



**Health  
Information  
and Quality  
Authority**

An tÚdarás Um Fhaisnéis  
agus Cáilíocht Sláinte

# Draft report for public consultation

## Appendices

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

23 April 2019



## CONTENTS

About the Health Information and Quality Authority .....	4
Acknowledgements .....	5
<b>Appendix 1</b> .....	<b>6</b>
<b>1.1 Full list of countries with ongoing or planned PrEP programmes*</b> ...	<b>6</b>
<b>Appendix 2</b> .....	<b>21</b>
<b>2.1 Characteristics of HIV notifications in 2017</b> .....	<b>21</b>
<b>2.2 Additional characteristics of HIV notifications in 2017 by risk group</b> 22	
<b>Appendix 3</b> .....	<b>23</b>
<b>3.1 Clinical effectiveness search strategy</b> .....	<b>23</b>
<b>3.2 Data collection, management and analysis</b> .....	<b>25</b>
<b>3.3 List of studies included in review of clinical effectiveness</b> .....	<b>26</b>
<b>3.4 List of studies excluded from review of clinical effectiveness</b> .....	<b>28</b>
<b>3.5 Additional efficacy results</b> .....	<b>34</b>
<b>Appendix 4</b> .....	<b>35</b>
<b>4.1 Excluded studies from review of cost-effectiveness</b> .....	<b>35</b>
<b>4.2 CHEC-list evaluation of the quality of included studies</b> .....	<b>39</b>
<b>4.3 List of studies at risk of bias</b> .....	<b>40</b>
<b>4.5 Additional cost-effectiveness study information</b> .....	<b>41</b>
<b>Appendix 5</b> .....	<b>52</b>
<b>5.1 Correction factor</b> .....	<b>52</b>
<b>5.2 Costs</b> .....	<b>53</b>
<b>5.3 Parameter distributions in probabilistic analysis</b> .....	<b>62</b>

## 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.

## Acknowledgements

HIQA would like to thank all of the individuals and organisations who provided their time, advice and information in support of this health technology assessment (HTA).

Particular thanks are due to the Expert Advisory Group (EAG) and the individuals within the organisations listed below who provided advice.

### The membership of the EAG was as follows:

<b>Dr Louise Campbell</b>	Lecturer in Medical Ethics, NUI Galway
<b>Dr Susan Clarke</b>	Consultant in Infectious Disease, Gay Men's Health Service and representative of Infectious Disease Society of Ireland (IDSI)
<b>Dr Patricia Harrington</b>	Health Information and Quality Authority
<b>Dr Derval Igoe</b>	Specialist in Public Health Medicine, Health Protection Surveillance Centre (HPSC)
<b>Dr Felicity Lamrock</b>	National Centre for Pharmacoeconomics (NCPE)
<b>Andrew Leavitt</b>	ACT UP Dublin
<b>Dr Fiona Lyons</b>	Clinical Lead in Sexual Health (until September 2018), HSE Sexual Health and Crisis Pregnancy Programme and representative from Society for the Study of Sexually Transmitted Diseases in Ireland (SSSTDI)
<b>Siobhan O'Dea</b>	Manager, Gay Men's Health Service
<b>Kate O'Flaherty</b>	Head of Health and Wellbeing, Department of Health
<b>Dr Éamon Ó Murchú</b>	Health Information and Quality Authority (Project Lead)
<b>Dr Mairin Ryan</b>	Director of HTA, Health Information and Quality Authority (Chair)
<b>Adam Shanley</b>	National Outreach Worker, Gay Men's Health Service
<b>Noel Sutton</b>	Gay Health Network
<b>Dr Conor Teljeur</b>	Health Information and Quality Authority

### 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
<b>Australia</b>	Demonstration projects (3)	Demonstration project (1)	<ul style="list-style-type: none"> <li>• MSM</li> <li>• Men</li> <li>• Transgender women</li> <li>• Transgender men</li> <li>• Serodifferent couples</li> <li>• N-PEP users</li> <li>• High-risk individuals</li> <li>• Women</li> </ul>	<ul style="list-style-type: none"> <li>• Private sector</li> <li>• Public sector</li> <li>• Pharmacies</li> <li>• Hospitals</li> <li>• Testing centers</li> <li>• Primary/general health clinics</li> <li>• NGOs</li> </ul>	Approved	No	Yes	
<b>Belgium</b>	<b>National Level (1)</b>		<ul style="list-style-type: none"> <li>• MSM</li> </ul>	Testing centers, Primary/general health clinics	Approved	Approved	Yes	HIV plan 2014-2019 Belgium
<b>Benin</b>	Demonstration project (1) (completed, still providing PrEP)		<ul style="list-style-type: none"> <li>• FSW</li> </ul>	Primary/general health Clinics	No	No	No	

<b>Botswana</b>	Implementation project (1)	<b>National level (1)</b>	Not available	Not available	Approved	Planned	Yes	
<b>Brazil</b>	Demonstration projects (5)  <b>National level (1)</b>	Demonstration project (1) Implementation project (1)	<ul style="list-style-type: none"> <li>• MSM</li> <li>• MSW</li> <li>• AGYW</li> <li>• CSW</li> <li>• FSW</li> <li>• Adolescent men</li> <li>• Transgender women</li> <li>• Transgender men</li> <li>• Serodifferent couples</li> </ul>	<ul style="list-style-type: none"> <li>• Public sector</li> <li>• Hospitals</li> <li>• Testing centers</li> <li>• Primary/general health clinics</li> <li>• NGOs</li> </ul>	Approved	No	Yes	
<b>Burkina Faso</b>	Demonstration project (1)		<ul style="list-style-type: none"> <li>• MSM</li> <li>• MSW</li> </ul>	<ul style="list-style-type: none"> <li>• Public sector</li> <li>• NGOs</li> </ul>	No	No	No	
<b>Canada</b>	<b>National level (1)</b>		<ul style="list-style-type: none"> <li>• MSM</li> <li>• Transgender women</li> </ul>	<ul style="list-style-type: none"> <li>• Public sector</li> <li>• Hospitals</li> </ul>	Approved	Approved	Yes	<p>Guidance for the use of PrEP in British Columbia (2016)</p> <p>Canadian guideline on HIV pre-exposure prophylaxis and nonoccupatio</p>

							nal postexposure prophylaxis
<b>China</b>	Demonstration project (1)	Not available	Not available	No	No	No	
	Implementation project (1)						
<b>Cote d'Ivoire</b>	Demonstration project (1)	<ul style="list-style-type: none"> <li>• MSM</li> <li>• MSW</li> </ul>	<ul style="list-style-type: none"> <li>• Public sector</li> <li>• NGOs</li> </ul>	No	Planned	No	
	Implementation project (1)						
<b>Democratic Republic of the Congo</b>	Implementation project (1)	Not available	Not available	No	No	No	
<b>Dominican Republic</b>	Implementation project (1)	Not available	Not available	No	No	No	



<b>England</b>	Implementation project (1)	Not available	<ul style="list-style-type: none"> <li>• MSM</li> <li>• Transgender women</li> <li>• Highrisk individuals</li> </ul>	Not available	Approved	Approved	Yes	British HIV Association/British Association for Sexual Health and HIV (2012)  BHIVA/BASH H guidelines on the use of HIV pre-exposure prophylaxis -- Version for Public Consultation
<b>Ethiopia</b>	Implementation project (1)		Not available	Not available	No	No	No	
<b>France</b>	Implementation project (1)  <b>National Level (1)</b>		<ul style="list-style-type: none"> <li>• MSM</li> <li>• Men</li> <li>• Transgender women</li> <li>• Women</li> </ul>	<ul style="list-style-type: none"> <li>• Public sector</li> <li>• Hospitals</li> </ul>	Approved	Approved	Yes	ANSM Pre-exposure Prophylaxis Guidelines (2017)

<b>Georgia</b>	Demonstration project (1)		<ul style="list-style-type: none"> <li>• MSM</li> <li>• Transgender women</li> </ul>	Not available	No	No	No	THE GEORGIAN NATIONAL HIV/AIDS STRATEGIC PLAN FOR 2016–2018
<b>Germany</b>	Implementation project (1)		Not available	Not available	Approved	Approved	No	Integrated Strategy for HIV, Hepatitis B and C and Other Sexually Transmitted Infections
<b>Greece</b>	Demonstration project (1)		<ul style="list-style-type: none"> <li>• MSM</li> </ul>	Not available	Approved	Approved	No	
<b>Haiti</b>	Implementation project (1)		Not available	Not available	No	No	Yes	
<b>India</b>	Demonstration projects (2)		<ul style="list-style-type: none"> <li>• FSW</li> </ul>	<ul style="list-style-type: none"> <li>• Public sector</li> <li>• NGOs</li> </ul>	No	Approved	No	
<b>Israel</b>		<b>National level (1)</b>	Not available	Not available	Approved	Approved	No	
<b>Japan</b>	Demonstration project (1)		<ul style="list-style-type: none"> <li>• MSM</li> <li>• Men</li> </ul>	Not available	No	No	No	

<b>Kenya</b>	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)	<ul style="list-style-type: none"> <li>• MSM</li> <li>• MSW</li> <li>• AGYW</li> <li>• FSW</li> <li>• Adolescent Men</li> <li>• Men</li> <li>• Serodifferent couples</li> <li>• High-risk individuals</li> <li>• Women</li> <li>• Injecting drug users</li> </ul>	<ul style="list-style-type: none"> <li>• Private sector</li> <li>• Public sector</li> <li>• Hospitals</li> <li>• Testing centres</li> <li>•</li> <li>Primary/general health clinics</li> <li>• Research clinics</li> <li>• Family planning clinics</li> <li>• NGOs</li> <li>• Mobile clinics</li> </ul>	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)
<b>Laos</b>	Implementation project (1)		Not available	Not available	No	No	No	
<b>Lesotho</b>	Implementation projects (2)		AGYW	Not available	Approved	Approved	Yes	National Guidelines on the Use of Antiretroviral Therapy For HIV Prevention and Treatment

								(2016)
<b>Malawi</b>	Implementation project (1)	Clinical trial (1)	<ul style="list-style-type: none"> <li>• MSM</li> <li>• AGYW</li> <li>• FSW</li> <li>• Pregnant women</li> </ul>	Research clinics	Approved	Planned	No	The National HIV Prevention Strategy (2015-2020)  Malawi Guidelines for Clinical Management of HIV in Children and Adults (2016)
<b>Malaysia</b>		Demonstration projects (2)	<ul style="list-style-type: none"> <li>• MSM</li> <li>• Transgender women</li> </ul>	<ul style="list-style-type: none"> <li>• Private sector</li> <li>• Public sector</li> <li>• Hospitals</li> <li>• Family planning clinics</li> <li>• NGOs</li> </ul>	No	No	No	
<b>Mali</b>	Demonstration project (1)	Not available	<ul style="list-style-type: none"> <li>• MSM</li> <li>• MSW</li> </ul>	<ul style="list-style-type: none"> <li>• Public sector</li> <li>• NGOs</li> </ul>	No	No	No	
<b>Mexico</b>	Demonstration project (1)	Implementation project (1)	<ul style="list-style-type: none"> <li>• MSM</li> <li>• Transgender women</li> <li>• Transgender men</li> </ul>	<ul style="list-style-type: none"> <li>• Public sector</li> <li>• Hospitals</li> <li>• Testing centres</li> <li>•</li> </ul>	Planned/in progress	No	No	

				Primary/general health clinics • NGOs				
<b>Morocco</b>	Implementation project (1)		• MSM • FSW	• NGOs	No	No	No	
<b>Mozambique</b>	Demonstration project (1)  Implementation project (1)		• MSM • FSW • Women	Private sector	Planned/in progress	Pending	No	
<b>Namibia</b>	Demonstration project (1)  Implementation projects (2)	<b>National level (1)</b>	• AGYW • Pregnant women	Not available	Approved	No	Yes	National Guidelines For Antiretroviral Therapy (2016)
<b>Netherlands</b>	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)
<b>New</b>	Demonstration	Not available	• MSM	• Public sector	Approved	No	Yes	Australasian

<b>Zealand</b>	project (1)  <b>National level (1)</b>	<ul style="list-style-type: none"> <li>• Transgender women</li> <li>• High-risk individuals</li> </ul>	<ul style="list-style-type: none"> <li>• Pharmacies</li> <li>• Hospitals</li> <li>• Primary/general health clinics</li> </ul>				Society for HIV, Viral Hepatitis and Sexual Health Medicine HIV pre-exposure prophylaxis: clinical guidelines
<b>Norway</b>	<b>National level (1)</b>						
<b>Nigeria</b>	Demonstration project (1)	<ul style="list-style-type: none"> <li>• Men</li> <li>• Serodifferent couples</li> <li>• Women</li> </ul>	<ul style="list-style-type: none"> <li>• Private sector</li> <li>• Public sector</li> <li>• Hospitals</li> </ul>	Approved	Approved	No	NATIONAL GUIDELINES FOR HIV PREVENTION TREATMENT AND CARE (2016)  National Strategic Framework on HIV and AIDS: 2017-2021

<b>Peru</b>	Demonstration projects (3)	Implementation project (1)	<ul style="list-style-type: none"> <li>• MSM</li> <li>• Transgender women</li> <li>• Transgender men</li> </ul>	<ul style="list-style-type: none"> <li>• Public sector</li> <li>• Hospitals</li> <li>• Testing centres</li> <li>• Primary/general health clinics</li> <li>• NGOs</li> </ul>	Approved	No	No	
<b>Philippines</b>	Demonstration project (1)		<ul style="list-style-type: none"> <li>• MSM</li> <li>• Transgender women</li> </ul>	Not available	No	No	No	
<b>Portugal</b>	<b>National level (1)</b>		Not available	Not available	Approved	Approved	No	
<b>Scotland</b>	<b>National level (1)</b>		Not available	Not available	Approved	Approved	Yes	Scottish Medicines Consortium Truvada Assessment (2017)
<b>Slovenia</b>		Demonstration project (1)	<ul style="list-style-type: none"> <li>• MSM</li> <li>• Transgender women</li> <li>• Serodifferent couples</li> <li>• Pregnant women</li> </ul>	Not available	Approved	Approved	No	
<b>South Africa</b>	Demonstration project (1)	<ul style="list-style-type: none"> <li>• Clinical trials (2)</li> <li>•</li> </ul>	<ul style="list-style-type: none"> <li>• MSM</li> <li>• AGYW</li> <li>• CSW</li> </ul>	<ul style="list-style-type: none"> <li>• Private sector</li> <li>• Public sector</li> <li>• Testing</li> </ul>	Approved	Approved	Yes	

	(completed and still providing PrEP)	Demonstration projects (2) • Implementation project (1)	<ul style="list-style-type: none"> <li>• FSW</li> <li>• Adolescent men</li> <li>• Men</li> <li>• Transgender women</li> <li>• Women</li> <li>• Pregnant women</li> </ul>	centres • Primary/general health clinics • Research clinics • Family planning clinics • NGOs				
	Clinical trial (1)							
	Demonstration projects (4)							
	Implementation projects (4)							
	Open label extension (1)							
	Product introduction and supports (2)							
<b>Spain</b>	Implementation projects (3)		<ul style="list-style-type: none"> <li>• MSM</li> <li>• Transgender women</li> </ul>	<ul style="list-style-type: none"> <li>• Hospitals</li> <li>• NGOs</li> </ul>	Approved	Approved	Yes	Documento de consenso de GESIDA sobre control y monitorización de la infección por
	Demonstration project (1)							



el VIH (2018)

<b>Swaziland</b>	Implementation projects (2)  Demonstration projects (3)	Not available	<ul style="list-style-type: none"> <li>• MSM</li> <li>• MSW</li> <li>• AGYW</li> <li>• FSW</li> <li>• Adolescent men</li> <li>• Men</li> <li>• Transgender women</li> <li>• Transgender men</li> <li>• Serodifferent couples</li> <li>• High-risk individuals</li> <li>• Women</li> </ul>	<ul style="list-style-type: none"> <li>• Private sector</li> <li>• Public sector</li> <li>• Hospitals</li> <li>•</li> <li>Primary/general health clinics</li> <li>• Family planning clinics</li> </ul>	Approved	Approved	No	
<b>Taiwan</b>	Demonstration project (1)	<b>National level (1)</b>	Not available	Not available	Approved	No	Yes	Taiwan National Pre-Exposure Prophylaxis Guidelines (2016)
		Demonstration project (1)						

<b>Tanzania</b>	Implementation projects (1)		• AGYW	Not available	Approved	Pending	No	
	Demonstration project (1)							
<b>Thailand</b>	<b>National level (1)</b>	Demonstration project (1)	• MSM • AGYW • FSW	• Public sector • Testing centres • NGOs	Approved	Approved	Yes	Thailand National Guidelines on HIV/AIDS Treatment and Prevention 2017
	Demonstration projects (4)		• Adolescent men • Men • Transgender women • Transgender men • Serodifferent couples • Women • Injecting drug users					
	Implementation projects (4)							
<b>Togo</b>	Demonstration project (1)		• MSM • MSW	• Public sector • NGOs	No	No	No	
<b>Uganda</b>	<b>National level (1)</b>	Clinical trial (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
	Demonstration project (1)	Product Introduction and Support (1)						
	Implementation projects							

								for Prevention and Treatment of HIV in Uganda (2016)
<b>Ukraine</b>	Implementation project (1)  Demonstration project (1)		<ul style="list-style-type: none"> <li>• MSM</li> <li>• Men</li> </ul>	Not available	Submitted/awaiting approval	Planned	No	
<b>USA</b>	Clinical trial (1)  Demonstration projects (3)  Implementation project(1)  <b>National level (1)</b>	Demonstration project (1)	<ul style="list-style-type: none"> <li>• MSM</li> <li>• FSW</li> <li>• Men</li> <li>• Transgender women</li> <li>• Transgender men</li> <li>• High-risk individuals</li> <li>• Women</li> <li>• Injecting drug users</li> </ul>	<ul style="list-style-type: none"> <li>• Private sector</li> <li>• Public sector</li> <li>• Primary/General health clinics</li> <li>• Family planning clinics</li> <li>• Home</li> </ul>	Approved	Approved	Yes	National HIV/AIDS Strategy for the United States: Updated to 2020  CDC Clinical Practice Guidelines (2014)
<b>Vietnam</b>	Implementation projects (4)		Not available	<ul style="list-style-type: none"> <li>• Private sector</li> <li>• Public sector</li> <li>• Primary/general health clinics</li> </ul>	No	No	No	

<b>Wales</b>	<b>National level (1)</b>		Not available	Not available	Approved	Approved	Yes	
<b>Zambia</b>	Implementation projects (2)		• AGYW	Not available	Approved	Planned	Yes	
<b>Zimbabwe</b>	Product introduction and support (1)  Implementation projects (2)  Open label extension (1)	Clinical trials (2)	<ul style="list-style-type: none"> <li>• MSM</li> <li>• MSW</li> <li>• AGYW</li> <li>• FSW</li> <li>• Transgender women</li> <li>• Transgender men</li> <li>• Serodifferent couples</li> <li>• Women</li> <li>• Pregnant women</li> </ul>	<ul style="list-style-type: none"> <li>• Public sector</li> <li>• Research clinics</li> </ul>	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	%
<b>Number of HIV Diagnosis</b>	492	-
<b>Rate of diagnoses (per 100,000 population)</b>	10.3	-
<b>Sex</b>	Male (%)	76.4
	Female (%)	23.6
	Male to Female ratio	-
<b>Age</b>	Median age of adult cases (years)	-
	Age range of adult cases (years)	-
	Young people aged 15-24 years (%)	8.3
	Aged 50 and older (%)	14.0
<b>Probable Route of Transmission</b>	MSM (%)	53.3
	Heterosexual (%)	33.1
	Infecting Drug Use (%)	3.5
	Mother to Child Transmission (%)	0.0
	Other (%)	1.4
	Unknown (%)	8.7
<b>Region of Birth</b>	Born in Ireland (%)	26.4
	Born Abroad (%)	62.6
	Unknown (%)	11.0
<b>Co-infection</b>	Acute STI (%)	13.6
	TB (%)	3.5
<b>Previous history of testing</b>	Previously tested positive abroad (%)	38.5
	Transfer of care (% among those previously positive abroad) (%)	87.9

Source: HPSC HIV in Ireland 2017 Report.

## 2.2 Additional characteristics of HIV notifications in 2017 by risk group

### 3.1 MSM

		All Diagnoses	New diagnoses (not previously positive)	Previously positive
<b>Total (n)</b>		262	151	111
<b>Age</b>	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
<b>Region of Birth</b>	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
<b>Co-infections</b>	Acute STI (%)	22.5	17.2	29.7

Source: HPSC HIV in Ireland 2017 Report

### 3.2 Heterosexuals

		Male	Female	Total
<b>Total (n)</b>		63	100	163
<b>Age</b>	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
<b>Region of Birth</b>	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
<b>Co-infections</b>	Acute STI (%)	6.3	1.0	3.1
	TB (%)	4.8	8.0	6.7
<b>Previous history of testing</b>	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 immunodeficiency 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 immunodeficiency 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 IMMUNODEFICIENCY 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
<b>#3</b>	'pre-exposure prophylaxis' OR 'preexposure prophylaxis' OR prep OR 'anti-retroviral chemoprophylaxis' OR 'antiretroviral chemoprophylaxis' OR 'chemoprevention'/syn OR 'hiv prophylaxis' OR 'chemoprophylaxis'/syn
<b>#2</b>	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
<b>#1</b>	'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 immunodeficiency virus':ti OR 'human immunodeficiency 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 immunodeficiency syndrome':ti OR 'acquired immunodeficiency syndrome':ab OR 'acquired immunodeficiency syndrome':ti OR 'acquired immunodeficiency syndrome':ab OR 'acquired immuno-deficiency syndrome':ab



## 3.2 Data collection, management and analysis

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

<sup>†</sup>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](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>.
6. Grohskopf LA, Chillag KL, Gvetadze R, Liu AY, Thompson M, Mayer KH, et al. Randomized trial of clinical safety of daily oral tenofovir disoproxil fumarate among HIV-uninfected men who have sex with men in the United States. *Journal of acquired immune deficiency syndromes (1999)*. 2013;64(1):79-86.
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, Mgodhi 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, Mgodhi 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, Nosedá 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
<b>Female</b>	7	14	49.4	-21.5, 80.8	0.11
<b>Male</b>	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 Excluded studies from review of cost-effectiveness

Reason for exclusion	Study
<b>Non-oral PrEP (n=5)</b>	Adamson 2017 <sup>(1)</sup> , Glaubius 2016 <sup>(2)</sup> , Moodley 2016 <sup>(3)</sup> , Walensky 2012 <sup>(4)</sup>
<b>Conference abstract (n=19)</b>	Anderson 2009 <sup>(5)</sup> , Bely 2009 <sup>(6)</sup> , Bernard 2016 <sup>(7)</sup> , Bórquez 2015 <sup>(8)</sup> , Cambiano 2015 <sup>(9)</sup> , Cambiano 2016 <sup>(10)</sup> , Damm 2016 <sup>(11)</sup> , Durand-Zaleski 2016 <sup>(12)</sup> , Garnett 2016 <sup>(13)</sup> , Kenyon 2015 <sup>(14)</sup> , Koppenhaver 2011 <sup>(15)</sup> , Musenge 2016 <sup>(16)</sup> , Nichols 2014 <sup>(17)</sup> , Nichols 2016 <sup>(18)</sup> , Obiero 2013 <sup>(19)</sup> , Pilkington 2018 <sup>(20)</sup> , Quaife 2018 <sup>(21)</sup> , Vaidya 2015 <sup>(22)</sup> , Ying 2015 <sup>(23)</sup>
<b>Systematic review (n=10)</b>	Cambiano 2016 <sup>(24)</sup> , Gomez 2013 <sup>(25)</sup> , Gordon 2013 <sup>(26)</sup> , Hankins 2014 <sup>(27)</sup> , Hellinger 2013 <sup>(28)</sup> , Kahn 2011 <sup>(29)</sup> , Mugo 2016 <sup>(30)</sup> , Schackman 2012 <sup>(31)</sup>
<b>Generalised population epidemic studies (n=6)</b>	Abbas 2007 <sup>(32)</sup> , Alistar 2014 <sup>(33)</sup> , Cremin 2013 <sup>(34)</sup> , Hallett 2011 <sup>(35)</sup> , Long 2013 <sup>(36)</sup> , Pretorius 2010 <sup>(37)</sup> ,
<b>Inappropriate intervention (n=9)</b>	Chen 2014 <sup>(38)</sup> , Cremin 2017 <sup>(39)</sup> , Drabo 2016 <sup>(40)</sup> , Price 2016 <sup>(41)</sup> , Punyacharoensin 2016 <sup>(42)</sup> , Ross 2016 <sup>(43)</sup> , Shen 2018 <sup>(44)</sup> , Jewell 2015 <sup>(45)</sup> , Mitchell 2015 <sup>(46)</sup>

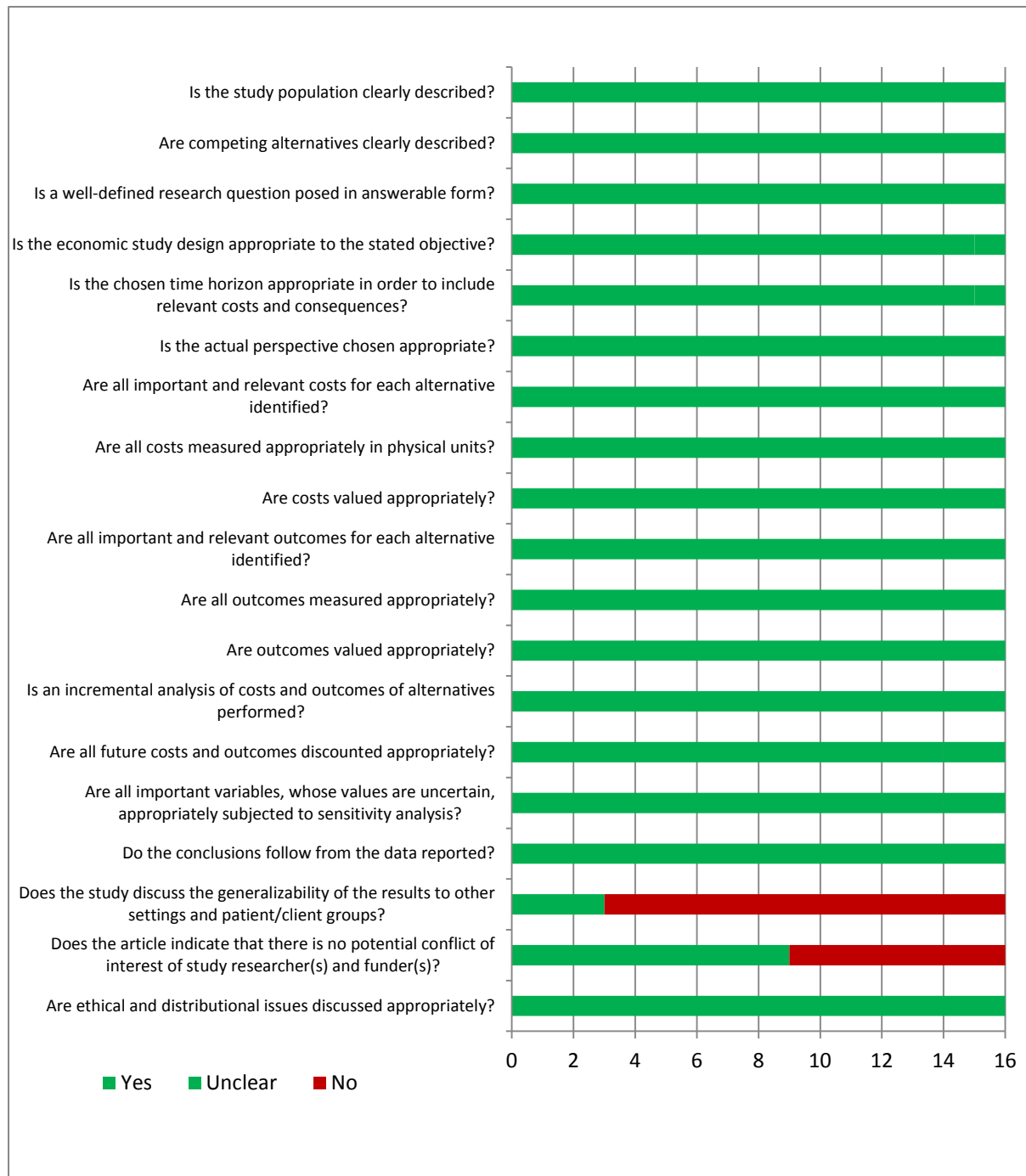
1. Adamson BJS, Carlson JJ, Kublin JG, Garrison LP. The potential cost-effectiveness of pre-exposure prophylaxis combined with HIV vaccines in the united states. *Vaccines*. 2017;5(2).
2. Glaubius RL, Hood G, Penrose KJ, Parikh UM, Mellors JW, Bendavid E, et al. Cost-effectiveness of injectable preexposure 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.
15. Koppenhaver RT, Sorensen SW, Farnham PG, Sansom SL. The cost-effectiveness of pre-exposure prophylaxis in men who have sex with men in the United States: An epidemic model. *Journal of Acquired Immune Deficiency Syndromes*. 2011;58(2):e51-e2.
16. Musenge E. A cost-effective and focused model for HIV prevention. *The Lancet HIV*. 2016;3(9):e402-e3.
17. Nichols BE, Baltussen R, Van Dijk JH, Thuma PE, Nouwen JL, Boucher CAB, et al. Cost-effectiveness of PrEP in HIV/AIDS control in Zambia: A stochastic league approach. *Journal of Acquired Immune Deficiency Syndromes*. 2014;66(2):221-8.
18. Nichols BE, Boucher CA, Van Der Valk M, Rijnders BJ, Van De Vijver DA. PrEP is only cost-effective among MSM in the Netherlands when used on demand. *Topics in Antiviral Medicine*. 2016;24(E-1):456.
19. Obiero AO, Odoyo JB, Ondondo RO, Rono BK, Odondi JO, Bukusi EA. Cost analysis of recruitment strategies used in the partners pre-exposure prophylaxis (PrEP) clinical trial at Kisumu Site, Kenya. *Sexually Transmitted Infections*. 2013;89.
20. Pilkington V, Nkwolo N, Pozniak A, Whitlock G, Hill A. How many people need to take PrEP to prevent one new HIV infection? Meta-analysis of 32 HIV incidence studies in 64,741 patients. *HIV Medicine*. 2018;19:S51.
21. Quaife M, Terris-Prestholt F, Eakle R, Cabrera Escobar MA, Kilbourne-Brook M, Mvundura M, et al. The cost-effectiveness of multi-purpose HIV and pregnancy prevention technologies in South Africa. *Journal of the International AIDS Society*. 2018;21.
22. Vaidya N, Campbell JD. A cost-effectiveness analysis of pre-exposure prophylaxis for HIV: A us payer perspective. *Value in Health*. 2015;18(3):A236-A7.
23. Ying R, Heffron R, Baeten J, Celum C, Katabira E, Bulya N, et al. Cost-effectiveness of preexposure prophylaxis for high-risk HIV-discordant couples. *Topics in Antiviral Medicine*. 2015;23:511.
24. Cambiano V, Miners A, Phillips A. What do we know about the cost-effectiveness of HIV preexposure prophylaxis, and is it affordable? *Current opinion in HIV and AIDS*. 2016;11(1):56-66.
25. Gomez GB, Borquez A, Case KK, Wheelock A, Vassall A, Hankins C. The Cost and Impact of Scaling Up Pre-exposure Prophylaxis for HIV Prevention: A Systematic Review of Cost-Effectiveness Modelling Studies. *PLoS Medicine*. 2013;10(3).
26. Gordon D. Pre-exposure prophylaxis (PrEP): Is it cost-effective? *AIDS Reader*. 2013.
27. Hankins CA. Untangling the cost-effectiveness knot: Who is oral antiretroviral HIV pre-exposure prophylaxis really for? *Expert Review of Pharmacoeconomics and Outcomes Research*. 2014;14(2):167-70.
28. Hellinger FJ. Assessing the cost effectiveness of pre-exposure prophylaxis for HIV prevention in the US. *Pharmacoeconomics*. 2013;31(12):1091-104.
29. Kahn JG, Marseille EA, Bennett R, Williams BG, Granich R. Cost-effectiveness of antiretroviral therapy for prevention. *Current HIV Research*. 2011;9(6):405-15.

30. Mugo NR, Ngure K, Kiragu M, Irungu E, Kilonzo N. The preexposure prophylaxis revolution; From clinical trials to programmatic implementation. *Current opinion in HIV and AIDS*. 2016;11(1):80-6.
31. Schackman BR, Eggman AA. Cost-effectiveness of pre-exposure prophylaxis for HIV: a review. *Current Opinion in HIV & AIDS*. 2012;7(6):587-92.
32. Abbas UL, Anderson RM, Mellors JW. Potential impact of antiretroviral chemoprophylaxis on HIV-1 transmission in resource-limited settings. *PLoS ONE*. 2007;2(9).
33. Alistar SS, Grant PM, Bendavid E. Comparative effectiveness and cost-effectiveness of antiretroviral therapy and pre-exposure prophylaxis for HIV prevention in South Africa. *BMC Medicine*. 2014;12(1).
34. Cremin I, Alsallaq R, Dybul M, Piot P, Garnett G, Hallett TB. The new role of antiretrovirals in combination HIV prevention: A mathematical modelling analysis. *AIDS*. 2013;27(3):447-58.
35. Hallett TB, Baeten JM, Heffron R, Barnabas R, de Bruyn G, Cremin Í, et al. Optimal uses of antiretrovirals for prevention in HIV-1 serodiscordant heterosexual couples in South Africa: A modelling study. *PLoS Medicine*. 2011;8(11).
36. Long EF, Stavert RR. Portfolios of biomedical HIV interventions in South Africa: A cost-effectiveness analysis. *Journal of General Internal Medicine*. 2013;28(10):1294-301.
37. Pretorius C, Stover J, Bollinger L, Bacaër N, Williams B. Evaluating the Cost-Effectiveness of Pre-Exposure Prophylaxis (PrEP) and Its Impact on HIV-1 Transmission in South Africa. *PLoS ONE*. 2010;5(11).
38. Chen A, Dowdy DW. Clinical effectiveness and cost-effectiveness of HIV pre-exposure prophylaxis in men who have sex with men: Risk calculators for real-world decision-making. *PLoS ONE*. 2014;9(10).
39. Cremin I, McKinnon L, Kimani J, Cherutich P, Gakii G, Muriuki F, et al. PrEP for key populations in combination HIV prevention in Nairobi: a mathematical modelling study. *The Lancet HIV*. 2017;4(5):e214-e22.
40. Drabo EF, Hay JW, Vardavas R, Wagner ZR, Sood N. A Cost-effectiveness Analysis of Preexposure Prophylaxis for the Prevention of HIV Among Los Angeles County Men Who Have Sex With Men. *Clinical Infectious Diseases*. 2016;63(11):1495-504.
41. Price JT, Wheeler SB, Stranix-Chibanda L, Hosek SG, Watts DH, Siberry GK, et al. Cost-Effectiveness of Pre-exposure HIV Prophylaxis During Pregnancy and Breastfeeding in Sub-Saharan Africa. *Journal of Acquired Immune Deficiency Syndromes: JAIDS*. 2016;72 Suppl 2:S145-53.
42. Punyacharoensin N, Edmunds WJ, De Angelis D, Delpech V, Hart G, Elford J, et al. Effect of pre-exposure prophylaxis and combination HIV prevention for men who have sex with men in the UK: a mathematical modelling study. *The lancet HIV*. 2016;3(2):e94-e104.
43. Ross EL, Cinti SK, Hutton DW. Implementation and Operational Research: A Cost-Effective, Clinically Actionable Strategy for Targeting HIV Preexposure Prophylaxis to High-Risk Men Who Have Sex With Men. *J Acquir Immune Defic Syndr*. 2016;72(3):e61-7.
44. Shen M, Xiao Y, Rong L, Meyers LA, Bellan SE. The cost-effectiveness of oral HIV pre-exposure prophylaxis and early antiretroviral therapy in the presence of drug resistance among men who have sex with men in San Francisco. *BMC Medicine*. 2018;16(1).
45. Jewell BL, Cremin I, Pickles M, Celum C, Baeten JM, Delany-Moretlwe S, et al. Estimating the cost-effectiveness of pre-exposure prophylaxis to reduce HIV-1 and HSV-2 incidence in HIV-serodiscordant couples in South Africa. *PLoS ONE*. 2015;10(1).
46. Mitchell KM, Lepine A, Terris-Prestholt F, Torpey K, Khamofu H, Folayan MO, et al. Modelling the impact and cost-effectiveness of combination prevention amongst HIV serodiscordant couples in Nigeria. *AIDS*. 2015;29(15):2035-44.
47. 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).

48. 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.
49. 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.
50. 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).
51. Gray RG, A. Discussion paper: Estimates of the number of people eligible for PrEP in Australia, and related cost-effectiveness. Kirby Institute & CSRH. 2017.
52. 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.
53. 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.
54. 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.
55. 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).
56. 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).
57. 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.
58. 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).
59. 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.
60. 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.
61. 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.
62. 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.
63. 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.

## 4.2 CHEC-list evaluation of the quality of included studies



### 4.3 List of studies at risk of bias

Study	Generalizability of results to other settings and patients/client groups	Conflict of interest
<b>Bernard (2017)</b> <sup>(47)</sup>	No	No conflict of interests.
<b>Cambiano (2018)</b> <sup>(48)</sup>	No	Personal fees paid to lead authors. One author received a grant from Gilead Sciences for other projects.
<b>Desai (2008)</b> <sup>(49)</sup>	No	No conflict of interests.
<b>Durand-Zaleski (2016)</b> <sup>(12)</sup>	No	Authors received grants and support from Gilead Sciences.
<b>Gomez (2012)</b> <sup>(50)</sup>	No	No conflict of interests.
<b>Gray (2017)</b> <sup>(51)</sup>	Yes	No conflict of interests.
<b>Juusola (2012)</b> <sup>(52)</sup>	No	Funding reported (National Institute of Health and the Department of Veterans Affairs). No conflict of interest reported.
<b>Lin (2016)</b> <sup>(53)</sup>	No	No financial disclosures were reported.
<b>Luz (2018)</b> <sup>(54)</sup>	No	No conflict of interests.
<b>MacFadden (2018)</b> <sup>(55)</sup>	No	Authors received research grants from and given lectures for Gilead Sciences.
<b>McKenney (2017)</b> <sup>(56)</sup>	No	No competing interests
<b>Nichols (2016)</b> <sup>(57)</sup>	No	Authors received research grants and personal fees from Gilead Sciences.
<b>Ong (2017)</b> <sup>(58)</sup>	Yes	No conflict of interests.
<b>Ouellet (2015)</b> <sup>(59)</sup>	No	No conflict of interests.
<b>Paltiel (2009)</b> <sup>(60)</sup>	No	Lead author acted as consultant for Gilead Science and received honoraria for teaching.
<b>Reyes-Uruena (2018)</b> <sup>(61)</sup>	No	No conflict of interests.
<b>Schneider (2014)</b> <sup>(62)</sup>	Yes	No conflict of interests.
<b>Suraratdecha (2017)</b> <sup>(63)</sup>	No	No conflict of interests.



## 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
<b>Bernard (2017)<sup>(47)</sup></b>	<ol style="list-style-type: none"> <li>1) Efficacy of PrEP: 49%</li> <li>2) Dosing regimen: daily</li> <li>3) Incidence of HIV: n/a</li> <li>4) Prevalence of HIV: 9.8%</li> <li>5) Assume 69.9% are aware of their HIV status.</li> </ol>	<p>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</p>	<p>PrEP coverage 36%: Incremental QALYS 220,000 PrEP coverage 40.5%: Incremental QALYS 25,000 PrEP coverage 45%: Incremental QALYS 24,000</p>	<p>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</p>	<p>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)</p>	N/A
<b>Cambiano (2018)<sup>(48)</sup></b>	<ol style="list-style-type: none"> <li>1) Efficacy of PrEP: 86%</li> <li>2) Dosing regimen: event-based PrEP (mean 5 pills per week)</li> <li>3) Incidence of HIV: 2.0 per 100 person-years (90%: 0.7–4.3)</li> <li>4) Prevalence of HIV: n/a</li> <li>5) 40,000 MSM initiated in Year 1</li> </ol>	<p>Currency (year): GBP (No cost year) Country: United Kingdom Model type: dynamic individual-based stochastic model Perspective: health System Discount rate: 3.5%</p>	<ol style="list-style-type: none"> <li>1) Cumulative mean number of HIV: 134,600 (61,700 to 264,300)</li> <li>2) Number of HIV infections averted: 44,300 (3,330;97,600)</li> <li>3) Proportion of HIV infections</li> </ol>	<p>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 £)</p>	<p>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)</p>	<ol style="list-style-type: none"> <li>1. 80% probability of cost-effectiveness £20,000 ICER</li> <li>2. 75% probability of cost-effectiveness £13,000 ICER</li> <li>3. PrEP cost saving can occur as</li> </ol>

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

						<p>levels reported all three ICERs &gt;\$100,000 at when care cost were low and adherence 33%.</p> <p>3) At base-case and high HIV case costs 39% of scenarios were cost saving.</p> <p>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.</p>
<b>Durand (2016)<sup>(12)</sup></b>	<ol style="list-style-type: none"> <li>1) Efficacy of PrEP: 86%</li> <li>2) Dosing regimen: on demand (15.6 tablets per month)</li> <li>3) Incidence of HIV: IPERGAY</li> <li>4) Prevalence of HIV: IPERGAY</li> <li>5) NNT: 17.2</li> <li>6) 5.68 infections averted/100 person-years</li> <li>7) Zero cost for placebo arm</li> </ol>	<p>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)</p>	None	<ol style="list-style-type: none"> <li>1) Annual PrEP ART Cost: €3,117</li> <li>2) Annual PrEP Program cost: €4,271 (SD €2,446)</li> <li>3) Cost of HIV infection averted: €75,258</li> </ol>	1) Cost saving for 7.5 years	<ol style="list-style-type: none"> <li>1) Generic price (€2,771/pp): Cost saving up to 13 years.</li> <li>2) International market price (€1,517/pp): Cost saving up to 20 years.</li> </ol>

<p><b>Gomez (2012)<sup>(50)</sup></b></p>	<ol style="list-style-type: none"> <li>1) Efficacy of PrEP: 92% (40;99)</li> <li>2) Dosing regimen: daily</li> <li>3) Incidence:             <ol style="list-style-type: none"> <li>(i) MSM 2.0/100PY</li> <li>(ii) High Risk MSM: 3.5/100PY</li> </ol> </li> <li>4) Prevalence: 0.2</li> <li>5) Adherence: good (95%), average (45%), poor (15%)</li> <li>6) Threshold for Peru: \$5,401/DALY averted.</li> </ol>	<p>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</p>	<ol style="list-style-type: none"> <li>1) DALY averted per infection undiscounted: 27.12</li> <li>2) DALY averted per infection discounted: 11.5</li> </ol>	<ol style="list-style-type: none"> <li>1) Annual PrEP ART cost: \$420–600</li> <li>2) PrEP intervention cost: \$525–830</li> <li>3) ART cost: \$1,000–3500</li> </ol>	<p>N/A</p>	<ol style="list-style-type: none"> <li>1) Low (5%) and high (20%) coverage scenarios.</li> <li>2) The three levels of adherence.</li> <li>3) Across all scenarios highest estimated cost per DALY averted \$1,126–\$1,780 (\$1,036–\$4,254).</li> <li>4) Six main scenarios (coverage &amp; prioritization): \$447–\$1779/DALY.</li> </ol>
<p><b>Gray (2017)<sup>(51)</sup></b></p>	<ol style="list-style-type: none"> <li>1) Efficacy of PrEP: 99%</li> <li>2) Dosing regimen: daily</li> <li>3) Incidence: n/a</li> <li>4) Prevalence: n/a</li> <li>5) High adherence: 90%</li> </ol>	<p>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</p>	<ol style="list-style-type: none"> <li>1) 30-0-0 scenario.</li> <li>2) Infections averted: 4,720 (2,510–6,440).</li> <li>3) QALYs gained: 2,190 (1,160–2,840)</li> </ol>	<ol style="list-style-type: none"> <li>1) Annual PrEP ART cost: \$10,249</li> </ol>	<ol style="list-style-type: none"> <li>1) Incremental cost of PrEP programme: \$205,242,910</li> <li>2) Cost per QALY gained: \$102,400</li> </ol>	<ol style="list-style-type: none"> <li>1) Eight update scenarios modelled for high/medium/low risk MSM</li> <li>2) Infections averted range: 4,720–11,330.</li> <li>3) QALY gained range: 2,190–6,270.</li> </ol>
<p><b>Juusola (2012)<sup>(52)</sup></b></p>	<ol style="list-style-type: none"> <li>1) Efficacy of PrEP: 44%</li> <li>2) Dosing regimen: daily</li> <li>3) Incidence: 0.8%</li> <li>4) Prevalence: 12.3%</li> <li>5) 90% reduction in sexual infectivity due to ART used for treatment of HIV infection.</li> </ol>	<p>Currency (year): USD (no cost year) Country: USA Type: deterministic dynamic compartmental Perspective: societal discount rate: 3% Time horizon: 20 Years</p>	<p>All MSM incremental QALYS (i) 100% coverage: 2,217,732 (ii) 50% coverage: 1,263,673 (iii) 20% coverage: 550,166</p>	<ol style="list-style-type: none"> <li>1) Annual PrEP ART cost: \$9,312</li> <li>2) Annual HIV ART cost: \$15,589</li> <li>3) Annual HIV care cost: \$4,130–6,934</li> <li>4) Annual AIDS care</li> </ol>	<p>PrEP in 20% of all MSM: \$172,091/QALY PrEP coverage of 100% high-risk MSM: \$52,433/QALY \$600,000 per</p>	<ol style="list-style-type: none"> <li>1) PrEP cost, efficacy and quality-of-life impacted cost effectiveness.</li> <li>2) Sexual disinhibition had no impact.</li> </ol>

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

	<p>4) HIV prevalence: 5.2–23.7%</p> <p>5) PrEP-induced resistance made first and second line ART 10% less effective.</p> <p>6) Cost effectiveness threshold of \$8,540.</p>	<p>Time horizon: n/a</p> <p>Lifetime utility values: n/a</p> <p>ICER in dollars per year of life saved (YLS).</p>			<p>when the cost was less than \$100/month PrEP remained cost effective until incidence was reduced to 0.9/100PY</p>	<p>(i) Incidence of HIV</p> <p>(ii) PrEP ART cost</p> <p>(iii) PrEP effectiveness.</p> <p>3) PrEP was cost effective until drug costs were &gt;\$100/month.</p> <p>4) PrEP was cost effective up to incidence of 0.9/100PY.</p>
<p><b>MacFadden (2016)<sup>(55)</sup></b></p>	<p>1) Efficacy of PrEP: 44%</p> <p>2) Dosing regimen: daily</p> <p>3) Incidence of HIV: 0.62–1.14 per 100PY</p> <p>4) Prevalence of HIV: n/a</p> <p>5) No female sexual partners were included.</p> <p>6) Tested PrEP in endemic equilibrium</p> <p>7) The cost of PrEP remained stable (that is, did not model on-demand dosing)</p> <p>8) QALY ratio for PrEP users was 1.</p> <p>9) ART adherence for patients with HIV was excellent.</p>	<p>Currency (year): CAD (2015)</p> <p>Country: Canada</p> <p>Model type: dynamic transmission perspective: health system</p> <p>Discount rate: 3%</p> <p>Time horizon: 20 years</p> <p>Utility values</p> <p>1) PrEP: 1</p> <p>2) Unidentified HIV+ (CD4&gt;200): 0.91</p> <p>3) Unidentified HIV+ (CD4&gt;200): 0.89</p> <p>4) Unidentified AIDS: 0.73</p> <p>5) Identified AIDS: 0.73</p> <p>6) On ART: 0.83</p> <p>Tengs and Lin 2002</p>	<p>All MSM incremental QALYS</p> <p>(i) 100% coverage: 5,430</p> <p>(ii) 75% coverage: 5,363</p> <p>(iii) 50% coverage: 4,413</p> <p>(iv) 25% coverage: 2,673</p> <p>High-risk MSM incremental QALYS</p> <p>(i) 100% coverage: 2,951</p> <p>(ii) 75% coverage: 3,080</p> <p>(iii) 50% coverage: 2,321</p> <p>(iv) 25% coverage: 1,417</p>	<p>All MSM PrEP costs (billions):</p> <p>(i) 100% coverage: \$4.37</p> <p>(ii) 75% coverage: \$3.80</p> <p>(iii) 50% coverage: \$2.65</p> <p>(iv) 25% coverage: \$1.36</p> <p>High-risk MSM PrEP costs (millions)</p> <p>(i) 100% coverage: \$269</p> <p>(ii) 75% coverage: \$239</p> <p>(iii) 50% coverage: \$162</p> <p>(iv) 25% coverage: \$79.8</p> <p>1) Annual PrEP ART Cost: \$10,012</p> <p>2) Initial/Subsequent clinic visits: \$305/\$100</p>	<p>*No base-case all scenario analysis.</p>	<p>All MSM cost/QALY gained:</p> <p>(i) 100% coverage: \$792,763</p> <p>(ii) 75% coverage: \$696,297</p> <p>(iii) 50% coverage: \$587,050</p> <p>(iv) 25% coverage: \$495,175</p> <p>High-risk MSM cost/QALY gained:</p> <p>(i) 100% coverage: \$68,203</p> <p>(ii) 75% coverage: \$56,084</p> <p>(iii) 50% coverage: \$46,818</p> <p>(iv) 25% coverage: \$34,999</p> <p>99% efficacy of PrEP cost/QALY:</p> <p>25-100% Coverage: \$15,275–44,427</p>

				3) Annual cost HIV+ (on ART) = \$15,264		
<b>McKenney (2017)<sup>(56)</sup></b>	<ol style="list-style-type: none"> <li>1) Efficacy of PrEP: 56%</li> <li>2) Dosing regimen: daily</li> <li>3) Incidence of HIV: 0.19 (0.05-0.4)</li> <li>4) Prevalence of HIV: n/a</li> <li>5) Base-case Chen et al.</li> <li>6) Updated the per-act probability of HIV: 0.0138 (0.0102–0.0186)</li> </ol>	<p>Currency: USD (no cost year) Country: USA Model type: decision analytic Perspective: societal Discount rate: 3% (Chen et al.) Time horizon: lifetime (1 year of PrEP) Utility values: HIV+ CD4 cell count &gt;350cells/µl: 0.94 HIV+ CD4 cell count 200-350cells/µl: 0.82 Infected AIDS: 0.7 Tengs and Lin 2002</p>	<p>Discounted QALY gained per case of HIV averted: 2.24</p> <p>QALY loss per additional STI: 0.02</p>	<ol style="list-style-type: none"> <li>1) Lifetime HIV cost: \$327,503</li> <li>2) Annual PrEP ART cost: \$10,711 (\$4,772-15,000)</li> </ol>	<p>Base-case: \$64,000/QALY gained</p> <p>All scenarios cost saving when the cost of PrEP is reduced by 60%.</p> <p>All scenarios are cost saving at high levels of efficacy/adherence .</p>	<p>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.</p>
<b>Nichols (2016)<sup>(57)</sup></b>	<ol style="list-style-type: none"> <li>1) Efficacy of PrEP: 86%</li> <li>2) Dosing regimen: daily and on-demand</li> <li>3) Incidence of HIV: n/a</li> <li>4) Prevalence of HIV: n/a</li> <li>5) Average of 4,500 MSM on PrEP at full scale-up.</li> <li>6) Daily and on-demand have same effectiveness.</li> <li>7) On-demand costs half as much as daily dosing.</li> <li>8) No change in sexual behaviour</li> </ol>	<p>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 &gt;350cells/µl: 0.94 HIV+ CD4 cell count 200-350cells/µl: 0.82 Infected AIDS: 0.7 Tengs and Lin 2002 Infected on ART: 0.94</p>	N/A	<ol style="list-style-type: none"> <li>1) Annual PrEP ART cost (Daily): €7,400</li> <li>2) Annual PrEP ART cost (on-demand): €3,850</li> <li>3) One time additional costs during first year of treatment: €1,130–3,539</li> <li>4) Cost of ART for HIV: €12,468–13,505</li> </ol>	<p>Daily PrEP</p> <p>Stable HIV epidemic – cost per QALY gained: €7,800 (100% efficacy) to €20,000 (40% efficacy).</p> <p>On-demand PrEP</p> <p>Stable HIV epidemic – cost per QALY gained: cost saving (100% efficacy) to €9,100 (40% efficacy).</p>	<ol style="list-style-type: none"> <li>1) Univariate sensitivity analysis.</li> <li>2) Daily PrEP the discount rate for costs and QALYs had most profound effect.</li> <li>3) ICERs: €5,200–15,000</li> <li>4) On-demand PrEP the cost of ART had most profound effect.</li> <li>5) ICERs: €700–3,700.</li> <li>6) Efficacy &gt;90%</li> </ol>

		(assumption based on Tengs and Lin)			At current epidemic all cost per QALY gained <€20,000.	<p>all ICER &lt;€10,000.</p> <p>7) Efficacy &gt;90% and cost of PrEP reduced by 50% intervention is cost saving.</p> <p>8) Daily PrEP declining HIV epidemic – cost per QALY gained: €13,100 (100% efficacy) to €26,000 (40% efficacy)</p> <p>9) On-demand PrEP declining HIV epidemic – cost per QALY gained: €1,400 (100% efficacy) to €9,100 (40% efficacy)</p>
<b>Ong (2017)<sup>(58)</sup></b>	<ol style="list-style-type: none"> <li>1) Efficacy of PrEP: 86%</li> <li>2) Dosing regimen: daily and on-demand (4 tablets per week).</li> <li>3) Incidence of HIV: 3.3/100PY</li> <li>4) Prevalence of HIV: n/a</li> <li>5) Risk compensation: 20%</li> <li>6) Assumption of no disutility between HIV infection and diagnosis.</li> <li>7) Cumulative lifetime incidence without PrEP: 16.96%.</li> </ol>	<p>Currency (year): GBP (2015) Country: United Kingdom Type: decision analytic Perspective: health provider Discount rate: 3.5% Time horizon: lifetime (1 Year PrEP Utility values: 1) Disutility HIV: 0.11 2) Utility of men &gt;75 years old with HIV:</p>	<ol style="list-style-type: none"> <li>1) 118 HIV infections averted.</li> <li>2) 361 (discounted) QALYs saved.</li> </ol>	<p>Annual PrEP ART Cost: £4,331 PEP: £772 Annual ART HIV cost: £4,741 Annual HIV care &gt;200CD4 cost: £4,734 Annual HIV care &lt;200CD4 cost: £7,479 Annual cost of undiagnosed HIV infection: £0 (£0–</p>	<p>Base-case: cost saving -£7,227 (Efficacy 86%, 3.3/100PY, risk compensation 20%)</p> <p>23 years until cumulative saving from HIV care costs averted for the year-1 investment to</p>	<ol style="list-style-type: none"> <li>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</li> </ol> <p>At 86% efficacy PrEP scenarios:</p>



	8) After Year 1 incidence was reduced to 1.35 per 100PY and PrEP was no longer indicated	0.75. Tengs and Lin 2002		2,499) Year 1 program cost: 22.5m.	breakeven.	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
<b>Ouellet (2015)<sup>(59)</sup></b>	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.
<b>Paltiel (2009)<sup>(60)</sup></b>	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
<b>Reyes-Uruena (2018)<sup>(61)</sup></b>	1) Efficacy of PrEP: 86% 2) Dosing regimen: daily and on-demand 3) Incidence of HIV: 2%	Currency (year): euro (2016) Country: Spain Model type: n/a	Incremental QALYS: (i) Undiscounted: 16.99 (ii) 3% discount: 4.19	Annual PrEP Program cost (ART Cost): (i) Daily: €7,176.54 (€5,873.90)	ICER daily PrEP: Undiscounted: €6,281.62	ICER Daily PrEP: (i) 3% discount: €57,424.80 (ii) 5% discount:

	<p>4) Prevalence of HIV</p> <p>5) MSM willing to take PrEP: 5,989–10,972 (1.86–3.4%)</p> <p>6) Six outpatient visits per year and incur laboratory costs.</p> <p>7) Salary losses due to PrEP €536</p> <p>8) Salary losses due to HIV: €5,661</p>	<p>Perspective: n/a</p> <p>Discount rate: 3%/5%</p> <p>Time horizon: n/a</p> <p>Utility values:</p> <p>Reduction in QALY in asymptomatic HIV infection: 0.94</p> <p>Tengs and Lin</p>	<p>(iii) 5% discount: 2.36</p> <p>Incremental life years:</p> <p>(i) Undiscounted: 14.9</p> <p>(ii) 3% discount: 3.5</p> <p>(iii) 5% discount: 1.9</p>	<p>(ii) On-demand: €7,176.54 (€2,936.90)</p> <p>HIV costs: €13,481.97</p>	<p>ICER on-demand PrEP:</p> <p>Uundiscounted: -3767.36</p>	<p>€155,829.82</p> <p>ICER On-Demand PrEP:</p> <p>(ii) 3% discount: €16,706.73</p> <p>(ii) 5% discount: €43,329.57</p>
<p><b>Schneider (2014)<sup>(62)</sup></b></p>	<p>1) Efficacy of PrEP: 95%</p> <p>2) Dosing regimen: daily and on-demand</p> <p>3) Incidence of HIV: n/a</p> <p>4) Prevalence of HIV: n/a Approximately 10% of MSM.</p> <p>5) 60,000 MSM</p> <p>6) Adherence of 75%</p> <p>7) No sexual disinhibition in the base-case</p>	<p>Currency (year): AUD (2013)</p> <p>Country: Australia</p> <p>Model type: dynamic transmission</p> <p>Perspective: health provider</p> <p>Discount rate: 3%</p> <p>Time horizon: 10 year</p> <p>Utility values:</p> <p>HIV+ CD4 cell count &gt;350cells/μl (Asymptomatic): 0.94</p> <p>HIV+ CD4 cell count 200–350cells/μl (Symptomatic): 0.82</p> <p>Infected AIDS: 0.7</p> <p>Tengs and Lin 2002</p>	<p>Target group, coverage: QALY</p> <p>All MSM</p> <p>(i) 10%: 605</p> <p>(ii) 20%: 1,477</p> <p>(iii) 30%: 2,142</p> <p>MSM&gt;10 partners</p> <p>(i) 15%:922</p> <p>(ii) 30%:1,503</p> <p>MSM&gt;20 partners</p> <p>(i) 15%: 878</p> <p>(ii) 30%:1,395</p> <p>MSM&gt;50 partners</p> <p>(i) 15%: 228</p> <p>(ii) 30%: 571</p> <p>MSM SDC:</p> <p>(i) 15%: 527</p> <p>(ii) 30%: 1,067</p>	<p>Target group, coverage: Incremental cost (billion)</p> <p>All MSM</p> <p>(i) 10%: \$3.16</p> <p>(ii) 20%: \$6.31</p> <p>(iii) 30%: \$9.52</p> <p>MSM&gt;10 partners</p> <p>(i) 15%: \$1.66</p> <p>(ii) 30%: \$3.31</p> <p>MSM&gt;20 partners</p> <p>(i) 15%: \$1.28</p> <p>(ii) 30%: \$2.55</p> <p>MSM&gt;50 partners</p> <p>(i) 15%: \$0.31</p> <p>(ii) 30%: \$0.65</p> <p>MSM SDC (millions):</p> <p>(i) 15%: \$4.42</p> <p>(ii) 30%: \$12.35</p> <p>Annual PrEP ART cost: \$9,596.97</p> <p>PrEP annual monitoring cost: \$765</p> <p>Annual HIV ART cost: \$10,685–31,411</p> <p>Annual HIV medical</p>	<p>Target Group, Coverage: ICER/QALYG</p> <p>All MSM</p> <p>(i) 10%: \$521,848</p> <p>(ii) 20%: \$427,149</p> <p>(iii) 30%:\$180,146</p>	<p>Target group, coverage: ICER/QALYG</p> <p>MSM&gt;10 partners</p> <p>(i) 15%: \$180,146</p> <p>(ii) 30%: \$220,252</p> <p>MSM&gt;20 partners</p> <p>(i) 15%: \$145,960</p> <p>(ii) 30%: \$183,195</p> <p>MSM&gt;50 partners</p> <p>(i) 15%: \$134,185</p> <p>(ii) 30%: \$113,673</p> <p>MSM SDC:</p> <p>(i) 15%: \$8,399</p> <p>(ii) 30%: \$11,575</p>

				costs: \$3,097–7,883		
<b>Suraratdecha (2017)<sup>(63)</sup></b>	<ol style="list-style-type: none"> <li>1) Efficacy of PrEP: 75%</li> <li>2) Dosing regimen: daily</li> <li>3) Incidence of HIV: n/a</li> <li>4) Prevalence of HIV: 11.6% and 5.2%</li> <li>5) Baseline ART coverage 30%</li> <li>6) Cost effectiveness threshold: \$17,449</li> </ol>	<p>Currency (year): USD (No cost year) Country: Thailand Model type: dynamic transmission (OPTIMA) Perspective: health provider Discount rate: 3% Time horizon: 5 years</p>	<p>PrEP to high-risk MSM: (i) DALYs averted: 7,857 (ii) HIV infection averted: 555</p> <p>PrEP to all MSM: (i) DALYs averted: 19,368 (ii) HIV infection averted: 1368</p>	<p>Annual PrEP ART costs: \$14,106 Total annual PrEP Cost: \$17,206</p> <p>PrEP to high-risk MSM: lifetime treatment cost (millions): \$3.99</p> <p>PrEP to all MSM: lifetime treatment cost (millions): \$9.84</p>	<p>PrEP to all MSM: (i) \$/DALY averted: \$7,089</p> <p>(ii) \$/HIV infection averted: \$100,367</p>	<p>80% chance of cost effectiveness in high MSM: \$4836 per DALY averted</p> <p>PrEP to high-risk MSM: (i) \$/DALY averted: \$4,836 (ii) \$/HIV infection averted: \$68,468</p>

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

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

2. Investigations: first clinical assessment			
	Test	Cost (2018 €)	Source
<b>4<sup>th</sup> generation venous blood HIV test</b>	HIV Antigen/Antibody (architect)	10.67	National Virus Reference Laboratory
<b>Chlamydia and gonorrhoea testing*</b>	GC/CT NAAT	31.74 per site	National Virus Reference Laboratory
<b>Syphilis testing</b>	Syphilis serology	10.05	National Virus Reference Laboratory
<b>HBV testing**</b>	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
<b>HCV testing</b>	HCV antibody	13.09	National Virus Reference Laboratory
<b>Serum creatinine and eGFR***</b>	Urea and Electrolytes	12.26	St James's Laboratory
<b>HAV IgG testing if previous vaccination not reported****</b>	HAV IgG	15.86	National Virus Reference Laboratory
<b>Vaccination review*****</b>	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/1.73m<sup>2</sup>: Measure creatinine and eGFR three monthly whilst on PrEP.

eGFR < 60 mls/min/1.73m<sup>2</sup>: At baseline if eGFR is < 60 mls/min/1.73m<sup>2</sup> assess for relevant medical conditions, nephrotoxic drugs and strongly consider renal referral before commencing PrEP. In follow up, if eGFR falls to < 60 mls/min/1.73m<sup>2</sup> 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 > 90 ml/min/1.73m<sup>2</sup>: if the eGFR falls whilst on PrEP but remains > 60 ml/min/1.73m<sup>2</sup> 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
<b>Clerical staff</b>	10	4.22	2019 Salary Scales Irish Department of Health & Time in Motion Study (GUIDE - 2013)
<b>Medical review (50% performed by clinical nurse specialist and 50% by consultant or specialist registrar)</b>	10	11.90	2019 Salary Scales Irish Department of Health
<b>Total: €16.12</b>			

\*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
<b>Clerical staff</b>	5–10	2.11	2019 Salary Scales Irish Department of Health & Time in Motion Study (GUIDE - 2013)
<b>Medical review and STI screen (by clinical nurse specialist/advanced nurse practitioner)</b>	15	13.50	2019 Salary Scales Irish Department of Health
<b>Phlebotomy</b>	12	6.00	2019 Salary Scales Irish Department of Health & Time in Motion Study (GUIDE - 2013)

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

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

\*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)**

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

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

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

\*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
<b>4<sup>th</sup> generation venous blood HIV test</b>	HIV Antigen/Antibody (architect)	10.67	National Virus Reference Laboratory
<b>Chlamydia and Gonorrhoea testing*</b>	GC/CT NAAT	31.74 per test	National Virus Reference Laboratory
<b>Syphilis testing</b>	Syphilis serology	10.05	National Virus Reference Laboratory
<b>HBV testing (annual)</b>	HBV surface antigen; anti-core antibody and surface antibody (architect)	37.44	National Virus Reference Laboratory
		<b>3-monthly cost</b>	<b>9.36</b>
<b>HCV testing (annual)</b>	HCV antibody	13.09	National Virus Reference Laboratory
		<b>3-monthly cost</b>	<b>3.27</b>
<b>HAV IgG testing if previous vaccination not reported**</b>	HAV IgG	15.86	National Virus Reference Laboratory
<b>Vaccination review**</b>	In line with NIAC recommendations		
	4. HBV vaccination is recommended for all people attending STI clinics		
	5. HAV vaccination is recommended for MSM		

6. 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)
<b>Total staff resource use: €58.95</b>			

**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)
<b>Total staff resource use: €17.72</b>			

**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)
<b>Total staff resource use: €10.22</b>			

**Investigations: first visit**

Investigations: First visit			
	Test	Cost	Source

<b>(2018 €)</b>			
<b>4<sup>th</sup> generation venous blood HIV test</b>	HIV Antigen/Antibody (architect)	10.67	National Virus Reference Laboratory
<b>Chlamydia and Gonorrhoea testing*</b>	GC/CT NAAT	31.74 per site	National Virus Reference Laboratory
<b>Syphilis testing</b>	Syphilis serology	10.05	National Virus Reference Laboratory
<b>HBV testing</b>	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
<b>HCV testing</b>	HCV antibody	13.09	National Virus Reference Laboratory
<b>Serum creatinine and eGFR</b>	Urea and Electrolytes	12.26	St James's Laboratory
<b>Urinalysis</b>	Urinary protein	8.16	St James's Laboratory
	Urinary creatinine	8.16	St James's Laboratory
	Urinary electrolytes	8.16	St James's Laboratory
<b>Liver profile</b>	(includes ALT)	12.14	St James's Laboratory
<b>Total Investigations: €183.61</b>			

### Investigations: second visit

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

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

### Investigations: third visit

<b>Investigations: third visit</b>			
	<b>Test</b>	<b>Cost (2018 €)</b>	<b>Source</b>
<b>4<sup>th</sup> generation venous blood HIV test</b>	HIV Antigen/Antibody (architect)	10.67	National Virus Reference Laboratory
<b>Total Investigations: €10.67</b>			

**Table 5.8. Cost — Treating one episode of rectal chlamydia**

Staff resource use			
	Time	Cost (2019 €)	Source
<b>Clerical Staff</b>	10 minutes	4.22	2019 Salary Scales Irish Department of Health & Time in Motion Study
<b>Medical review (Consultant or Specialist Registrar)</b>	30 minutes	48.73	2019 Salary Scales Irish Department of Health
Cost of treatment/investigations			
<b>Chlamydia testing (GC/CT NAAT)*</b>		31.74 per test	National Virus Reference Laboratory
<b>Cost of medications (doxycycline 100mg twice daily for 7 days)</b>		8.80	
<b>Total Cost</b>		<b>€125.23</b>	
<b>Vary by 50% to account for regional differences</b>		<i>Min</i> €62.615	
		<i>Max</i> €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
dist_NPhigh_HIV	age-specific mortality 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_NPmedlow	Distribution associated with	Gamma	alpha: 57, lambda: 156	0.36538

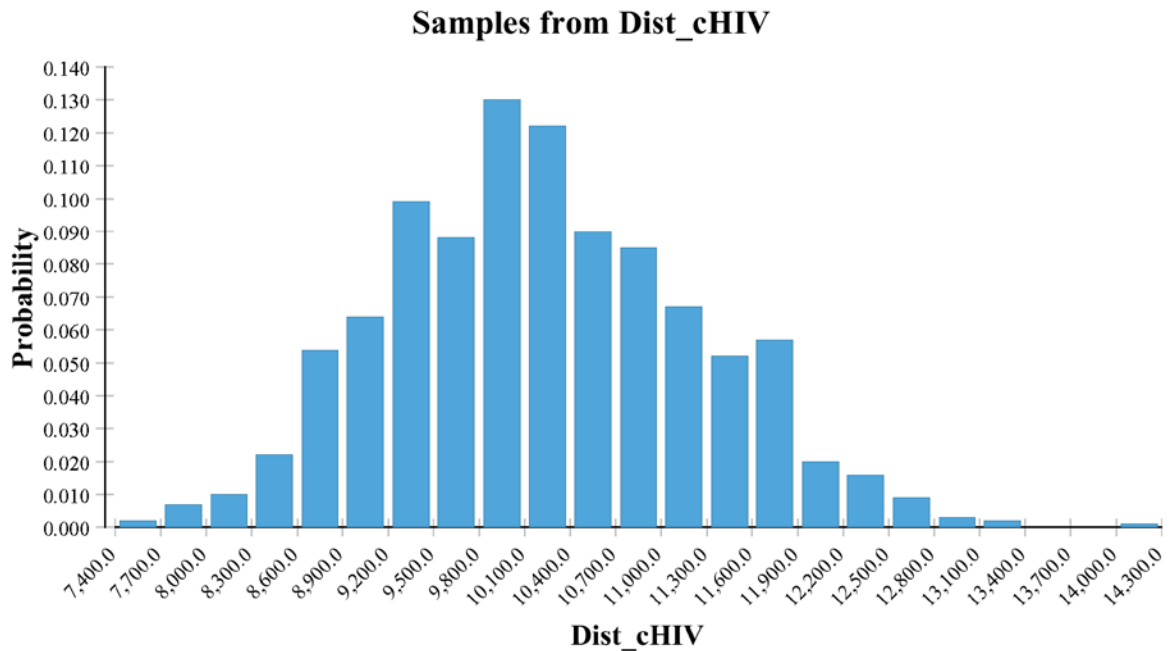
Name of parameter in model	DESCRIPTION	TYPE	Alpha, Beta, Lambda, mean or SD	Expected Value
w	transition probability high risk (PrEP) to medium/low			
dist_Phigh_Phigh	Distribution associated with transition probability high risk (PrEP) to high risk (no PrEP)	Gamma	alpha: 112, lambda: 214	0.52336
dist_prop_Chlamydia	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 proportion	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



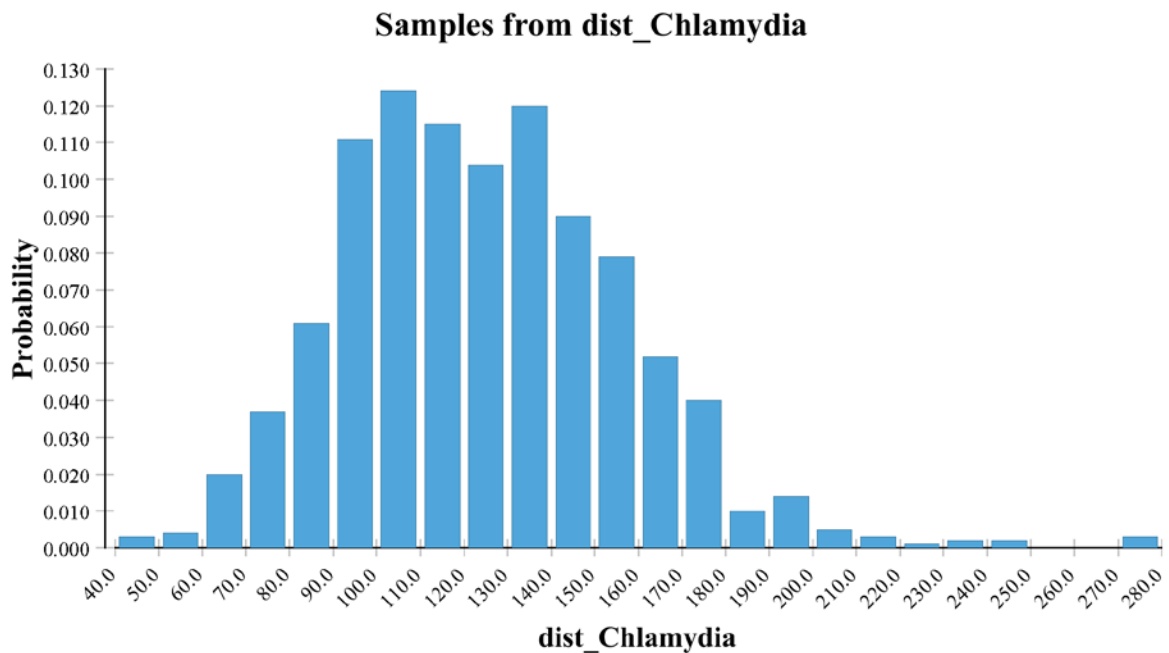
Name of parameter in model	DESCRIPTION	TYPE	Alpha, Beta, Lambda, mean or SD	Expected Value
Dist_uHIV	for HIV positive Distribution associated with utility value for HIV+ individuals	Beta	subtype: 2, alpha: $\frac{((0.89)^2) * (1 - (0.89))}{((0.008)^2) - (0.89)}$ , beta: $\frac{((1 - (0.89)) * ((1 - (0.89)) * (0.89)))}{((0.008)^2) - 1}$	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)

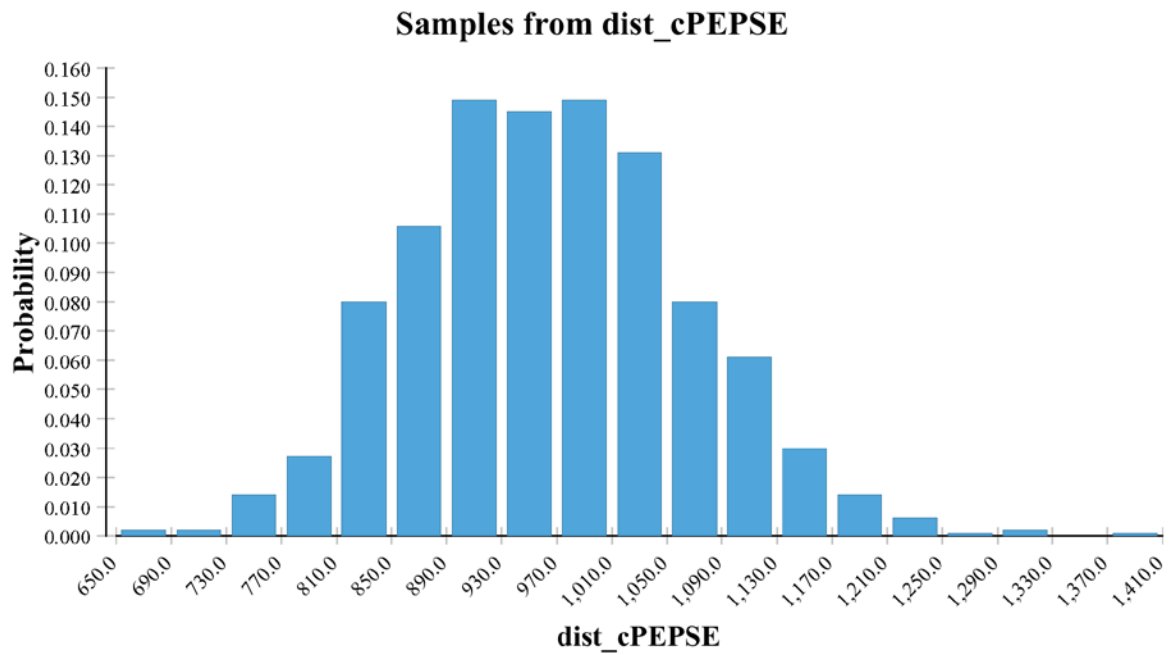
1. Distribution associated with annual cost of HIV



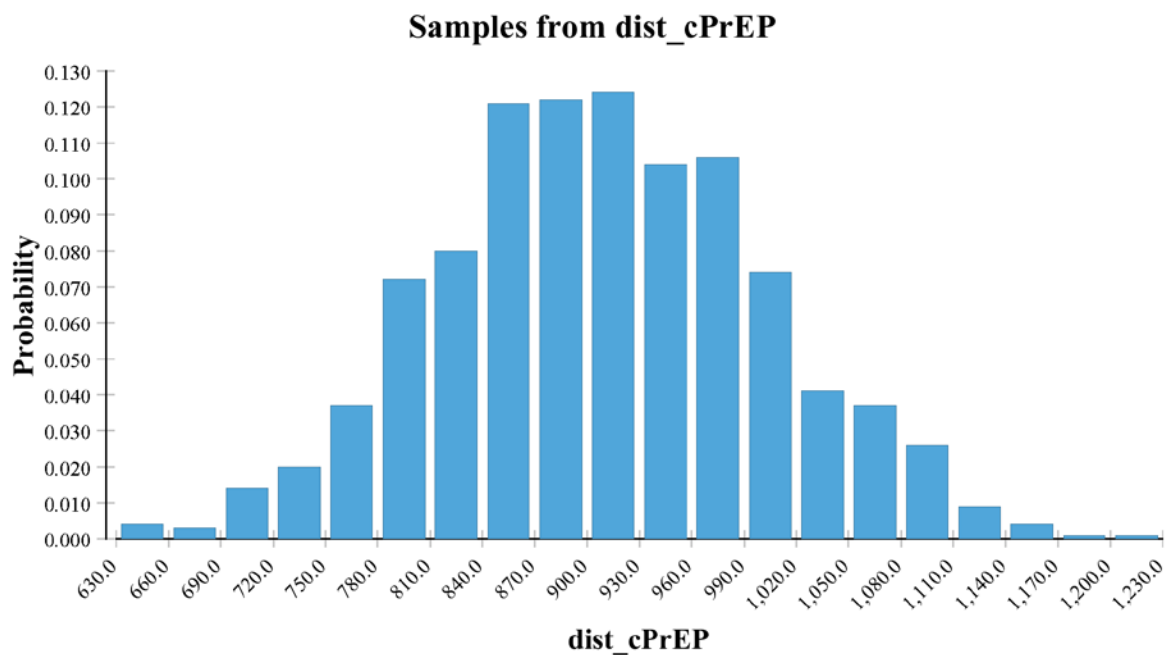
2. Distribution associated with cost of treating chlamydia



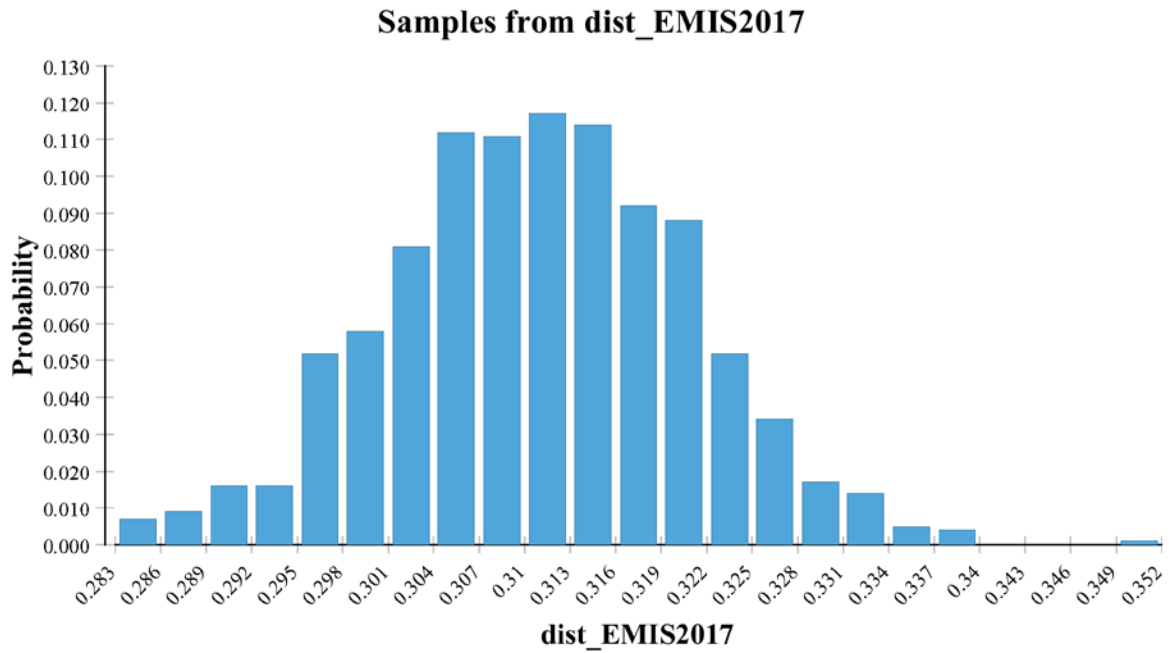
### 3. Distribution associated with cost of PEPSE



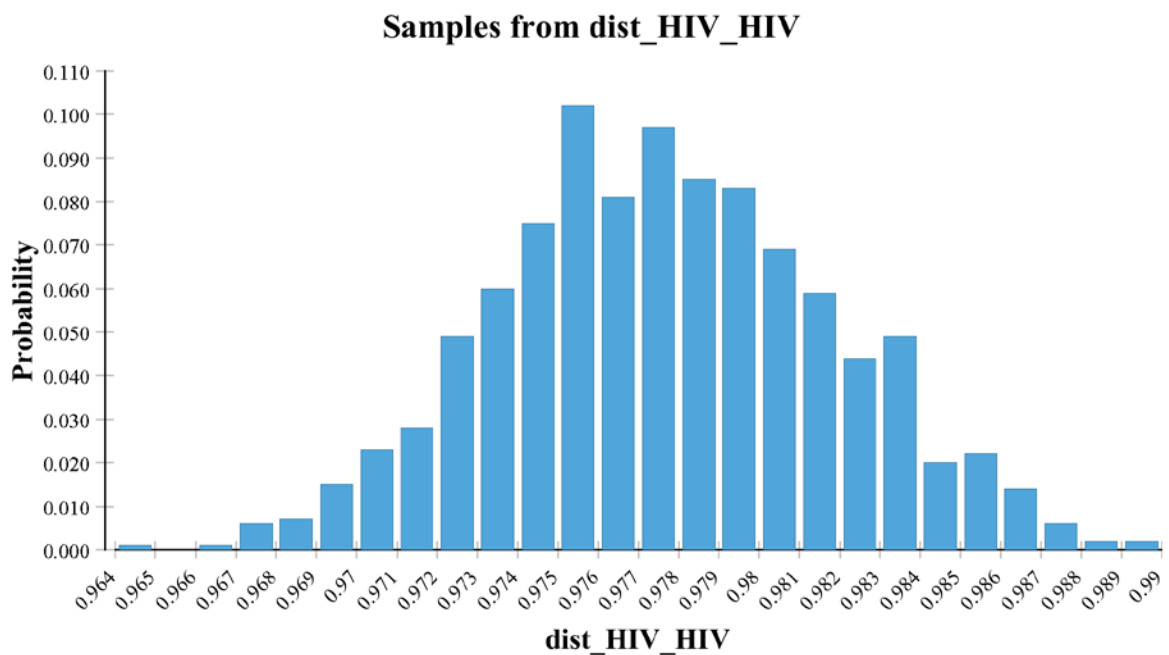
### 4. Distribution incremental cost PrEP (prog+drug)



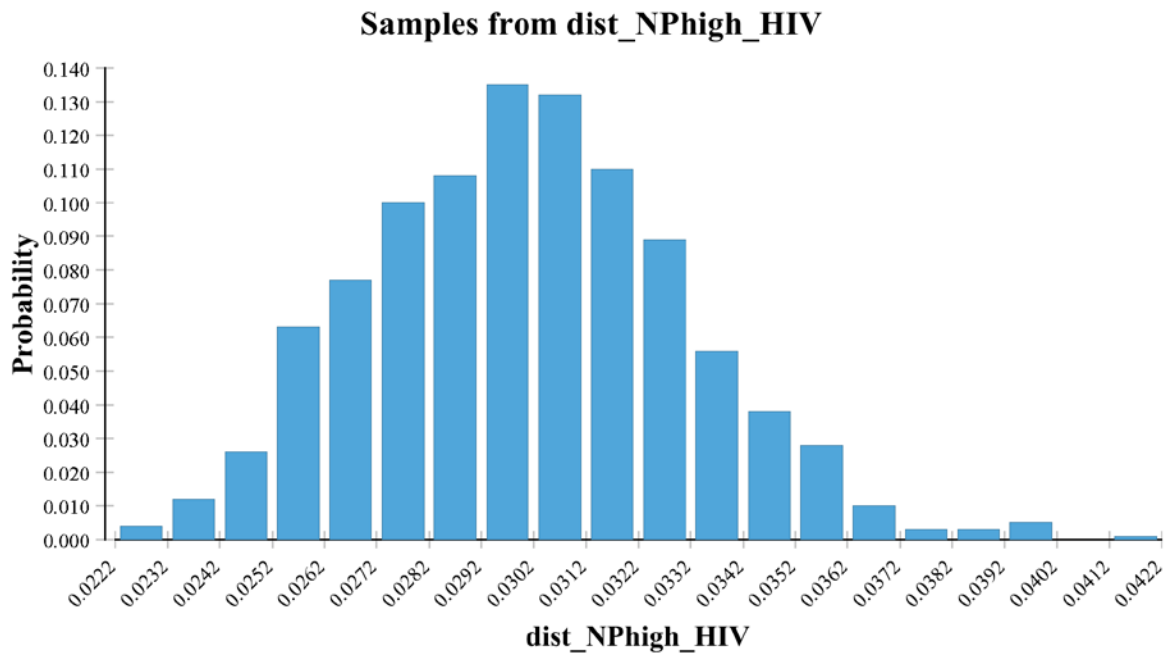
## 5. Distribution associated with EMIS Ireland 2017 eligible proportion



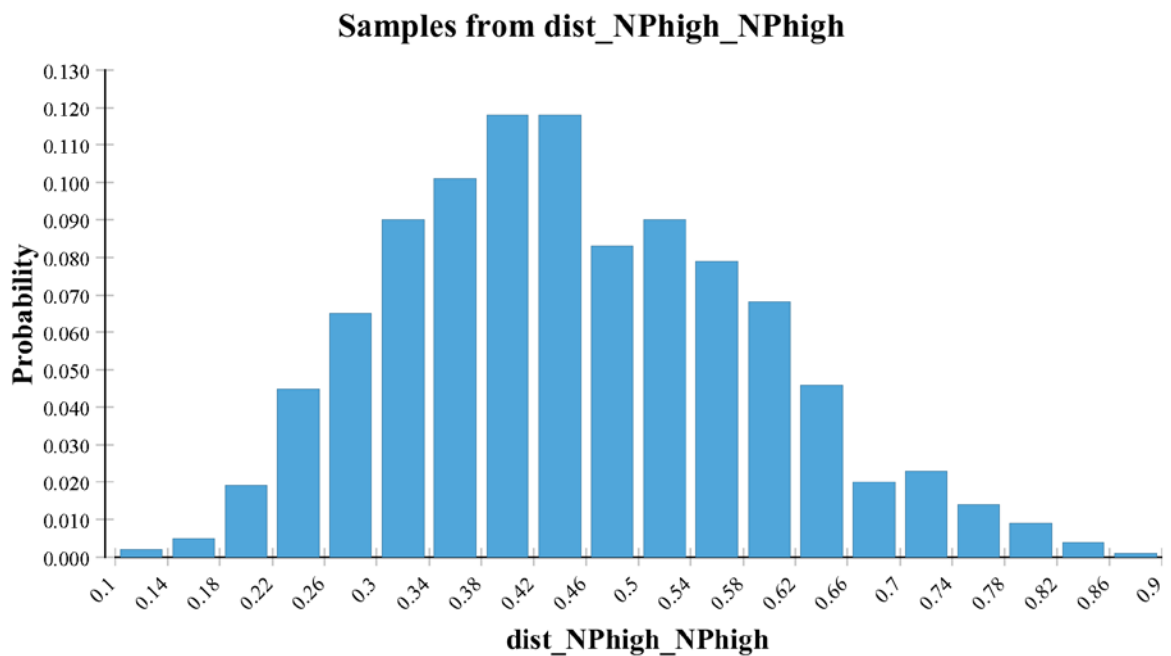
## 6. Distribution associated with transition probability HIV+ to HIV+



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

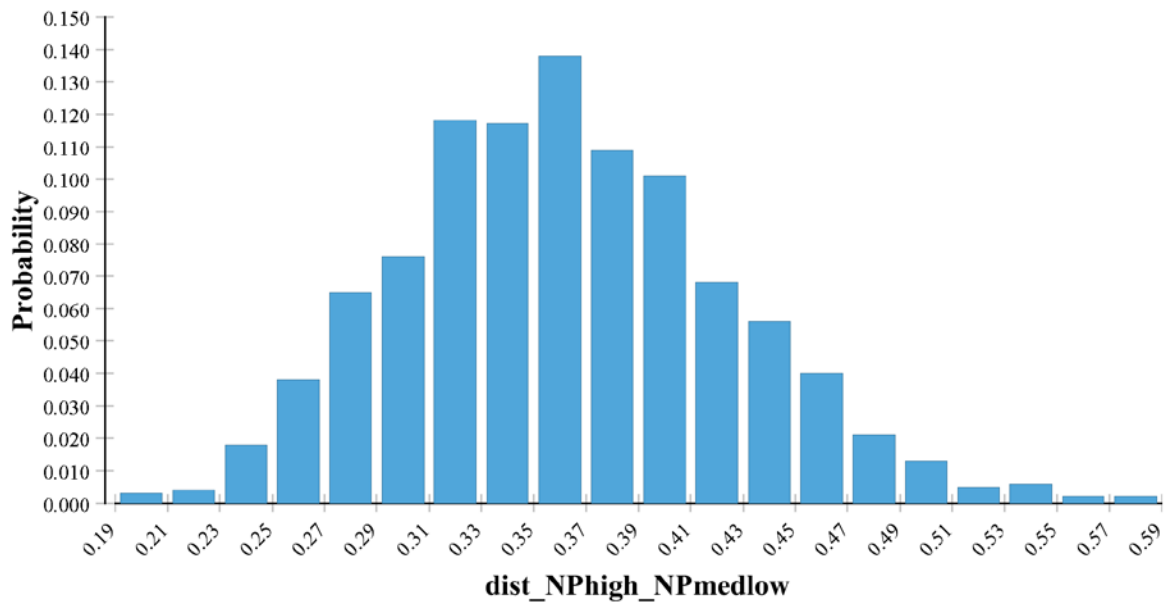


## 8. Distribution associated with transition probability high risk (no PrEP) to high risk (no PrEP)



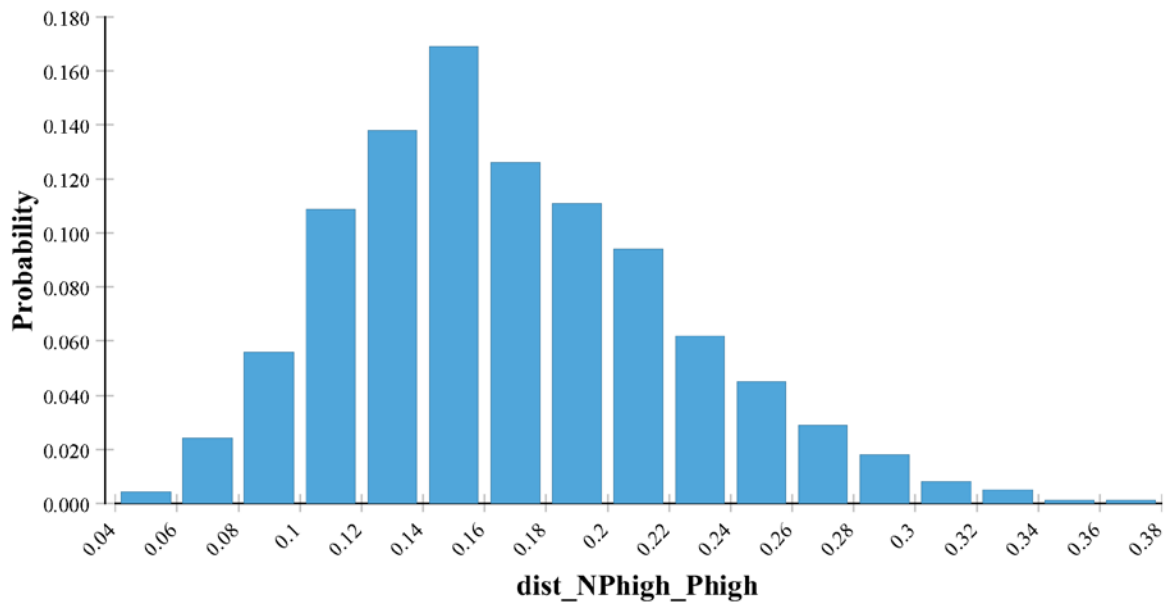
### 9. Distribution associated with transition probability high risk (no PrEP) to medium/low

Samples from dist\_NPhigh\_NPmedlow



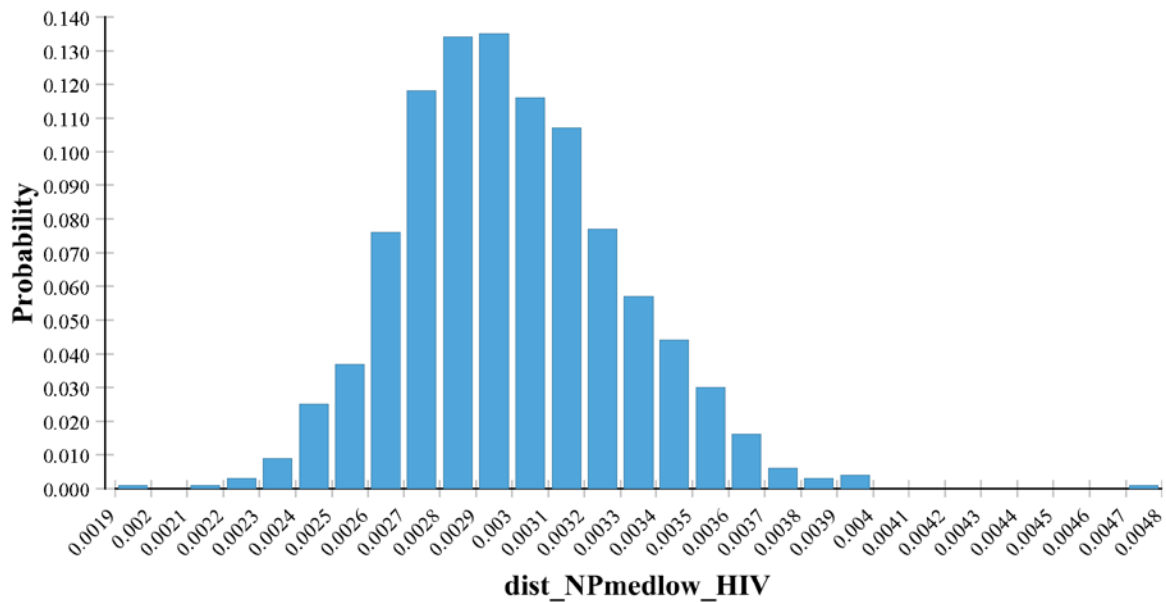
### 10. Distribution associated with transition probability high risk (PrEP) to high risk (PrEP)

Samples from dist\_NPhigh\_Phigh



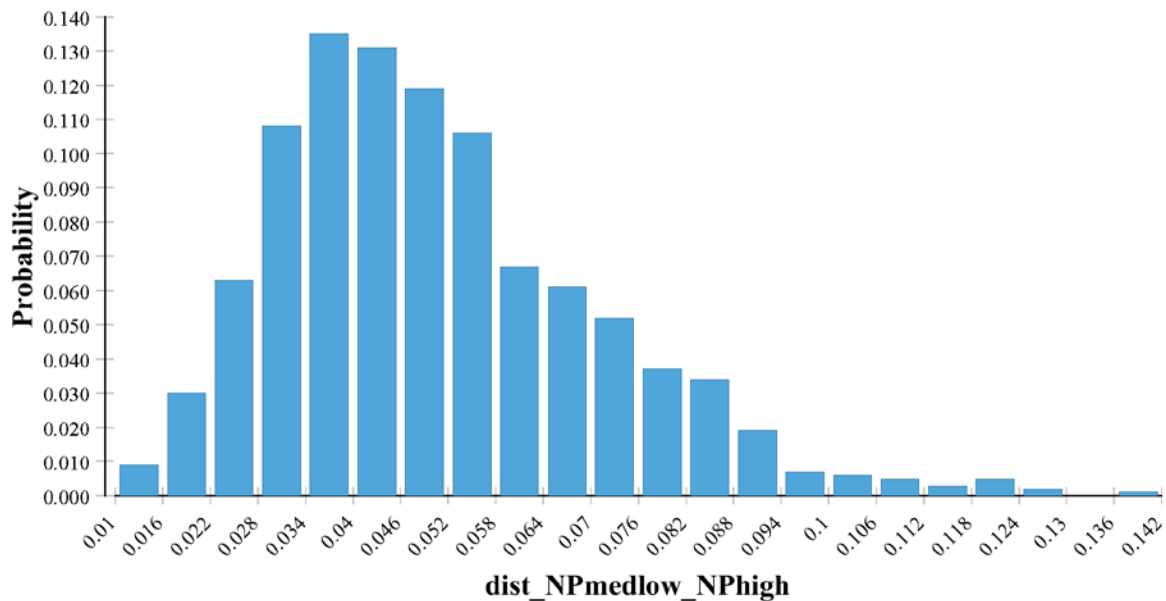
### 11. Distribution associated with transition probability medium/low risk to HIV+

Samples from dist\_NPmedlow\_HIV

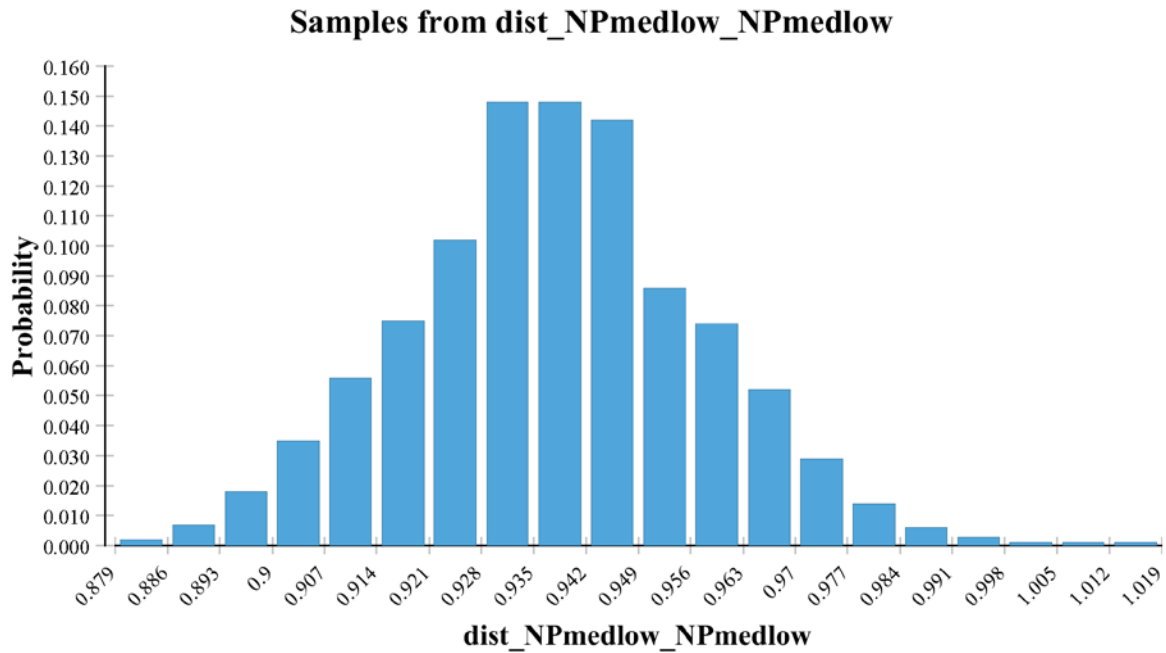


### 12. Distribution associated with transition probability medium/low to high risk (no PrEP)

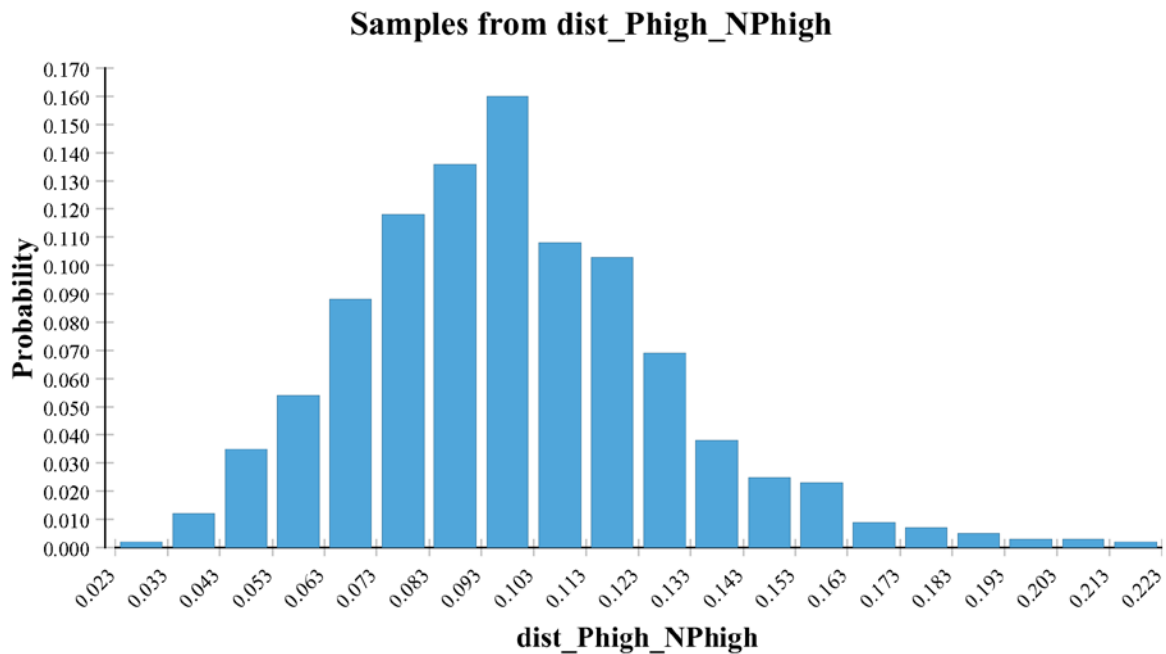
Samples from dist\_NPmedlow\_NPhigh



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



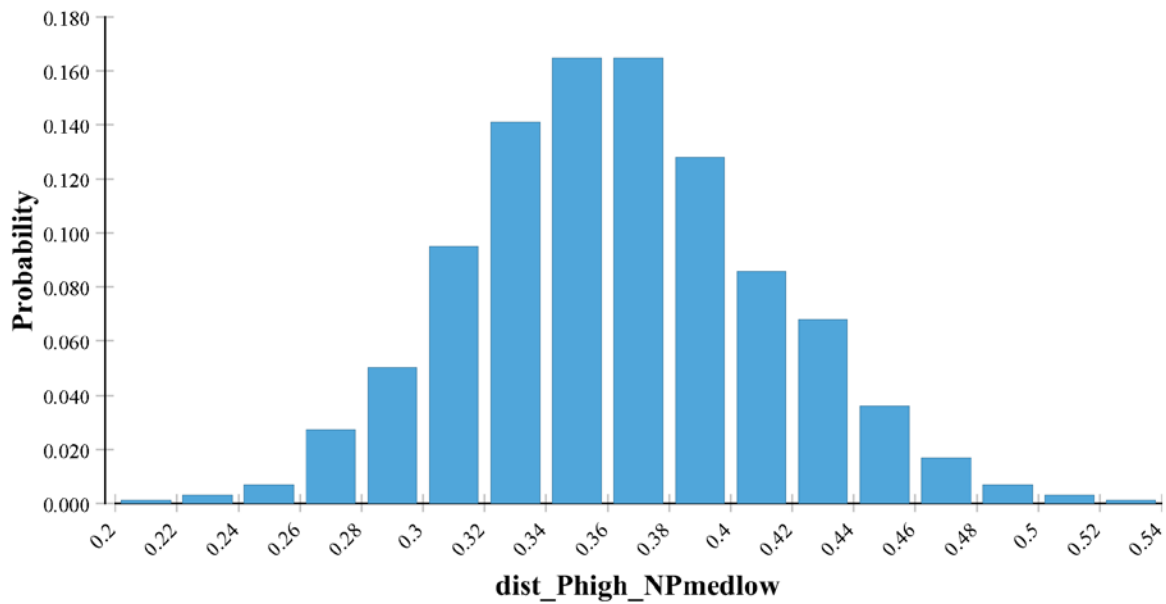
### 14. Distribution associated with transition probability high risk (PrEP) to high risk (no PrEP)





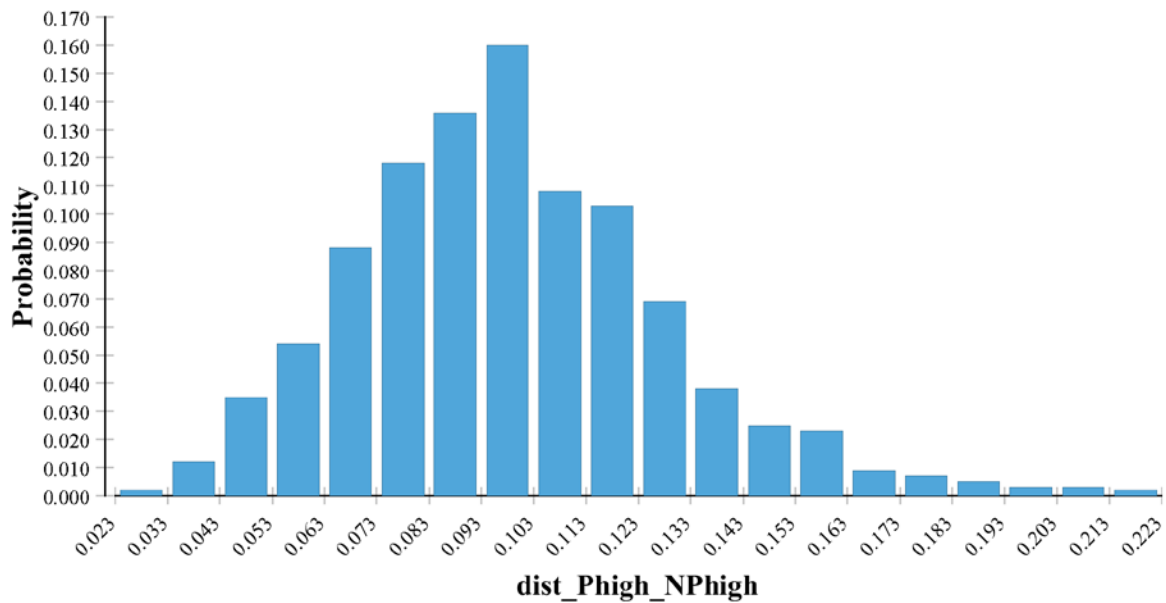
### 15. Distribution associated with transition probability high risk (PrEP) to medium/low

Samples from dist\_Phigh\_NPmedlow



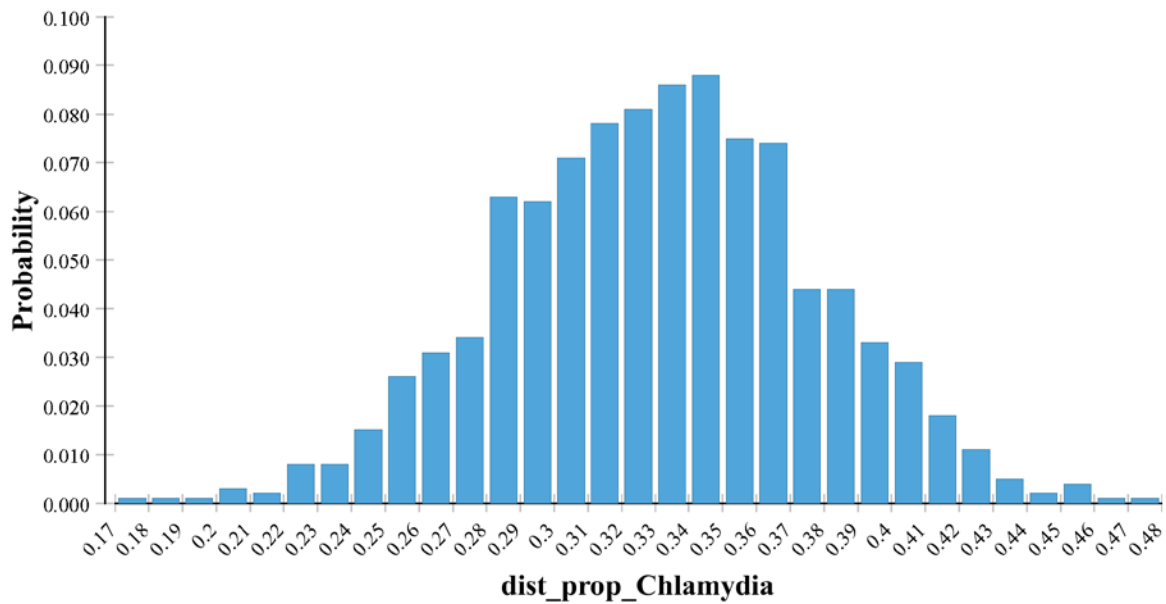
### 16. Distribution associated with transition probability high risk (PrEP) to high risk (no PrEP)

Samples from dist\_Phigh\_NPhigh



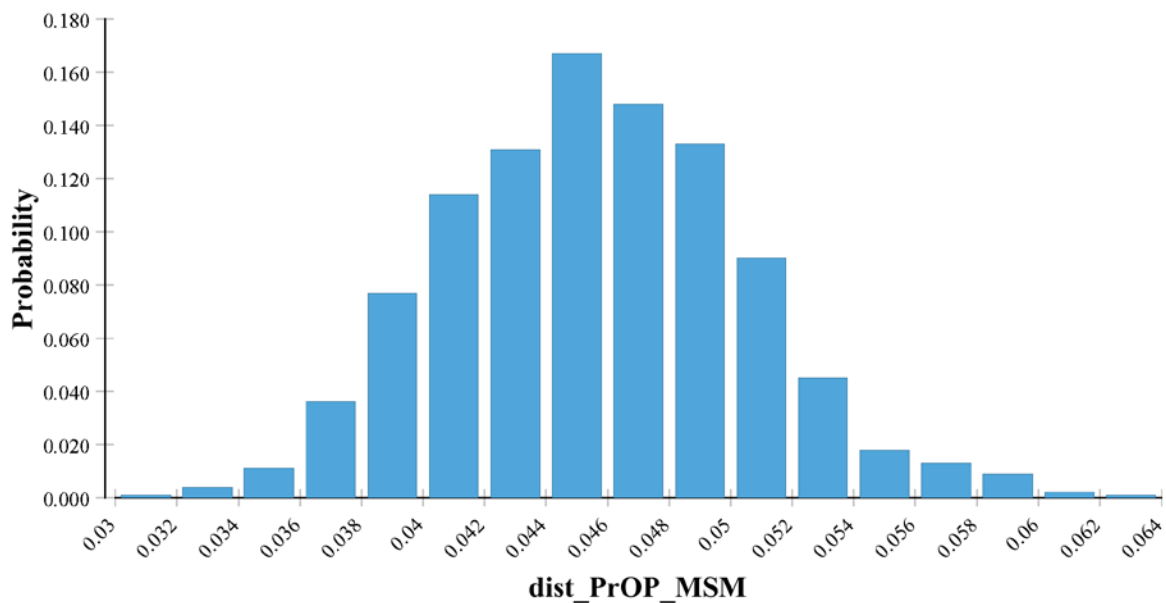
### 17. Distribution associated with the increased proportion who acquire rectal chlamydia on PrEP

Samples from dist\_prop\_Chlamydia

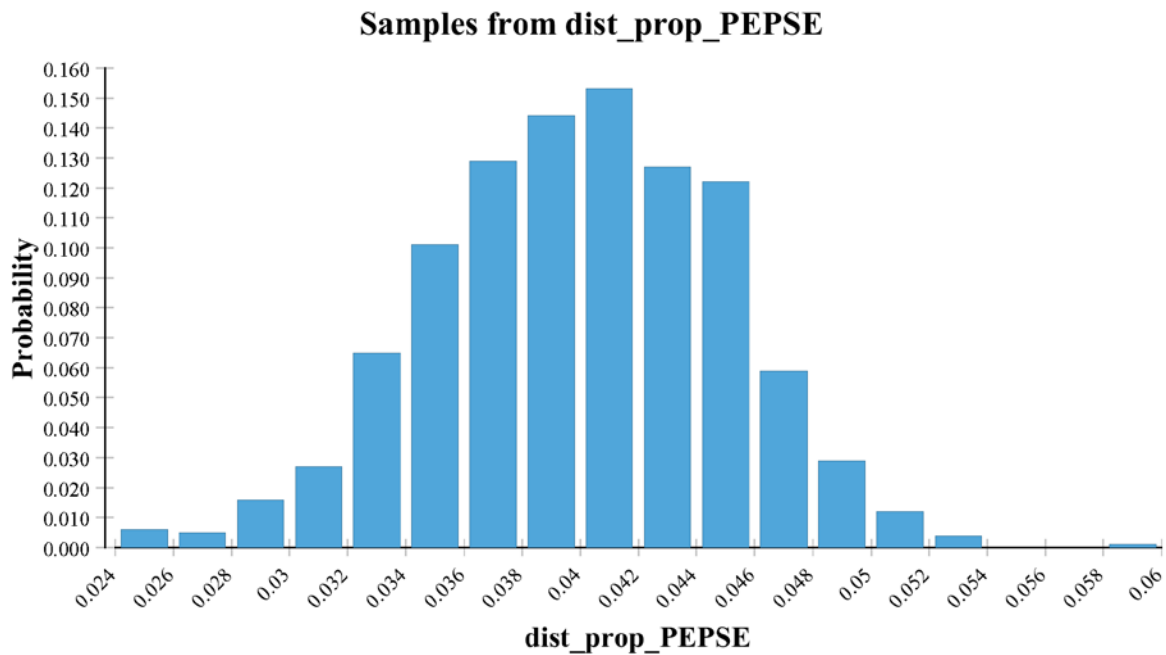


### 18. Distribution associated with proportion of men who are MSM

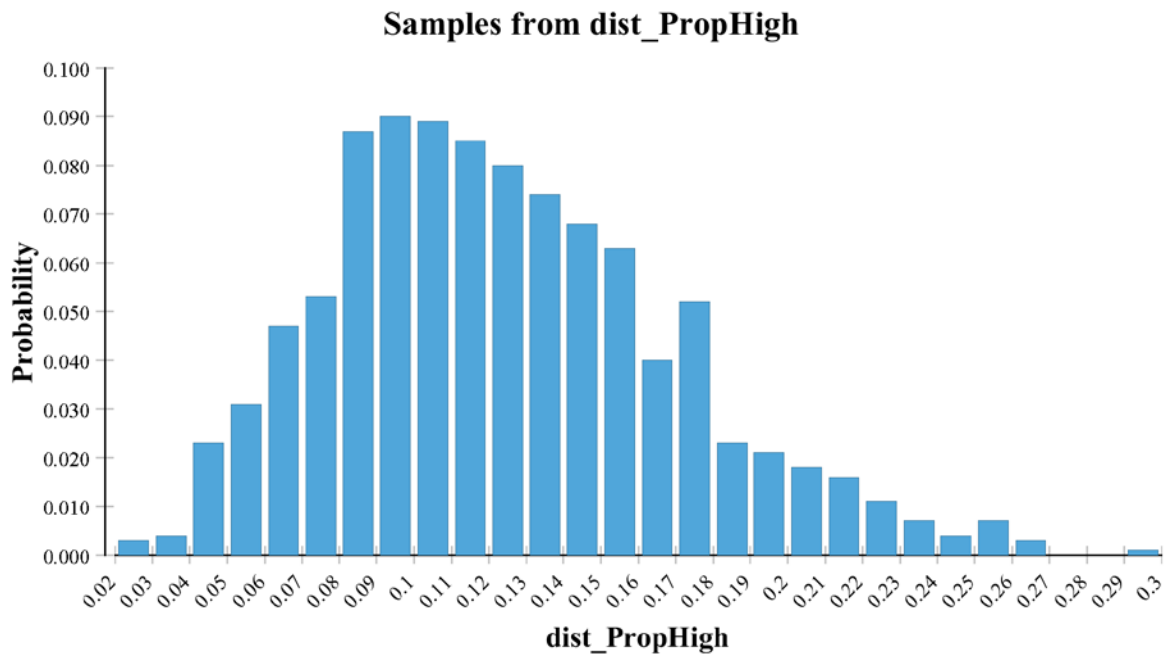
Samples from dist\_PrOP\_MSM



### 19. Distribution associated with proportion who obtain PEPSE annually

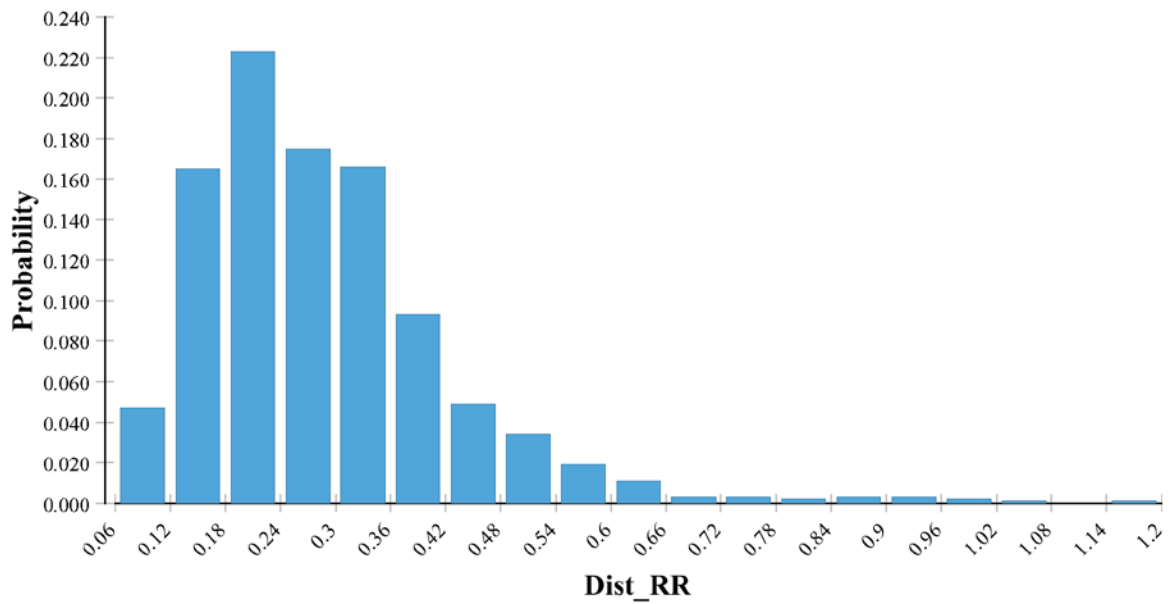


### 20. Distribution associated with the proportion of MSM at substantial risk of HIV



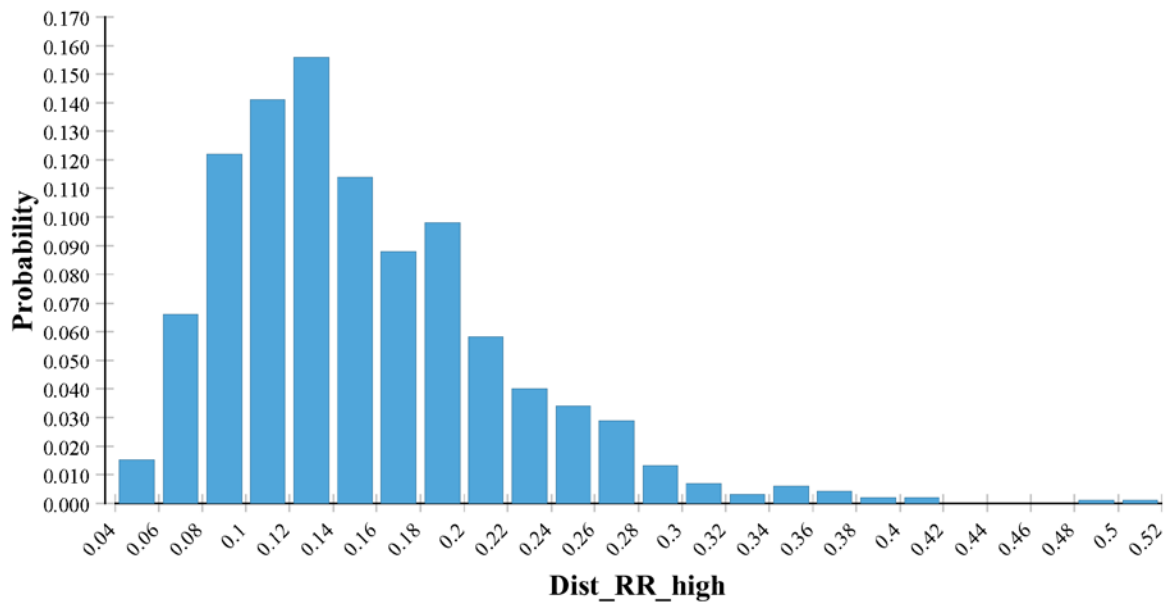
## 21. Distribution associated with efficacy of PrEP - meta-analysis of all trials

Samples from Dist\_RR



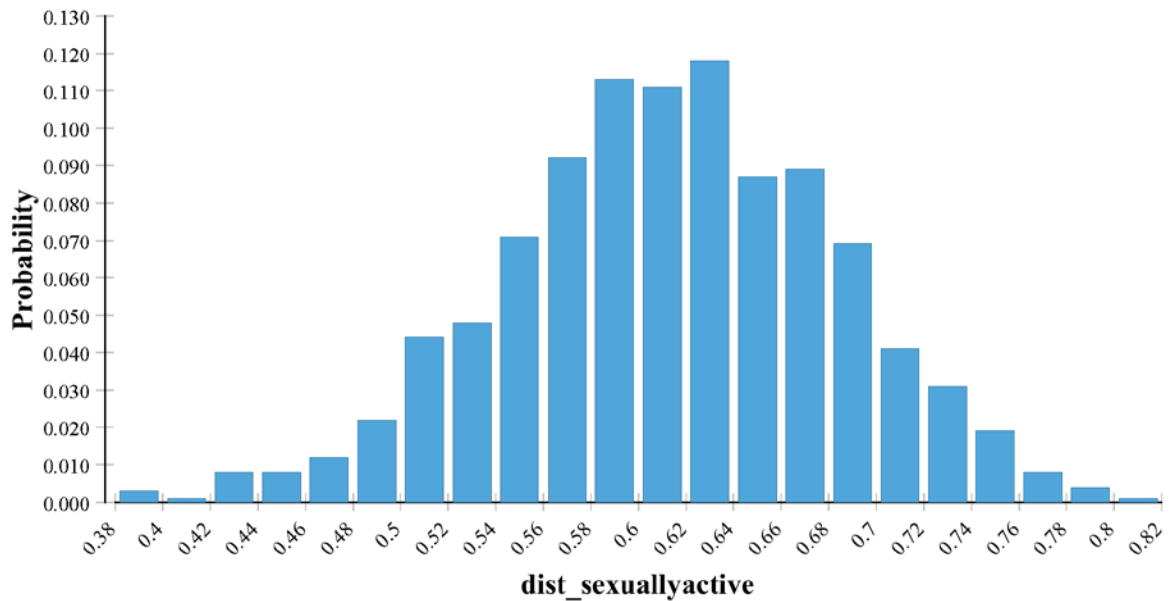
## 22. Distribution associated with RR of efficacy: PrEP from PROUD and IPERGAY

Samples from Dist\_RR\_high



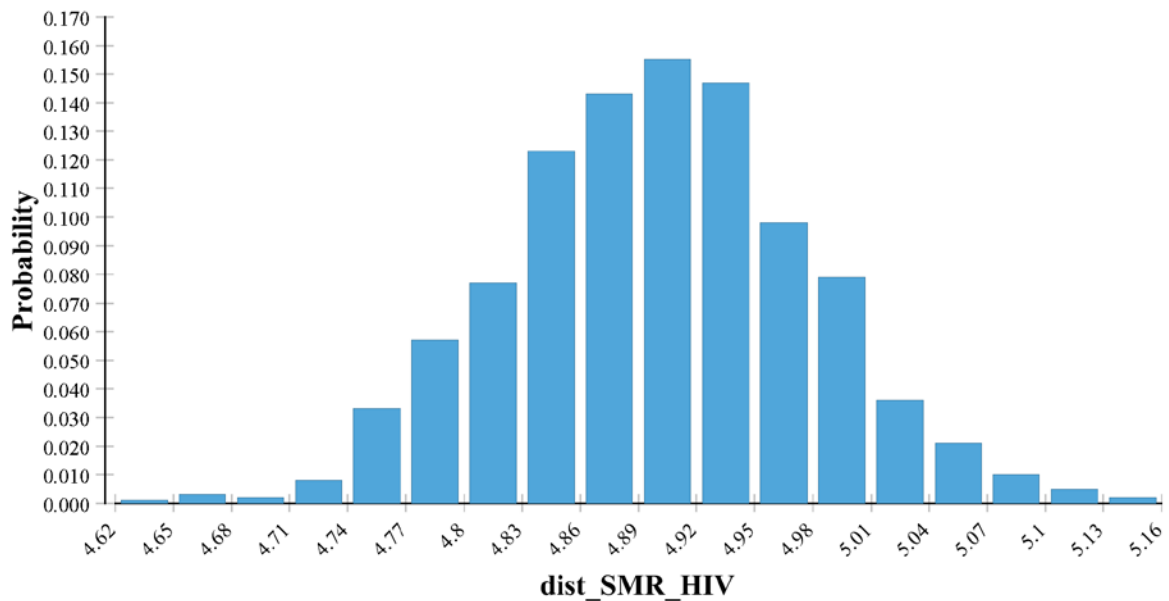
### 23. Distribution associated with sexually active proportion

Samples from dist\_sexuallyactive

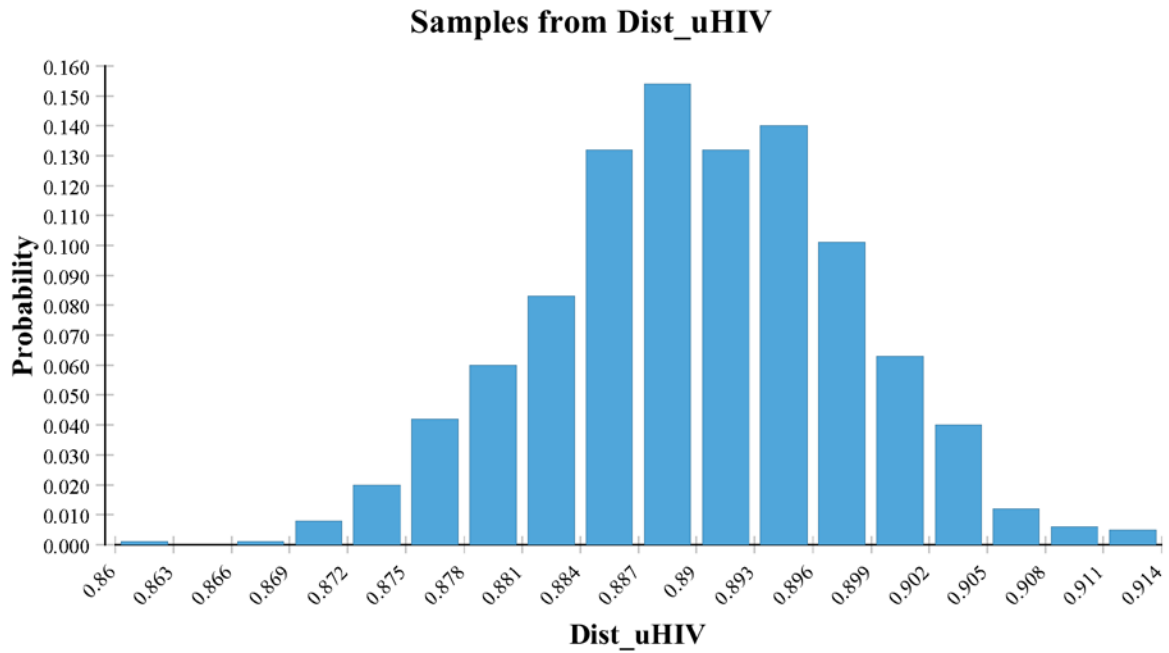


### 24. Distribution associated with Standardised Mortality Ratio for HIV positive

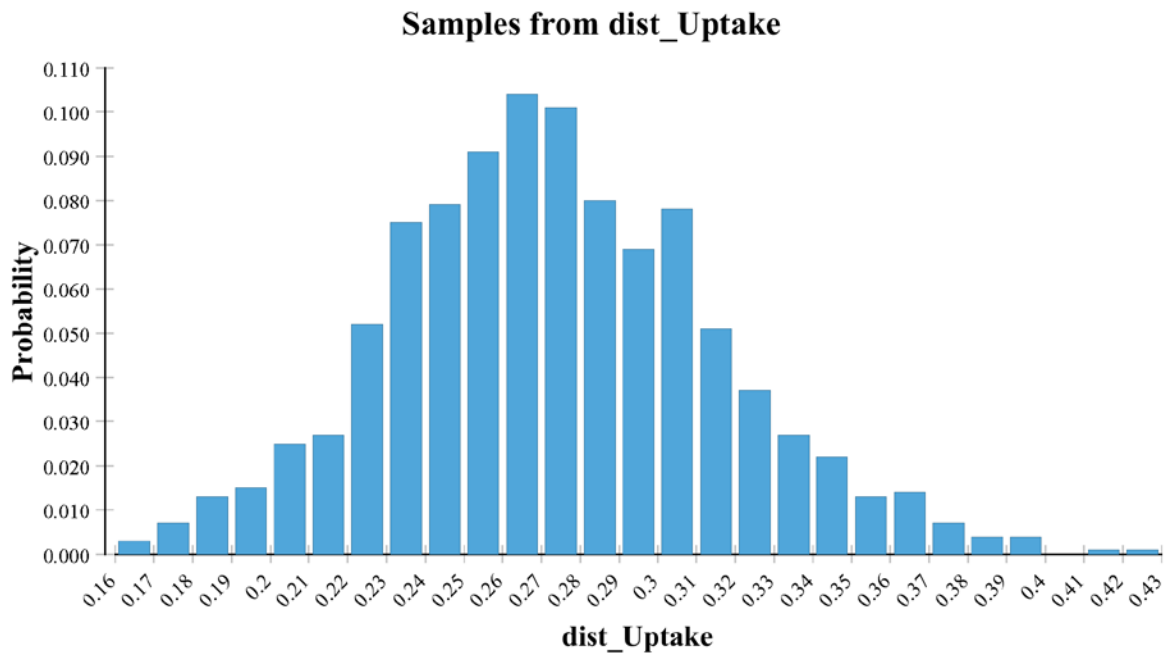
Samples from dist\_SMR\_HIV



## 25. Distribution associated with utility value for HIV+ individuals



## 26. Distribution associated with the uptake rate of PrEP



**Published by the Health Information and Quality Authority**

**For further information please contact:**

**Health Information and Quality Authority  
Dublin Regional Office  
George's Court  
George's Lane  
Smithfield  
Dublin 7**

**Phone: +353 (0) 1 814 7400**

**Email: [info@hiqa.ie](mailto:info@hiqa.ie)**

**[www.hiqa.ie](http://www.hiqa.ie)**

**© Health Information and Quality Authority 2019**