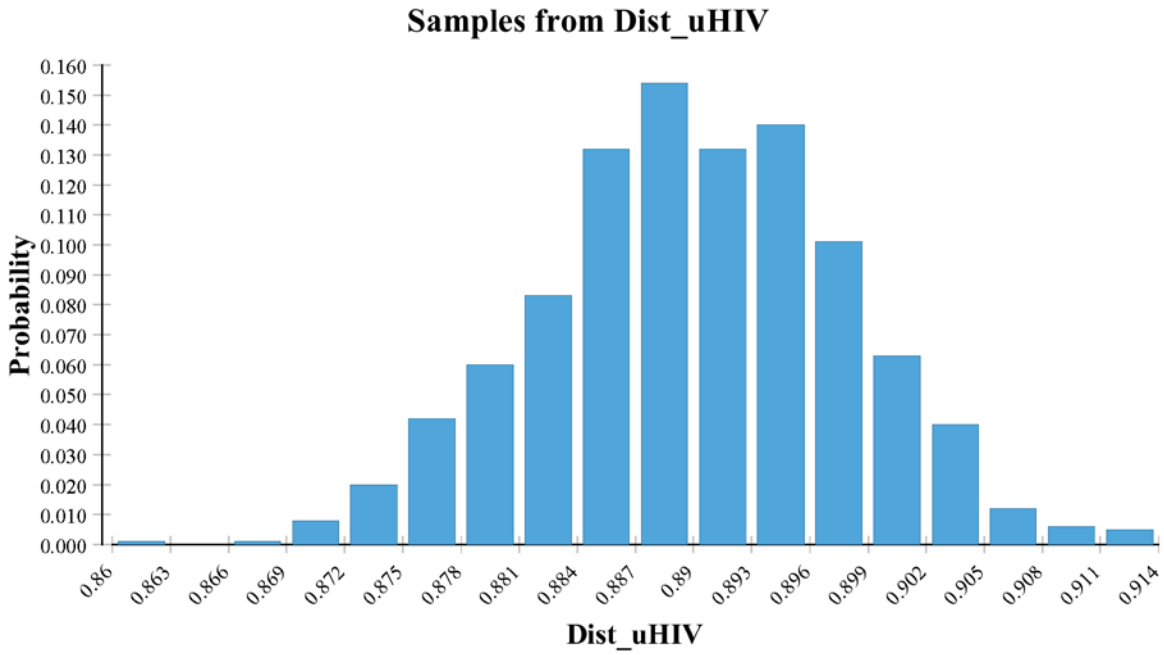
23. Distribution associated with sexually active proportoin



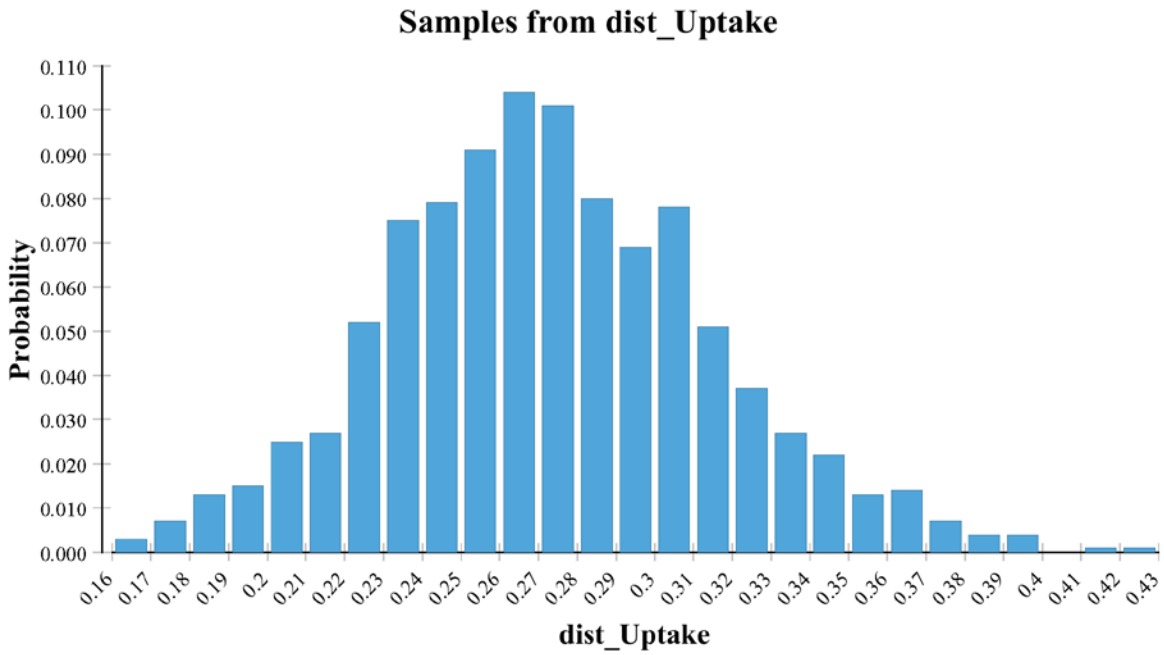
24. Distribution associated with standardised mortality ratio for HIV positive



25. Distribution associated with utility value for HIV+ individuals



26. Distribution associated with the uptake rate of PrEP



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