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Review

Likely impact of pre-exposure prophylaxis on HIV epidemics among men who have sex with men

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Abstract. Rapid developments in the field of HIV pre-exposure prophylaxis (PrEP) with antiretrovirals offer a promise to bring HIV transmission among gay and other men who have sex with men (MSM) to zero by 2030. This review evaluates studies, which modelled the impact of PrEP on HIV diagnoses, and discusses the progress towards PrEP implementation. Studies in English, conducted after 2010 among MSM in countries of the Organization for Economic Cooperation and Development (OECD) were reviewed. Six modelling studies were included, three of which had been conducted outside the US. None of the published models showed that PrEP alone can reduce HIV diagnoses to zero and eliminate HIV transmission by 2030. However, PrEP in combination with other biomedical interventions can reduce HIV diagnoses on the population level by ~95%. Other upcoming biomedical prevention strategies may strengthen combination prevention. Access to PrEP remains limited, even in the OECD countries. Modelling studies can assist governments with decision-making about PrEP implementation and add urgency to the implementation of PrEP. More work is needed on modelling of the impact of PrEP on HIV diagnoses trends outside the US where PrEP implementation is in its early stages.

Additional keywords: combination prevention, effect, HIV/AIDS, implementation, mathematical model, pre-exposure prophylaxis (PrEP), review.

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Introduction

On 10 June 2016, the General Assembly of the United Nations reaffirmed the commitment of its member States and Governments to achieve the UNAIDS 90–90–90 treatment targets by 2020 and to end the AIDS pandemic by 2030. These targets are ambitious, but self-motivating. They show a determination of the international community to end the HIV epidemic using new biomedical prevention approaches based on testing and antiretroviral medications.[1] At the same time, the General Assembly expressed deep concerns that the HIV epidemic continues to be a global emergency, the progress in reducing HIV infection is slow and the scale-up of combination prevention programs remains limited.[2] Indeed, the global number of new HIV infections decreased only by 6% during 2010–15,[3] and there has been no decline in HIV diagnoses among gay and other men who have sex with men (MSM).[4]

In high- and middle-income nations of the Organization for Economic Cooperation and Development (OECD), HIV transmission among MSM is a major contributor to the ongoing epidemic, and in many countries, it has been growing. In 2014, in countries of Western and Central Europe and North America, 49% of new HIV infections were diagnosed among MSM,[5] while in Australia, this proportion was even higher at 75%.[6] Increases in HIV infections among MSM were observed despite significant progress towards the ambitious 90–90–90 targets set by UNAIDS for 2020, with respect to the levels of HIV testing, treatment and viral load suppression. The UK (latest available data – 2013) has achieved two out of three UNAIDS targets: 86% of people estimated to be living with HIV were diagnosed, 90% of those diagnosed received antiretroviral (ART) treatment and 90% of those on treatment had an undetectable viral load.[7] In the US (latest available data – 2011), these indicators were 86%, 43% and 81%, respectively,[8] in Australia they were 88%, 73% and 92%, respectively,[6] and similar patterns were observed in high-income European countries.[9]

This obvious disparity between the trends in HIV diagnoses and progress towards the UNAIDS 2020 targets is troubling. It points to an obvious gap in HIV prevention and a need to embrace new primary prevention methods. Among new prevention tools currently known to be effective with MSM is antiretroviral-based pre-exposure prophylaxis of HIV (PrEP). A daily pill containing tenofovir disoproxil fumarate (TDF) and emtricitabine (TDF/FTC) has successfully passed rigorous investigations in randomised clinical trials and has been shown to be safe and efficacious in preventing HIV infection in several key population groups including MSM.[10] TDF/FTC PrEP has been even more effective in open-label PrEP trials, which attracted high-risk MSM. For example, annual HIV incidence

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among MSM participants who did not receive PrEP was 8.9% and 6.6% in the UK[11] and French[12] trials, respectively. TDF/FTC PrEP reduced the risk of HIV infection by 86% in both studies. A recent review by Gilead Sciences, Inc. found zero HIV infections among PrEP users in 17 out of 32 PrEP demonstration projects internationally.[13] People at highest risk for HIV are motivated users and are most likely to use PrEP appropriately.[10,11] No major safety issues have been raised with respect to drug resistance or side-effects among TDF/FTC PrEP users.[10] Daily TDF/FTC PrEP is a promising option for primary HIV prevention and is now recommended in national or regional guidelines in the US, Europe and Australia,[3,12–14] as well as by the WHO guidelines globally.[14]

In the last 5 years, the field of HIV prevention research with PrEP has made dramatic achievements and has rapidly progressed from clinical trials to implementation research. However, despite universal optimism that PrEP holds a significant promise to downturn HIV transmission among MSM, the jury is still out on the issue as to whether PrEP can actually bring HIV transmission to zero and achieve the UNAIDS 2030 prevention target on time. To address this issue, two questions are at the focus of this review: (i) what is the potential impact of PrEP on HIV transmission among MSM?; and (ii) what do we know about current PrEP implementation?

Methods

Focus on the nations of the OECD

In recent years, increases in HIV diagnoses have been observed in many OECD countries, where epidemics are often concentrated among MSM.[15] These trends have mostly been attributed to treatment optimism among MSM and complacency as to safe drug use and sexual practices. An overhaul of HIV prevention methods among MSM is needed. As pharmacokinetics studies have shown, TDF/FTC PrEP is particularly suited for HIV prevention among MSM.[16,17] To date, most of the research on TDF/FTC PrEP among MSM has been conducted in OECD counties.[18] This part of the world is currently leading PrEP implementation efforts.

Literature search

This review is limited to publications in English after 2010 (the year when the first evidence of PrEP efficacy was published[19]). To identify all published studies that evaluated PrEP impact on HIV diagnoses among MSM, a literature search was conducted using EndNote X6 in the Web of Science (Topic Searcher, TS) combined database (Thomson Reuters, New York, NY, USA) and in PubMed. The following search terms were used: ('impact' OR 'effect') AND ('tenofovir' OR 'TDF') AND ('pre-exposure prophylaxis' OR 'preexposure prophylaxis' OR 'chemoprophylaxis' OR 'antiretroviral prophylaxis' OR 'PrEP') AND ('HIV') AND ('men who have sex with men' OR 'MSM' OR 'homosexual men') AND ('modelling'). The search and screening process is presented in Fig. 1. Thirty-four references were found and abstracts retrieved; eight publications were identified as eligible for review because they described the modelling of impact of PrEP for HIV prevention among MSM, and two were excluded. Both were conducted in non-OECD countries; one evaluated an impact of a limited PrEP access program in Peru, and the other one compared the impact of PrEP among Indian MSM where PrEP targets were based on sexual roles.[20,21] The remaining six publications were reviewed and are described in Table 1.

Review

Studies, models and input indicators

Among the selected six studies, three[22–24] focused on modelling the impact of PrEP on HIV diagnoses in the US (including one study that looked at the US and Peru MSM[22]), and the other three studies presented models for the UK,[25] Australia[26] and South Korea.[27]

As to the methods, two studies used a stochastic model, which estimated probability distributions of HIV diagnoses by allowing for random variation in one or more input indicators over time;[22,26] three studies applied deterministic models;[23–25] and one study described their method as a mathematical simulation model.[27] All six studies were selected because they modelled HIV diagnoses over time, but three of the studies also

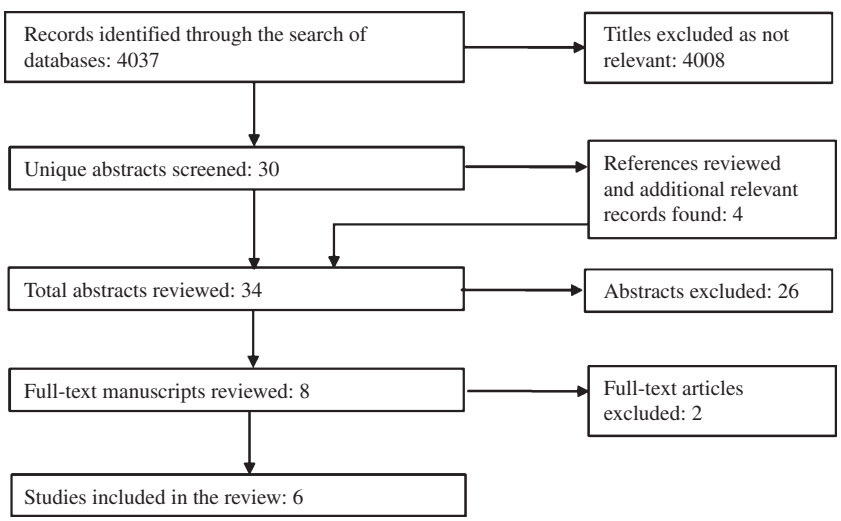

Fig. 1. Search and screening process.

Table 1. Studies on the impact of pre-exposure prophylaxis (PrEP), provided to men who have sex with men (MSM), on HIV diagnoses in countries of the Organization for Economic Cooperation and Development (OECD)

TDF/FTC, tenofovir disoproxil fumarate/emtricitabine; ART, antiretroviral treatment

Study first author	Journal, year of publication	Country/ setting	Model	Time horizon	Input indicators and assumptions	Estimated reduction in HIV diagnoses	Cost per infection averted (PIA)
Carnegie *et al.*[22]	JAIDS, 2015	US and Peru	Dynamic stochastic network models	10 years	• PrEP uptake - 20%, 40% and 60% (uptake defined as accepting at least one prescription); • Adherence - negligible, low and high (corresponding to 0, 2 and 4 doses per week, with per-contact risk reduction of 0%, 75% and 90%, respectively); • Five different targeting strategies: – Men practising receptive sex; – Men in the top two quintiles of the distribution of numbers of condomless anal intercourse contacts (CAI40); – Men in the uppermost fifth quintile (CAI20); – Men in serodiscordant partnerships; – Men in serodiscordant partnership and CAI20; • Risk compensation – increases from 50% to 300%	• Low PrEP uptake and adherence when targeting all men – **<1%;** • High PrEP uptake and adherence, targeting men who engage in receptive condomless anal sex – **~50%;** • Highest level of condomless casual sex (~1.5–7 contacts per month) – **~30%**	Not estimated
Juusola *et al.*[23]	Ann Intern Med, 2012	US	Deterministic dynamic compartmental model	20 years	• MSM population – 4.3 million; • PrEP coverage – 20%; • PrEP efficacy – 44%; • Assumptions: – Behaviour – no change in partner numbers or condom use; – Annual testing coverage among MSM – 67%; – Reduction in risk behaviour due to testing/counselling – 20%; • Cost of TDF/FTC PrEP US$ 776 per person per month	• 100% of MSM start PrEP – **51%;** • 20% of MSM start PrEP – **13%**; • 100% of *high-risk* MSM start PrEP – **52%**; • 20% of *high-risk* MSM start PrEP – **13%**.	• PrEP accessible to all MSM - US$ 1.6 million PIA (249 156 infections averted, 51% from status quo); • Prioritisation of PrEP to all high-risk MSM - US$0.6 million PIA (167 143 infections averted, 34% from status quo); • Prioritisation of PrEP to 20% of high-risk MSM - US$0.4 million PIA (41 061 infections averted, 8% from status quo)

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Table 1. (*continued*)

Study first author	Journal, year of publication	Country/ setting	Model	Time horizon	Input indicators and assumptions	Estimated reduction in HIV diagnoses	Cost per infection averted (PIA)
Kessler *et al.*[24]	AIDS, 2014	US	Equilibrium results from a Monte Carlo simulation of HIV progression and a deterministic compartmental model	20 years	• Proportion of men who are MSM – 6%; • PrEP uptake – 50%; • Adherence – 63%; • PrEP efficacy – 44%; • Assumptions: – Behaviour – probability of multiple partnerships (sexually active MSM) 44%; – Annual testing coverage – 31%; – cost of TDF/FTC PrEP US$ 806 per person per month	• 50% of all MSM start PrEP – **19%**; • 50% of *high-risk* MSM start PrEP – **15%**; • 70–100% of high-risk MSM start PrEP and cost is reduced by 50% – **40%**	• Prioritisation of PrEP to high-risk MSM – US$ 1.1 million PIA (8390 infections averted); • To all MSM – US$ 1.6 million PIA (10 989 infections averted)
Kim *et al.*[27]	PLoS ONE, 2014	South Korea	Mathematical model, projection - up to 40 years	5-year increments up to 40 years	• PrEP efficacy - 44%; • Seven scenarios compared with current situation, five of them included PrEP: Scenario 1: PrEP + unsafe sex behaviour does not increase; Scenario 2: PrEP + 10% increase in unsafe sex; Scenario 3:) PrEP + 20% increase in unsafe sex; Scenario 4: PrEP + 30% increase in unsafe sex; Scenario 5: Combination prevention intervention (PrEP plus 99% of HIV+ men are diagnosed and on ART within a year of being infected)	Impact in 10 years: • Scenario 1 – **77%**; • Scenario 2 – **70%**; • Scenario 3 – **61%**; • Scenario 4 – **51%**; • Scenario 5 with no change in unsafe behaviour – **95.9%**	Not estimated
Punyacharoensin *et al.*[25]	Lancet HIV, 2016	UK	Deterministic partnership-based mathematical model. Seven combinations of interventions were compared, including PrEP	2014–2020	• PrEP coverage – 25%, 50%, 75% and 100%; • PrEP effectiveness – 20%, 40%, 60%, 80% and 100%; • Behaviour: – Low sexual activity (on a verage, <1 new male sexual partner per year) and high sexual activity (>1 new sexual partner a year); – Two types of sexual partnerships: one-off and repeat partnerships	• All MSM start PrEP – **59%** (9955 infections averted); • All high-activity MSM start PrEP – **51%** (8665 infections averted) • On average, a 1% increase in PrEP coverage led to an increase of 1.9% in effect. A 1% increase in PrEP effectiveness led to an increase of 1.25% in effect	Not estimated

Schneider *et al.*[26]	Clin Infect Dis; 2014	New South Wales, Australia	Stochastic agent-based model	10 years (2010–2020)	• PrEP coverage – 10–30%, 15–30% of MSM with >10–50 sexual partners per 6 months, and 15–30% of HIV-negative MSM in discordant regular partnerships; • PrEP adherence – 75% (defined as drug detected in blood); • PrEP efficacy – among individuals who are adherent, 95% against wild virus and 40% against PrEP-drug resistant virus; • Assumptions: – Behaviour – no change in number of partners or unsafe sex	• 30% of all MSM start PrEP – **30%**; • A combination of all available interventions including PrEP – **96%**	• All MSM have access to PrEP – AUS$ 2.1 (US$ 1.6) million PIA (535 infections averted); • Prioritisation of PrEP to 30% of high-risk MSM – AU$ 2.5 (US$ 1.8) million PIA (718 infections averted)

presented their evaluation of the cost per one infection averted (cost PIA, estimated from the provider perspective in all three cases).[23,24,26] Cost PIA is also included in Table 1.

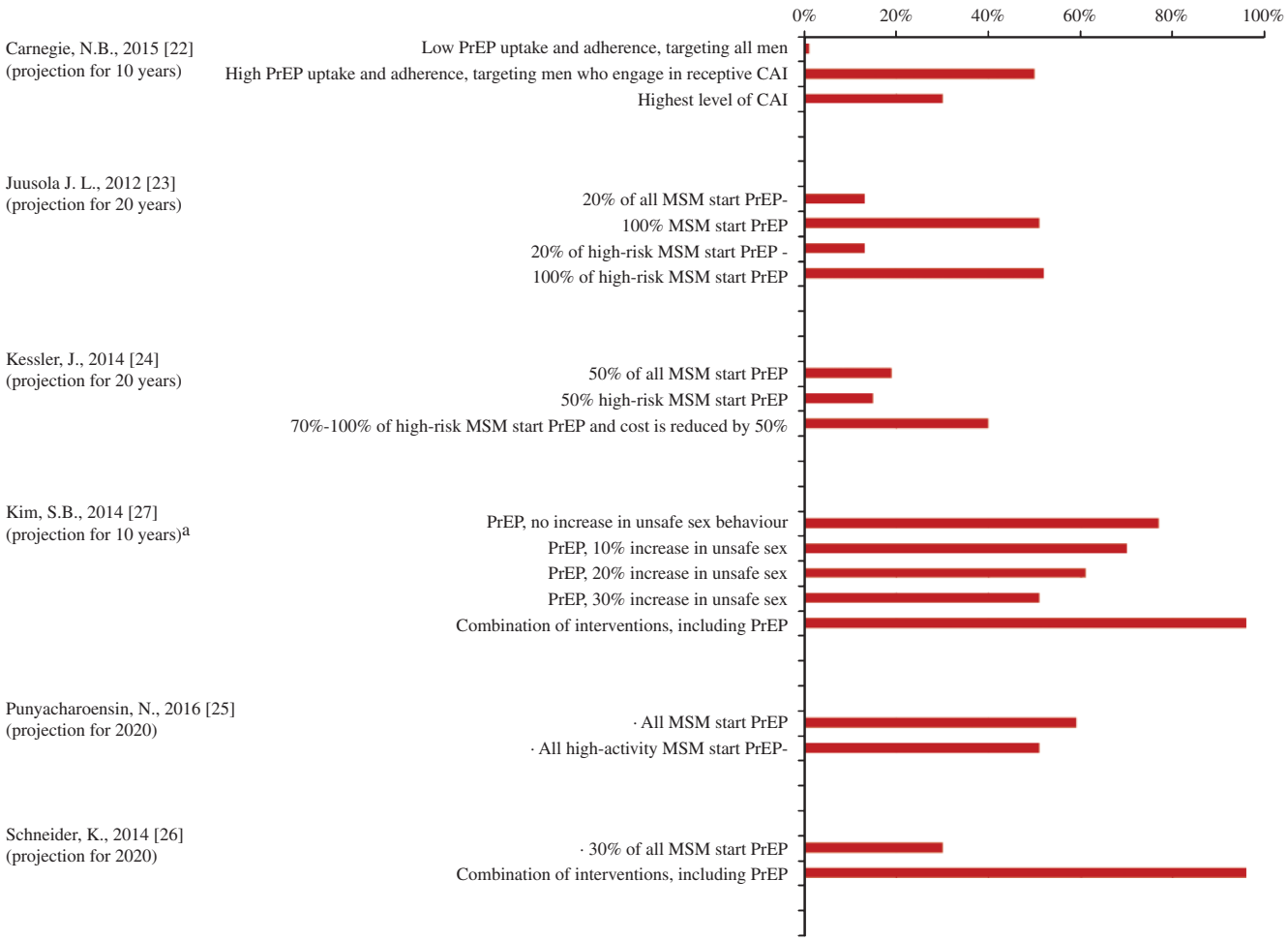
The key input indicators included PrEP efficacy, and assumptions about coverage, adherence, HIV testing and/or behaviour change, as well as a concurrent use of other HIV prevention strategies. Three out of six modelling studies, mainly published in the earlier days of PrEP trials (in 2012[23] and 2014[24,27]), included a PrEP efficacy of 44% in their models. This was the finding of the intent-to-treat analysis from the iPrEx study (also known as the *Chemoprophylaxis for HIV Prevention in Men* trial or *the PrEP Initiative*).[19] Modelling studies conducted later (2014–2016[22,25,26]) took on board the newly emerging evidence from the French–Canadian trial, IPERGAY,[12,28] and the UK demonstration study, PROUD;[11,29] both showed a PrEP efficacy of 86% (that is higher than expected at the time). Carnegie *et al.* imputed per-contact HIV-risk reduction of 0%, 75% and 90%.[22] Schneider *et al.*[26] used 95% efficacy against wild virus and 40% efficacy against PrEP-drug resistant virus. The most recent study by Punyacharoensin *et al.* took yet another approach, assessing PrEP effectiveness from 0% to 100%, with 20% increments.[25]

As to PrEP coverage, the earliest published study in this set[23] considered a PrEP coverage of 20%, while later studies considered a range of higher coverage scenarios. For instance, the latest study, published in 2016, looked at PrEP coverage of 25%, 50%, 75% and 100% in comparison with no PrEP use.[25] As to adherence, Kessler *et al.*[24] and Schneider *et al.*[26] considered adherence of 63% and 75%, respectively, while Carnegie *et al.* used adherence cut-offs of zero, two and four pills per week, with a corresponding per-contact risk reduction of 0%, 75% and 90%, respectively.[22]

Two studies considered an increase in unsafe risk behaviour over time,[22,27] including one that tested an increase in risk compensation from 50% to 300%, while other studies assumed no change in behaviour, and one study (published in 2012)[23] that assumed a reduction in risk behaviour due to HIV testing and counselling. Interestingly, the US studies included two very differing assumptions about annual texting probability: 31% in Kessler *et al.*[24] and 67% in Juusola *et al.*[23]

Potential impact of PrEP on HIV transmission among MSM

Among the six reviewed modelling studies, three made projections as to the impact of PrEP on HIV diagnoses for up to 10 years, with potential effect by 2020 (Fig. 2 and Table 1);[22,25,26] two used a time horizon of 20 years (with effect by 2030);[23,24] and one looked as far as 40 years ahead (using 5-year increments).[27] None of these models showed PrEP alone to be able to reduce HIV diagnoses to zero, regardless of the time horizon. Only in combination with other available HIV prevention strategies, including early treatment as prevention, was PrEP able to approach the HIV prevention goal. While this was predicted by two studies, their timeframes were different; one predicted it was possible in 10 years,[26] while the other one forecast this outcome would take 20 years.[27] In general, the impact of PrEP on HIV diagnoses varied broadly. An intervention with low uptake of PrEP and low levels of



a - Kim *et al* lade projections for 40 years with 5-year increments. Presented here is their projection for 10 years.

Fig. 2. Impact of pre-exposure prophylaxis (PrEP) on HIV diagnoses. MSM, men who have sex with men; CAI, condomless anal intercourse.

adherence among users (particularly if offered without any targeting) was shown to have no effect whatsoever.[22] Generally, interventions that are targeted to and achieve high coverage in high-risk MSM, have a potential to have a higher impact on HIV diagnoses, as can be seen in some,[22,23] but not all[25] models. At least one study[27] predicted that when PrEP is accompanied by increases in risk compensation, such behavioural change undermined and reduced the protective effect of PrEP. That study also revealed a reverse dose–response relationship between sexual risk behaviour and the protective effect of PrEP.

One study[24] suggested that two factors have a synergistic effect on HIV diagnoses, specifically, a high uptake of PrEP among high-risk gay men and a 50% reduction in the cost of PrEP. However, the resulting impact of PrEP on HIV diagnoses in 10 years would still be modest at 40%.

Three of the six studies reported the cost of implementing PrEP per one HIV infection averted. Juusola *et al*. reported that PrEP accessible to all MSM will cost ~US$1.6 million dollars PIA; prioritisation to high-risk MSM may bring the cost PIA down by 68%, but will result in fewer infections averted (reductions in HIV diagnoses by 51% and 34%, respectively).[23] Kessler *et al*. also showed a potential cost-benefit from targeting PrEP to high-risk MSM in comparison to a program with access to PrEP for all MSM (cost PIA of US$1.1 million vs US$1.6 million, respectively)[24] The cost saving, however, would also come with fewer infections averted (8390 vs 10 989, respectively). Only one study reported the estimated cost of providing PrEP outside of the US – an Australian study reported by Schneider *et al*. in 2014.[26] In that study, one HIV infection averted in the Australian context would cost US$1.8 million if PrEP is available to all MSM or $1.6 million if PrEP is targeted to high-risk MSM (the difference in the number of infections averted will be 535 vs 718, respectively).

In this review, we do not specifically focus on the assessment of PrEP cost-effectiveness over time, because this was done by a recent review conducted by Cambiano *et al*.[30] Cambiano *et al*. reported on seven studies that evaluated cost-effectiveness of PrEP or the cost of introducing PrEP as a HIV prevention strategy in key population groups, including MSM. The key conclusions of that review were that among MSM in North America, PrEP cost-effectiveness can vary from PrEP being cost-effective, to being too expensive for providers at a cost of US$160 000 per quality-adjusted life-year gained. That review also suggested that better, more precise cost-effectiveness

models can be achieved if the calibrations consider local HIV incidence, the levels of PrEP uptake, the effects of providing PrEP within a package of HIV prevention interventions (combination prevention), as well as the effects of PrEP on other prevention approaches.

Current PrEP implementation in OECD countries

As the reviewed modelling studies show, any substantive impact of PrEP on HIV diagnoses, regardless of any timelines, can only be achieved with considerable PrEP coverage. Currently, access to PrEP remains limited. In the US, the original TDF/FTC has been approved by the US Food and Drug Administration as PrEP for preventive purposes in 2012. However, universal PrEP access has not yet been achieved and PrEP uptake varies by state. For example, in California, New York and Washington, states that are known for their sizeable MSM communities, a history of participating in PrEP research and strong HIV prevention advocacy, increases in PrEP uptake have been observed, particularly after 2013.[13] Although there are sizeable gay communities in other US jurisdictions as well, some states of the US South and Midwest have not seen any significant PrEP uptake among MSM.

In other OECD countries, access to PrEP remains limited, mainly due to regulatory approval issues and/or high cost of TDF/FTC, which is protected by complex intellectual property (IP) laws.[31] Westerhaus and Castro have investigated the balance between the public health need of increasing the ART distribution (not only for HIV treatment but also for its prevention) and the restrictions imposed by IP laws. They suggested restricting the effect of these laws for low- and middle-income countries' ability to access generic drugs.[31] This issue still remains unresolved in the OECD countries, which face high ART prices for PrEP under the current IP laws.

Meanwhile, to guide PrEP prescribing, local and national PrEP prescribing guidelines have been released in the US,[32,33] Australia,[34,35] Europe[36] and South Africa. The original TDF/FTC for PrEP has now been approved by regulatory authorities in Australia,[37] South Africa and France;[18] positive opinion on preventative use of TDF/FTC was released by the European Committee for Medicinal Products for Human Use (CHMP)[38] and applications for regulatory approvals are being considered in Canada and the UK.[18]

Some OECD counties are taking PrEP implementation forward, while others have not yet begun the process. In France, the national government authorised Truvada prophylaxis on 23 November 2015, and is fully reimbursing the cost of PrEP and related services.[39] By 20 July 2016, more than 1000 patients were able to access PrEP in more than 90 clinics across France; both daily and on-demand PrEP is now prescribed to MSM in France.[40] In Australia, state governments of the three most populous states (New South Wales (NSW), Victoria and Queensland) have announced funding for expanded PrEP implementation programs. These programs, which will be set-up within a research framework, will provide access to daily TDF/FTC PrEP for a total of ~8000 MSM over the next 2 years.[41] The largest of these three programs, the EPIC-NSW study in NSW, started on 1 March 2016 and by 20 July 2016 had already enrolled more than 2000 MSM in ~20 clinics.[42] This evidence-based study intends to enrol 3700 high-risk MSM and evaluate the impact of providing PrEP to them over a 2-year period. EPIC-NSW will evaluate the impact of this approach on HIV incidence in the study and on HIV diagnoses in the state. In the UK, however, PrEP implementation has been stalled by a lack of regulatory approval and by the recent (21 March 2016) decision by the National Health Service (NHS) to not support provision of PrEP.[43] Over 6000 people are annually diagnosed with HIV in the UK, ~55% of them are MSM;[43] the local PrEP demonstration study, PROUD, has convincingly demonstrated high PrEP efficacy in the UK context and advocacy is growing for the NHS to reconsider this decision.[44] In other OECD counties, small-scale demonstration studies are underway in Belgium, Canada and the Netherlands.[18]

Discussion and Conclusion

Several interesting findings emerge from this review of PrEP impact modelling studies and PrEP implementation in the OECD countries. Overall, there have been only a few modelling studies, and only three have been conducted outside the US. Their complexity has evolved as more evidence has emerged about PrEP and better input indicators have become available for calibrating the models.

PrEP is a necessary and powerful new tool for HIV prevention. However, none of the published models[22–27] showed that PrEP alone can reduce HIV diagnoses to zero, regardless of the time horizon, which means that PrEP alone cannot achieve the ambitious UNAIDS goal of eliminating HIV transmission by 2030 (and certainly not by 2020). Two studies[26,27] predicted that only in combination with other available HIV prevention strategies, such as regular testing, early treatment initiation for HIV positive people and behavioural interventions, can PrEP enable us to reduce HIV diagnoses by ~95% and come close to the UNAIDS HIV prevention goal. Other upcoming biomedical prevention strategies may turn out to be useful additions in the future, and help end the HIV epidemic within the timeframe. For MSM, such additional strategies may include long-lasting PrEP options (e.g. injectable implants, to improve PrEP adherence and effectiveness), on-demand PrEP (for people who do not fall into the targeted categories of high-risk, frequently exposed to HIV MSM), HIV vaccines and curative treatment. Unfortunately, these options are still some way off[45] and may not be able to help in achieving the UNAIDS targets by 2030.

Access to PrEP remains limited, even in the OECD countries. High cost of PrEP per one infection averted, including the high cost of TDF/FTC, is an important impediment for PrEP implementation. Three modelling studies[23,24,26] showed that the monetary costs can be somewhat reduced by first targeting PrEP to the high-risk MSM, but these gains can result in some delays in achieving the HIV prevention targets. Indeed, the matter of PrEP cost may not be resolved without addressing the complex issue of IP laws, which restrict access to the medications. Addressing the issue of access to ARVs for treatment and prevention is a public health imperative in OECD countries and globally.[31]

While access to PrEP remains limited, some OECD counties have started PrEP implementation. In November 2015, the French government approved free, subsidised access to PrEP for MSM,[39] and three Australian state governments (in NSW, Victoria and Queensland) are subsidising large PrEP implementation programs. In the UK, progress with PrEP access has slowed with the NHS decision to not subsidise PrEP.[43] Some other OECD countries are working towards PrEP implementation.[18]

Where PrEP implementation has progressed, it appears that the following factors have played an important role: the strength of the local evidence base about HIV transmission (good surveillance and research data to better understand how to target PrEP), government support (with a clear HIV prevention strategy and measureable prevention targets), supportive health profession and health services (ready and willing to prescribe PrEP) and strong community advocacy putting pressure on the HIV sector and adding urgency to the implementation of PrEP. Such factors have been shown to be present in the US, France and Australia, and PrEP implementation in these countries has begun.[40,41]

Mathematical models have their limitations; they depend on input indicators and the complexity of estimation methods. However, in combination with clear HIV prevention targets, such modelling exercises are very useful. They can assist governments in their decision-making about PrEP implementation. They can propose the most suited scenarios for the roll-out of PrEP and indicate population groups to target. They are informative for the allocation of limited resources. Modelling studies are also instrumental in adding urgency to the implementation of PrEP. Therefore, more work is needed on modelling the impact of PrEP on the HIV epidemic outside the US where PrEP implementation is in its early stages.

Conflicts of interests

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