HIV IRELAND REPORT 05-2017

Pre-exposure Prophylaxis (PrEP) Scoping and Policy Options Review

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Final Paper Submitted 5th May 2017

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Introduction

HIV Ireland, and the Gay Health Network have been to the forefront of Irelands response to HIV over the past 30 years. The importance of our work, past and present, cannot be underestimated, especially now with new HIV diagnoses in Ireland increasing to their highest level on record. Since 2011, Ireland has experienced a 35% increase in new HIV diagnoses. In 2017, there are on average 10 new HIV diagnoses every week.

Against this backdrop, HIV Ireland and the Gay Health Network play a key role in supporting people who live with HIV, and crucially, an increasingly important role in HIV prevention. We believe this policy options paper will play a key part in the widening conversation around HIV prevention, and the crucial role PrEP can play in reducing new HIV infections.

We would like to sincerely thank Dr. Ann Nolan for producing this important document. We would equally like to thank all participants in the research who gave of their time and expertise. The richness of the document reflects the breadth of knowledge and expertise that exists within Ireland when it comes to HIV and sexual health.

HIV is a highly stigmatised, chronic illness. The impact it can have on a person's health and wellbeing is profound. We believe that PrEP can significantly contribute to negating that potential reality for many people in the future.

To quote Dr. Nolan, 'PrEP promises to be one of the most important innovations in the global response to HIV, and Ireland's escalating epidemic suggests that we cannot afford to be left behind.'

We wholeheartedly endorse that view.

Niall Mulligan
Executive Director
HIV Ireland

Noel Sutton
Chairperson
Gay Health Network

15th June 2017 – Irish AIDS Day

Executive Summary

This policy options review and evidence-scoping of Pre-Exposure Prophylaxis (PrEP) for HIV prevention has been commissioned by HIV Ireland Ltd (HIVI) and the Gay Health Network (GHN). The primary aim of this paper is to provide evidence-based guidance on PrEP efficacy, while establishing the views of key populations affected by HIV, and stakeholders directly and indirectly involved in the provision of HIV services throughout Ireland.

This study relies significantly on existing evidence for PrEP particularly reviews conducted by the World Health Organisation (WHO), the National Institutes for Health and Care Excellence (NICE), the National Health Service (Wales), the United States Centre for Disease Control and Prevention (CDC), and the British HIV Association (BHIVA) to reach conclusions about policy options for PrEP in Ireland.

PrEP is a biomedical HIV prevention strategy meaning that it uses antiretroviral drugs to protect HIV-negative people from HIV infection. In August 2016, the European Commission granted marketing authorisation for once-daily Truvada® (emtricitabine 200 mg/tenofovir disoproxil 245 mg; FTC/TDF) in combination with safer-sex practices to reduce the risk of sexually acquired HIV-1 infection among uninfected adults at high risk, which means that once-daily Truvada® is licensed for PrEP in Ireland.

The Evidence-base for PrEP Efficacy

The World Health Organisation's (WHO) Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection, Recommendations for a public health approach - Second edition (2016) recommends that oral PrEP should be offered as an additional prevention choice for people at substantial risk of HIV. WHO's systematic review and meta-analysis of PrEP trials demonstrated that PrEP is effective in reducing the risk of acquiring HIV infection. It was found that the level of protection did not differ by age, sex, regimen (TDF versus FTC + TDF) or mode of acquiring HIV (rectal, penile or vaginal exposure) but detectable drug levels in the blood are strongly correlated with the prophylactic effect, emphasising the importance of adherence to PrEP.

The sources upon which this study relies - WHO; European Centre for Disease Prevention and Control (ECDC); the European AIDS Clinical Society; British HIV Association (BHIVA); the National Institute for Health and Care Excellence (NICE); the United States Centre for Disease Control (CDC); the Scottish HIV Pre-Exposure Prophylaxis Short Life Working Group and the National Health Service (NHS) Wales - conclude that the quality of the evidence base for PrEP efficacy is robust.[1]. Trials with potentially transferable findings include:

1. WHO, *Consolidated Guidelines,* 2016; Nandwani R and Valiotis G, on behalf of the Scottish HIV Pre-Exposure Prophylaxis Short Life Working Group. *PrEP in Scotland.* Scottish Health Protection Network (SHPN) October 2016; NICE, Pre-exposure prophylaxis of HIV in adults at high risk: Truvada (emtricitabine/tenofovir disoproxil), 2016; BHIVA-BASHH Position Statement on PrEP in the UK: Update 2016; Center for Disease Control, US Public Health Service, Pre-exposure Prophylaxis for the Prevention of HIV Infection in the United States, 2014; ECDC GUIDANCE HIV and STI prevention among men who have sex with men, 2015; Jones, A., Couzins, Z., Preparing for PrEP? – A Review of the Current Evidence for Pre-exposure Prophylaxis (PrEP) to prevent HIV infection in Wales, NHS Wales, 2017; European AIDS Clinical Society.

1. The iPrEx study was a double-blind RCT evaluating once-daily Truvada® or placebo in 2,499 HIV-negative men or transgender women who have sex with men with evidence of high-risk behaviour for HIV infection. Once daily Truvada® reduced the relative risk of acquiring HIV infection by 44% compared with placebo;
2. The Partners PrEP study was a double-blind RCT evaluating once-daily single agent tenofovir disoproxil or Truvada® or placebo in 4,747 HIV-negative individuals in a heterosexual partnership with a person already infected with HIV in Kenya and Uganda. Once-daily Truvada® reduced the relative risk of acquiring HIV infection by 75% compared with placebo;
3. The PROUD study was an open-label trial of once-daily Truvada® in 544 HIV-negative men or transgender women who have sex with men in England. Participants were randomised to start PrEP with Truvada immediately on study entry or after a deferral period. Once-daily Truvada reduced the relative risk of acquiring HIV infection by 86% compared with no prophylaxis;
4. The IPERGAY study was a double-blind RCT evaluating Truvada® or placebo taken 'on demand' before and after sexual activity in 414 high-risk MSM in France and Canada. Participants took a median of 15 tablets per month and reduced the relative risk of acquiring HIV infection by 86% compared with placebo.

The Bangkok Tenofovir Study is the only large-scale study conducted with people who inject drugs (PWID). Over 2, 400 PWID were enrolled and with optimal adherence a 70% reduction in HIV incidence was reported but in general, this RCT reported a 48.9% reduction in HIV using once daily Tenofovir disoproxil fumarate (TDF) without Emtricitabine (FTC) among PWID. The policy context for this study differs significantly from the Irish context and as such, the high levels of adherence may not be relied upon.

While these population trials provide generally unbiased indicators of the effect of PrEP on HIV incidence rates, they do not provide insight into the effectiveness of PrEP in real-world clinical care settings. Implementation research is needed in diverse settings not least in terms of supporting adherence and the capacity of already over-stretched health systems to respond effectively to increased demand. It is also largely unknown how PrEP may affect behavioural and social outcomes in the medium to long term. The RCTs described here noted few changes in terms of sexual behaviours but trials provide a high level of psycho-social support that may not be replicated in real-world settings.

The cost-effectiveness of PrEP is frequently cited as a key barrier to PrEP implementation and Gilead Science's application for a Supplementary Protection Certificate for once-daily Truvada® is a significant threat to taking PrEP to scale in Europe. Cost effectiveness analysis appears to be particularly sensitive to key variables such as HIV incidence, levels of adherence, demand for PrEP, risk behaviours, the cost of drugs and other clinical interventions required to support PrEP programmes: as such cost-

effectiveness studies conducted in other jurisdictions are of limited value to the Irish context. While France is the only country in Europe currently providing PrEP through the public health service, a number of countries are implementing or planning to implement PrEP demonstration projects.

National and International PrEP Policy Context

The national and international policy architecture for PrEP is well established. The transnational dimensions of health are facilitated through governance structures which foregrounds global and local connectivity. Ireland emphasises an all-of-government approach with policy coherence prioritised between the Health Service Executive and Irish Aid's global health and HIV partnership portfolio, illustrating the extent to which health policy is increasingly perceived to be international in scope. PrEP is already governed – directly and indirectly - by international policy instruments that have been ratified by Ireland. The most recent of these, the 2016 United Nations Political Declaration on HIV and AIDS: On the Fast-Track to Accelerate the Fight against HIV and to End the AIDS Epidemic by 2030, was adopted at the United Nations General Assembly High-Level Meeting on AIDS in June 2016, and includes explicit commitment to the adoption of evidence-based prevention measures including PrEP. Furthermore, UNAIDS is a key partner in Ireland's Global Health and HIV Portfolio to which overseas development assistance commits €2.7 million per annum.[2] To fast track actions to achieve 2020 targets, the new Action plan for the health sector response to HIV in the WHO European Region 2017-2022 emphasises the need for member states to optimise prevention efforts through the prioritisation of evidence-based HIV prevention urging a particular focus on key populations, 'with inclusion of novel approaches such as pre-exposure prophylaxis (PrEP) for populations at substantial risk of HIV acquisition'[3] Also of continuing relevance, the Dublin Declaration, 2004 commits member states in Europe and Central Asia to act collectively in tackling the HIV/AIDS epidemic, setting out a number of actions to accelerate the achievement of this commitment. The most recent special report under the Dublin Declaration 2016 particularly emphasised the need to reduce HIV infections in Europe using a range of prevention interventions including PrEP. Finally, at national level, policy provision for PrEP is contained in the National Sexual Health Strategy 2015-2020 which urges the implementation of guidelines for the appropriate use of antiretroviral therapy in HIV prevention.

2. 2015 budget allocation
3. WHO Europe, *Action plan for the health sector response to HIV in the WHO European Region,* 2017-2022, Geneva

An Overview of Findings and Recommendations

Following careful consideration of the evidence-base for PrEP, this study conducted a wide range of key informant interviews with stakeholders in Ireland including civil society activists, policy makers, health care providers and researchers, pharmaco-economists, international development specialists, with two focus group discussions (FGD) undertaken with MSM and people living with HIV. Given the paucity of data available on the potential or rationale for introducing PrEP in Ireland, opportunities to verify or triangulate information were limited. In order to present a clearer picture of the Irish-specific landscape, data from this research was collated with pre-existing Irish-specific grey literature and academic sources, with outlier issues and/or data corresponding to ToR requirements not previously considered. The primary findings and recommendations resulting from this process are presented here in summary:

1. Policy options for the introduction of PrEP into Ireland as indicated by the evidence base governing PrEP efficacy; the global, regional and national policy context; the high risk profile of most at-risk populations; the epidemiology of HIV in Ireland, which reflects broader European trends; the views of health care providers and key stakeholders working directly and indirectly in HIV, and the views of potential end users, point to one option: This review identified overwhelming support for the introduction of PrEP for populations at substantial risk of HIV in Ireland as part of a comprehensive package of HIV prevention interventions.
2. An albeit limited level of self-administered PrEP use among MSM appears evident in Ireland, but which nonetheless requires urgent intervention by statutory services in collaboration with civil society who may be well placed to provide immediate information, education and guidance for PrEP users. It is recommended as a first step, that the safety concerns posed by the online purchase and self-administration of PrEP in Ireland must immediately prompt the funding and establishment, within existing specialist sexual health clinics, of information, advice and clinical monitoring services until such time as PrEP is made available through the HSE.
3. The evidence base, while currently dependent on RCTs and a small number of implementation studies, which are increasing in number, clearly demonstrates PrEP efficacy particularly for MSM and transsexual women. Notwithstanding the absence of context-transferable evidence for key populations other than MSM and trans women, the World Health Organisation recommends that oral PrEP should be offered as an additional prevention choice for all people at substantial risk of HIV as part of a combination of prevention approaches, which is widely supported by contributors to this review, while recognising that the primary beneficiaries of potential PrEP introduction are likely to be MSM in practice.

4. PrEP in practice is marked by a number of unknowns with regard to adherence levels, the potential for risk compensation, and of particular concern to health care providers interviewed in this study, the capacity of an already over-stretched sexual health service to absorb a cohort of HIV-negative clients. Implementation research is needed in diverse settings not least in terms of supporting adherence and the capacity of already over-stretched health systems to respond effectively to increased demand. It is also largely unknown how PrEP may affect behavioural and social outcomes in the medium to long term. The vast majority of contributors to this review favoured an implementation or demonstration study as a first step not least because the budget impact may be contained, any unintended consequences more easily offset and issues resolved before PrEP is taken to scale. Concerns about the cost of PrEP were frequently cited as a perceived barrier to PrEP implementation: this is a Europe-wide concern, not just an Irish one. Clinical interventions are not cost-neutral and the actual cost of once-daily Truvada® for PrEP is likely to impact significantly on the budget for HIV and sexual health. An implementation trial would facilitate cost-containment until such time as generic substitutions are licensed for PrEP in Europe. As a first step, it is recommended that GHN and HIVI support the introduction of an implementation study, which may be more easily and speedily sanctioned, until such time as PrEP may be taken to scale.
5. The cost-effectiveness of PrEP appears to be particularly sensitive to key variables such as HIV incidence, levels of adherence, willingness to use PrEP, risk behaviours, the cost of drugs and other clinical interventions required to support PrEP programmes: as such cost-effectiveness studies conducted in other jurisdictions are of limited value to the Irish context. The potential cost of PrEP is perceived to be a barrier to implementation in Ireland. In the medium to long term, there is a role for advocacy in challenging the HSE to explore the cost-saving potential of generic substitution of ARVs which have been found to be acceptable to patients and HIV health care providers, while Return on Investment analysis should be considered in conjunction with budget impact and cost effectiveness analysis which may prove to be a more propitious cost benefit benchmark for PrEP implementation in Ireland.
6. Coupled with concerns about the cost of PrEP and the capacity of the health system to respond to the clinical requirements of PrEP introduction, some participants raised questions as to whether PrEP should be made available to non-Irish citizens. This is problematic in public health terms given that at least 55% of HIV cases diagnosed in Ireland originate from other countries. [4] Additionally, 35% (n=94) of people testing HIV+ in Ireland in 2015 were born in sub-Saharan Africa, and over half (53%) of female cases were born in sub-Saharan Africa. To fail to provide PrEP to non-Irish citizens

4. Geographic origin is unknown in 15% of cases (HPSC, 2015, p.12-13)

may potentially offset any HIV prevention gains and institute non-coherence between Ireland's national and international health policy commitments. It is recommended that policy advocacy must ensure that PrEP implementation does not operate eligibility on the basis of citizenship but works to ensure inclusiveness on public health terms and in the interests of a 'whole-of-government' approach.

7. Europe's Action plan for the health sector response to HIV in the WHO European Region, 2017-2022 urges member states to "collect and analyse timely and high-quality epidemiological data to understand how, where and among whom new HIV infections are occurring, develop HIV estimates, monitor risk behaviours and estimate the size of key populations in need of services."[5] Ireland's failure to prioritise and invest in the collection of epidemiological data is a significant risk to cost-effectiveness, budget impact and service planning estimates for PrEP and other interventions, while also precluding full engagement and reporting against high profile international commitments, including 90-90-90 targets. A number of participants in this study raised the need for increased behavioural surveillance investment to help identify and better off-set risk by early intervention. There is a role for civil society to champion improved surveillance systems in Ireland so that new technologies (like PrEP) are supported by robust epidemiological data and evidence.
8. Civil society advocacy is central to the realisation of particularly contested policy issues, and plays a key role in holding government and statutory service providers to account. While advocates for PrEP implementation are an important part of the process, Ireland's relatively conservative political culture points to a generally cautious approach to policy change for sexual health. Views were divided on the best approach to policy advocacy for PrEP but it is suggested that advocacy platforms for PrEP might be best served by campaigns targeting key policy makers, while mobilising political champions to engage stakeholders in dialogue to help remove some of the barriers to PrEP implementation. Civil society representatives need to be prepared for media interest in PrEP with a factually based public health narrative that is devoid of emotive arguments and rests on sound science.
9. Finally, it is a flawed rationale that renders the statutory services ever the subject of complaint when private interests like Gilead Science Inc are the primary reason why PrEP affordability and cost effectiveness is questionable. Gilead's application for an SPC for Truvada® is the single most significant threat to taking PrEP to scale in Europe not just in Ireland and this issue requires strong civil society engagement.

5. WHO Europe, 2016, p.8

Conclusion

A combination of the evidence for PrEP efficacy coupled with the risk profile of key populations in Ireland, increasing incidence of HIV reflecting broader European trends, PrEP's policy coherence with Ireland's international policy position, and a high level of support for PrEP implementation among key stakeholders and potential end-users, points to the need for immediate steps to be taken to make PrEP available to key populations at substantial risk of HIV acquisition as part of a comprehensive package of HIV prevention measures. At an absolute minimum, the failure to provide HIV testing and clinical monitoring to MSM who are self-purchasing and administering PrEP is a risk to the individual and broader public health. While multidrug resistance levels are generally low, the risks are increased if people with an undiagnosed HIV infection are acquiring PrEP online. The global, regional and national policy context actively advocates PrEP implementation and the requirements to prioritise HIV prevention in member states of the European Union where sexually acquired HIV incidence rates are raising exponentially must render PrEP a policy priority in Ireland.

Limitations of the Review

This policy options review and evidence-scoping of PrEP for HIV prevention was time-limited with parameters and scope clearly determined by the Terms of Reference. It relies significantly on existing evidence for PrEP particularly reviews conducted by a range of multilateral, national and international institutes for health to reach conclusions about policy options for PrEP in Ireland. Much of the information synthesised and presented in this paper was provided by those with direct or indirect involvement in HIV and sexual health in Ireland and is consequently not free of bias. The reviewer has endeavoured to critique key informant responses where possible but the paucity of grey or academic sources relating to PrEP in Ireland limited the robustness of this exercise. The limitations imposed by time and the breadth of ToR requirements; the paucity of the Irish-specific evidence base; the poor participation of stakeholders from outside Dublin and stakeholder bias necessitates some generalised findings. As such, the findings and conclusions presented herein must be interpreted with caution.

CONTENTS

1. Introduction

This policy options review of Pre-Exposure Prophylaxis (PrEP) for HIV prevention has been commissioned by *HIV Ireland Ltd (HIVI)* and the *Gay Health Network (GHN)*. It provides a time-limited scoping of the evidence base underscoring PrEP efficacy while examining the Irish context, and real and perceived barriers to PrEP implementation. The primary aim of this policy options review is to provide evidence-based guidance to both *HIVI* and the *GHN* while establishing the views of key populations affected by HIV, and stakeholders directly and indirectly involved in the provision of HIV services throughout Ireland, to enable informed policy dialogue and an advocacy platform for PrEP.

The author wishes to emphasise that this paper is not a comprehensive review of the evidence for PrEP and should not be read as such. Systematic reviews of the evidence base have been effectively undertaken by better resourced multilateral and national institutions for health in other jurisdictions. This study draws on existing evidence for PrEP, relying in part on reviews conducted by the World Health Organisation (WHO), the National Institutes for Health and Care Excellence (NICE), the National Health Service (Wales), the United States Centre for Disease Control and Prevention (CDC), and the British HIV Association (BHIVA) to reach conclusions about policy options for PrEP in Ireland. There is no scope to revisit or critique that evidence base here other than as background against which PrEP efficacy may support and provide reference for the primary data collected through key informant interviews with stakeholders throughout Ireland.

PrEP is a biomedical HIV prevention strategy meaning that it uses antiretroviral drugs to protect HIV-negative people from HIV infection. Antiretrovirals (ARVs) are currently used in multiple ways to prevent the transmission of HIV in Ireland and internationally:

1. from mother-to-child during pregnancy and childbirth (prevention of mother-to-child transmission, PMTCT);
2. post-exposure to HIV by a person who is HIV-negative (Post-exposure Prophylaxis, PEP); and
3. in the treatment of HIV-positive people, ARVs suppress the viral load to decrease the risk of onward transmission of the virus. This is known as Treatment-as-Prevention (TasP).

PrEP represents an additional intervention for use of ARVs in the prevention of new HIV infections in Ireland, though this is not without some challenges in terms of feasibility, cost and its place in the competition for health priorities. In August 2016, the European Commission granted marketing authorisation for once-daily Truvada®(emtricitabine 200 mg/tenofovir disoproxil 245 mg; FTC/TDF) in combination with safer-sex practices to reduce the risk of sexually acquired HIV-1 infection among uninfected adults at high risk, which means that once-daily Truvada® is licensed for PrEP in Ireland. However, while PrEP is currently available to buy on prescription from the pharmacy

in St. James's Hospital, Dublin, it is not available through the Health Service Executive. This policy options review, involving a scoping[6] of the evidence base supported by key informant (KI) interviews with a wide range of stakeholders, will provide evidence-based guidance to both *HIV Ireland Ltd* and the *Gay Health Network* in accordance with the Terms of Reference *(see Appendix A)* on the potential of PrEP to enhance current HIV prevention efforts and inform advocacy and policy dialogue in Ireland.

1.1 A Global, Regional & National Overview of HIV: Incidence and Prevalence in Ireland

In 2015 there were 2.1 million new HIV infections worldwide, and while AIDS-related deaths have declined in almost all regions of the world between 2010 and 2015, the number of newly acquired HIV infections has barely declined or remained static during the same period.[7] UNAIDS reports that key populations at increased risk of HIV infection include gay men and other men who have sex with men (MSM), sex workers, people who inject drugs (PWID), transgender people, and prisoners. Analysis of data available to UNAIDS suggests that more than 90% of new HIV infections in central Asia, Europe, North America, the Middle East and North Africa in 2014 were among people from key populations and their sexual partners[8]. Notwithstanding continuing prevention efforts, there has been only a minimal decline in the number of HIV diagnoses per 100,000 population over the last decade in the EU/EEA area, with a rate of 6.6 per 100,000 in 2006 (29,156 cases) compared with 6.3 per 100,000 (32,483 cases) in 2015[9]. In the 31 countries of the EU/EEA, the highest proportion of HIV diagnoses was reported to be in MSM (42%) in 2015, with heterosexual contact the second most common transmission mode (32%). Transmission arising from injecting drug use accounted for 4% of HIV diagnoses[10]. The European Centre for Disease Prevention and Control (ECDC) and the WHO Regional Office for Europe report that one third (37%) of the total number of people diagnosed were not born in the reporting country.

The epidemic in Ireland reflects both global and regional trends reporting relatively stable rates of HIV diagnoses between 2010 and 2014 with a notable increase of 30% between 2014 and 2015[11]. In 2015, there were 485 cases of HIV notified in Ireland - a rate of 10.6 per 100,000 population compared to an EU/EEA average incidence rate of 6.3 per 100,000 - which the Health Protection Surveillance Centre (HPSC) reports is 'the highest rate ever reported in Ireland'[12]. While epidemic patterns and trends vary significantly across European countries, sustained increases in the number of infections among MSM are particularly

6. Defined as an exercise which due to time and resource limitations aims to rapidly map the key concepts underpinning a research area and the main sources and types of evidence available – see Mays, N., Roberts, E., & Popay, J. (2001). Synthesising research evidence. In N. Fulop, P. Allen, A. Clarke, & N. Black (Eds.), Studying the organisation and delivery of health services: Research methods (pp. 188-219). London: Routledge
7. UNAIDS, *Global AIDS Update, 2016:* Geneva, Switzerland, p. 2-3
8. Ibid, p.8-9
9. Ibid, p.X
10. European Centre for Disease Prevention and Control/ WHO Regional Office for Europe. *HIV/AIDS surveillance in Europe 2015*. Stockholm: ECDC; 2016.
11. Health Protection Surveillance Centre (HPSC), *HIV in Ireland - 2015 Report*: Dublin, Ireland, 5th October 2016
12. Ibid, p. 4

noteworthy. Ireland is one of only 15 countries in the region where sex between men constituted over 50% of new HIV diagnoses in 2015[13] and one of only 4 countries - Bulgaria, Cyprus, Malta – where substantial increases in MSM transmission is noted between the period 2005-2015.[14]

Sex between men and women is the second most commonly reported mode of transmission in the EU/EEA region, accounting for 32% (9,545) of HIV diagnoses and 27% (130) of cases notified in Ireland. More than one-third (37%; 2,494) of heterosexually acquired HIV in the EU/EEA originate from countries with generalised epidemics. The highest proportions of these were observed in Germany (60%), France (49%) and Ireland (58%) in 2015. The HPSC reports that in excess of one third (34%) of MSM diagnosed with HIV in Ireland were born in Latin America, 33% in Ireland and 17% in Europe, while at least 55% of cases originate from other countries.[15]

Transmission through injecting drug use has decreased in many countries in East Europe. However, in 2015 injecting drug use accounted for one third of new diagnoses reported with more than half of those new cases diagnosed in Russia. Ireland experienced an 81% increase in the number of people who inject drugs (PWID) testing positive for HIV in 2015 compared to 2014. The HPSC reports that this increase was due to an outbreak of recently acquired HIV infection among PWID living in Dublin in 2014/2015, primarily among homeless chaotic polydrug users, many of whom were injecting snow blow, a synthetic cathinone or short-acting stimulant[16]. Patterns of needle and syringe re-use and having a sexual partner who was also injecting drugs were also risk factors within this group.

The ECDC and WHO Regional Office for Europe point to an alarmingly high number – 48% - of late diagnoses in the European Region which contributes to ill-health, early death and increases the risk of onward HIV transmission. Again Ireland broadly reflects this trend with 45% of all HIV diagnoses presenting late in 2015. The HPSC emphasise, however, that the proportion of people who presented late was much lower (31%) among those who had a previous HIV diagnosis abroad compared to those who did not self-report a previous diagnosis abroad (52%)[17]. Demographic data points to a 3:2 male to female ratio with 76% of all HIV cases notified in Ireland in 2015 male and 24% female with a median age at diagnosis of 34 years, broadly reflecting EU/EEA age and gender characteristics. Eight per cent of diagnoses notified in Ireland were young people between the ages of 15 and 24 years, while 9.3% were over 50 years when diagnosed.

The HPSC collates data on newly diagnosed cases of HIV and AIDS in Ireland annually but a study of the demographics and clinical status of all people living with HIV infection in Ireland has not been undertaken. This data is available in other jurisdictions: for example, the HIV and AIDS Reporting System (HARS) in the United Kingdom (UK) is a consultation based, disaggregate dataset which is submitted on a quarterly basis,

13. European Centre for Disease Prevention and Control/ WHO Regional Office for Europe. *HIV/AIDS surveillance in Europe 2015*. Stockholm: ECDC; 2016, p.1
14. Ibid, p.3
15. Geographic origin is unknown in 15% of cases (HPSC, 2015, p.12-13)
16. Health Protection Surveillance Centre (HPSC), *HIV in Ireland - 2015 Report:* Dublin, Ireland, 5th October 2016, p28
17. Ibid, p.18

and reported by all outpatient HIV service providers. The HARS dataset conducts an annual survey of HIV prevalence which serves to support commissioning services and enhance surveillance outputs.[18] Using data from six adult hospitals caring for HIV positive patients in Ireland, Tuite et al retrospectively identified the number of patients accessing specialist care for HIV over a 12-month period from July 2009 to June 2010 to estimate diagnosed prevalence rates for people living with HIV in Ireland by region.[19] Using data from the 2011 Census for ages 15-59 (international age-range requirement) the authors estimated that Ireland's HIV prevalence rate is 1.09/1000 for 15-59 year olds with prevalence estimated at 2.25/1000 in the Dublin region.[20] The relatively high prevalence estimate in the Dublin region prompted the authors to conclude that routine opt out testing for HIV in healthcare settings should be considered, a finding that is supported by a follow on study in an Emergency Department in Dublin in which an opt-out blood borne virus screening programme was piloted over a 10-month period in 2015 resulting in 7 new late HIV diagnoses not all of whom were representative of high risk key populations[21].

1.2 Scope of the Policy Options Review of Pre-Exposure Prophylaxis (PrEP)

The scope of this time-limited policy options review of PrEP commenced with an initial scoping of the evidence base within parameters that were defined by *HIV Ireland* and the *Gay Health Network*: these included the pros and cons underscoring PrEP as a biomedical HIV prevention intervention; real and perceived barriers to PrEP implementation, and an assessment of PrEP efficacy in terms of key populations. The paucity of data available on the Irish context was a limiting factor in *Phase 1, Desk Review/ Scoping of Academic and Grey Literature Sources* and this gap was somewhat addressed by *Phase 2, key informant (KI) interviews* which were conducted with a wide range of stakeholders. The primary aim of this project is to provide evidence-based policy guidance to both *HIV Ireland Ltd* and the *Gay Health Network* in accordance with the Terms of Reference (see Appendix A) and inform advocacy and policy dialogue.

The combined assessment requirements are grouped under three headings, presented in *Figure 1.2*:

18. Public Health England, HIV Surveillance Systems, https://www.gov.uk/guidance/hiv-surveillance-systems [accessed 30th March 2017]
19. Helen Tuite, M Horgan, PWG Mallon, SJ McConkey, Busi Mooka, Fiona Mulcahy, Cathal Walsh, A O'Hora, Darina O'Flanagan, Colm Bergin, Catherine Fleming, Patients accessing ambulatory care for HIV-infection: epidemiology and prevalence assessment - Irish Medical Journal, Volume 108, Number 7, July/August 2015
20. Ibid
21. O'Connell S, Lillis D, Cotter A, O'Dea S, Tuite H, Fleming C, et al. (2016) Opt-Out Panel Testing for *HIV, Hepatitis B and Hepatitis C in an Urban Emergency Department: A Pilot Study.* PLoS ONE 11(3): e0150546. doi:10.1371/journal.pone.0150546

Figure 1.2: Scope of the Policy Options Review

Assessment of	Criteria and review questions	Source of Evidence
Pros & cons of PrEP/ experiences in other jurisdictions	PrEP efficacy as established by clinical trials	Desk review/scoping exercise
	Implementation research in other jurisdictions	Desk review/Interviews
	Real and perceived barriers to PrEP implementation	Desk review/Interviews
PrEP in an Irish context	Policy, feasibility, cost effectiveness	Interviews with limited document review
	Prevalence of high risk behaviours & perspectives of potential end-users (key populations)	Interviews/FGDs[22]
Policy/advocacy guidance	Effective advocacy for PrEP implementation in Ireland	Interviews
	Transnational dimensions of policy transfer for PrEP	Document review
	Ability to influence	Document review / interview

22. Focus Group Discussion

2. Methodology

The methodology for the PrEP policy options scoping comprised three phases: Phase 1 - document review & scoping the evidence base; Phase 2 - schedule of interviews, and Phase 3 - data analysis and report production.

2.1 Phase 1: Desk Review[23]

This review applied qualitative research methods in the social sciences.[24] The development of the research instrument was primarily informed by the core aims defining the review as indicated by *HIVI* and the *GHN* in *Appendix A*. Phase 1 commenced with a scoping of the evidence base for PrEP to which 8 contract days were initially allocated and to a wide range of grey literature sources provided by HIVI and the GHN. While parameters for inclusion were quite wide, the sheer breadth of the evidence base and the project time limitation prompted a more focused and narrowed search which included articles and documents published from 2015 only. The initial stages of Phase 1 aimed to fulfil the requirements of the ToR by assessing recurring themes in the literature in order to focus the document search and identity key issues for inclusion in key informant interviews: *WHO's Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection, Recommendations for a public health approach - Second edition (2016)* served to direct the initial thematic scoping in conjunction with parameters defined by HIVI and the *GHN*.

Databases and HIV/AIDS-specific journals included in Phase 1: document review and scoping of the evidence base, were: *PubMed; Science Direct; Cochrane Database; British Medical Journal (BMJ); the Lancet; Journal of the International Association of Providers in AIDS Care; Journal of the International Association of Physicians in AIDS Care; International Journal of STD and AIDS; Journal of AIDS Policy and Law, and the Journal of Addiction.* A document review synthesis collapsed all data gathered in Phase 1 against the requirements of the ToR under four primary thematic headings as dictated by desk review findings *(see Appendix B)*. These were *public health effectiveness of PrEP; adherence to PrEP; feasibility of PrEP; risk compensation/disinhibition arising as a result of PrEP, and the cost effectiveness of PrEP.*

The questions posed by the ToR and the primary themes arising from the desk review informed the development of the research instrument developed to gather data on the Irish context, which was the primary data gap evident from the literature review.

23. The complete desk review matrix is an extremely large document – too unwieldy to include in Appendices – but is available on request from the author.
24. Bryman, A., *Social Research Methods: 4th Edition.* 2012, Oxford: Oxford University Press; Creswell, J.W., *Qualitative Inquiry and Research Design: Choosing Among Five Traditions.* 1998, Thousand Oaks, CA: Sage; Rubin, H.J., Rubin, I.S., *Qualitative Interviewing: The Art of Hearing Data.* Second Edition. 2005, Thousand Oaks, CA: Sage Publications; Gomm, R., Social research methodology: a critical introduction, (2008) Palgrave Macmillan 2nd Edition

2.2 Phase 2: Interviews with key informants and stakeholders

The desk review phase was followed by 17 semi-structured key-informant interviews; two focus group discussions (FGDs) and a number of email submissions *(see Appendix C)*. Thirty-two invitations to interview were issued, with 17 accepted resulting in a response rate of 53%. The remaining 47% were either unavailable for interview or did not respond to the initial invitation to interview or follow-up. Email submissions were received by four informants or in response to follow-up queries. Key stakeholders were either centrally or peripherally involved in the clinical or psychosocial support of people living with HIV in Ireland or involved in the PrEP debate in other jurisdictions. The sample included health care providers, pharmaco-economists, health researchers, epidemiologists, pharmacists, civil society activists, and international actors. The first FGD included 11 MSM who were potential end-users of PrEP and the second FGD was held with 6 people living with HIV including women from sub-Saharan Africa and MSM. The research methodology employs a generic purposive participant sample but snowball sampling - a method in which selected participants propose other key informants – provided five additional key informants to the review, not all of whom were available to participate when invited to do so. The timeframe identified for completion of the review process – 20 days – necessitated review by both synchronous and asynchronous methods. Six key stakeholders, some of whom are not resident in Ireland, were interviewed by telephone (asynchronous of place), while the remaining were interviewed by face-to-face (synchronous) methods. E-mail contact to verify data or clarify issues arising in FGD was also employed. The interview schedules while encompassing the measures indicated by the ToR and reflecting the 5 themes arising from scoping the literature and document review, were adapted to reflect the various specialisations of KIs, and in some instances, focused specifically on one or two areas of expertise.

2.3 Phase 3: Analysis of evidence and recommendations

This final phase aggregated data from various sources in an assessment matrix to support triangulation and analyses of all information and data collected. This report will present the findings in Chapter 4 in accordance with the criteria specified by the ToR, while reflecting themes arising in interview. The final chapter will combine the evidence base presented in Chapter 3 with Irish context data presented in Chapter 4 to arrive at clear recommendations for PrEP advocacy and policy dialogue. The final chapter will further outline a global, regional and national policy framework for PrEP.

2.4 Limitations of the Review

This policy options review was capacity (one person) and time-limited to 20 days with a 5-day extension authorised at write-up to facilitate inclusion of all data collected by the process. The capacity of the researcher to follow-up with key stakeholders and incorporate the enormous volume of additional data submitted throughout the process for inclusion in analysis is also limited and as such all data presented here must be interpreted in that context.

As PrEP, while licensed, is currently not available via the health system in Ireland, interviews focusing on the Irish context were primarily theoretical as there is no hard evidence upon which claims about PrEP may be made. As such, this research is not unbiased as it draws heavily on the perspectives of sector insiders including sexual health clinical and technical specialists; civil society HIV service providers; epidemiologists; pharmaco-economists; policy makers and potential end-users. A number of senior civil servants, arguably the health policy decision makers, declined to be interviewed and/or did not respond to invitations to interview. Hence, any clear indications as to whether or not PrEP is likely to be introduced in Ireland cannot be definitively answered here. The relatively low response rate (53%) despite follow-up with all those invited to participate, would appear to suggest some reluctance to engage, at least publicly, in the PrEP debate in Ireland.

The research is weakened by the poor participation of stakeholders from outside Dublin. While invitations to interview were issued to clinical and psychosocial services providers in Cork, Galway and Limerick, only the Sexual Health Centre in Cork opted to participate. As such, regional perspectives are not well represented in the findings. It is equally problematic that KIs selected for interview and willing to participate were primarily sector insiders and more likely to support the introduction of PrEP. Consequently, it has not been possible to address stakeholder bias or adequately address the reasons why some may not support the introduction of PrEP into Ireland. As such, the findings herein must be interpreted with caution.

3. Overview of the Evidence-base for PrEP

This chapter will summarise some of the key issues arising from a scoping of the evidence base for PrEP efficacy and will include examination of issues around product safety. An assessment of the evidence base for key populations in terms of adherence, efficacy and the phenomenon of risk compensation will be considered, followed by the evidence for cost effectiveness including the risks associated with Gilead Science Inc.'s recent application for a Supplementary Protection Certificate (SPC) for once-daily Truvada®. This chapter will conclude with a review of multilateral and national guidelines for PrEP with the status of implementation in other jurisdictions.

3.1 The Evidence Base for PrEP Efficacy

The World Health Organisation's Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection, Recommendations for a public health approach - Second edition (2016) recommends that oral PrEP should be offered as an additional prevention choice for people at substantial risk[25] of HIV replacing previous guidance advocating PrEP for MSM. In preparing the updated guidelines, WHO embarked a systematic review and meta-analysis of PrEP trials containing TDF, which demonstrated that PrEP is effective in reducing the risk of acquiring HIV infection. It was found that the level of protection did not differ by age, sex, regimen (TDF versus FTC + TDF) or mode of sexual acquisition (rectal, penile or vaginal exposure) but detectable drug levels in the blood are strongly correlated with the prophylactic effect, emphasising the importance of adherence to PrEP.[26] WHO announced that it will publish comprehensive implementation guidance for PrEP in 2016 but this has not been published at time of writing.

As indicated at the outset, the scope of this review does not provide for an objective assessment of randomised controlled trials (RCTs) which have found PrEP to be effective in reducing the sexual transmission of HIV in both men and women. While large-scale population trials are important and generally unbiased indicators of an effect, they operate some limitations not least in terms of the applicability of results in real-world scenarios. The background incidence in the PROUD study was so high, for example, that the same effect may not be replicable in practice. That said PROUD was a UK-based study that was conducted in a routine clinical practice and as such its lessons are transferable to the Irish context but both clinicians and study participants were aware of the allocation of treatment thus introducing the risk of bias. A number of RCTs included in WHO's meta-analysis were conducted in sub-Saharan Africa where the epidemiology of the HIV epidemic is vastly different, and social and cultural characteristics too divergent to assume transferability to people living in Ireland. Some modelling studies have suggested that the public health impact of PrEP may be hampered by slow uptake, poor adherence,

25. *Substantial risk* of HIV infection is provisionally defined as HIV incidence around 3 per 100 person-years or higher in the absence of PrEP. HIV incidence higher than 3 per 100 person-years has been identified among some groups of men who have sex with men, transgender women in many settings, and heterosexual men and women who have sexual partners with undiagnosed or untreated HIV infection (WHO, *Consolidated Guidelines,* 2016, p.53)
26. Ibid, p.52

or increases in risk behaviour (risk compensation/disinhibition)[27] To address these issues, more than 20 demonstration projects and Open Label Extensions (OLE)[28] of PrEP RCTs are currently planned or ongoing and will contribute to our understanding of PrEP uptake and delivery beyond the RCT setting.[29]

The time and resource limitations of this policy options study precluded an in-depth review or critique of the evidence base for PrEP and relies on better resourced and well established expertise as emphasised in the introduction. The sources upon which much of section 3.1 is based conclude that the quality of the evidence base for PrEP efficacy is robust. These sources include the WHO; European Centre for Disease Prevention and Control (ECDC); the European AIDS Clinical Society; British HIV Association (BHIVA); the National Institute for Health and Care Excellence (NICE); the United States Centre for Disease Control (CDC); the Scottish HIV Pre-Exposure Prophylaxis Short Life Working Group and the National Health Service (NHS) Wales.[30] The evidence summary provided by NICE and reinforced by NHS Wales and the Scottish Short Life Working Group on PrEP, reviews four main trials considered most appropriate to the potential provision of PrEP in a UK setting: these are iPrEX study[31]; the Partners PrEP study[32]; the PROUD study[33], and the IPERGAY study.[34] While significant differences exist between the national insurance model of healthcare service delivery in the UK and the Irish two-tier hybrid system of private and public services, the epidemiology and characteristics of HIV infection in the two jurisdictions is similar. Summary highlights from these trials are replicated for information purposes here as arguably trial results are transferable to the Irish context:

1. The iPrEx study was a double-blind RCT evaluating once-daily Truvada®® or placebo in 2,499 HIV-negative men or transgender women who have sex with men with evidence of high-risk behaviour for HIV infection. It was conducted in Peru, Ecuador, Brazil, the US, Thailand and South Africa. Once daily Truvada® reduced the relative risk of acquiring HIV infection by 44% compared with placebo. Self-

27. 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 Med.* 2013;10(3):e1001401.
28. An open-label trial or extension is a clinical trial in which both the researchers and participants know which treatment is being administered.
29. Wilton J, Senn H, Sharma M, Tan DHS, Pre-exposure prophylaxis for sexually-acquired HIV risk management: a review, 28 April 2015 Volume 2015:7 Pages 125—136
30. WHO, *Consolidated Guidelines,* 2016; Nandwani R and Valiotis G, on behalf of the Scottish HIV Pre-Exposure Prophylaxis Short Life Working Group. PrEP in Scotland. Scottish Health Protection Network (SHPN) October 2016; NICE, Pre-exposure prophylaxis of HIV in adults at high risk: Truvada (emtricitabine/tenofovir disoproxil), 2016; BHIVA–BASHH Position Statement on PrEP in the UK: Update 2016; Center for Disease Control, US Public Health Service, Pre-exposure Prophylaxis for the Prevention of HIV Infection in the United States, 2014; ECDC GUIDANCE HIV and STI prevention among men who have sex with men, 2015; Jones, A., Couzins, Z., Preparing for PrEP? – A Review of the Current Evidence for Pre-exposure Prophylaxis (PrEP) to prevent HIV infection in Wales, NHS Wales, 2017; European AIDS Clinical Society.
31. Grant RM, Lama JR, Anderson PL et al. for the iPrEx study team (2010) Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. New England Journal of Medicine 30; 363: 2587–99
32. Baeten JM, Donnell D, Ndase P et al. for the Partners PrEP study team (2012) Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. New England Journal of Medicine 367:399–410; Baeten JM, Donnell D, Mugo NR et al. for the Partners PrEP study team (2014) 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. Lancet Infectious Diseases 14: 1055–64
33. McCormack S, Dunn DT, Desai M et al. (2016) 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 387: 53–60
34. Molina JM, Capitant C, Spire B et al. for the ANRS IPERGAY study group (2015) On-demand preexposure prophylaxis in men at high risk for HIV-1 infection. New England Journal of Medicine 373: 2237–46

reported adherence levels were at odds with drug level monitoring which found emtricitabine or tenofovir in only 9% of people with HIV infection and 51% of people who were HIV-negative, while 3 people had an emtricitabine-resistant infection and no one reported a tenofovir-resistant infection;

2. The Partners PrEP study was a double-blind RCT evaluating once-daily single agent tenofovir disoproxil or Truvada® or placebo in 4,747 HIV-negative individuals in a heterosexual partnership with a person already infected with HIV (i.e. serodiscordant heterosexual couples) in Kenya and Uganda. Once-daily Truvada® reduced the relative risk of acquiring HIV infection by 75% compared with placebo, while 1 person had an emtricitabine-resistant infection and 1 person had a tenofovir-resistant infection;
3. The PROUD study was an open-label trial of once-daily Truvada® in 544 HIV-negative men or transgender women who have sex with men in England. Participants were randomised to start PrEP with Truvada® immediately on study entry or after a deferral period. Once-daily Truvada® reduced the relative risk of acquiring HIV infection by 86% compared with no prophylaxis; adherence levels were high and while 2 people in the immediate Truvada® group who had HIV infection at baseline or at the 4-week visit developed an emtricitabine-resistant mutation, no participants developed a tenofovir-resistant mutation;
4. The IPERGAY study was a double-blind RCT evaluating Truvada® or placebo taken 'on demand' before and after sexual activity in 414 high-risk men who have sex with men in France and Canada. Participants took a median of 15 tablets per month and reduced the relative risk of acquiring HIV infection by 86% compared with placebo; adherence varied throughout the course of the trial with rates of detection for tenofovir diphosphate and emtricitabine 86% and 82% respectively and none of the 16 people who developed HIV infection after enrolment had resistant mutations to tenofovir or emtricitabine.

The Bangkok Tenofovir Study[35] is the only large-scale study conducted with people who inject drugs (PWID). Over 2, 400 PWID were enrolled and provided regular HIV testing and risk reduction counselling. With optimal adherence a 70% reduction in HIV incidence was reported but in general, this RCT reported a 48.9% reduction in HIV using once daily Tenofovir disoproxil fumarate (TDF) without Emtricitabine (FTC) among PWID. The policy context for this study differs significantly from the Irish context and as such, the high levels of adherence may not be relied upon. This trial which was funded by the US CDC, was overshadowed by ethical

35. Choopanya K, Martin M, Suntharasamai P, Sangkum U, Mock PA, Leethochawalit M, Chiamwongpaet S, Kitisin P, Natrujirote P, Kittimunkong S, Chuachoowong R. 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. The Lancet. 2013 Jun 21;381(9883):2083-90. Available from: https://www.cdc.gov/nchhstp/newsroom/docs/factsheets/archive/prep-idu-factsheet- 508.pdf [accessed 4th April 2017]

and methodological controversy[36]. Trial findings, however, led the U.S. Centers for Disease Control and Prevention to recommend that PrEP be considered "as one of several prevention options for persons at very high risk for HIV acquisition through the injection of illicit drugs"[37]

As emphasised above, while these population trials provide generally unbiased indicators of the effect of PrEP on HIV incidence rates, they do not provide insight into the effectiveness of PrEP in real-world clinical care settings. Implementation research is needed in diverse settings not least in terms of supporting adherence and the capacity of already over-stretched health systems to respond effectively to increased demand. It is also largely unknown how PrEP may affect behavioural and social outcomes in the medium to long term. The RCTs described here noted few changes in terms of sexual behaviours but trials provide a high level of psycho-social support that may not be replicated in real-world settings. WHO notes that while daily dosing was the preferred choice for the majority of users, implementation research is required to establish how best to adapt PrEP to diverse and changing sexual practices. It is also required to establish whether frequent HIV and renal monitoring could be reduced; how best to maximise support for PrEP users while minimising cost, while integrating PrEP into existing services.

3.1.1 PrEP Safety [38]

While Truvada® has long been licensed for use as treatment for people who are HIV positive, the adverse effects when used for PrEP is less well understood. The summary of product characteristics (SPC) provides an indication of potential side effects, which need to be factored into its use as PrEP:

1. Renal (kidney) failure, renal impairment, elevated creatinine[39], hypophosphataemia[40] and proximal tubulopathy[41] have been reported with the use of tenofovir disoproxil for treating HIV infection. The SPC recommends that creatinine clearance is calculated in all people before starting Truvada® for either treatment or prevention and renal function should also be monitored during use. In the iPrEx study, elevated creatinine levels were seen in 2% of the Truvada® group and 1% of the placebo group but this reversed when the drug was stopped. Elevated creatinine levels were also seen in 18% of the Truvada® group and 10% of the placebo group (p=0.03) in the IPERGAY study, but none led to discontinuation of the study drug. In PROUD, 3/275 people in the immediate Truvada® group interrupted treatment because of high creatinine

36. Wolfe, Daniel. 2013. "Beyond the Hype: PrEP for People Who Inject Drugs." http://www.huffi ngtonpost.com/daniel-wolfe/beyond-the-hype-prep-for-_b_3437910.html [Accessed 5 April 2017]; Mathers, B.M. et al. 2010. "HIV prevention, treatment and care services for people who inject drugs: a systematic review of global, regional, and national coverage." Lancet 375: 1014-1028.
37. Caitlin Kennedy and Virginia Fonner, Pre-exposure prophylaxis for people who inject drugs: A systematic review, WHO, 2014, p. 3
38. *Adapted from* NICE, Pre-exposure prophylaxis of HIV in adults at high risk: Truvada (emtricitabine/tenofovir disoproxil), 2016, p. 8
39. A chemical waste molecule that is passed through the kidneys to be processed and excreted in urine.
40. Abnormally low level of phosphate in the blood.
41. A form of renal disease.

levels, but the study drug was restarted in all these people. It has been reported that a large study is planned, to take place in North America and Europe, of Descovy® a new alternative to Truvada®®. This drug substitutes the old formulation of tenofovir, tenofovir disoproxil fumarate (TDF) with a new one, tenofovir alafenamide (TAF), in combination with emtricitabine. TAF is already licensed for HIV treatment and reaches higher intracellular levels and lower plasma levels requiring lower dosage, while producing fewer kidney and bone-related side-effects. Its efficacy as PrEP in humans is unknown but 15 centres in eight European countries have registered interest in joining the study: Austria, Denmark, France, Germany, Ireland, the Netherlands, Spain and the UK.[42];

2. In a sub-study of iPrEx a decrease in bone mineral density of −0.91% in the spine −0.61% in the hip was seen with Truvada® compared with placebo by 24 weeks. Among all participants in the iPrEx study there were fractures in 1.7% of the Truvada® group and 1.4% of the placebo group so the adverse effect is marginal but nonetheless noteworthy;
3. Chronic hepatitis B or C in people prescribed antiretroviral therapy (ART) poses an increased risk for severe and potentially fatal hepatic adverse reactions. The safety and efficacy of Truvada® for PrEP in people with hepatitis B or C has not been established;
4. The most frequently reported adverse reactions by people taking Truvada® are nausea (12%) and diarrhoea (7%). No new adverse reactions were identified from the iPrEx and Partners PrEP studies, and the most frequent adverse reaction reported in the Truvada® group in the iPrEx study was headache (1%). In both iPrEx and IPERGAY there were increased rates of gastrointestinal disturbance with Truvada® compared with placebo. In the Partners PrEP study, there were increased reports of gastrointestinal side effects and fatigue in the Truvada® group, mainly during the first month. In PROUD, 21/275 (8%) people in the immediate Truvada® group interrupted or missed doses because of adverse events.

WHO guidance recommends creatinine testing before starting PrEP and quarterly during PrEP use for the first 12 months, then annually thereafter; hepatitis B surface antigen (HBsAg) is preferred; support to optimise adherence, particularly through initial adverse effects including gastrointestinal disturbance; support is also required to ensure that PrEP users are fully informed about important aspects of taking PrEP including that it reaches protection after 7 doses and that full protection may require 4 doses for anal sex and 7 doses for vaginal sex. HIV testing is required before PrEP is offered and regularly with STI screening while PrEP is taken.[43]

42. PrEP Access in Europe Initiative (undated but circa 2016)
43. WHO, *Consolidated guidelines,* 2016, p.57-59

Six trials measured and reported cases of TDF or FTC drug resistance, with 8 (18%) HIV infections identified with resistance to TDF or FTC occurring among 44 trial participants acutely HIV-infected at enrolment. Additionally, 6 (2%) TDF or FTC drug-resistant infections occurred out of 533 cases of incident HIV infection postrandomization across study arms including five FTC mutations among participants randomised to PrEP and one mutation identified in a participant randomised to placebo[44]. The New England Journal of Medicine recently reported the case of a 43-year-old man in Toronto who notwithstanding strict adherence to PrEP contracted a drug-resistant strain of HIV.[45]

3.2 PrEP and Key Populations: Efficacy, Adherence and Risk Compensation

The first edition of WHO's Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection, Recommendations for a public health approach in 2014 recommended, on the basis of the evidence then available, that PrEP be offered to MSM deemed to be at substantial risk for HIV. On the basis of further evidence of the effectiveness and acceptability of PrEP, WHO has now broadened the recommendation to include all population groups at substantial risk of HIV infection.[46] A systematic review and meta-analysis of PrEP which supports this recommendation illustrates that PrEP is effective in reducing the risk of acquiring HIV infection and that the level of protection did not differ by age, sex, regimen (TDF versus FTC + TDF) or mode of sexual acquisition of HIV (rectal, penile or vaginal exposure). Fonner *et al's 2016* systematic assessment of oral PrEP containing TDF across populations in 15 RCTs found PrEP to be effective in reducing risk of HIV acquisition across types of sexual exposure, sexes, PrEP regimens, and dosing schemes. [47] The review further reported that PrEP appears to present few significant safety risks, and no evidence of behavioural risk compensation in this collaborative, unbiased review and meta-analysis of the RCT evidence base, which was conducted by the John Hopkins Bloomberg School of Public Health in Maryland, Virginia, the Medical University of South Carolina, and the WHO.

While the PrEP context-transferable evidence base appears more robust in the case of MSM as indicated by 3.1 – PROUD, IPERGAY, iPrEX - compared to other key populations affected by HIV as indicated by NICE and NHS Wales (see section 3.1 above), meta-analysis of all RCTs appears to suggest that PrEP is effective in terms of reducing HIV transmission in all key populations. However, as indicated above, real-world implementation

44. Fonner, Virginia A.; Dalglish, Sarah L.; Kennedy, Caitlin E.; Baggaley, Rachel; O'Reilly, Kevin R.; Koechlin, Florence M.; Rodolph, Michelle; Hodges-Mameletzis, Ioannis; Grant, Robert M. *Effectiveness and safety of oral HIV preexposure prophylaxis for all populations,* AIDS: 31 July 2016 - Volume 30 - Issue 12 - p 1973–1983 doi: 10.1097/QAD.0000000000001145
45. Multidrug-Resistant HIV-1 Infection despite Preexposure Prophylaxis N Engl J Med 2017; 376:501-502 February 2, 2017DOI: 10.1056/NEJMc1611639 [accessed 5th April 2017]
46. Substantial risk of HIV infection is provisionally defined as HIV incidence around 3 per 100 person-years or higher in the absence of PrEP. HIV incidence higher than 3 per 100 person-years has been identified among some groups of men who have sex with men, transgender women in many settings, and heterosexual men and women who have sexual partners with undiagnosed or untreated HIV infection (WHO, *Consolidated Guidelines,* 2016, p.53)
47. Fonner, Virginia A.; Dalglish, Sarah L.; Kennedy, Caitlin E.; Baggaley, Rachel; O'Reilly, Kevin R.; Koechlin, Florence M.; Rodolph, Michelle; Hodges-Mameletzis, Ioannis; Grant, Robert M. *Effectiveness and safety of oral HIV preexposure prophylaxis for all populations,* AIDS: 31 July 2016 - Volume 30 - Issue 12 - p 1973–1983 doi: 10.1097/QAD.0000000000001145

of PrEP in clinical settings may reveal unintended consequences and while scale-up of PrEP appears to be underway in a number of jurisdictions (see 3.4.1), some implementation questions remain unanswered. For example, the extent to which PrEP may contribute to reductions in HIV incidence outside of clinical trial settings is largely unknown[48] although initial data are promising: sexual health clinics in London have recently reported a substantial decline in the number of new HIV infections among MSM and while PrEP may be contributing to that decline it is more likely to be as a result of combination prevention, which includes testing and treatment-as-prevention (TasP). Speaking at the British HIV Association conference in Liverpool in April 2017, it is reported that Valerie Delpech from Public Health England acknowledged the possible contribution of PrEP and the fact that it may have more impact in the future[49]. The *I Want PrEP Now* campaign in the UK reports that 2000 men have been purchasing generic PrEP through its website, while services offered by some clinics to test for drug concentrations and adverse events related to PrEP have been well used. A Lancet Editorial reported that while the decline in infections cannot with certainty be linked to PrEP, "the temporal correlation is compelling."[50] The government of New South Wales in Australia has also reported a drop to a five year low in HIV incidence which is attributed to the introduction in March 2016 of *Expanded PrEP Implementation in Community,* the EPIC trial.[51]

The efficacy of PrEP is dependent on multiple factors not least adherence with which it is strongly correlated. Emtricitabine 200 mg/ tenofovir disoproxil 245 mg; FTC/TDF appears efficacious to different degrees depending on biological, social and cultural factors – for example, stigma associated with taking PrEP has been highlighted by sex workers in countries where HIV is endemic and everybody knows that the brand name is a HIV drug, whereas this may be less of an issue in concentrated contexts.

Transgender women frequently report a disproportionate burden of HIV infection: Three RCTs assessing the efficacy of PrEP in men or transgender women who have sex with men, found that once-daily Truvada® (emtricitabine/tenofovir disoproxil 200 mg/245 mg) reduced the relative risk of acquiring HIV[52]. A subgroup analysis from the iPrEX trial focused on the experiences of 339 (14%) of participants who self-identified as "trans," identified as female, or who used feminising hormones. Higher tenofovir concentrations after oral dosing were found in the rectum compared with the vagina, which may explain the near complete protection observed with PrEP dosing of 4–6 tablets per week among men and trans women who have sex with men, whose HIV exposure is primarily by anal intercourse. By contrast seroconversion was observed among several vaginally exposed

48. Wilton J, Senn H, Sharma M, Tan DHS, Pre-exposure prophylaxis for sexually-acquired HIV risk management: a review, 28 April 2015 Volume 2015:7 Pages 125—136
49. Pebody, R. *The large fall in HIV diagnoses in London gay men is real and thanks to combination prevention, not just PrEP,* NAM AIDSMAP, 6th April 2017
50. Editorial www.thelancet.com/hiv Vol 4 February 2017 [accessed 6th April 2017]
51. NSW Government. Health. *HIV notifications fall to a five year low.* http://www.health.nsw.gov.au/news/Pages/20170304_00.aspx [accessed 6.4.2017]
52. NICE, Pre-exposure prophylaxis of HIV in adults at high risk: Truvada (emtricitabine/tenofovir disoproxil), 2016, p.4

non-trans women at this same level of PrEP use.[53] One review suggests that drug-drug interactions with feminising hormones may explain the lower doses of FTC or TDF concentrations.[54] Lower adherence levels were also observed among trans women but the reasons for this are not well understood. Qualitative research suggests that trans women tend to prioritise gender-affirming care over HIV prevention[55]

In 18 PrEP-related studies - 15 RCTs and three observational OLE or demonstration projects - PrEP was found to be most effective in studies with high adherence, reducing infection risk by 70%. Fonner *et al* observed that the level of protection is strongly correlated with adherence to the extent that PrEP significantly reduced infection risk in studies with moderate adherence levels, but showed no effect in studies with low adherence.[56] A number of studies observed that younger participants had poorer adherence compared with older participants and while PrEP was found not to be effective in preventing HIV infection among women aged less than 25 years (FEM-PrEP) it reduced infection among women aged less than 30 years in Partners PrEP.[57] The ``I Am Men's Health'' programme applied an innovative methodology involving co-location of PrEP services with community supports and weekly attendance to generate adherence to PrEP in 23 mostly young black MSM living below the poverty line. Despite multiple risk factors for HIV in the population, adherence to PrEP was 73%, with a median adherence of 82% for participants who had taken PrEP for at least 1 month.[58] Additional research is clearly needed on how to support adherence, especially for adolescents and young women although injectable formulations and (sustained release) implants, currently in development, offer the potential to mitigate current compliance challenges.[59]

In women, some studies have suggested a possible biological mechanism for different rates of protection according to primary transmission route, in that higher rates of drug concentration have been found in rectal tissue compared with vaginal tissue.[60] Fonner *et al's* systematic review and meta-analysis, however, did not find differences in the protective effects of PrEP between men and women. FEM-PrEP and Partners PrEP both reported that the effectiveness of contraception is

53. Grant, R.M., Jae M. Sevelius, Juan V. Guanira, Jana Villayzan Aguilar, Suwat Chariyalertsak, DrPH,k and Madeline B. Deutsch, *Transgender Women in Clinical Trials of Pre-Exposure Prophylaxis, J Acquir Immune Defic Syndr* 2016;72:S226–S229
54. Mayer KH et al. - *Antiretroviral pre-exposure prophylaxis implementation in the United States: a work in progress,* Journal of the International AIDS Society 2015, 18(Suppl 3):19980
55. Sevelius JM, Keatley J, Calma N, et al. 'I am not a man': Trans-specific barriers and facilitators to PrEP acceptability among transgender women. Glob Public Health. 2016:1–16. 16.
56. Ibid.
57. 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. *J Acquir Immune Defic Syndr* 2013; 64:87–94; Murnane PM, Heffron R, Ronald A, Bukusi EA, Donnell D, Mugo NR, et al. Pre-exposure prophylaxis for HIV-1 prevention does not diminish the pregnancy prevention effectiveness of hormonal contraception. AIDS 2014; 28:1825–1830.
58. Giffin W. Daughtridge, S. CaitlinConyngham, Noel Ramirez, Helen C. Koenig, MD, MPH, *'I Am Men's Health' Journal of the International Association of Providers of AIDS Care (JIAPAC)* Vol 14, Issue 2, pp. 103 – 107 First published date: October-20-2014
59. Hope, Thomas J. and Jeanne M. Marrazzo, 'A shot in the arm for HIV prevention? Recent successes and critical thresholds', AIDS Research and Human Retroviruses, xi, 31 (2015), 1055–1059
60. Cottrell ML, Yang KH, Prince HMA, Kashuba ADM. *Predicting effective Truvada PrEP dosing strategies with a novel PK-PD model incorporating tissue active metabolites and endogenous nucleotides (EN). HIV Research for Prevention (HIV R4P).* Cape Town, South Africa. Abstract OA22.06 LB.; Patterson KB, Prince HA, Kraft E, Jenkins AJ, Shaheen NJ, Rooney JF, et al. *Penetration of tenofovir and emtricitabine in mucosal tissues: implications for prevention of HIV-1 transmission. Sci Transl Med* 2011; 3: 112re114.

not altered by PrEP.[61] FEM-PrEP and Partners PrEP also evaluated the potential effects of PREP on adverse pregnancy-related events and the risk of adverse pregnancy-related events did not differ between PrEP and the placebo arms. Both FEM-PrEP and VOICE trials enrolled high-risk heterosexual women in sub-Saharan Africa, and demonstrated variable adherence with low levels of efficacy raising initial concerns that PrEP may not work for women. However, TDF-based oral PrEP was effective for women in the Partners PrEP and TDF2 studies[62]

Owing to differences in condom use and risk compensation measurement across studies, meta-analysis of trial data was not possible in Fonner *et al's* systematic review. The literature does not provide a definitive consensus on risk compensation, but whether real or imagined, health care providers have reported concerns about risk compensation.[63] This finding was echoed in interviews conducted with Irish stakeholders in this study. A systematic review of behavioural outcomes from RCTs conducted by Koechlin et al (2016) reported that the majority of participants did not anticipate hypothetical PrEP use would lead to increased risk behaviours[64] and this is consistent with Fonnar et al's meta-analysis of PrEP outcomes, which showed no significant effect on sexual behaviour with PrEP use.[65] No difference in condom use across arms was detected with some even showing increases in condom use throughout trial duration[66]. Similarly, in studies comparing PrEP with no-PrEP, which more accurately reflect real-life scenarios than RCTs, studies reported either no change in condom use across arms or slight increases in condom use over time.[67] The PROUD trial used sexually transmitted infections (STIs) among MSM participants as a proxy for unprotected sexual intercourse and found similar rates across immediate and delayed PrEP arms.[68] A study in clinical practice in San Francisco, however, indicated a 40% drop-off rate in condom use among PrEP users.[69] In transgender people, one study in South America found anecdotally that condom use may decrease with PrEP[70].

61. Callahan R, Nanda K, Kapiga S, Malahleha M, Mandala J, Ogada T, et al. Pregnancy and contraceptive use among women participating in the FEM-PrEP trial. *J Acquir Immune Defic Syndr* 2015; 68:196–203; Murnane PM, Heffron R, Ronald A, Bukusi EA, Donnell D, Mugo NR, et al. Pre-exposure prophylaxis for HIV-1 prevention does not diminish the pregnancy prevention effectiveness of hormonal contraception. *AIDS* 2014; 28:1825–1830.
62. Wilton J, Senn H, Sharma M, Tan DHS, *Pre-exposure prophylaxis for sexually-acquired HIV risk management: a review, 28 April 2015 Volume 2015:7 Pages 125—136*
63. Doblecki-Lewis, S. and Deborah Jones, *Community Federally Qualified Health Centers as Homes for HIV Preexposure Prophylaxis: Perspectives from South Florida,* Journal of the International Association of Providers of AIDS Care 2016, Vol. 15(6) 522–528
64. Koechlin, F.M., Fonner, V.A., Dalglish, S.L. et al. Values and Preferences on the Use of Oral Pre-exposure Prophylaxis (PrEP) for HIV Prevention Among Multiple Populations: A Systematic Review of the Literature, AIDS Behav (2016). doi:10.1007/s10461-016-1627-z
65. Fonner, Virginia A.; Dalglish, Sarah L.; Kennedy, Caitlin E.; Baggaley, Rachel; O'Reilly, Kevin R.; Koechlin, Florence M.; Rodolph, Michelle; Hodges-Mameletzis, Ioannis; Grant, Robert M. *Effectiveness and safety of oral HIV preexposure prophylaxis for all populations,* AIDS: 31 July 2016 - Volume 30 - Issue 12 - p 1973–1983 doi: 10.1097/QAD.0000000000001145
66. Ibid
67. 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. J Acquir Immune Defic Syndr* 2013; 64:87–94; 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. J Acquir Immune Defic Syndr* 2013; 64:79–86.
68. Fonner *et al* 2016
69. Volk JE, Marcus JL, Phengrasamy T, et al. *No new HIV infections with increasing use of HIV preexposure prophylaxis in a clinical practice setting* [published online September 1, 2015]. Clin Infect Dis. 2015. pii: civ778
70. Galea JT, Kinsler JJ, Salazar X, et al. *Acceptability of preexposureprophylaxis as an HIV prevention strategy: barriers and facilitators to pre-exposure prophylaxis uptake among at risk Peruvian populations.* Int J STD AIDS. 2011;22(5):256–62.

There is significant variability between groups and contexts with women in one US study indicating that taking PrEP would result in a decrease in condom use,[71] while women in a study in Ghana demonstrated a decrease in number of sexual partners and rate of unprotected sex acts.[72] One study found that 20% of young women expected to use condoms less frequently if they took PrEP.[73]

In serodiscordant couples, 3% of Chinese partners said they would increase their number of partners if PrEP was available to them and 12% said they would decrease condom use.[74] However, in Kenya, 25% of respondents said they would stop using condoms if PrEP were available to them.[75] The longitudinal Partners PrEP analysis reported decreasing frequency of unprotected intercourse with HIV-positive study partners but also noted increased frequency of unprotected intercourse with outside partners over time[76].

A study in Kenya and South Africa reported that female sex workers raised concerns that their colleagues might see PrEP as an opportunity to forego condoms to increase earnings[77] which reflects concerns also raised in interview by the Sex Workers Alliance Ireland (SWAI) for this research. SWAI argue that the recent introduction of the Criminal Law (Sexual Offences) Act 2017 which criminalises the purchase of sexual services will decrease sex workers' income thus encouraging higher risk activity as sex workers strive to make a living.

Two of the randomised trials were conducted in European MSM populations and while in both trials the HIV incidence in the control group was much higher than anticipated (9.0/100 person years in PROUD and 6.6/100 person years in IPERGAY) the reduction in HIV was also the highest reported to date (86% in both trials). PROUD also demonstrated the feasibility of delivering PrEP through sexual health clinics using simple and easy to apply inclusion criteria[78]. The PROUD study demonstrated high levels of adherence (86%) but these are estimates based on prescription records. While PROUD reported STIs during the study with slightly higher rates in the PrEP group compared to the placebo group (57% vs 50%) the study concluded that compared to HIV risk from condomless sex, the difference was not statistically significant. This is difficult to call not least because the background incidence of HIV in the PROUD study was so extraordinarily high, but given that STI rates were similar in both groups, it is reasonable to suggest that sexual behaviour may have been quite similar in each group. IPERGAY is a very different

71. Wingood GM, Dunkle K, Camp C, et al. *Racial differences and correlates of potential adoption of preexposure prophylaxis: results of a national survey.* J Acquir Immune Defic Syndr. 2013;63(Suppl 1):S95–101.
72. Guest G, Shattuck D, Johnson L, et al. *Acceptability of PrEP for HIV prevention among women at high risk for HIV.* J Women's Health. 2010;19(4):791–8.
73. Rubtsova A, Wingood G, Dunkle K, Camp C, DiClemente R. *Young adult women and correlates of potential adoption of preexposure prophylaxis (PrEP):* results of a national survey. Curr HIV Res. 2014;11(7):543–8.
74. Mijiti P, Yahepu D, Zhong X, et al. *Awareness of and willingness to use oral pre-exposure prophylaxis for HIV prevention among HIV-serodiscordant heterosexual couples: a cross-sectional survey in Xinjiang, China.* PLoS ONE. 2013;8(7): e67392.
75. Fowler N, Arkell P, Abouyannis M, James C, Roberts L. Attitudes of serodiscordant couples towards antiretroviral-based HIV prevention strategies in Kenya: a qualitative study. AIDS Patient Care STDs. 2015;29(1):33–42.
76. Fonner et al 2016
77. Mack N, Evens EM, Tolley EE, et al. The importance of choice in the rollout of ARV-based prevention to user groups in Kenya and South Africa: a qualitative study. J Int AIDS Soc. 2014;17(3 Suppl 2):19157.
78. BHIVA–BASHH Position Statement on PrEP in the UK: Update 2016, p.3

study from PROUD, in that it studied 'on-demand'[79] PrEP which is not licensed for use in the EU: this trial also reported good adherence (43% per cent reported that they had taken it according to the protocol; 29% had taken some doses; and 28% had not taken any) and there was no evidence of risk compensation identified by the study.

Finally, the context transferable data for PWID is perhaps weaker than for any other key population notwithstanding recommendations by the WHO[80] and CDC PrEP Guidelines.[81] The Bangkok Tenofovir Study[82], which underscores these recommendations, is the only large-scale study conducted with PWID. As previously outlined, the RCT reported that with optimal adherence a 70% reduction in HIV incidence is possible but overall effectiveness in terms of reducing HIV incidence rates was found to be 48.9% with once daily TDF without FTC. The social and policy context for this study differs significantly from the Irish context and as such, the high levels of adherence may not be relied upon. Evidence suggests that single interventions do not produce substantial and sustained reductions in HIV transmission among PWID but rather a high coverage of combination biomedical, harm reduction and structural approaches are required.[83] Coupled with the fact that HIV incidence is low among PWID in Ireland due to successful harm reduction interventions, the European Commission have only licensed Gilead's Once-Daily Truvada® for reducing the risk of sexually acquired HIV-1 in August 2016. However, the European AIDS Clinical Society (EACS) guidelines from 2015 and WHO's 2016 guidelines recommend PrEP for people at high-risk of acquiring HIV infection in combination with other preventive interventions, including the use of condoms. As such, it is likely to be the case in practice that eligibility criteria informed by WHO and EACS guidance would extend PrEP to PWID and their sexual partners if all clinical requirements are met. It should be noted however that NHS England's proposed eligibility and exclusion criteria of individuals whose injecting drug use is their only risk of HIV acquisition have been excluded from proposed PrEP provision, on the grounds that "current HIV incidence in this group in the UK is too low for PrEP to be cost effective"[84].

79. Differs from daily dosage of one Truvada pill and instead prescribes two Truvada pills from one day to two hours before sex is anticipated.
80. WHO, *Consolidated Guidelines,* 2016; US CDC
81. US Public Health Service, Pre-exposure Prophylaxis for the Prevention of HIV Infection in the United States: A Clinical Guideline, 2014. "PrEP is recommended as one prevention option for adult injection drug users (IDU) at substantial risk of HIV acquisition" p9
82. Choopanya K, Martin M, Suntharasamai P, Sangkum U, Mock PA, Leethochawalit M, Chiamwongpaet S, Kitisin P, Natrujirote P, Kittimunkong S, Chuachoowong R. 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. The Lancet. 2013 Jun 21;381(9883):2083-90. Available from: https://www.cdc.gov/nchhstp/newsroom/docs/factsheets/archive/prep-idu-factsheet- 508.pdf [accessed 4th April 2017]
83. Marshall, B. D. L., and Milloy, M.-J. (2016) *Improving the effectiveness and delivery of pre-exposure prophylaxis (PrEP) to people who inject drugs.* Addiction, doi: 10.1111/add.13597
84. NHS England, *Clinical Commissioning Policy Proposition: Pre-exposure prophylaxis (PrEP) to prevent the acquisition of HIV in adults Reference:* November 2016 [draft]

3.3 Cost Effectiveness

Cost effectiveness studies are context and epidemic-specific and as such few conclusions can be drawn from studies conducted in other jurisdictions. The cost-effectiveness of PrEP appears to be particularly sensitive to key variables such as HIV incidence, levels of adherence, willingness to use PrEP, risk behaviours, the cost of drugs and other clinical interventions required to support PrEP programmes. Presenting at the ECDC PrEP conference in 2016, modelling experts emphasised the challenges of cost effectiveness modelling in a situation where substantial short-term budget impact has a potential longer-term public health benefit and cost saving.[85]

Cost effectiveness studies have been undertaken in a number of countries and settings, including the Netherlands, Australia, Canada and the United Kingdom but there appears to be no clear indication that PrEP is cost-effective.[86] The Dutch study was based on mathematical modelling to predict the effectiveness and cost-effectiveness of PrEP in daily usage and 'on-demand' and demonstrated that 'on-demand' PrEP would be cost-saving if the price was reduced by 30-40% but daily PrEP would not[87]. The Canadian study found that targeting PrEP at the highest risk MSM is likely to improve cost-effectiveness,[88] and the Australian study found that cost-effectiveness is only achieved when targeted at all discordant MSM partnerships. Other scenarios did not generate cost-effectiveness ratios that would constitute value for money.[89]

In the United Kingdom – where the cost of drugs is generally lower than in Ireland – two studies have demonstrated that PrEP would not be cost-effective unless the price of *Truvada*® is cut substantially[90]. The first of these conducted by Ong et al estimated the cost and cost effectiveness of a proposed daily oral PrEP programme covering 10,000 high-risk MSM attending genitourinary medicine clinics in England. Cambiano *et al* modelled

85. Jones, A., Couzins, Z., Preparing for PrEP – A Review of the Current Evidence for Pre-exposure Prophylaxis (PrEP) to prevent HIV infection in Wales, NHS Wales, 2017, p.13
86. Cambiano V., Miners A., Dunn D., McCormack S., Ong K., Gill N., et al. Is PrEP for HIV prevention cost-effective in MSM in the UK? Glasgow: University College London; 2015; Ong KJ., Desai S., Desai M., Nardone A., Hoek AJ van., Gill ON. Cost and cost-effectiveness of an HIV pre-exposure prophylaxis (PrEP) programme for high-risk men who have sex with men in England: results of a static decision analytical model. The Lancet. 13 November 2015; Available at: http://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(15)00854-5.pdf (Accessed: 6th April 2017); Nichols B. PrEP is Only Cost-Effective Among MSM in the Netherlands When Used on Demand. Conference on Retroviruses and Opportunisitc Infections (CROI) 2016; 25 February 2016; Boston, Massachusetts; 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. September 2016; Available at: DOI:10.1016/S1473-3099(16)30311-5 (Accessed: 6th April 2017); 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. 4 January 2014; 58(7): 1027–1034. Available at: DOI:10.1093/cid/cit946 (Accessed: 6th April 2017); 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): 23–29. Available at: DOI:10.1155/2015/964512 (Accessed: 6th April 2017)
87. Nichols B. PrEP is Only Cost-Effective Among MSM in the Netherlands When Used on Demand. Conference on Retroviruses and Opportunisitc Infections (CROI) 2016; 25 February 2016; Boston, Massachusetts; 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. September 2016; Available at: DOI:10.1016/S1473-3099(16)30311-5 (Accessed: 6th April 2017)
88. 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): 23–29. Available at: DOI:10.1155/2015/964512 (Accessed: 6th April 2017)
89. 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. 4 January 2014; 58(7): 1027–1034. Available at: DOI:10.1093/cid/cit946 (Accessed: 6th April 2017)
90. Ong KJ., Desai S., Desai M., Nardone A., Hoek AJ van., Gill ON. Cost and cost-effectiveness of an HIV pre-exposure prophylaxis (PrEP) programme for high-risk men who have sex with men in England: results of a static decision analytical model. The Lancet. 13 November 2015; Available at: http://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(15)00854-5.pdf (Accessed: 6th April 2017)

the cost of PrEP to 5,000 gay men at risk of HIV infection.[91] The models have been criticised for relying on the observed HIV infection rates in sexual health clinic attendees, rather than the higher infection rates seen in those not taking PrEP in the PROUD study. However, the background HIV incidence rate in PROUD is extremely high and whether or not such rates may be witnessed beyond an RCT is open to question. Ong and Cambiano therefore base their models on the likely infection rate in the absence of PrEP which in the UK based on clinic attendees is 3.3% rather than the 9% seen in PROUD.[92] The models are also criticised for scenario assumptions of lower adherence and decreases in condom use over time, while operating on the premise that the cost of HIV treatment is likely to fall at a faster rate than the cost of PrEP. Cost effectiveness modelling studies are marked by limitations but so are RCTs and as such the true cost of an intervention like PrEP can never be accurately known until it is implemented and managed for results: as Nobel Prize winning physicist, Niels Bohr, commented somewhat ironically, "Prediction is very difficult, especially if it's about the future."

Perhaps the most significant threat to both cost effectiveness and plans to upscale PrEP across Europe is Gilead Science, Inc. recent application for a Supplementary Protection Certificate (SPCs) for Truvada®. An SPC prolongs the term of patents for pharmaceutical products for a maximum of five additional years, which if granted in the case of Truvada® would extend the patent until 2022 thus preventing cheaper generics from acquiring licenses for PrEP in the European market. SPCs are governed by EU law and in early 2017 a UK court referred Gilead Science's application to the Court of Justice of the European Union (CJEU), for further clarification on the SPC regulation. A decision is awaited at time of writing.

3.4 PrEP Guidelines

PrEP is supported by a robust evidence base and implementation of PrEP programmes is supported by clinical guidance currently operationalised by key multilateral and national institutes for health. Primary guidance for PrEP implementation is presented here with review studies conducted in England, Scotland and Wales proposing PrEP implementation:

1. **World Health Organisation, *Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection, Recommendations for a public health approach - Second edition (2016):***

   Recommendation:
   Oral pre-exposure prophylaxis (PrEP) containing TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches (strong recommendation, high-quality evidence);

91. Cambiano V., Miners A., Dunn D., McCormack S., Ong K., Gill N., et al. Is PrEP for HIV prevention cost-effective in MSM in the UK? Glasgow: University College London; 2015
92. AIDSMAP, *Second Cost Effectiveness study finds that large PrEP programmes may need drug price cut to be affordable.* http://www.aidsmap.com/Second-UK-cost-effectiveness-study-finds-that-large-PrEP-programmes-may-need-drug-price-cut-to-be-affordable/page/3000951/ [accessed 6th April 2014]

2. **US Public Health Service, Pre-exposure Prophylaxis for the Prevention of HIV Infection in the United States, A Clinical Practice Guideline,2014**

Recommendation:
Daily oral PrEP with the fixed-dose combination of tenofovir disoproxil fumarate (TDF) 300 mg and emtricitabine (FTC) 200 mg has been shown to be safe and effective in reducing the risk of sexual HIV acquisition in adults; therefore,

- PrEP is recommended as one prevention option for sexually-active adult MSM (men who have sex with men) at substantial risk of HIV acquisition;
- PrEP is recommended as one prevention option for adult heterosexually active men and women who are at substantial risk of HIV acquisition;
- PrEP is recommended as one prevention option for adult injection drug users (IDU) at substantial risk of HIV acquisition;
- PrEP should be discussed with heterosexually-active women and men whose partners are known to have HIV infection (i.e., HIV-discordant couples) as one of several options to protect the uninfected partner during conception and pregnancy so that an informed decision can be made in awareness of what is known and unknown about benefits and risks of PrEP for mother and foetus.

3. **European AIDS Clinical Society, 2017**

Recommendations:
- PrEP should be used in adults at high-risk of acquiring HIV infection when condoms are not used consistently. Before PrEP is initiated, HBV serology status should be documented;
- Recommended in HIV-negative men who have sex with men (MSM) and transgender individuals when condoms are not used consistently with casual partners or with HIV-positive partners who are not on treatment. A recent STD, use of post-exposure prophylaxis or chemsex may be markers of increased risk for HIV acquisition;
- May be considered in HIV-negative heterosexual women and men who are inconsistent in their use of condoms and have multiple sexual partners where some of whom are likely to have HIV infection and not being on treatment;
- PrEP is a medical intervention that provides a high level of protection against HIV acquisition but does not protect against other STDs and should be used in combination with other preventive interventions. PrEP should be supervised by a doctor, experienced with sexual health and use of HIV medicines, possibly as part of a shared care arrangement.

4. **British HIV Association (BHIVA) and British Association for Sexual Health and HIV (BASHH), Position Statement on PrEP, May 2016**

Recommendation:

- PrEP should be made available within a comprehensive HIV prevention package to:
- Men who have sex with men, trans men and trans women who are engaging in condomless anal sex;
- HIV-negative partners who are in serodiscordant heterosexual and same-sex relationships with a HIV-positive partner whose viral replication is not suppressed;
- Other heterosexuals considered to be at high risk.

5. **National Health Service, England, Clinical Commissioning Policy Proposition: Pre-exposure prophylaxis (PrEP) to prevent the acquisition of HIV in adults [draft, 2016]**

Policy Statement:
Policy Statement NHS England proposes to routinely commission Pre Exposure Prophylaxis for the treatment of adults at high risk of HIV acquisition in accordance with the criteria outlined in this document;

Proposed Criteria for Commissioning:
Prescribing of ARVs for HIV pre-exposure prophylaxis TDF/emtricitabine will be prescribed as an intermittent regimen for MSM, trans women and trans men clinically assessed as being at high risk of HIV acquisition. Based on clinical assessment of individual clinical need, a daily regimen may be indicated and this will need to be fully documented. Daily TDF/emtricitabine will be prescribed for heterosexuals clinically assessed as being at high risk of HIV acquisition.

6. **Nandwani R and Valiotis G, on behalf of the Scottish HIV Pre-Exposure Prophylaxis Short Life Working Group. *PrEP in Scotland.* Scottish Health Protection Network (SHPN) October 2016**

Recommendations:

- The HIV PrEP Short Life Working Group strongly recommends that people at the highest risk of HIV in Scotland are provided with the option of PrEP as part of a wider targeted national prevention programme delivered by the NHS in sexual health services, subject to delivery of the programme at a cost effective price and reflecting SMC advice where applicable;
- Pending a decision on the availability of NHS-funded PrEP medication, the HIV PrEP Short Life Working Group recommends that the Executive Leads endorse specialist sexual health services targeting support to

provide advice and clinical monitoring to individuals who have either self-purchased PrEP medication or are considering doing so.

7. **Jones, A., Couzins, Z., Preparing for PrEP? – A Review of the Current Evidence for Pre-exposure Prophylaxis (PrEP) to prevent HIV infection in Wales, NHS Wales, 2017**

Recommendation:

- Pending the outcome of the decision from the All Wales Medicines Strategy Group (AWMSG) regarding NHS provision of PrEP medication, the HIV Expert Group recommends that the specialist sexual health services provide advice and clinical monitoring to individuals who have accessed PrEP medication outside of the NHS or are considering doing so;
- Additional funding will be required for specific support and monitoring of PrEP in specialist sexual health services;
- Formal structures should be in place centrally to monitor and evaluate the use of PrEP in Wales, to include: the outcomes regarding infection (HIV and other STIs); usage of PrEP (length of use, on demand or continual); behavioural changes (perceived risk of activity and condom use);
- Information regarding PrEP should be produced centrally, in collaboration with key stakeholders, as part of a revised HIV prevention programme;
- PrEP should not be considered in isolation but be seen as part of a comprehensive package of HIV prevention. Support needs to be given to allow for earlier diagnosis and linkage to other interventions that may reduce the incidence of STIs;
- Information regarding PrEP is constantly evolving, therefore central oversight needs to continue with updates being provided to services on a regular basis and public messaging revised accordingly.

8. **Australian National PrEP Guidelines, 2016: The Australian Commentary outlines the ASHM recommendations on how to effectively implement the US Public Health Service Guidelines in Australia. This Commentary is embedded in the US Public Health Service Clinical Practice Guidelines.**

Recommendation:

- PrEP is indicated for HIV-negative adults who are at ongoing high risk for HIV infection. HIV-negative status should be confirmed as close to initiation of PrEP as possible, ideally on the same day but not more than 7 days before the prescription is given, by using the standard-of-care testing procedures.

9. **NICE, Pre-exposure prophylaxis of HIV in adults at high risk: Truvada® (emtricitabine/tenofovir disoproxil), 2016**

There is no NICE guidance on pre-exposure prophylaxis for HIV but this evidence summary provides a comprehensive overview of evidence appropriate to population characteristics, health system and the policy context in the UK.

3.4.1 PrEP implementation in other jurisdictions

Taking PrEP to scale i.e. national implementation programmes, has been slow to evolve, which is surprising given the quality of the evidence supporting PrEP efficacy. PrEP is currently not available on the NHS in England, Scotland or Wales notwithstanding evidence reviews which have been undertaken in each jurisdiction, referred to throughout this chapter. NHS England announced in December 2016 that it will fund an extension to national HIV prevention programme with the aim of supporting those most at risk and reducing the incidence of HIV infection[93]. Following the recent Court of Appeal ruling that NHS England in collaboration with local authorities, has the power, but not the obligation, to fund PrEP a large scale clinical trial which will include 10,000 participants over the next three years at a cost of £10 million will be rolled out in 2017. NHS England emphasises that while the evidence supporting the clinical effectiveness of PrEP is strong, implementation questions that they claim should be answered before PrEP is rolled out on a national basis, should be answered. While not specified, evidence reviews from England, Scotland and Wales suggest that these questions pertain to the cost effectiveness of PrEP including the cost of clinical management, adherence, uptake, and levels of risk compensation/disinhibition.[94] While unstated, Gilead Science's application for an SPC, which effectively prevents cheaper generic manufacturers from seeking marketing authorisation for their equivalent products, is likely to be a factor here as the cost of the NHS rises to almost 10% of GDP[95]. Some NHS sexual health clinics – the most well known of which is 56 Dean Street in London – provides free HIV testing, STI screening and follow up to people who have purchased generic PrEP online.

It was reported at the 21st International AIDS Conference in Durban in 2016 that more than 79,000 people in the United States have commenced PrEP in the last four years as widely advocated and endorsed by the CDC (see below). In New York City, a blueprint to reduce the incidence of HIV from 3000 new diagnoses per annum to 750 by the end of 2020 includes statewide implementation of PrEP with collaboration among a wide range of clinical providers, HIV testing, primary prevention and

93. NHS England, *NHS England announces major extension of national HIV prevention programme with Public Health England and funding for ten new specialised treatments,* 4th December 2016. https://www.england.nhs.uk/2016/12/hiv-prevention-pregramme/ [accessed 7th April 2017]
94. Jones, A., Couzins, Z., Preparing for PrEP? – A Review of the Current Evidence for Pre-exposure Prophylaxis (PrEP) to prevent HIV infection in Wales, NHS Wales, 2017; European AIDS Clinical Society; NICE, Pre-exposure prophylaxis of HIV in adults at high risk: Truvada (emtricitabine/tenofovir disoproxil), 2016; Nandwani R and Valiotis G, on behalf of the Scottish HIV Pre-Exposure Prophylaxis Short Life Working Group. *PrEP in Scotland.* Scottish Health Protection Network (SHPN) October 2016
95. World Bank, Global Health Expenditure, http://data.worldbank.org/indicator/SH.XPD.TOTL.ZS [accessed 7th April 2017]

support services.[96] At a Conference on Retroviruses and Opportunistic Infections (CROI) in Seattle in February, 2017, Demetre C Daskalakis from *NYC Department of Health and Mental Hygiene, New York,* presented compelling evidence that the provision of PrEP as part of a broader HIV treatment and prevention package can make overarching objecting of the blueprint, Ending the Epidemic, appear achievable. NYC's approach to HIV prevention is system wide and engages multiple stakeholders in PrEP delivery including STI clinics and community centres to operate a `status neutral' model in which HIV testing is the gateway to a system of either HIV treatment or HIV prevention *(see figure 3.4.1)*.

PrEP is widely available on the health system in France and on 11th April 2017, Scotland announced that PrEP would shortly be available on the NHS[97]. Many countries in Western Europe have either developed guidance for PrEP or made provision for PrEP in existing treatment guidelines. At present, the lower-income countries of central and Eastern Europe are showing very little interest in PrEP notwithstanding the emergence of generalised epidemics in this region. At time of writing, France is the only country providing PrEP through its public health service. The National Agency for Drug Safety has authorised a Recommendation for Temporary Use (RTU) of Truvada® for PrEP for three years, which can be renewed. As of July 2016, 1,077 people were reported to be receiving PrEP through the public health system, with 90 clinics offering PrEP assessment and prescription[98]. PrEP eligibility criteria are as follows:

- Anal sex without a condom with at least two different sexual partners in the last 6 months;
- Episodes of STIs in the past 12 months;
- Multiple PEP treatments in the last 12 months;
- Use of drugs during sex.

A PrEP demonstration project (PROUD) is completed in the UK and demonstration projects are ongoing in Belgium, Italy and the Netherlands, all of which are being implemented in healthcare settings. The target populations are MSM at high risk of HIV in Belgium, MSM and transgender people at high risk of HIV in the Netherlands, and sero-discordant heterosexual couples in Italy.

In Europe and Central Asia, PrEP demonstration projects are planned in a further 15 countries. National policy and clinical guidelines for PrEP are under development in Ireland, Romania and Ukraine as reported under the Dublin Declaration.[99]

The Danish Society for Infectious Diseases recommended in 2015 that PrEP should be considered for MSM who are not HIV-infected and who regularly have condomless anal intercourse with different

96. New York State, Department of Health, Get tested, Treat Early, Stay Safe: End AIDS, 2015
97. Boseley, Sarah, People at risk of HIV in Scotland to be given PrEP drug on NHS, *The Guardian Newspaper.* https://www.theguardian.com/society/2017/apr/10/people-risk-hiv-scotland-prep-drug-nhs-aids [accessed 11th April 2017]
98. European Centre for Disease Prevention and Control. Evidence brief: Pre-exposure prophylaxis for HIV prevention in Europe. Stockholm: ECDC; 2016.
99. Ibid, p.2

partners. Repeated STIs are also a proxy for PrEP. However, PrEP is not recommended for heterosexuals on the basis that transmission among heterosexuals in Denmark has not reached a degree that justifies the use of PrEP. Danish guidelines provide for both daily dosage and 'on demand' regimens. In Spain the GeSIDA group of the Spanish Society of Infectious Diseases and Clinical Microbiology released Guidelines on PrEP in June 2016, which recommend that PrEP should be offered to MSM and trans women who have had condomless sex in the last six months, and who have had more than two partners OR an STI diagnosis OR have sought PEP OR have had "chemsex". These guidelines also recommend that PrEP may be considered for people who are not MSM or trans women where a person, a) is in a serodiscordant relationship with an HIV-positive person with an unsuppressed viral load; b) injects drugs and has shared equipment; c) has had transactional sex for food or shelter; or d) is otherwise socially vulnerable and at high risk of HIV.

3.4.2 Barriers to PrEP implementation in Europe

An ECDC Evidence Brief on PrEP in Europe reported in October 2016 that the cost of Truvada®, the cost of service delivery and feasibility are the main obstacles to PrEP implementation[100]. Thirty-one countries identified the cost of drugs as the primary issue preventing or limiting PrEP implementation, and 24 of these countries rated the issue of high importance. A further 23 countries identified the cost of service delivery as an issue of high or medium importance, and 19 countries identified feasibility as an issue of high or medium importance. A number of countries also expressed concerns about the impact of PrEP on transmission of other STIs, on condom use, eligibility criteria, and adherence and compliance with dosing regimens.[101] Gilead Science, Inc. recent application for a SPC for Truvada® will potentially reinforce obstacles to PrEP rollout on a wider scale in Europe not least in terms of extending the duration of the cost barrier.

100. European Centre for Disease Prevention and Control. Evidence brief: Pre-exposure prophylaxis for HIV prevention in Europe. Stockholm: ECDC; 2016.
101. Ibid, p.6

Chapter Summary

- A high quality, robust evidence base supports PrEP efficacy, with two RCTs demonstrating that once-daily Truvada® may reduce the relative risk of acquiring HIV infection in MSM and trans women by 86% and by 75% in sero-discordant heterosexual couples compared with placebo ;
- The World Health Organisation recommends that oral PrEP should be offered as an additional prevention choice for all people at substantial risk of HIV as part of a combination of prevention approaches;
- The Bangkok Tenofovir Study is the only large-scale study conducted with PWID demonstrating a 48.9% reduction in HIV incidence but its findings may not be transferable to an Irish context;
- PrEP efficacy is strongly correlated with adherence;
- Implementation research is needed in diverse settings to support optimal adherence and to assess how PrEP may affect behavioural and social outcomes in the medium to long term;
- Six trials measured and reported low levels of drug resistance;
- The cost-effectiveness of PrEP appears to be particularly sensitive to key variables such as HIV incidence, levels of adherence, willingness to use PrEP, risk behaviours, the cost of drugs and other clinical interventions required to support PrEP programmes: as such cost-effectiveness studies conducted in other jurisdictions are of limited value to the Irish context;
- PrEP programmes are supported by clinical guidance currently operationalised by key multilateral and national institutes for health in Europe and the USA;
- France is the only country in Europe currently providing PrEP through the public health service, but a number of countries are implementing or planning to implement PrEP demonstration projects;
- The cost of Truvada®, the cost of service delivery and feasibility are the main obstacles to PrEP implementation in Europe;
- Gilead Science's application for an SPC for Truvada® is a significant threat to taking PrEP to scale in Europe.

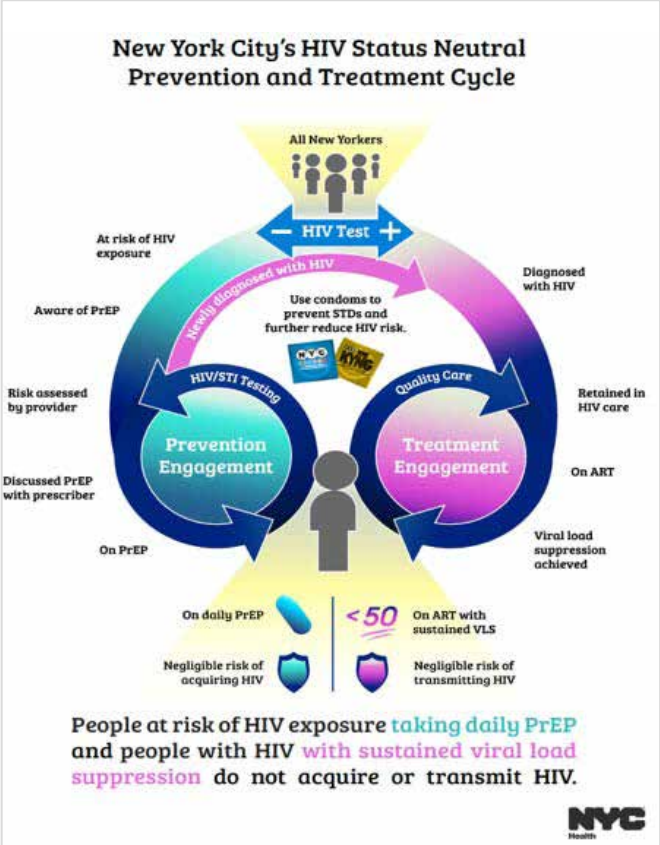


Figure 3.4.1
Source: Department of Health and Mental Hygiene https://www1.nyc.gov/assets/doh/downloads/pdf/ah/neutral-prevention-treatment-cycle.pdf [accessed 7th April 2017]

4. Findings: PrEP in the Irish Context

This chapter will present Irish-specific evidence for PrEP, primarily the findings from key informant interviews conducted with a range of stakeholders including civil society activists, policy makers, health care providers, pharmaco-economists, international development specialists, and two focus group discussions (FGD) undertaken with MSM and HIV positive people between March and April 2017. Queries put to a range of sources including pharmacists and national health insurers are also included here where responses were issued either by telephone or email. Given the paucity of data available on the potential or rationale for introducing PrEP in Ireland, opportunities to verify or triangulate information were limited. Therefore, in order to present a clearer picture of the Irish-specific landscape, data from this research is presented so as to reinforce existing grey literature and academic sources where possible, with outlier issues and/or data corresponding to ToR requirements presented in section 4.6. This Chapter also includes analysis in the context of the evidence base presented in Chapter 3 or additional sources of evidence with recommendations for consideration or policy dialogue presented in bold. This is not an unbiased sample, however, and as such, findings must be interpreted with some caution.

4.1 Multiple risk behaviours for HIV and STIs

The Men who have sex with men Internet Survey Ireland (MISI) 2015 captures the sexual health knowledge, attitudes, needs and behaviour of over 3,000 men in the Republic of Ireland. A small number of respondents - 2% - said they were using PrEP even though it is not available in Ireland through the Health Service Executive.[102] Thirty-seven per cent of men in this survey had never tested for HIV and 61% had not tested for HIV in the last year, while 67% of respondents were definite about their HIV status, the remaining third were unsure with 29% believing that it was `probably negative', 0.2% `probably positive' and 4% `didn't know'. Seventy nine percent of HIV positive respondents reported that they were on ART and of those on ART, 91% were virally suppressed. Nine percent of men reported having a newly diagnosed STI in the last 12 months and among those who reported testing for STIs within the last 12 months, 21% had a newly diagnosed STI. Seventy-one per cent of men who ever had sex with a man had condomless anal intercourse (CAI), 55% had CAI in the last 12 months and 47% reported CAI within the last 6 months. Men most likely to report CAI with a non-steady partner were men with a lower level of education, men who were unemployed and HIV positive men. When steady and non-steady partners were combined 69% of men reported sex with more than one partner, and 25% had CAI with more than one partner in the last 12 months. Seventy-seven percent of HIV positive men reported more than one CAI partner[103].

102. Kate O'Donnell, Margaret Fitzgerald, Peter Barrett, Mick Quinlan and Derval Igoe, MISI 2015 – Findings from the men-who-have-sex-with-men internet survey, Health Service Executive, 2016, p.91
103. Ibid, p.VIII

Seven percent of men reported using drugs associated with chemsex (sex under the influence of psychoactive drugs) during the last year, with usage more common among respondents living in Dublin, and those who were HIV-positive. These findings are consistent with a similar study conducted by the Dean Street Clinic in London in which chemsex behaviour tended to accelerate after a HIV diagnosis[104]. The Dean Street research also found higher rates of chemsex episodes in the aftermath of relationship break-up, and following migration to London. Sexually active episodes while under the influence of drugs tended to last from between 12 and 48 hours and while 45% reported between 4 and 10 partners per episode, 11% reported 10 or more partners per episode.[105] Data in the initial stages of collection by the Gay Men's Health Service (GMHS) in Dublin points to a significantly higher proportion of recreational drug use among men attending the service compared to the Dean Street cohort[106]. This data which is capturing a higher risk profile among men attending the GMHS will help to inform the Sexual Health and Crisis Pregnancy Programme Working Group on PrEP and the national multidisciplinary multisectoral group in their assessment of MSM PrEP eligibility.

A study to assess the prevalence of chemsex among attendees at Ireland's only dedicated sexual health clinic for MSM presented at the Society for the Study of Sexually Transmitted Diseases in Ireland (SSSTDI) Autumn Meeting in November 2016 reported that of 486 convenience sampling questionnaires included in analysis, 27% had engaged in chemsex reporting use of crystal meth, G, ketamine, mephedrone, NPS, cocaine, ecstasy or other stimulants during sex.[107] Use of drugs during sex was more likely to be reported by 25-39 yr olds (31%) compared to men aged 18-24 and the over 40 age groups (20%). Gamma-Hydroxybuteric Acid or 'G' is a central nervous system depressant that produces a stimulant effect at lower doses, was the most commonly used drug reported by men in this study. Half of these men had used 2 or more drugs at last chemsex episode and 9% had ever injected drugs for/during a chemsex episode. Of the 27% who reported engaging in chemsex, they were almost two and a half times more likely to have had more than 10 sexual partners within the previous 12 months. Of 486 men participating in the study, 1 in 3 did not use a condom at last anal sex but those who reported engagement in chemsex were more likely to have engaged in CAI at last anal intercourse. In excess of two thirds (71%) of those who had engaged in chemsex had ever been diagnosed with an STI, compared with 56% of those who had not engaged in chemsex[108]. While this study is limited by the fact that it is only representative of men attending an MSM health service, it reinforces initial data emerging from this service (referred to above) which suggests that there is a cohort of MSM in Ireland demonstrating high and multiple risk behaviours for HIV.

104. Stuart, D. Nneka Nwokolo, Alan McOwan, Margherita Bracchi, Marta Boffito, ChemSex: *Data on Recreational Drug Use and Sexual Behaviour in Men Who Have Sex with Men (MSM) from a Busy Sexual Health Clinic in London, UK,* Chelsea and Westminster Hospital Trust, 2016
105. Ibid
106. Email communication with Siobhán O'Dea, Gay Men's Health Service, 15th March 2017. This data will be presented when analysed at a later date.
107. Glynn, R., *Chemsex use among MSM attending a sexual health clinic in Dublin,* SSSTDI Autumn Meeting, 26th November 2016
108. Ibid, slides 9-14

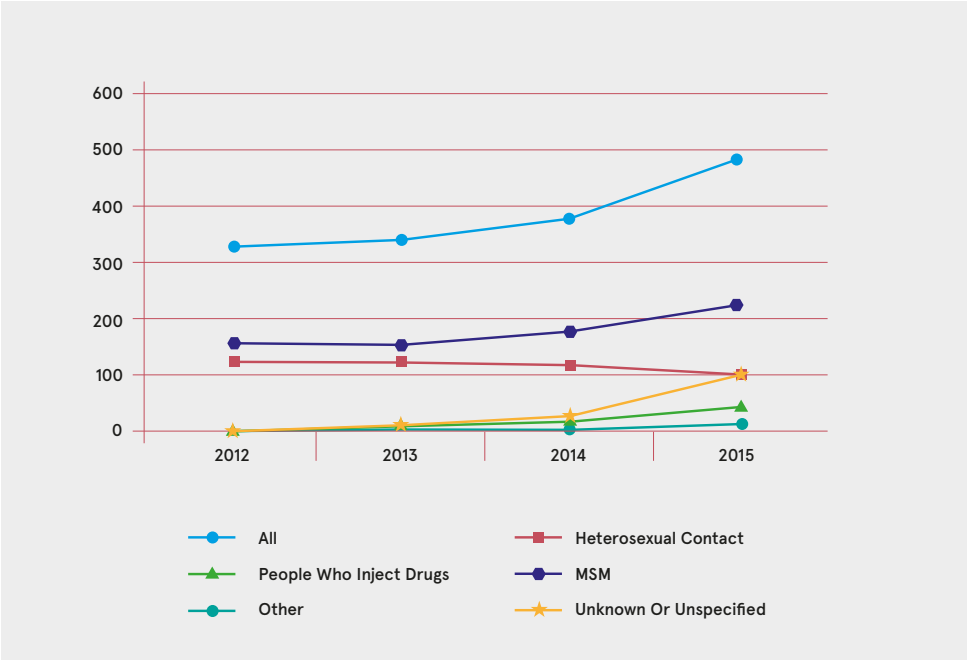
Other recreational drug use was reported by 36% of respondents in the MISI Ireland study, the most common drug of choice being cannabis, ecstasy and cocaine. Recreational drug use was found to be more common among younger men, students, and those living in Dublin peaking among 20-24 year olds and HIV positive men.[109] These MISI data appears to reinforce these findings – and in fact suggests - a slightly higher prevalence of chemsex among MSM in Ireland compared to survey data recently published by Squirt.org, an online platform for MSM sex that surveyed 22,248 members in 2016. This survey found that chemsex had been practiced by 30% of survey respondents while 39% of respondents said they would consider engaging in chemsex and 61% said they would not. The drug of choice for study participants was crystal meth (36%), followed by marijuana (19%), cocaine (13%), and MDMA, better known as ecstasy (11%)[110]. Of relevance here, the survey also inquired about safe sex practices for those who engage in chemsex: 93% of respondents said that they don't use protection for oral sex, while 51% said they don't use protection for penetration. Eighty-nine per cent reported that they knew their current HIV status, 63% said they knew the HIV status of their partner, and 45% said they disclose their HIV status to their partners. A further 37% said they don't know their HIV status. Twenty-three per cent of survey participants reported that they were HIV positive, with 19% saying they were positive, but undetectable and 68% who reported that they were HIV negative. Slightly higher percentages – 3% - were taking PrEP in this survey compared to the MISI cohort.

In the Dean Street study[111] 64% reported zero condom use, while initial data emerging from the GMHS appears to suggest that a slightly higher proportion of men who have completed an anonymous behavioural questionnaire, report that they do not use condoms for either insertive or receptive anal intercourse.[112]

In 2016 a national multidisciplinary multisectoral group was established with representation from the Sexual Health and Crisis Pregnancy Programme, STI and Infectious Disease services, Public Health Departments, the Health Protection Surveillance Centre, Laboratory services, the Gay Health Network, HSE Gay Men's Health Service (GMHS), and Positive Now, an all-Ireland network of HIV positive people, in response to increasing trends in HIV and STIs amongst MSM in Ireland. As outlined in section 1.1 between 2014 and 2015, HIV notifications among MSM increased by 21%, while early infectious syphilis (EIS) increased by 53%.[113] As indicated by figure 4.1 below, the number of MSM testing HIV positive in Ireland has been increasing exponentially since 2013 with 223 cases, 58% of all new diagnoses, where the probable mode of transmission was known, reported in MSM in 2015.

109. Ibid, p.74
110. Squirt.org. *Prevalence of Drug-fuelled sex or Chemsex in the gay community,* http://www.squirt.org/press/chemsex [accessed 10th April 2017]
111. Stuart, D. Nneka Nwokolo, Alan McOwan, Margherita Bracchi, Marta Boffito, ChemSex: *Data on Recreational Drug Use and Sexual Behaviour in Men Who Have Sex with Men (MSM) from a Busy Sexual Health Clinic in London, UK,* Chelsea and Westminster Hospital Trust, 2016
112. Email communication with Siobhán O'Dea, Gay Men's Health Service, 15th March 2017
113. Health Service Executive, *Epi-Insight: Disease Surveillance Report of the National Disease Surveillance Centre,* volume 17 issue 5 May 2016

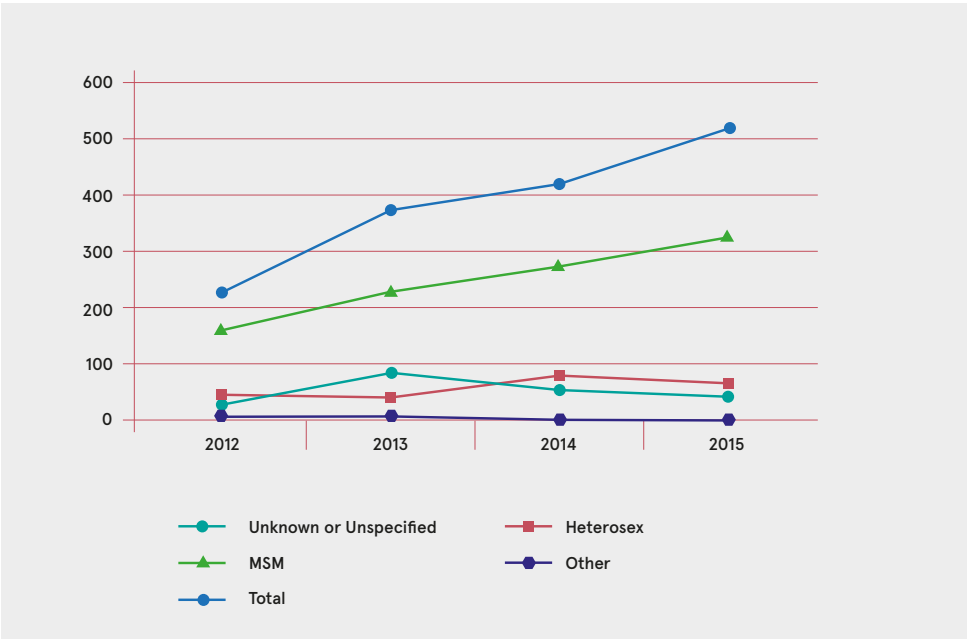
Figure 4.1: Number of HIV notifications in Ireland by reported probable route of transmission, 2012-2015



Source: Epi-Insight: Disease Surveillance Report of the National Disease Surveillance Centre, volume 17 issue 5 May 2016

There has also been a steady increase in EIS in MSM with 214 cases notified among this group in 2015, an increase of 53% on 2014. In the same year, MSM accounted for 87% of diagnoses of EIS – see Figure 4.2:

Figure 4.2: Number of notifications of EIS in Ireland by probable mode of transmission, 2012-2015



Source: Epi-Insight: Disease Surveillance Report of the National Disease Surveillance Centre, volume 17 issue 5 May 2016

The risk profile of other groups affected by HIV is virtually impossible to establish as the same level of behavioural surveillance is not available in Ireland. Provisional data from the HPSC illustrates that 29 cases of heterosexually acquired Syphilis and 402 cases of Gonorrhoea were notified in 2016 but 45% of all STIs where gender is known were acquired by women.[114] In addition, some level of risk is indicated by the *Healthy Ireland 2015* survey in which a large number of respondents (87%) answered questions about their sexual health. As identified by the HPSC for this research, the Healthy Ireland instrument may provide an entry point for gathering a more complete behavioural surveillance dataset. The 2015 data currently tells us very little about who is at risk for HIV but it points to high risk sexual behaviours in the general population with only 24% reporting that they had used a condom when they last had sex, and 47% reporting that they did not use any form of contraception the last time they had sex. Seventeen per cent of those were having sex outside a steady relationship and not using contraception.[115] The perspectives of representatives or health care providers working with key populations other than MSM have contributed to this research but few conclusions may be drawn due to the very small size of the sample.

4.2 Comparing results with the Flash! PrEP in Europe: Ireland Report

The Flash! PrEP in Europe online survey which is conducted by the French HIV organisation, AIDES and the University of Amsterdam was officially launched on 15th June 2016. Initial results for Ireland revealed a high level of PrEP awareness with 92% (n=335) of MSM demonstrating awareness of PrEP, 72.5% of which demonstrated correct knowledge, and 27.5% incorrect or partially correct knowledge.[116] Sixty-six per cent of MSM reported a probable or definite intention to use PrEP if and when it becomes officially available[117] with only 15% reporting that they would probably or definitely not use PrEP if it were available in Ireland. Reflecting the findings of the focus group discussion in this study, 62% of MSM believed that PrEP should be available either free-of-charge or covered by health insurance, while 32% expressed the view that those who use it should pay some of the costs. Community health centres, STI clinics and General Practitioners were favoured by survey participants as the 'best places to prescribe PrEP'.[118] In this study however, the MSM FGD overwhelmingly preferred to access PrEP in a specialist clinic/ hospital where staff are sensitive to and understand MSM lifestyles. Some men pointed to extremely negative experiences of accessing PEP in non-specialist centres where junior doctors were found to be unfamiliar with the treatment. General Practitioners (GPs) were also considered unsuitable to administer PrEP given that fees are likely to be charged and

114. Health Protection Surveillance Centre, Sexually Transmitted Infections (STIs) in Ireland, 2016 Provisional Data
115. *Healthy Ireland Survey, 2015*, (Dublin: Stationary Office), p.57
116. University of Amsterdam, AIDES, Plus. Flash! *PrEP in Europe Country Report Ireland. Early Results.* 2017, p.7
117. This may be due to the sampling method, which distributed flyers through drug-related organisations in Dublin, HIV-related organisations, LGBT-related organisations, migrants-related organisations, and provided regular information about the survey on Facebook® and twitter® HIV Ireland pages. The survey organisers also sponsored posts and adverts on Facebook® with a website banner posted on drugs.ie
118 Ibid, p.9

similar to non-specialist centres, men reported a lack of understanding of gay lifestyles among some GPs.

Forty-five per cent of those 'maybe, probably or definitely' interested in using PrEP in the Flash! PrEP in Europe study reported that they 'somewhat or strongly agreed' with the statement that 'they would rather have condomless sex' while 38% somewhat or strongly disagreed with this statement. This ambiguity and general lack of consensus on risk compensation was also reported by 90% (n=11) of MSM focus group participants in this study. One participant said that "The only reason I would want to go on PrEP is so that I would no longer need to use condoms." and this view was shared by a number of men, and a significant range of civil society and health care professionals who participated in this study. However, this view was not unanimous with other FGD participants suggesting that for them PrEP provides "an opportunity to add another layer or prevention." or similarly, "I want it for those times when I might make a stupid mistake." The diversity of views around risk compensation in the context of PrEP reflects wider ambiguity around this issue not least in the evidence base which provides no definitive consensus.

The Flash! PrEP in Europe study reported that ninety-eight per cent of men 'maybe, probably or definitely' interested in using PrEP said that it would make them feel safer and 89% that they would feel more in control, views also expressed by men participating in the FGD. Sixty-nine per cent 'somewhat or strongly agreed' that they would have a more satisfying sex life if PrEP were available, which was a view also shared by men in the FGD, and 60% self-identified themselves at risk of acquiring HIV. The significant minority (n=61) who 'probably or definitely' would not take PrEP were for reasons including that they do not want to take medication every day (1 participant in the FGD); concerned about side effects; do not want to pay for PrEP, or were afraid of being seen in a negative light, of acquiring STIs or do not perceive themselves to be at risk for HIV. Ten men (2.7%) said they are or have been participating in a PrEP study and of the remainder (N=355) 12 (3.4%) were informal PrEP users. It has not been possible to confirm the existence of a PrEP study at the GUIDE clinic in St. James's Hospital but this *Flash! PrEP* report supports anecdotal evidence which emerged in the MSM FGD. A number of men who participated in the FGD at Outhouse on 22nd March 2017 said that they were using PrEP which they had purchased in generic form online at a cost of $150 for three months supply using guidance provided by the UK-based *I want PrEP Now* website. One participant said "The biggest concern for me as a PrEP user is that I am breaking the law by buying PrEP online." a concern shared by a number of men in the FGD. Men importing PrEP in the FGD reported that they knew of people who had provided an address in Northern Ireland where online purchase of up to 3 months supply of medication online is permitted. The men had not experienced themselves or knew of anyone who had had the PrEP supply seized by customs and one participant reported that at least one clinician has advised that in the event that an import of generic PrEP is seized, he/she would be prepared

to provide a retrospective prescription to satisfy customs officials. Men participating in this focus group and a FGD with HIV+ people expressed fears and concerns around the lack of clinical monitoring and support for people using generic PrEP that they have purchased online: one participant reported that he has but one functioning kidney following a cancer diagnosis, while others raised concerns about the impact of PrEP on haemochromatosis and/or potential interactions with performance enhancing drugs, which had been raised by health care personnel in one dedicated sexual health clinic.

The ambiguity surrounding PrEP access, the lack of knowledge, information and clinical monitoring was raised by many as the greatest cause for concern currently. Drug resistance was highlighted by a number of HIV+ contributors to this study, who argued that drug resistant strains of HIV are a threat to the safety of positive and negative people. While as the evidence in chapter 3 highlights, these risks are low but concerns are nonetheless valid. Finally, the risks of purchasing medication online from unknown sources are well established, not to mention illegal under Irish law. The obvious health risks raised by men in the MSM FGD around the lack of clinical support for PrEP is a real cause for concern in terms of personal safety, the negative consequences of drug interactions, and pre-existing health complications. Equally, the potential side effects of taking once-daily Truvada® or a generic alternative as outlined in section 3.1.1 highlight the potentially serious consequences of self-administration of PrEP. The potential to increase resistant strains of HIV is increased by the risk that a person who is unaware of an existing HIV infection commences PrEP. One dedicated sexual health clinic said in interview that they are providing HIV testing and clinical monitoring to men who are taking PrEP but this is unofficial and neither funded nor supported by the HSE. As such, this service which is based on the goodwill of the people providing it is dependent on word of mouth and constrained by lack of capacity and resource limitations. As also advocated by the HIV PrEP Short-life Working Group in Scotland and while acknowledging that such interventions are not cost neutral, the safety concerns posed by the online purchase and self-administration of PrEP in Ireland must immediately prompt the funding and establishment, within existing specialist sexual health clinics, of information, advice and clinical monitoring services until such time as PrEP is made available through the HSE.

4.3 Comparing results with the PrEP Access in Europe Report

The PrEP Access in Europe Report published by the PrEP in Europe Initiative (PiEi) reported anecdotal evidence that some doctors are currently prescribing Truvada®® off label to HIV-negative individuals in at least ten countries in Europe. This report largely reinforces the findings of the *Flash! PrEP* in Europe Study with regard to the ways in which MSM are accessing PrEP, findings which are also validated by disclosures by MSM in the FGD undertaken by this study. *The PrEP Access in Europe Report* suggests that in the vast majority of these cases, access to PrEP is

through private practice where clients pay the full cost of the drug, which in Ireland is €700 for one box of 30 pills[119], which is also confirmed by this study. The report includes an anonymous quotation, which incorrectly cites the cost of Truvada®® and also incorrectly claims that PrEP is only available through the pharmacy in St. James's Hospital: "IRELAND: "PrEP is only available to be dispensed from one pharmacy, based in the Sexual Health clinic (GUIDE) at St. James' Hospital and comes at the full price (around €400 for a month). I would also imagine there would be extra cost involved for liver [and] renal function tests and regular HIV tests if in the private system.""[120]

It is also reported that people in Ireland are accessing PrEP through HIV-positive friends, who either share the Truvada®® pills that are no longer needed by them for treatment, or by going back to clinics for more, claiming that they have lost the prescription or the bottle.[121]

Generic versions of PrEP are available from online pharmacies and while supply of prescription medicines by mail order (including the internet) is prohibited in Ireland, the PrEP Access in Europe report claims that this method of acquiring PrEP is increasingly prevalent in Ireland as outlined above.[122] While imports may potentially be seized by customs officials, it is claimed that customers are using parcel forwarding options based in countries that do allow generic drug importation. The UK, for example, and consequently Northern Ireland, permits three months' supply of medicine for personal use. At least one pharmacy offers customers south of the border, the opportunity to direct medicines purchased online to Newry, where they may be collected.[123] Some clinics in Europe are offering unofficial drug-level testing to ensure that people are acquiring the correct levels of emtricitabine and tenofovir disoproxil fumarate as one specialist sexual health clinic confirmed is also occurring in Ireland. The PrEP Access in Europe report confirms – as raised by MSM in the FGD - that Ireland is one of a number of countries in which people are accessing PrEP in this way: "Ireland: "It is possible for people to order generic Truvada® online to a UK address which is then redirected. Anecdotally, this passes through customs and VAT is applied before delivery with no further issues""[124]

119. Confirmed in correspondence with Miriam Moriarty, Chief II Pharmacist, Genito-Urinary Medicine and Infectious Diseases, St. James's Hospital on 10th April 2017. It should also be noted, however, that a prescription issued privately by an Infectious Diseases specialist would be brought to a community pharmacy to be dispensed, where the actual costs may be higher.
120. PrEP in Europe Initiative, *PrEP Access* in Europe, October 2016, p.13
121. Ibid, p.14
122. Ibid, p.15
123 McNally's Pharmacy, Newry, Co. Down - http://www.mcnallyspharmacy.com/index.php?option=com_content&view=article&id=45&Itemid=109 [accessed 10th April 2017]
124 Ibid, p.15

4.4 Comparing Results with *Towards preparedness for PrEP: PrEP awareness and acceptability among MSM at high risk of HIV transmission who use socio-sexual media in four Celtic nations: Scotland, Wales, Northern Ireland and The Republic of Ireland: an online survey*

The *Social Media, Men who have Sex with Men and Sexual Health (SMMASH)* survey collected anonymous, online self-completion questionnaires with MSM in Scotland, Wales, Northern Ireland and the Republic of Ireland in 2013. SMMASH sought information on socio-demographic factors, sexual health and sexual behaviours in the previous 12 months with HIV-negative/status unknown high-risk men (n=386) drawn from Scotland (44%, n=170), Wales (22%, n=85), the Republic of Ireland (19.9%, n=73) and Northern Ireland (14%, n=54). Participation generally reflected the relative population size of each country although Scotland was over-represented (+7%) and the Republic of Ireland under-represented (–9.5%)[125].

The survey found that participants were more likely to be aware of PrEP if they lived in Northern Ireland (compared with Wales or Republic of Ireland), reported frequent (daily or more often) gay social media use, lived near the commercial gay scene, reported an HIV test or an STI test in the last year, reported regular HIV testing at least every 6 months or regular STI testing at least every year. The multivariate regression model revealed that only regular (at least every 6 months) HIV testing remained independently associated with PrEP awareness. Participants reporting ≥10 anal and ≥5 CAI partners in the last year demonstrated significantly increased likelihood that they would use PrEP if it were available. Notably, an almost twofold difference between the Republic of Ireland and Northern Ireland in terms of PrEP awareness prompted the authors to recommend local health promotion initiatives for new HIV prevention technologies[126]. MSM FGD participants in this study were all PrEP-aware but some younger participants attended in anticipation of learning about PrEP which was not the focus of the discussion. FGD participants involved in outreach to MSM said that they are experiencing constant requests for information about PrEP – where it may be purchased, how it works etc – and this increasing demand for education and information on PrEP was raised by both civil society and health care providers in this study.

125 Frankis, J, Young, I, Lorimer, K, Davis, M, & Flowers, P., *Towards preparedness for PrEP: PrEP awareness and acceptability among MSM at high risk of HIV transmission who use sociosexual media in four Celtic nations: Scotland, Wales, Northern Ireland and The Republic of Ireland: an online survey, Sexually Transmitted Infections,* 2016, 92, 4, p. 279, Publisher Provided Full Text Searching File, EBSCOhost, viewed 27 February 2017.
126 Ibid, 282

4.5 Comparing Results with *Antiretroviral Therapy (ART) for HIV Prevention: Attitudes and practice amongst healthcare providers in HIV and STI care in Ireland*[127]

A cross sectional survey of attitudes to PrEP, TasP and Post-Exposure Prophylaxis (PEP) among HIV and STI health care providers presented at the Autumn meeting of the Society for the Study of Sexual Transmitted Diseases in Ireland (SSSTDI) in November 2016, revealed that 100% of medical, nursing and pharmacists who completed the self administered anonymous online questionnaire had heard of PrEP. A further 83% 'agreed or strongly agreed' with the statement that "PrEP should be available in Ireland to individuals at high risk for HIV", while 91% indicated that they were 'likely or very likely' to recommend PrEP to high risk individuals. In excess of 90% 'agreed or strongly agreed' that PrEP should only be implemented as part of an overall HIV prevention programme, while up to 70% believed that the use of PrEP will encourage patients to engage in riskier behaviours. Less than 40% believed that the use of PrEP may disseminate ARV drug resistance, and circa 35% believed that the use of PrEP will result in less funding for general sexual health services. Less than 40% expressed concern about side effects and less than 10% that PrEP may not be efficacious.

While the methods deployed to collect data in the Garvey *et al* (2016) study[128] (self-administered anonymous online questionnaire) presented at the SSSTDI conference were entirely different to the qualitative methods used in this study, a number of the same themes reported in Garvey et al also arose in semi-structured key informant interviews used here with a range of health care professionals working in HIV and sexual health in Ireland.

Each of the themes raised by health care providers in Garvey *et al* (2016) study[129] will be explored here in light of the more in-depth qualitative data collected by this process:

1. "Who is going to look after this cohort, the services are already bursting at the seams."[130]

Health care providers interviewed in this study raised similar concerns identifying the capacity of the health care system to respond to HIV-negative people at risk as one of the barriers to PrEP implementation in Ireland. Sexual health services were described by one participant as 'crisis managing' clients requiring PEP and fails to envisage how PrEP might be incorporated into the treatment-to-prevention continuum of care. One dedicated sexual health centre reported an increasing number of MSM are requesting clinical support for PrEP, which they have purchased in generic form online. With significant capacity constraints, including

127 Garvey P, Kiernan J, O'Leary A, Hurley C, Lyons F, *Antiretroviral Therapy (ART) for HIV Prevention: Attitudes and practice amongst healthcare providers in HIV and STI care in Ireland,* SSSTDI Autumn Meeting, 26th November 2016
128 Ibid
129 Ibid
130 Ibid, slide 18

recent budgetary cuts, this service is by necessity provided 'beneath the radar' as there is neither the staffing nor the resources to support a system of expansion. This clinic emphasised that their client base frequently present with a very high risk profile, with increasing episodes of chemsex reported, but that PrEP taken to scale needs to be supported by adequate resources. It was argued by this and many other providers contributing to this study that an implementation trial needs to be the first step so that feasibility issues may be addressed and the best way to make PrEP available to everyone who needs it identified (see below for further discussion). One health researcher argued that capacity issues should not outweigh the need for prioritisation of a prevention intervention like PrEP that promises such significant public health gains.

2. "The non availability of PrEP is hugely concerning and is impacting on new HIV infection rates. The gay sex landscape has changed... Unsafe sex is now routinely part of the sexual repertoire and the use of recreational drugs have impacted on MSM sexual practises"[131]

As indicated by section 1.1 increases in the number of MSM testing positive for HIV is an international phenomenon, not just an Irish one. Notwithstanding, both civil society and health care professional participants in this study echoed this concern with one dedicated sexual health centre pointing to an increasing number of MSM with multiple levels of risk including CAI and chemsex episodes attending the service. A significant number of health care providers argued that Ireland has largely failed to control the HIV epidemic with rising rates of HIV and STIs annually prompting the question as to whether Ireland needs to start viewing the epidemic as a public health emergency? One dedicated sexual health service pointed to a 44% increase in requests for PEP between 2015 and 2016, while it was also reported that a number of MSM are taking performance enhancing drugs, which coupled with illicit drug use requires prompt intervention. One provider argued that from a public health perspective, there is a duty of care to those – very often women - who may unknowingly be at risk of HIV. A number of men attending the FGD in Outhouse also raised the fact that Ireland has become a 'sex positive' culture in recent years with an ever increasing number of sex parties available: as such, the sexual health service needs to evolve in parallel with changes in culture and society.

3. "I do not consider it to be an appropriate use of taxpayers' money. Condoms are a cheaper alternative" [132]

This view was *not* expressed or shared by any participant in this study. While a small number of health care providers said that they may initially have had doubts about PrEP when factoring the competition for

131 Ibid, slide 18
132 Ibid, slide 18

health priorities within an already constrained health system, all of these reported that they had now reversed that view in favour of PrEP given the public health benefits and overwhelming evidence for PrEP efficacy. All participants expressed the view that PrEP should be seen as one prevention intervention among an arsenal of measures that are targeted and appropriate to the needs of the individual, but should not replace the emphasis on condom use to prevent HIV and STIs.

If at its most basic, the principles of public health are understood to be rooted in the prevention of disease, the promotion of health and prolonging life then the evidence appears to suggest that PrEP is an appropriate public health intervention in the context of the risk profile of the community it serves. While there are multiple ways in which the evidence may be interpreted – for example, economic or political perspectives - policy options from a public health perspective are largely limited to one: PrEP is an effective public health intervention and while some participants in this study expressed reservations or concerns around how PrEP should be implemented, *all* contributors to this study supported the implementation of PrEP on public health grounds.

4. "Politically, supplying PrEP free of charge would cause difficulty in the context of rationing of healthcare" [133]

That PrEP should be provided free-of-charge at the point of delivery was contested in this study. A significant number of health care personnel did not believe that PrEP should be provided free-of-charge on the basis that a significant number of prevention interventions in others areas of healthcare are not free to those who need them. Meningococcal B is a serious life-threatening illness that primarily affects children under the age of 5 years: it is prevented by a vaccine that was only made available through the General Medical Service (GMS) to children born after 1st October 2016. No rationale, it was argued, can advocate that PrEP be free-of-charge when antibiotics, contraception, the vaccine for chicken pox and Orlistat, a drug for treating obesity, are some of the numerous examples of prevention interventions in other areas of healthcare that are not funded by the GMS[134] scheme. People on low incomes will have access to PrEP if they are medical card holders. A FGD with HIV+ people mirrored this view suggesting that medical card holders should pay prescription charges and those who can pay should be obliged to make a contribution towards the cost of PrEP on the basis that it is a short-term intervention rather than chronic condition requiring treatment for life. MSM participating in the FGD entirely disagreed with this position, unanimously arguing that PrEP should be entirely free at the point of access: "It's back to us as a community – we are entitled to it [PrEP free-of-charge]" while others suggested that some people would be prepared to pay for PrEP – "Some people would be willing to pay but I don't think

133 Ibid, slide 18
134 Either cost-limited or free-of-charge to medical card holders and refundable to tax payers above €144 per month limit

we should have to pay." This tension between the provider perspective and the end-user perspective is not unusual, but in light of prevention interventions in other areas of healthcare that are comparable to PrEP it seems improbable that PrEP will be made available free-of-charge if implementation is taken to scale.

This study contacted both VHI and Laya Health Insurance seeking conformation as to whether or not PrEP is now or may be covered in the future. Only VHI responded on 29th March as follows:

Thank you for your e-mail of 20/3/17 below enquiring if Vhi cover Pre-exposure Prophylaxis (PrEP). We confirm Pre-exposure Prophylaxis (PrEP) is not covered under our Member Rules Terms and Conditions. We are sorry our reply cannot be more favourable on this occasion.

4.6 New Findings

This study explored a number of issues relating to PrEP that are not explored by previous studies focusing on Ireland. These findings are as follows:

1. Reasons why PrEP should be introduced into the health care system in Ireland

As already indicated, while this is far from an unbiased exercise in that all participants were directly or indirectly associated with HIV and sexual health services, that PrEP should be introduced into Ireland was almost unanimously supported. There were 2 participants who qualified their support for PrEP implementation, with one preferring to see the evidence from implementation trials in other jurisdictions before committing to PrEP in Ireland, and a second who, while not opposed in principle, advocated greater emphasis on testing and TasP rather than PrEP. The evidence base for PrEP efficacy is irrefutable, it was argued, which coupled with the high risk profile of some MSM in particular (see section 4.1), warrants immediate implementation. It was argued by a number of health care providers that Ireland has failed to control the HIV epidemic and while PrEP is not a silver bullet, it provides a significant contribution to the range of HIV prevention interventions that currently exist. Behavioural surveillance data strongly supports PrEP roll-out to MSM in Ireland but the evidence in terms of demand for PrEP, the risk profile or evidence of self-administration of PrEP is not available for other key populations affected by HIV.

2. Barriers to PrEP implementation

The most significant barrier to PrEP implementation in Ireland by participants in this study is Gilead Science, Inc.'s application for a Supplementary Protection Certificate (SPCs) for Truvada®. If granted, the term of the patent for Truvada® may be extended up to 2022 preventing cheaper generics from acquiring licenses for PrEP in the European market. This will have a knock-on effect on both cost effectiveness and budget impact (see below) which may delay introduction of PrEP not

only in Ireland but also in Europe. Other barriers to PrEP implementation raised by participants include the potential for other areas of the health service to object to PrEP among the competition for health priorities, and national debate which is bound to become emotive and argued along axes of morality and values rather than public health objectives.

3. Who should get PrEP?

Responses to this question appear to have been determined by sector-alignment: health care providers were more likely to advocate that PrEP should be made available to those in greatest need and/or at highest risk of HIV as part of a broader prevention and treatment package as per WHO, BHIVA, and CDC guidelines, while civil society actors and the focus group discussion with MSM argued primarily that PrEP should be available to anyone who wishes to take it. The FGD in particular made the point that HIV is a special concern for LGBTI communities and as such PrEP must be central to a national HIV and sexual health response. Some men entirely rejected the notion of eligibility criteria on the basis that the health system should respect an individual's self-assessment of their own risk. This is understandable if unrealistic, however, as the health system, at least in the initial stages, is more likely to opt for a low-risk, lower budget-impact option which makes PrEP available to people of high risk of acquiring HIV as advocated by the WHO. While this level of caution is undoubtedly required to get PrEP over the policy line, the unintended consequences of limiting access to PrEP may prompt some men to put themselves at risk in order to meet the required criteria but only an implementation trial will determine the detail in this regard. The SHCPP Working Group for PrEP appears to favour eligibility criteria selected by the French health system as most appropriate to Ireland. These criteria are indicated in France for all persons over the age of 18 who do not routinely use condoms during sexual intercourse and who are at high risk of contracting HIV. In particular, gay men and transgender people who have sex with men and at least one of the following criteria:

- Anal sex without a condom with at least two different sexual partners in the last 6 months;
- Episodes of STIs in the past 12 months;
- Multiple PEP treatments in the last 12 months;
- Use of drugs during sex[135].

As outlined above, while some behavioural surveillance is available for MSM, this same level of data is not available for other groups at risk of HIV, prompting calls by a number of participants in this study for increased behavioural surveillance investment to help identify and better off-set risk by early intervention as also advocated by WHO Europe. Improved surveillance is required to enable Ireland to both achieve and report

135 Provided by Dr. Fiona Lyons in personal email communication dated 10th March 2017.

against its 90-90-90 targets (by 2020, 90% of all people living with HIV will know their HIV status, 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy, and 90% of all people receiving antiretroviral therapy will have achieved viral suppression).

A small number of outliers argued that PrEP should not be extended to non-citizens of Ireland. This may be valid in cost-effectiveness terms, but it is almost certainly problematic in public health terms given that at least 55% of HIV cases diagnosed in Ireland originate from other countries. [136] Additionally, 35% (n=94) of people testing HIV+ in Ireland in 2015 were born in sub-Saharan Africa, and over half (53%) of female cases were born in sub-Saharan Africa. To fail to provide PrEP to non-Irish citizens may potentially offset any HIV prevention gains. HIV is a policy priority for Ireland's overseas aid programme at the Department of Foreign Affairs and Trade, and the HSE has articulated a commitment to working in global solidarity with developing countries to fulfil its responsibility to achieving a universal 'right to health'. *Healthy Ireland: A framework for improved health and wellbeing (2013-2025)* is explicitly committed to the principle of 'solidarity' with resource poor countries[137] and the Irish government's policy emphasis on a 'whole-of-Government' approach to realise policy coherence between departments and sectors means that any suggestion that non-Irish citizens may not access PrEP would contravene those policy commitments at national and international levels.

As outlined in section 3.2, WHO's *Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection, Recommendations for a public health approach* in 2016 recommend that PrEP be offered to all population groups at substantial risk of HIV infection. PrEP has been found to be effective in reducing the risk of acquiring HIV infection and that the level of protection does not differ by age, sex, regimen or sexual mode of acquiring HIV (rectal, penile or vaginal exposure).[138] However, the risk profile of key populations affected by HIV other than MSM is sadly lacking in an Irish context and as such it is virtually impossible to determine with any degree of accuracy the number of people likely to benefit from PrEP were it made available in Ireland. The MISI 2015 data is currently supporting an estimate of the number of MSM eligible for PrEP using the French health system eligibility criteria, but no such data exists for other population groups at risk of HIV. As such, only an implementation study will fill this gap in information. The scope of this research precluded in-depth assessment of key populations other than MSM in Ireland, and as such no firm conclusions may be drawn, but some interviews were conducted with key stakeholders from the Sex Workers Alliance Ireland (SWAI), a FGD with PositiveNow was conducted on behalf of this research, one interview conducted with a health care provider in the drugs sector and email communication was established with Ireland's

136. Geographic origin is unknown in 15% of cases (HPSC, 2015, p.12-13)
137. Health Service Executive, *Healthy Ireland: A Framework for Improved Health and Wellbeing, 2013-2025,* p.51
138. *Substantial risk* of HIV infection is provisionally defined as HIV incidence around 3 per 100 person-years or higher in the absence of PrEP. HIV incidence higher than 3 per 100 person-years has been identified among some groups of men who have sex with men, transgender women in many settings, and heterosexual men and women who have sexual partners with undiagnosed or untreated HIV infection (WHO, *Consolidated Guidelines,* 2016, p.53)

embassy in Uganda where PrEP is currently being rolled out on a national scale.

SWAI welcomed PrEP and felt it would provide sex workers with an added layer of protection, which, it was argued, has become more important since the introduction of the Criminal Law (Sexual Offences) Act 2017 which criminalises the purchase of sexual services. SWAI said that there is anecdotal evidence which suggests that this new legislation is resulting in a decrease in income which in turn encourages higher risk activity as women and men strive to make a living. SWAI also raised the fact that women from traditional societies are more likely than Irish sex workers to engage in condomless sex.

The Bangkok Tenofovir Study[139] as reported in Chapter 3 is the only large-scale study conducted with PWID and its findings cannot be said to be transferable to an Irish context. Equally, while the US CDC highlights that a 70% reduction in HIV incidence was found in this trial,, a closer look at the data reveals that this level of protection was only achieved with optimal adherence and so the overall reduction was found to be 48.9%. It is clear from this research that PrEP has not featured in policy dialogue within the drugs sector and is certainly not a policy priority. The one health care professional who did participate in this study from the drugs sector cautiously welcomed PrEP in principle, but felt that real-world implementation evidence is lacking with regard to PWID. This participant further argued that PWIDs cannot access methadone programmes, while frontline and proven interventions like needle exchange services have experienced cutbacks. As such, it was argued that funds for the injecting population may be better spent on improving access to proven interventions, while waiting to see the evidence for PrEP emerge from other jurisdictions. The *NHS Clinical Commissioning Policy Proposition: Pre-exposure prophylaxis (PrEP)* to prevent the acquisition of HIV in adults argued cogently that: "Compared to many countries, the prevalence of HIV among people who inject drugs (PWID) is low in the UK, largely due to highly successful needle exchange programmes....There is insufficient evidence to support routine commissioning for this sub-population."[140]

The FGD with HIV+ MSM and women from sub-Saharan Africa welcomed PrEP but highlighted a paucity of information and knowledge among non-MSM key populations. This group argued that anyone who felt they were at risk should be in a position to request an eligibility assessment, and highlighted important concerns around the PEP[141] to PrEP nexus in which anecdotal evidence suggests that some people are clinic-hopping to acquire PEP in order to use it as PrEP without medical supervision. The FGD raised valid concerns about the emergence of drug resistant strains of HIV which also would affect the treatment options for HIV+ people.

As outlined in Chapter 3, the Partners PrEP study was a double-blind RCT

139. Choopanya K, Martin M, Suntharasamai P, Sangkum U, Mock PA, Leethochawalit M, Chiamwongpaet S, Kitisin P, Natrujirote P, Kittimunkong S, Chuachoowong R. 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. The Lancet. 2013 Jun 21;381(9883):2083-90. Available from: https://www.cdc.gov/nchhstp/newsroom/docs/factsheets/archive/prep-idu-factsheet- 508.pdf [accessed 4th April 2017]
140. NHS England, 2016, p.17
141. Post Exposure Prophylaxis (see Introduction)

evaluating once-daily Truvada® which was administered to HIV-negative individuals in a heterosexual serodiscordant relationship in Kenya and Uganda. This trial reported a relative risk reduction of 75% compared with placebo. While it was not possible to interview serodiscordant heterosexual couples for this research, communication with the Irish Aid programme in Uganda reported that PrEP is a policy priority targeting *people who have multiple sexual partners; engage in transactional sex including sex workers; use or abuse injectable drugs and alcohol; have had more than one episode of an STI within the last twelve months; are part of a discordant couple, especially if the HIV positive partner is not on ART or has been on ART for less than six months; are recurrent users of PEP (3 consecutive cycles of PEP);engage in anal sex or are members of key populations who are unable or unwilling to achieve consistent use of condoms.*[142] It is, however, too early to assess demand for PrEP or to comment on the level of acceptability of PrEP in this sub-Saharan African context.

While there is a paucity of behavioural surveillance data supporting an estimate of key populations – other than MSM - eligible for PrEP using the French health system eligibility criteria, participants in this study – with the exception of the drugs sector health care provider for valid reasons outlined above – overwhelmingly supported WHO 2016 guidance that PrEP be offered to all population groups at substantial risk of HIV infection in Ireland. In the absence of behavioural surveillance for key populations other than MSM, the Scottish HIV PrEP Short Life Working Group estimated that 5% or less are likely to be eligible for PrEP.[143] In practice, it is likely that MSM engaging in high risk behaviours will be more likely to meet the eligibility criteria than others.

4. Implementation/demonstration study

The vast majority of contributors to this research argued for an implementation or demonstration study as a first step before national implementation is considered. The rationale underscoring this recommendation was two pronged: in the first instance, a number of participants felt that were too many unknowns with regard to PrEP in Ireland to justify wholesale national implementation not least in terms of the capacity of the health system to respond to an additional cohort of HIV-negative patients; the level of demand for PrEP; operationalisation of eligibility criteria; levels of adherence; risk compensation, and unforeseen or unanticipated circumstances of this intervention in an Irish context. Secondly, it was argued that a trial would limit the immediate budget impact of making PrEP available until such time as generic and cheaper formulations are available, which are more likely to contribute to cost effectiveness. On the other hand, some contributors argued against an implementation study believing that the evidence is robust enough: if we are truly committed to evidence-based medicine, one participant argued,

142. Email communication with Denis Busobozi, HIV Advisor, Irish Embasy, Uganda.
143. Nandwani R and Valiotis G, on behalf of the Scottish HIV Pre-Exposure Prophylaxis Short Life Working Group. *PrEP in Scotland.* Scottish Health Protection Network (SHPN) October 2016

PrEP should be introduced without delay. One service provider from the drugs sector argued that Ireland might be best served by waiting to see the evidence arising from implementation research conducted elsewhere before investing in an intervention whose evidence-base is built on data from RCTs with limited real world application.

Policy tends to be developed in incremental steps[144] and while the concept of evidence-based medicine seems entirely rational, the power of experts, and indeed evidence itself, is almost always contingent on alignment with political priorities.[145] The evidence for public health policy suggests that a new and potentially controversial intervention like PrEP will not be taken to scale immediately but will commence with an implementation trial targeting those most at risk. This is not least because the budget impact can be contained, any untended consequences more easily offset and outstanding questions about PrEP implementation in Ireland more easily answered.

5. Cost effectiveness of PrEP in Ireland

As outlined in section 3.3 above, cost effectiveness studies are context and epidemic-specific and as such few conclusions can be drawn from studies conducted in other jurisdictions. The cost-effectiveness of PrEP is particularly sensitive to key variables such as HIV incidence, levels of adherence, willingness to use PrEP, risk behaviours, the cost of drugs and other clinical interventions required to support PrEP programmes. As no cost-effectiveness study has been conducted in Ireland, no definitive claims can be made as to whether PrEP is likely to be cost effective in Ireland. As described in Chapter 3, two studies conducted in the UK - where HIV incidence is higher (based on 2015 data), the cost of once-daily *Truvada*® is lower, the overall epidemiology of HIV and the risk profile of MSM is similar (see section 4.1) to Ireland - have demonstrated that PrEP would not be cost-effective unless the price of *Truvada*® is cut substantially[146]. Consequently, it seems reasonable to extrapolate that once-daily Truvada® for PrEP is unlikely to be cost effective in Ireland either. Health care professionals from a range of sectors who contributed to this study pointed to the fact that budget impact tends to be more important than cost effectiveness. Budget Impact Analysis (BIA) is a tool to predict the potential financial impact of the adoption and diffusion of a new technology or intervention into the healthcare system[147].

144. Kingdon, J.W., *Agendas, Alternatives, and Public Policies - second edition.* 2003, New York, London: Longman; Kraft, M.E., Furlong, S., *Public Policy: Politics, Analysis and Alternatives.* 2013, London and Thousand Oaks California: Sage Publications; Stone, D., *Policy Paradox: The Art of Political Decision Making - Revised Edition.* 2002, New York: WW Norton & Company.
145. Nathanson, C.A., Sember, R., Parker, R., Contested Bodies: *The Local and Global Politics of Sex and Reproduction, in Sex Politics: Reports from the Front Lines,* R. Parker, Petchesky, R., Sember, R., Editor. 2007, Sexuality Policy Watch: Rio de Janeiro.
Nathanson, C.A., *The Contingent Power of Experts: Public Health Policy in the United States, Britain, and France.* Journal of Policy History, 2007. 19(1): p. 71-94.
146. Ong KJ., Desai S., Desai M., Nardone A., Hoek AJ van., Gill ON. Cost and cost-effectiveness of an HIV pre-exposure prophylaxis (PrEP) programme for high-risk men who have sex with men in England: results of a static decision analytical model. The Lancet. 13 November 2015; Available at: http://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(15)00854-5.pdf (Accessed: 6th April 2017)
147. Health Information and Quality Authority, *Guidelines for Budget Impact Analysis,* https://www.hiqa.ie/reports-and-publications/health-technology-assessments/guidelines-budget-impact-analysis [accessed 12.4.2017]

It addresses the affordability of the intervention in terms of the net annual financial cost of adopting the technology for a fixed number of years, whereas cost effectiveness evaluates whether an intervention provides value relative to health outcome (see example)[148].

A significant number of health care providers including two pharmaco-economists interviewed for this research argued that Gilead Sciences Inc need to make Truvada® available at an affordable price and that there is a need to negotiate a lower price for potential PrEP users in Ireland. As highlighted above, one of the most significant barriers to PrEP implementation was considered to be Gilead's application for an SPC for Truvada® potentially preventing access to cheaper generics regimens for up to five more years. There has been some reluctance, however, among health care providers to use generic ARVs for HIV treatment with one study demonstrating that while generic substitution would be acceptable to the majority of patients and health care providers in an Irish sample, the potential increase in pill burden and dosing frequency were identified as concerns or barriers to generic substitution.[149] The authors argue that the potential saving to the health service which could be redirected into the HIV service or indeed new prevention interventions like PrEP merits some consideration. The introduction of generic substitution has resulted in significant cost savings to the Irish health service in recent years but generic substitution for ARVs has not been considered. It has been estimated by the NHS that substitution with generic ARVs would result in a cost saving of £1.25 billion but there are clearly other implications that need to be factored with regard to ARV generic substitution.[150] While it has not been articulated by senior policy makers in health, the potential cost of PrEP is perceived to be the barrier to implementation in Ireland, a finding also reported by Garvey et al's study of health care providers discussed above.[151] Should costs appear to remain a barrier to PrEP implementation, there is a role for advocacy in challenging the HSE to explore the cost-saving potential of generic substitution of ARVs which have been found to be acceptable to the majority of patients and HIV health care providers in Kieran et al's (2017) study[152].

Other contributors to this research argued that the decision to implement PrEP or otherwise should be informed by multi-factor analysis and not just cost or budget impact. The New York State blueprint for ending the HIV epidemic by 2020 adopted a return on investment (ROI) analysis rather than either a cost effectiveness or budget impact analysis. The strategy argues that "The state's expenditures on efforts to end AIDS

148. Example: A cost-effectiveness analysis may indicate that Drug A is a good value relative to Drug B, because it has an incremental cost-effectiveness ratio (ICER) of €40,000 per Quality-Adjusted Life Year (QALY). This means that per person, the health system needs to spend €40,000 additional Euro to provide each patient with Drug A. If there are 3,000 patients within a health system that need this drug, the healthcare system will have to spend an additional €120 million Euro to treat these patients, which may not be affordable.
149. Kieran, J.A., O'Reilly, E., O'Dea, S., Bergin, C., O'Leary, A., *Generic substitution of antiretrovirals: patients' and health care providers'* opinions, International Journal of STD & AIDS 0(0) 1–8
150. Hill A, Hill T, Jose S, et al. Predicted savings to the UK National Health Service from switching to generic antiretrovirals, 2014–2018. J Int AIDS Soc 2014; 17: 19497.
151. Garvey P, Kiernan J, O'Leary A, Hurley C, Lyons F, *Antiretroviral Therapy (ART) for HIV Prevention: Attitudes and practice amongst healthcare providers in HIV and STI care in Ireland,* SSSTDI Autumn Meeting, 26th November 2016
152. Kieran et al, 2017, p.7

as an epidemic should be viewed as investments rather than costs"[153] Estimating the lifetime HIV-related medical care cost as $357,498, while achieving the goal of reducing new HIV infections from 3,000 to 750 per year by the end of 2020 would, it is estimated, result in a saving of $804.4 million. In relation to testing, New York State assessed the return on the public health investment of a large-scale HIV testing programme which demonstrated a return of $1.95 for every dollar invested.[154] ROI analysis should be considered in conjunction with budget impact and cost effectiveness analysis[155] which may prove to be a more propitious cost benefit benchmark for PrEP implementation in Ireland.

6. The Role of Advocacy

The role of advocacy in supporting PrEP implementation was contested and perceived quite differently across sectoral lines although this divide was not consistently held. Health care providers welcomed HIV advocacy in general on the basis that every heath care issue requires champions without which very little traction would be gained particularly in areas like HIV and sexual health which tend not to be policy priorities. Specifically in relation to PrEP however, some argued that in light of serious constraints in the health system which have been receiving significant media focus, overt-PrEP campaigns may not be helpful in taking – as a first step at least – an implementation/demonstration study over the policy line. On the other hand some civil society groups and MSM participants in the FGD were of the view that the failure to provide PrEP to MSM who wish to avail of it constitutes "homophobia, this is stigma" and were "very uncomfortable" with any suggestion that overt public discussion involving the media is likely to be debated along axes of values and morality rather than public health which may risk or delay PrEP implementation.

The Terrence Higgins Trust (THT) in the UK has already faced this dilemma in terms of Public Health England's reluctance to implement a PrEP programme. While engaging politicians in advocacy, THT found it efficacious to link political support with decision makers in the health services rather than engage them in public and/or controversial media debate. As is the case in Ireland, prominent politicians were not inclined to become involved in the debate in England, rather back-benchers and elected representatives not in government. THTs campaigns are factually based focusing on the public health benefits of PrEP in the context of a HIV epidemic that is spiralling in the UK with push back against narratives that seek to compare one disease with another. There has been some conservative backlash in the UK but it is a minority platform that has not gained significant traction. No backlash has been identified in Scotland since announcing that PrEP would be available on the NHS, however.

153. New York State, 2015 Blueprint, p.14
154. Ibid
155. Ireland is currently not in a position to report against these targets

Policymaking for sexual health and other contested domains in Ireland tends to favour a covert and ambiguous approach[156]. The divisive and polarising nature of debate on moral issues in Irish life has rendered policy and law reform in these areas highly problematic for politicians and civil servants, with changes driven and frequently successfully implemented from the ground up[157]. Given Ireland's relatively cautious and sometimes conservative social and political culture, advocacy platforms for PrEP might be best served by campaigns targeting key policy makers, while mobilising political champions to engage stakeholders in dialogue to help remove some of the barriers to PrEP implementation. Furthermore, civil society representatives need to be prepared for media interest in PrEP with a factually based public health narrative that is devoid of emotive arguments and rests on sound science.

It emerged in the course of this research that some groups are using the system of PQs (Parliamentary Questions) as a way of acquiring information on the status of PrEP from the Sexual Health and Crisis Pregnancy Programme's Working Group on PrEP. PQs are usually reserved as the final stage in a process of advocacy if at all not least because they tend to yield extremely cautious and benign answers from government representatives, while placing a significant administrative burden on key civil servants. The perceived need for PQs may be better met by improved channels of communication between community representatives on the Working Group and their constituency.

156. Butler, S. and Mayock, P. 'An Irish solution to an Irish problem': Harm reduction and ambiguity in the drug policy of the Republic of Ireland, in International Journal of Drug Policy, 16:6 (2005), p. 421; Shane Butler, *Alcohol, Drugs and Health Promotion in Modern Ireland* (Dublin: Institute of Public Administration, 2002)
157. Nolan, A., Larkan, F, *Vectors of transnationality in the adoption of a liberal public health response to HIV and AIDS in Ireland,* Global Social Policy 16(3) · December 2015 DOI: 10.1177/1468018115620458; Nolan, A. (forthcoming May 2018), *Covert policy: the Church, the State and the gay community response to the emergence of AIDS in Ireland,* Journal of Policy History; Nolan, A., (forthcoming 2018) *Transforming School-based Sex Education Policy in the Initial Era of AIDS in Ireland,* Irish Educational Studies

4.7 Chapter Summary & Conclusions

- All participants expressed the view that PrEP should be seen as one prevention intervention among an arsenal of measures that are targeted and appropriate to the needs of the individual, and should not replace the emphasis on condom use to prevent HIV and STIs;
- PrEP is an effective public health intervention and while some participants in this study expressed reservations or concerns around how PrEP should be implemented, all contributors to this study supported the implementation of PrEP on public health grounds;
- The safety concerns posed by the online purchase and self-administration of PrEP in Ireland must immediately prompt the funding and establishment, within existing specialist sexual health clinics, of information, advice and clinical monitoring services until such time as PrEP is made available through the HSE.
- Data in the initial stages of collection by the Gay Men's Health Service (GMHS) in Dublin points to a significantly higher proportion of recreational drug use and other high risk behaviours among men attending the service compared to the Dean Street Clinic in London;
- The risk profile of other groups affected by HIV is virtually impossible to establish as the same level of behavioural surveillance is not available in Ireland although high STI incidence rates among women and patterns of risk behaviour are evident in general populations surveys;
- MSM interviewed for this study argued that Ireland has become a `sex positive' culture in recent years with an ever increasing number of sex parties available: as such, sexual health services need to evolve in parallel with changes in culture and society;
- In light of prevention interventions in other areas of healthcare that are comparable to PrEP, it seems improbable that PrEP will be made available free-of-charge if implementation is taken to scale;
- A number of participants in this study raised the need for increased behavioural surveillance investment to help identify and better off-set risk by early intervention. Improved surveillance is also required to enable Ireland to both achieve and report against its 90-90-90 commitments: by 2020, 90% of all people living with HIV will know their HIV status, 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy, and 90% of all people receiving antiretroviral therapy will have achieved viral suppression;
- To fail to provide PrEP to non-Irish citizens may potentially offset any HIV prevention gains. HIV is a policy priority for Ireland's overseas aid programme at the Department of Foreign Affairs and Trade, and the HSE has articulated a commitment to working in global solidarity with developing countries to fulfil its responsibility to achieving a universal `right to health'. Healthy Ireland: A framework for improved health and wellbeing (2013-2025) is explicitly committed to the principle of `solidarity' with resource poor countries. The Irish government's policy emphasis on a `whole-of-Government' approach to realise policy coherence between departments and sectors means

that any suggestion that non-Irish citizens may not access PrEP would contravene those policy commitments at national and international levels;

- Participants in this study overwhelmingly supported WHO 2016 guidance which advocates that PrEP be offered to all population groups at substantial risk of HIV infection in Ireland;
- The potential cost of PrEP is perceived to be a barrier to implementation in Ireland. There is a role for advocacy in challenging the HSE to explore the cost-saving potential of generic substitution of ARVs which have been found to be acceptable to the majority of patients and HIV health care providers;
- Return on Investment analysis should be considered in conjunction with budget impact and cost effectiveness analysis in the context of the 90-90-90 targets[158] - 90 per cent of people living with HIV must know their status; 90 per cent of people with diagnosed HIV infection must be on sustained antiretroviral therapy; and 90 per cent of people receiving antiretroviral therapy must have viral suppression – which may prove to be a more propitious cost benefit benchmark for PrEP implementation in Ireland;
- Advocacy platforms for PrEP might be best served by campaigns targeting key policy makers, while mobilising political champions to engage stakeholders in dialogue to help remove some of the barriers to PrEP implementation. Civil society representatives need to be prepared for media interest in PrEP with a factually based public health narrative, that is devoid of emotive arguments and rests on sound science;
- The perceived need for PQs may be better met by improved channels of communication between community representatives on the Working Group and their constituency.

158 Ireland is currently not in a position to report against these targets

5. Policy Options

The primary aim of this literature scoping and policy options review has been to provide evidence-based guidance to both *HIVI* and the *GHN* on PrEP efficacy, while establishing the views of key populations affected by HIV, and stakeholders directly and indirectly involved in the provision of HIV services throughout Ireland. It is intended to enable an informed policy platform to realise effective advocacy for PrEP and as such this chapter will commence with an overview of the policy framework for PrEP at global, regional and national levels before concluding with policy options as determined by this review. Section 5.2 spotlights a combination of evidence-based findings from Chapter 3 combined with Irish-specific findings presented in Chapter 4 to present policy options and considerations for PrEP policy dialogue and advocacy. Detailed findings are contained in the body of this paper with highlights summarised here.

5.1 Global, Regional and National Policy Framework for PrEP

The transnational dimensions of health, in particular, are facilitated and realised through governance structures which emphasise global and local connectivity[159]. Transnationalism and the multidimensionality of policy transfer intensifies the global-local nexus for HIV and AIDS policy. Ireland emphasises on an *all-of-government* approach with policy coherence prioritised between the HSE and Irish Aid's global health and HIV partnership portfolio, illustrating the extent to which health policy is increasingly perceived to be international in scope. PrEP is already governed – directly and indirectly - by international policy instruments that have been ratified by Ireland. The most recent of these, the 2016 United Nations Political Declaration on HIV and AIDS: On the Fast-Track to Accelerate the Fight against HIV and to End the AIDS Epidemic by 2030, was adopted at the United Nations General Assembly High-Level Meeting on AIDS in June 2016, and mandated UNAIDS to support countries in reporting on the commitments in the Political Declaration[160]. Paragraph 48 is explicit in its endorsement of PrEP:

> 48. (We) Welcome the important progress achieved in research for new biomedical tools for prevention, notably regarding treatment as prevention, pre-exposure prophylaxis and antiretroviral-based microbicides and voluntary medical male circumcision, but also recognize that research and development must be accelerated, including for long-acting formulations of pre-exposure prophylaxis, preventive and therapeutic HIV vaccines and curative interventions;

159. Obinger, H., Schmitt, C., Starkea, P., *Policy Diffusion and Policy Transfer in Comparative Welfare State Research*, Social Policy & Administration, Vol. 47, NO. 1, February 2013, PP. 111–129; Browne, T., Craddock, S., Ingram, A., *Critical Interventions in Global Health: Governmentality, Risk, and Assemblage*, Annals of the Association of American Geographers, 102(5) 2012, pp. 1182–1189; Kanbur, R., Sumner, A., *Poor Countries or Poor People? Development Assistance and the New Geography of Global Poverty*, Journal of International Development J. Int. Dev. 24, 686–695 (2012); Dolowitz, D., Marsh, D., *Learning from Abroad: The Role of Policy Transfer in Contemporary Policy-Making*, Governance: An International Journal of Policy and Administration, Vol. 13, No. 1, January 2000; Yeates, N., *Social Politics and Policy in an Era of Globalization: Critical Reflections*, Social Policy and Administration, 1999, 33 (4): p372-389;

160. This Political Declaration was built on three previous political declarations: the 2001 Declaration of Commitment on HIV/ AIDS, the 2006 Political Declaration on HIV/AIDS and the 2011 Political Declaration on HIV and AIDS. Member States unanimously adopted the 2001 Declaration at the United Nations General Assembly Special Session on HIV/ AIDS in 2001. The 2001 Declaration reflected global consensus on a comprehensive framework to achieve Millennium Development Goal 6: halting and beginning to reverse the HIV epidemic by 2015.

While four sub-paragraphs of paragraph 62 directly and indirectly endorse PrEP interventions, particularly in areas of high incidence, paragraph 62g is explicit in its commitment to the adoption of evidence-based prevention measures "that reflect the specific nature of each country's epidemic by focusing on geographic locations, social networks and populations that are at higher risk of HIV infection." However, this paragraph also places particular emphasis on the need for each country to ensure that "resources for HIV prevention are spent as cost-effectively as possible and to ensure that particular attention is paid to those populations at highest risk, depending on local circumstances." this is likely to affect those who believe that PrEP should be available to anyone who wishes to take it (see section 4.6 – Who should get PrEP?)

UNAIDS is a key partner in Ireland's *Global Health and HIV Portfolio* to which overseas development assistance commits €2.7 million per annum[161] and is therefore committed to 90-90-90 targets by 2020: 90% of all people living with HIV will know their HIV status, 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy, and 90% of all people receiving antiretroviral therapy will have achieved viral suppression. To fast track actions to achieve the 2020 targets, the new *Action plan for the health sector response to HIV in the WHO European Region 2017-2022* emphasises the need for member states to optimise prevention efforts through the prioritisation of evidence-based HIV prevention urging a particular focus on key populations, 'with inclusion of novel approaches such as pre-exposure prophylaxis (PrEP) for populations at substantial risk of HIV acquisition'[162]

The Dublin Declaration, 2004 commits member states in Europe and Central Asia to act collectively in tackling the HIV/AIDS epidemic, setting out a number of actions to accelerate the achievement of this commitment. The countries also committed to closely monitor and evaluate the implementation of the actions outlined in the Declaration, along with those of the Declaration of Commitment of the United Nations General Assembly Session on HIV/AIDS. As such, the most recent special report under the Dublin Declaration 2016 particularly emphasises the need to reduce HIV infections in Europe as "Coverage of key prevention interventions, including condom promotion and distribution, behaviour change interventions, pre-exposure prophylaxis (PrEP) and harm reduction for people who inject drugs remains too low in many countries to make a real impact."[163]

At national level, policy provision for PrEP is contained in the National Sexual Health Strategy 2015-2020 under action 3.29: "Develop and implement guidelines for the appropriate use of antiretroviral therapy in HIV prevention."

161. 2015 budget allocation
162. WHO Europe, *Action plan for the health sector response to HIV in the WHO European Region,* 2017-2022, Geneva
163. ECDC, *The status of the HIV response in the European Union/European Economic Area,* Dublin Declaration report, 2016

5.2 Policy options for PrEP Advocacy in Ireland: key recommendations and conclusions

This exploratory exercise has proved to have commenced with a misnomer in that policy options for the introduction of PrEP into Ireland as indicated by the evidence base governing PrEP efficacy; the global, regional and national policy context; the high risk profile of most at-risk populations; the epidemiology of HIV in Ireland, which reflects broader European trends; the views of health care providers and key stakeholders working directly and indirectly in HIV, and the views of potential end users, all point to one policy option: This review finds overwhelming evidence supporting the introduction of PrEP for populations at substantial risk of HIV in Ireland as part of a comprehensive package of HIV prevention interventions.

The evidence presented in Chapter 4 points to an albeit limited level of self-administered PrEP use among MSM, but which nonetheless requires urgent intervention by statutory services in collaboration with civil society who may be well placed to provide immediate information, education and guidance for PrEP users. It is recommended as a first step, that the safety concerns posed by the online purchase and self-administration of PrEP in Ireland must immediately prompt the funding and establishment, within existing specialist sexual health clinics, of information, advice and clinical monitoring services until such time as PrEP is made available through the HSE.

The evidence base, while currently dependent on RCTs and a small number of implementation studies, which are increasing in number, clearly demonstrates PrEP efficacy particularly for MSM and transsexual women. Two RCTs (PROUD and IPERGAY) demonstrated that once-daily Truvada® may reduce the relative risk of acquiring HIV infection in MSM and trans women by 86%. As indicated in Chapter 4, data in the initial stages of collection by the GMHS in Dublin points to a high proportion of recreational drug use while a significant proportion of men are reporting that they do not use condoms for either insertive or receptive anal intercourse. In sero-discordant heterosexual couples, the relative risk of HIV was reduced by 75%: it should be borne in mind; however, that the Partners' trial funded by the Bill and Melinda Gates Foundation was conducted in Kenya and Uganda which are countries characterised by generalised epidemics and as such may not be transferable to an Irish context. Equally, the Bangkok Tenofovir Study is the only large-scale study conducted with PWID demonstrating a 48.9% reduction in HIV incidence but its findings may also not be transferable to an Irish context, where HIV incidence is low among PWID due to generally successful harm reduction interventions. Contributors to this study from the drugs sector were reluctant to endorse PrEP for PWID due to the paucity of implementation evidence. It should be noted that NHS England's proposed eligibility and exclusion criteria of individuals whose injecting drug use is their only risk of HIV acquisition have been excluded from proposed PrEP provision, on the grounds that "current HIV incidence in this group in the UK is too low

for PrEP to be cost effective"[164]. While the risk profile of other groups affected by HIV is virtually impossible to establish as the same level of behavioural surveillance is not available in Ireland, high STI incidence rates among women and patterns of risk behaviour are evident in general population surveys. Consequently notwithstanding the absence of context-transferable evidence for key populations other than MSM and trans women, the World Health Organisation recommends that oral PrEP should be offered as an additional prevention choice for all people at substantial risk of HIV as part of a combination of prevention approaches, which is widely supported by contributors to this review, while recognising that the primary beneficiaries of potential PrEP introduction will be MSM in practice.

PrEP in practice is marked by a number of unknowns with regard to adherence levels, the potential for risk compensation, and of particular concern to health care providers interviewed in this study, the capacity of an already over-stretched sexual health service to absorb a cohort of HIV-negative clients. Implementation research is needed in diverse settings not least in terms of supporting adherence and the capacity of already over-stretched health systems to respond effectively to increased demand. It is also largely unknown how PrEP may affect behavioural and social outcomes in the medium to long term. The RCTs described here noted few changes in terms of sexual behaviours but trials provide a high level of psycho-social support that may not be replicated in real-world settings. WHO notes that while daily dosing was the preferred choice for the majority of users, implementation research is required to establish how best to adapt PrEP to diverse and changing sexual practices. It is also required to establish whether frequent HIV and renal monitoring could be reduced; how best to maximise support for PrEP users while minimising cost, while integrating PrEP into existing services.

The vast majority of contributors to this review favoured an implementation or demonstration study as a first step not least because the budget impact can be contained, any unintended consequences more easily offset and issues resolved before PrEP is taken to scale. Concerns about the cost of PrEP were frequently cited as a perceived barrier to PrEP implementation: this is a Europe-wide concern, not just an Irish one. Clinical interventions are not cost-neutral and the actual cost of once-daily Truvada® for PrEP is likely to impact significantly on the budget for HIV and sexual health. An implementation trail would facilitate cost-containment until such time as generic substitutions are licensed for PrEP in Europe. As a first step, it is recommended that GHN and HIVI support the introduction of an implementation study, which may be more easily and speedily sanctioned, until such time as PrEP may be taken to scale.

The cost-effectiveness of PrEP appears to be particularly sensitive to key variables such as HIV incidence, levels of adherence, willingness to use PrEP, risk behaviours, the cost of drugs and other clinical interventions

164. NHS England, *Clinical Commissioning Policy Proposition: Pre-exposure prophylaxis (PrEP) to prevent the acquisition of HIV in adults Reference:* November 2016 [draft]

required to support PrEP programmes: as such cost-effectiveness studies conducted in other jurisdictions are of limited value to the Irish context. The potential cost of PrEP is perceived to be a barrier to implementation in Ireland. In the medium to long term, there is a role for advocacy in challenging the HSE to explore the cost-saving potential of generic substitution of ARVs which have been found to be acceptable to patients and HIV health care providers, while Return on Investment analysis should be considered in conjunction with budget impact and cost effectiveness analysis which may prove to be a more propitious cost benefit benchmark for PrEP implementation in Ireland.

Coupled with concerns about the cost of PrEP and the capacity of the health system to respond to the clinical requirements of PrEP introduction, some participants raised questions as to whether PrEP should be made available to non-Irish citizens. This is problematic in public health terms given that at least 55% of HIV cases diagnosed in Ireland originate from other countries. [165] Additionally, 35% (n=94) of people testing HIV+ in Ireland in 2015 were born in sub-Saharan Africa, and over half (53%) of female cases were born in sub-Saharan Africa. To fail to provide PrEP to non-Irish citizens may potentially offset any HIV prevention gains. HIV is a policy priority for Ireland's overseas aid programme at the Department of Foreign Affairs and Trade, and the HSE has articulated a commitment to working in global solidarity with developing countries to fulfil its responsibility to achieving a universal 'right to health'. *Healthy Ireland: A framework for improved health and wellbeing (2013-2025)* is explicitly committed to the principle of 'solidarity' with resource poor countries. Importantly, the Irish government's policy emphasis on a 'whole-of-Government' approach to realise policy coherence between departments and sectors means that any suggestion that non-Irish citizens may not access PrEP would contravene those policy commitments at national and international levels. It is recommended that policy advocacy must ensure that PrEP implementation does not operate eligibility on the basis of citizenship but works to ensure inclusiveness on public health terms and in the interests of a 'whole-of-government' approach.

Europe's Action plan for the health sector response to *HIV in the WHO European Region, 2017-2022* urges member states to "collect and analyse timely and high-quality epidemiological data to understand how, where and among whom new HIV infections are occurring, develop HIV estimates, monitor risk behaviours and estimate the size of key populations in need of services."[166] Ireland's failure to prioritise and invest in the collection of epidemiological data is a significant risk to cost-effectiveness, budget impact and service planning estimates for PrEP and other interventions, while also precluding full engagement and reporting against high profile international commitments, including 90-90-90 targets. A number of participants in this study raised the need for increased behavioural surveillance investment to help identify and better off-set risk by early

165. Geographic origin is unknown in 15% of cases (HPSC, 2015, p.12-13)
166. WHO Europe, 2016, p.8

intervention. Part of the challenge to the statutory services in responding to new technologies like PrEP is that reliable estimates of the number of people likely to be eligible are wanting due to lack of epidemiological data and evidence supporting implementation. There is a role for civil society to champion improved surveillance systems in Ireland so that new technologies (like PrEP) are supported by robust epidemiological data and evidence.

Civil society advocacy is central to the realisation of particularly contested policy issues, and plays a key role in holding government and statutory service providers to account. While advocates for PrEP implementation are an important part of the process, Ireland's relatively conservative political culture points to a generally cautious approach to policy change for sexual health. Views were divided on the best approach to policy advocacy for PrEP but it is herein suggested that advocacy platforms for PrEP might be best served by campaigns targeting key policy makers, while mobilising political champions to engage stakeholders in dialogue to help remove some of the barriers to PrEP implementation. Civil society representatives need to be prepared for media interest in PrEP with a factually based public health narrative that is devoid of emotive arguments and rests on sound science.

It is a flawed rationale that renders the statutory services ever the subject of complaint when private interests like Gilead Science Inc are the primary reason why PrEP is not likely to be affordable. Gilead's application for an SPC for Truvada® is the single most significant threat to taking PrEP to scale in Europe not just in Ireland and this issue requires strong civil society engagement.

Conclusion

A combination of the evidence for PrEP efficacy coupled with the risk profile of key populations in Ireland, increasing incidence of HIV reflecting broader European trends, PrEP's policy coherence with Ireland's international policy position, and a high level of support for PrEP implementation among key stakeholders and potential end-users, points to the need for immediate steps to be taken to make PrEP available to key populations at substantial risk of HIV acquisition as part of a comprehensive package of HIV prevention measures. At an absolute minimum, the failure to provide HIV testing and clinical monitoring to MSM who are self-purchasing and administering PrEP is a risk to the individual and broader public health. While multidrug resistance levels are generally low, the risks are increased if people with an undiagnosed HIV infection are acquiring PrEP online. The global, regional and national policy context actively advocates PrEP implementation and the requirements to prioritise HIV prevention in member states of the European Union where sexually acquired HIV incidence rates are raising exponentially must render PrEP a policy priority in Ireland.

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Appendix A:

Terms of Reference provided by HIV Ireland Ltd and the Gay Health Network to guide Pre-exposure Prophylaxis (PrEP) Scoping and Policy Options Review

a. We need guidance on PrEP!
b. Your paper will help inform the decision making and future position of HIVI on PrEP.
c. The paper will be of sufficient integrity to be accepted and respected by external stakeholders in debates on the pros and cons of PrEP and its introduction into Ireland.
d. The paper will explore the main issues for and against PrEP and the experience of introducing PrEP in other jurisdictions.
e. The paper in particular will identify barriers to PrEP, both actual and perceived, and provide responses to these barriers.
f. The paper will explore PrEP within an Irish context i.e. any unique Irish factors relative to international experience of introducing PrEP.
g. The paper will explore PrEP and MSM but also other target groups where PrEP would be relevant (e.g. IVDU's, Sex Workers).
h. The paper will aim to engage with end users.
i. The paper will provide an objective and informed voice that can influence Government policy.

Appendix B: PrEP Desk Review Synthesis

Research Parameters	Themes				
	Public health effectiveness	**Adherence**	**Feasibility/knowledge/ willingness to take PrEP**	**Risks/Risk Compensation**	**Cost/cost effectiveness**
Guidance on PrEP	1. WHO: Oral PrEP containing TDF should be offered as an additional prevention choice for people **at substantial risk of HIV infection**[167] as part of combination HIV prevention approaches. This is a strong recommendation, supported by high-quality evidence; 2. PrEP should not displace or threaten the implementation of effective and well-established HIV prevention interventions, such as condom programming and harm reduction (WHO, 2016); 3. There is a need for synergy & a broad approach to harm reduction programming to include the offer of PrEP to address both sexual and injection-related health risks (Coleman et al 2016); 4. On 22 August 2016, the European Commission officially granted marketing authorisation for once daily Truvada® in combination with safer-sex practices to reduce the risk of sexually acquired HIV-1 infection among uninfected adults at high risk. The marketing authorization allows for the marketing of Truvada® for PrEP in all 28 countries of the European Union, subject to national regulatory authority approval of required pharmaco vigilance materials in each country.	1. Level of protection is strongly correlated with adherence. 12 trials on the effectiveness of oral PrEP have been conducted among serodiscordant couples, heterosexual men, women, MSM, Trans & PWID-all demonstrate that when adherence is high, significant levels of efficacy have been achieved. 2. Perfect compliance is not required to obtain benefits of PrEP but timing relative to HIV exposure is NB	1. A number of studies note high levels of acceptability and willingness to use PrEP but low levels of uptake; 2. PrEP is recommended for those facing a genuinely high risk of acquiring HIV. The benefit to be obtained from PrEP depends on the incidence rate of HIV and this factor has to be balanced against the (small) risks of the medication. Adverse events are infrequent, the benefits of treatment for those living with HIV are very high, whereas the benefits of PrEP to those who are HIV-negative depend entirely on their chance of acquiring infection; 3. Koechlin et al, 2016 systemmatic review identified strong interest & support for PrEP use amongst most populations at risk of HIV infection, and lesser (though still fairly high) interest among people who inject drugs. Notably, literature on heterosexual men, transgender people, adolescent girls and young women, and people who inject drugs is limited, thus calling for more research;	1. Literature does not provide a definite consensus on risk compensation but accurate to state that there is no conclusive evidence to support the claim that PrEP leads to risk compensation in sexual practices, such as decreased condom use or more sexual partners; 2. Given concerns about risk compensation, normative bodies continue to maintain that PrEP should be used together with condoms;	1. The HIV incidence threshold for cost-saving implementation of PrEP will vary, depending on the relative costs of PrEP versus treatment for HIV infection and the anticipated uptake & effectiveness of PrEP. PrEP costs are not limited to the cost of drugs and include costs for clinic staff, laboratory testing, pharmacy services, community education, provider education and monitoring and evaluation; 2. A systematic review of 13 cost-effectiveness studies found that key considerations to address in assessing cost-effectiveness of PrEP are cost, epidemic context, individual adherence level, PrEP programme coverage and prioritization strategy.

167 Substantial risk of HIV infection is provisionally defined as HIV incidence around 3 per 100 person-years or higher in the absence of PrEP (measure of incidence rates – result of events divided by time, in this case possibly 3 infections in group of 100 people in one year) HIV incidence higher than 2 per 100 person-years considered sufficient to warrant offering oral PrEP in the recommendations issued by the International Antiviral Society – USA expert panel in 2014 . Thresholds for offering PrEP may vary depending on a variety of considerations, including epidemiological context or trends, available resources and the relative costs, feasibility and demand for PrEP.

Research Parameters	Themes				
	Public health effectiveness	**Adherence**	**Feasibility/knowledge/ willingness to take PrEP**	**Risks/Risk Compensation**	**Cost/cost effectiveness**
Pros/in favour of PrEP	1. Stepping stone to the ultimate goal of HIV vaccine; 2. Low level of adverse events reported; 3. The risk of drug resistance is low but in case of large-scale implementation is unknown; 4. Access provides opps for accessing sexual health services, & people at substantial HIV risk often slip through gaps & have fewer HIV prevention options; 5. New infections among MSM in UK are down 40% - Lancet 2017 suggests that while, "The decline in infections cannot with certainty be linked to PrEP, the temporal correlation is compelling."	1. Different effectiveness findings between studies can be explained by differing adherence levels; 2. Low adherence levels in the efficacy trials raised concerns about the feasibility of PrEP as a public health strategy but recognised that real-life adherence to a product of demonstrated effectiveness would probably be different from adherence in a placebo-controlled trial, where participants are told that intervention efficacy is still unclear and that half of them are receiving a placebo.	1. The impact of PrEP on sexual practices may vary according to social & cultural contexts but may also provide opps for understanding how PrEP influences sexual practices leading to improved SH outcomes.	1. Koechlin et al 2016 systematic review found no significant effect on sexual behaviour with PrEP use – funded by WHO	1. Some trials find PrEP favourable in terms of cost-effectiveness but this finding is not transferable as CE is particularly context and epidemiologically dependent.
Cons/ opposition to PrEP	1. Neither cost nor value neutral; 2. Several studies noted subclinical declines in renal functioning and bone mineral density among PrEP users which reversed when PrEP discontinued; 3. Stigma is a driver of HIV and could be decreased or increased depending on how PrEP is implemented; 4. Resistance among some health care providers – ID staff do not manage HIV neg populations; 5. Destabilized the social norm of ``100% condom use,''; 6. Few side-effects reported - Mild nausea, diarrhoea, bloating and headache were reported in the first month by less than 1 in 10 people. These side effects then usually cease.	1. Studies with low adherence show no effect on reducing HIV; 2. Social & behavioural factors critical to compliance; 3. Younger populations have poorer adherence; 4. two people have become HIV positive even though they were adhering to PrEP. This was because they caught HIV from a partner who was already resistant to the drugs in PrEP. This is a very rare event.	1. The impact of PrEP may also realise adverse behavioural & social outcomes although trials have not brought any to light as yet; 2. Issues of equality & access are raised by PrEP; 3. Low levels of PrEP awareness reported across Celtic nations. Only one-third of high-risk MSM had heard of PrEP but over one-half would be willing to take a daily pill to prevent HIV infection.	1. IPERGAY trial, provided intensive counselling on the importance of safe sex and condom distribution & moreover, trail participants are selected assuming that they do not use condoms consistently and have multiple partners => an increased cost implication to minimise risk compensation.	1. Cost implications of M&E, HIV testing, STI screening, renal, HBV monitoring, adherence support etc. 2. Cost effectiveness relative to low incidence rate?

Research Parameters	Themes				
	Public health effectiveness	**Adherence**	**Feasibility/knowledge/ willingness to take PrEP**	**Risks/Risk Compensation**	**Cost/cost effectiveness**
Experience of introducing PrEP in other jurisdictions	1. Confining to MSM is more stigmatizing; 2. Australian guidance differs from guidelines in the US, SA, & EU in its approach to determining eligibility for PrEP-targets daily PrEP to those at high and ongoing risk of HIV infection, which in the Australian context is mainly MSM-considering expansion to those at moderate risk of HIV as access to PrEP improves.	1. Data from clinical trials and others indicate that most participants did not take oral PrEP as prescribed. Although adherence observed in clinical trials is likely to vary considerably from levels in the ``real world,'' trial results suggest that implementation programmes need to greatly increase adherence levels in order to maximize the likelihood that PrEP will have a population-level impact; 2. Despite the initial reports of PrEP efficacy, concerns were raised because of the less-than-optimal adherence in iPrEx (approximately 51% had detectable drug levels in their blood) and two PrEP studies in African women that did not demonstrate protection; US community-based clinics have reported high levels of patient adherence to PrEP.	1. Much of the data on the acceptability of PrEP is based on willingness to take PrEP (i.e., hypothetical receptivity) rather than actual intentions (i.e., planned behavioral action). 2. Intending to begin PrEP in US most common among men most at risk for HIV. 3. PEP used for PrEP – evidence of clinic hopping in EU countries & pill sharing; 4. Purchasing online at full cost/ or generic without medical supervision is widespread across Europe; 5. Some EU clinics offering drug testing to ensure quality of product purchased online;		1. In generalized epidemics, priority for the use of PrEP to people at substantial risk of acquiring HIV infection increases impact but some studies found PrEP to be cost-effective within the context of ART expansion only & others found no benefit; 2. In concentrated epidemics results vary widely. Studies have found PrEP to be cost-effective, depending on the cost of the drug and delivery systems when PrEP uptake is higher among people at substantial risk; 3. Canadian study concluded that 'on demand' (as opposed to continuous) PrEP strategy ranges from cost saving to largely cost-effective;

Research Parameters	Themes				
	Public health effectiveness	**Adherence**	**Feasibility/knowledge/ willingness to take PrEP**	**Risks/Risk Compensation**	**Cost/cost effectiveness**
Barriers to PrEP, both actual and perceived	1. Many of the issues raised in argument against PrEP are identical to those invoked against female contraception, namely, cost, safety, the potential impact on sexual behaviour and the potential for unforeseen health risks associated with longterm use- not new or specific to HIV; 2. Lack of data for targeting high-risk populations; 3. Advocates of prevention among SWs & PWIDs in some jurisdictions have argued that authoritarian states could implement mandatory PrEP programmes for KPs, resulting in human rights violations, or simply in the neglect of other effective prevention interventions,; 4. Current media focus on PrEP and MSM, encourages assumption that MSM should ``be responsible and just use condoms,'' & fails to take into account of the fact that for many MSM, condoms are not a feasible option; 5. More nuanced discussion is missing about the potential benefits of PrEP for women, including female sex workers and transwomen, for whom PrEP offers a prevention strategy that is under their control; 6. PrEP will ``medicalize'' what should properly be regarded as a structural and social issue ; 7. PrEP exemplifies global economic and health disparities in an intervention that caters to affected communities in rich countries when over half the people with HIV in the world still cannot get treatment; 8. A key challenge for Europe is to meet the needs of other high-risk groups, particularly migrants, for whom the links with community-based organizations and the healthcare system are much lower than for MSM	Perception of poor adherence levels.	1. In US men intending to begin PrEP were those with the least access to it; 2. US studies found barriers based on financial, insurance, and immigration status; 3. Knowledge of PrEP is low outside clinical trials;	1. Several studies with health care personnel capture concerns about risk compensation. For several participants, this discussion took on a moralistic tone; 2. One study with non-specialist healthcare providers found that the need to discuss sexual activity to assess risk and determine whether PrEP was appropriate was perceived as a major barrier to PrEP; 3. Perception that PrEP will increase behavioural disinhibition, resulting in new HIV transmissions, whether it will promote the development of resistant strains of HIV, and/or increase rates of STDs. 4. Concerns raised regarding rates of toxicity of the medications, because side effects may be less acceptable for individuals who are otherwise healthy than for people at risk of developing HIV without medication.	1. A common problem for all countries is the cost of the drug which makes large-scale national PrEP programmes look unaffordable. This is the underlying reason that the PrEP policy has stalled in England and Wales, where the National Health Service is only willing to contribute £2M to the early implementation activities (McCormack et al 2016); 2. Cambiano et al 2015 concluded that in UK the use of PrEP for MSM during periods of condomless sex is not cost effective at current antiretroviral prices, but it would become cost-effective if drug prices are reduced after patent expiry date.

Research Parameters	Themes				
	Public health effectiveness	**Adherence**	**Feasibility/knowledge/ willingness to take PrEP**	**Risks/Risk Compensation**	**Cost/cost effectiveness**
PrEP within an Irish context	1. IRELAND: "PrEP is only available to be dispensed from one pharmacy, based in the Sexual Health clinic (GUIDE) at St. James' Hospital and comes at the full price (around €400 for a month).	1. Perception is likely to have penetrated Irish health service providers	1. PrEP Access in Europe Initiative: "It is possible for people to order generic Truvada® online to a UK address which is then redirected. Anecdotally, this passes through customs and VAT is applied before delivery with no further issues." 2. Frankis et al 2017 identified low levels of PrEP awareness across these Celtic nations. Euro Prep 92% of sexually active MSM in Ireland are PrEP aware with 72% correctly knowledgeable.		1. Offering PrEP in situations where the incidence of HIV is higher than 3 per 100 person years is expected to be cost saving in many situations – HPSC input required. 2. Transaction costs involved for liver, renal function tests, STI screening and regular HIV tests; 3. Asked if PrEP should be free of charge & covered by health insurance, 62% of respondents said yes and 3% said no. 32% felt that people who use it should pay some of the cost.
PrEP & MSM	1. PrEP in the form of daily oral tenofovir(TDF)/emtricitabine (FTC) offers 90% reduction in HIV infection with adherence. The level of protection does not differ by age, sex, regimen & mode of acquiring HIV (rectal, penile or vaginal exposure)	1. In one US study with extremely vulnerable black young MSMs used innovative methodology to generate adherence: no participant seroconverted to HIV while in the program, & despite very high risk factors in the population, adherence to PrEP was excellent; 2. Concerns about adherence for MSM abating.	1. Feasibility & high levels of awareness, knowledge and willingness to take PrEP are reported in multiple studies.	1. The PROUD study, in the UK demonstrated that PrEP is feasible and effective and is not associated with significant changes in behavioural risk. 2. Data from regular clinical practice in San Francisco indicated a 40% drop-off rate in condom use among PrEP users; 3. Initial data from demonstration studies in MSM show that people who choose to take PrEP are those who report episodes of UAI & reported PrEP adherence is already high, with no subsequent risk compensation or change from their present condom use. 4. Among MSM, PrEP may become a choice among people at risk due to condomless anal sex, who feel that a daily pill may suit them better than condoms; 5. Increases in STIs predate PrEP-in the UK rates of other STIs have been increasing for the last decade, driven largely by infections in HIV-positive MSM but accompanied by a steady increase in syphilis, gonorrhoea and chlamydia in HIV-negative MSM	1. A mathematical modelling study on the cost-effectiveness of PrEP concluded that PrEP could prevent a significant number of infections among high-risk MSM (Desai 2008). Another mathematical modelling study that evaluated the cost-effectiveness of PrEP in South Africa showed that the cost-effectiveness of PrEP relative to ART decreases rapidly as ART coverage increases beyond three times its coverage in 2010 (Pretorius 2010).

Research Parameters	Themes				
	Public health effectiveness	**Adherence**	**Feasibility/knowledge/ willingness to take PrEP**	**Risks/Risk Compensation**	**Cost/cost effectiveness**
PrEP & Trans	1. More information is needed about interactions between PrEP and hormone therapy used by transgender people; 2. Because a relatively low percent of iPrEx participants were transgender women, there are insufficient data regarding PrEP safety, acceptability and efficacy for them. The iPrEx OLE study found that TDF/FTC concentrations were, on average, lower among transgender women compared with MSM. 3. Although suboptimal medication adherence is thought to explain some of the differences, the possibility that drug-drug interactions of exogenous feminizing sex hormones could alter intercellular FTC or TDF concentrations is under study. 4. Further studies of PrEP for transgender women are needed.	1. Additional research is needed on how to support adherence, especially for adolescents, young women and transgender people;	1. The iPrEx OLE project and the Partners Demonstration Project both show that PrEP implementation is feasible for different populations, including men and women.		

Research Parameters	Themes				
	Public health effectiveness	**Adherence**	**Feasibility/knowledge/ willingness to take PrEP**	**Risks/Risk Compensation**	**Cost/cost effectiveness**
PrEP & Women incl FSW	1. Of 10 randomized PrEP trials reporting HIV outcomes, women were included in six studies and men in seven studies. PrEP was effective for both men and women. The level of protection does not differ by age, sex, regimen & mode of acquiring HIV (rectal, penile or vaginal exposure); 2. Vaginal rings – potential for negative effects from sustained release forms; 3. Potential risk of occult infection[168] – variable distribution of antiretroviral drugs at exposed mucosal sites- PrEP does not get into the vaginal tissues as well as rectal tissues; 4. Tenofovir DF as a single drug is supported by several studies for reducing risk from heterosexual (vaginal) sex; 5. PrEP does not appear to affect the effectiveness of hormonal contraception; 6. If PrEP is to be introduced FSWs it should only be done after adequate capacity building, awareness building, & within the trusted spaces of CSOs.	1. Adherence among women has been high when open-label PrEP is provided; 2. Additional research is needed on how to support adherence, especially for adolescents, young women and transgender people; 3. Despite high levels of interest in PrEP in studies in Kenya & Sth India, concerns were expressed regarding the potential stigma associated with being recognized as someone who takes pills every day; privacy around the administration of PrEP; the possibility of being identified as being HIV positive; potential adverse effects of a new medication; and challenges with daily drug adherence; 4. Long-acting agents that combine PrEP with hormonal contraceptives), may offer an additional motivation for adherence. Preclinical or early clinical studies are already under way for such strategies in women;	1. Two placebo-controlled trials among women found significant barriers to uptake and adherence, including the social stigma of being identified as living with HIV because of taking the medication, cultural barriers and lack of family or social support. 2. The iPrEx OLE project and the Partners Demonstration Project both show that PrEP implementation is feasible for different populations, including men and women;	1. Koechlin et al systematic review 2016 found some sex workers raised concerns that their colleagues might see PrEP as an opportunity to forego condoms to increase earnings; 2. Adolescent Girls/Young Women One study found 20% of young women expected to use condoms less frequently if they took PrEP	1. A recent study in US designed to assess the predictors of HIV incidence among at-risk women found an annualized HIV incidence of 0.25%. This low level of HIV incidence would make it very difficult to conduct an efficacy trial to evaluate the benefit of PrEP for high-risk US women, because thousands would need to be enrolled in order to demonstrate efficacy. Given the low HIV incidence in US women, concerns have been raised about the chronic use of PrEP (given costs and toxicities) to prevent the rare likelihood that individual women would become HIV-infected – also issue for Ireland
PrEP & PWID	1. Daily PrEP reduces risk by 70% with adherence. The level of protection does not differ by age, sex, regimen & mode of acquiring HIV (rectal, penile or vaginal exposure); 2. PrEP is recommended for PWID by the American Centres for Disease control & the WHO;	1. Poor adherence to ARV's well documented for this KP; 2. Once study found high level of adherence among prisoners & those who self-identify as high-risk (Martin, 2017); 3. Adherence unclear in Bangkok study (further research)	1. The iPrEx OLE project and the Partners Demonstration Project both show that PrEP implementation is feasible for different populations, including men and women; 2. No interaction is expected between PrEP and heroin, methadone or methamphetamine.	1. Shrestha (2017) study of 400 opioid dependent drug users, willingness to initiate PrEP was high and correlated with being at elevated risk for HIV, but anticipated higher risk behaviors in PWID group even while on PrEP.	

168 An infection recognised by secondary manisfestation. In HIV when the virus establishes a beachhead at the site of mucosal transmission but does not become detectable as systemic infection.

Research Parameters	Themes				
	Public health effectiveness	**Adherence**	**Feasibility/knowledge/ willingness to take PrEP**	**Risks/Risk Compensation**	**Cost/cost effectiveness**
PrEP & hetero and/or sero-discordant	1. The level of protection does not differ by age, sex, regimen & mode of acquiring HIV (rectal, penile or vaginal exposure); 2. The Partners Demonstration Project, showed an overall relative risk reduction of 96% in an interim analysis suggesting that the use of PrEP as a bridge in serodiscordant couples whereby the HIV-negative partner takes PrEP for protection while waiting for the HIV-positive partner to start treatment and minimize viral load is efficacious; 3. PrEP has the potential to confer agency and control on HIV-uninfected persons who heretofore have had to depend on willingness of partners to use condoms or ARV as their primary prevention strategies; 4. 1460 heterosexual HIV infections were estimated as acquired in the UK by migrants living in the UK or by those born in the UK but it is not yet clear how to identify the heterosexuals at risk who would benefit from PrEP;		1. The iPrEx OLE project and the Partners Demonstration Project both show that PrEP implementation is feasible for different populations, including men and women.		

Research Parameters	Themes				
	Public health effectiveness	**Adherence**	**Feasibility/knowledge/ willingness to take PrEP**	**Risks/Risk Compensation**	**Cost/cost effectiveness**
Outlier/ implementation Issues	1. Provider training, linking PrEP to other health & community services recommended; 2. PrEP as part of combination prevention; HIV testing; renal function testing; Hep B, adherence & pregnancy monitoring; 3. Active surveillance during PrEP scale-up is warranted; 4. PrEP reshaping the sexual landscape eg online dating sites for MSM now offer an expanding variety of options for characterizing one's HIV status - HIV-negative & on PrEP; HIV-positive & not on treatment; HIV-positive with an undetectable viral load and I don't know; 5. Governments may need to see a demonstration of partnerships to be convinced that it is easy to accommodate PrEP within existing reconfigured services (McCormack et al, 2016)		1. Additional research is needed on how best to integrate PrEP with other services. PrEP is compatible with HIV testing, HIV treatment services, sexual health services, condom provision, behavioural counselling, harm reduction, empowerment programmes, contraceptive services, reproductive health services and primary health care. For e.g., PEP started after recent exposure to HIV can be transitioned to PrEP after 28 days if there is continuing substantial risk. 2. How best to integrate PrEP into existing services is not known and may vary in different settings; 3. The CDC released clinical guidelines in May 2014 state that data on the efficacy and safety of PrEP for adolescents are insufficient, & the risks & benefits of PrEP for adolescents should be weighed carefully in the context of local laws and regulations.	1. A compromise in PrEP messaging suggested by Ca'ceres CF et al 2015 could include stating 1) PrEP does not intend to replace condoms but to add to condom protection; 2) PrEP does not protect against bacterial STIs; 3) PrEP can become especially useful for those who have difficulties with consistent condom use, as long as it is taken as prescribed.	1. Across all trials, PrEP was provided in the context of a package of HIV prevention interventions, including regular HIV testing and counselling, provision of condoms, screening and treatment for STIs, adherence counselling and other options relevant to the study population, such as access to contraception for women and methadone maintenance therapy for people who inject opioids – transaction costs?

Appendix C – List of Participants

Face-to-face interviews:

Research Participant	Contribution Status
Dr. Fiona Lyons *Clinical Lead in Sexual Health* HSE Sexual Health and Crisis Pregnancy Programme	Participated
Dr. Paddy Mallon *Infectious Disease Specialist* Mater Misericordiae University Hospital, Dublin	Participated
Dr. Jennifer Kieran *Consultant in Clinical Pharmacology and Therapeutics* *& Adjunct Professor in Clinical Pharmacology and Therapeutics*** St James Hospital & Trinity College, Dublin	Participated
Dr. Anne Marie Liddy *Specialist Registrar in General Medicine and Clinical Pharmacology and an Assistant Professor within the Department of Pharmacology and Therapeutics, Trinity College* Trinity College, Dublin	Participated
Dr. Derval Igoe *Specialist in Public Health Medicine* Health Protection Surveillance Centre	Participated
Ms. Siobhán O'Dea *Manager* Gay Men's Health Service	Participated
Lorraine Gallagher *Development Specialist* *Irish Aid Programme* Dept of Foreign Affairs and Trade	Participated
Andrew Leavitt *Activist* ACT UP Dublin	Participated
Ms. Helen Deely *Head* Sexual Health & Crisis Pregnancy Programme	Dr. Fiona Lyons on behalf of SH&CPA
Ms. Breda Gahan *Global HIV and AIDS Programme Advisor* Dochas and Concern Worldwide, Dublin	Participated
Dr. Derek Freedman MD, FRCPI *Specialist in Sexual Health, STD and HIV* STD Clinics, Dublin	Unavailable to participate
Dr. Austin M O'Carroll *General Practitioner* Mountjoy St Medical Practice, Dublin	Participated
Dr. Eamon Keenan *Consultant Psychiatrist in Substance Misuse & Clinical Leader* The HSE National Addiction Services, Dublin	Unavailable to participate
Dr. Cillian De Gascun *Consultant Virologist & Laboratory Director National Virus Reference* Laboratory, University College Dublin	Participated
Dr. Gabriel Fitzpatrick Department of Public Health, HSE East	Did not respond to invitation to interview

Telephone interviews:

Research Participant	Participant Status
Alex Phillips *Campaign & Parliamentary Officer* Terrence Higgins Trust, London	Participated
Denis Busobozi *HIV Advisor* Embassy of Ireland, Uganda	Participated by email
Maureen Ndawana African Policy Network	Unavailable for interview
International Network of People Who Use Drugs	Unavailable for interview
Kate McGrew *Coordinator* Sex Workers Alliance Ireland, Dublin	Participated
AIDS West, Galway	Did not respond to invitation to interview
Deirdre Seery *CEO* Sexual Health Centre Cork	Participated
Richard Carson *CEO* ACET Ireland, Dublin	Participated by email
Anne Mason *Manager* GOSHH (Gender Orientation Sexual Health HIV), Limerick	Did not respond to invitation to interview
Dr. Helen Tuite *Specialist in Infectious Diseases* University Hospital, Galway	Did not respond to invitation to interview
Catherine Fleming *Clinical Lecturer* Dept of Medicine NUI, Galway	Did not respond to invitation to interview
Professor Mary Horgan *Dean* School of Medicine, University College Cork	Did not respond to invitation to interview
James O'Connor HIV Advocacy and Learning	Participated
Dr. Joe Barry *Professor & Head of Department Professorial Chair in Population Health Medicine* Trinity College, Dublin	Unavailable for interview
Miriam Moriarty *Chief II Pharmacist* Genito-Urinary Medicine and Infectious Diseases St James's Hospital	Participated by email
VHI	Participated by email
Laya Health Care	No response to query received.
Dean Street Clinic, London (invitation to interview with follow-up calls)	Did not respond to invitation to interview
New York Clinics	Did not respond to invitation to interview

Focus Group Discussions

Research Participant	Contribution Status
MSM organised by Outhouse and GHN	11 men participated
Positive Now (convened on behalf of the study by Dr. Erin Nugent)	4 men/2 women

HIV Ireland is a registered charity operating at local, National and European level. The principal aim of the organisation is too improve, through a range of support services, conditions for people living with HIV and AIDS and/or Hepatitis, their families and their caregivers while further promoting sexual health in the general population.

Our mission and vision is to contribute towards a significant reduction in the incidence and prevalence of HIV in Ireland and towards the realisation of an AIDS-free generation by advocating for individuals living with HIV, preventing new HIV infections and combating HIV-related stigma and discrimination.

Since 1987 HIV Ireland has been pioneering services in sexual health education and promotion, and has consistently engaged in lobbying and campaigning in the promotion of human rights. Our approach broadly reflects a harm minimisation model which emphasises practical rather than idealised goals. In relation to practical service provision we currently operate under two headings:

Community Support

- Counselling
- 1-1 Support
- Advocacy
- Community Outreach Work
- HIV & STI Community Testing
- Capacity Building with People Living with HIV

Prevention, Education & Training

- One day workshops on HIV, STI's and Sexual Health
- Sexual Health Training for Trainers Programme (Let's Talk About... Safer Sex)
- Free Condom Service (Just Carry One Campaign)
- Social Media work and campaigning
- Network Involvement

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