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Achieving 90-90-90 Human Immunodeficiency Virus (HIV) Targets Will Not Be Enough to Achieve the HIV Incidence Reduction Target in Australia

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Background. We estimated the human immunodeficiency virus (HIV) incidence reduction in Australia that would correspond to achieving the United Nations Program on HIV and AIDS (UNAIDS) 90-90-90 targets by 2020 and extended targets of 95-95-95 by 2030. This was done in combination with various scale-ups of HIV testing, primary prevention, and preexposure prophylaxis (PrEP) among high-risk men who have sex with men (MSM). These projections were evaluated against the target of achieving a 90% reduction in HIV incidence by 2030 compared with 2010 levels.

Methods. A mathematical model.

Results. Achieving 90-90-90 by 2020 was estimated to reduce incidence by 10% from 2010 levels. Achieving 95-95-95 by 2030 was estimated to reduce incidence by 17% from 2010 levels, with the first "95" being achievable by testing low- and high-risk MSM 2 and 4 times per year, respectively. This was improved to a 34% reduction by including a 5-year scale-up of PrEP to 30% coverage among high-risk MSM and to 45% by also increasing MSM condom use from 42% to 60%. However, even with 95-95-95, 2 and 4 tests per year for low- and high-risk MSM, 100% high-risk MSM PrEP coverage, and 100% MSM condom use, only an 80% reduction in incidence was possible by 2030.

Conclusions. Many countries, particularly those with low HIV prevalence, will struggle to achieve a 90% reduction in HIV incidence by 2030, even if UNAIDS targets are met. Most will require substantially higher levels of prevention coverage and higher testing frequencies to reach this target.

Keywords. elimination targets; HIV; mathematical model; men who have sex with men; PrEP.

In 2014, the United Nations Program on HIV and AIDS (UNAIDS) proposed the 90-90-90 global human immunodeficiency virus (HIV) targets [1], aiming to have 90% of people living with HIV (PLHIV) knowing their status, 90% of people diagnosed with HIV on treatment, and 90% of people on treatment with suppressed viral loads by 2020. Worldwide, the second and third targets are currently the closest to being reached [2], with the 2015 HIV care cascade estimated to be 57-80-83 [3]. In Australia, estimates suggest that the care cascade was approximately 90-83-92 in 2015 [4]. This is similar to many estimates for other high-income countries [5] and indicates that programs to facilitate more rapid treatment initiation following diagnosis should be pursued to reach the second UNAIDS target.

The UNAIDS 90-90-90 targets are linked to the Ending AIDS target set by the UN General Assembly [6], aiming to achieve a 90% reduction in HIV incidence by 2030 compared with 2010 levels [7]. However, modeling has shown that reaching the 90-90-90 objective without scaling up other interventions to reduce HIV transmission is unlikely to achieve the desired reduction in HIV incidence [8–10]. This is, in part, because when adopted in isolation, treatment as prevention is insufficient to produce very large declines in HIV transmission [11, 12]. For countries that already have moderate or high treatment coverage [5], the potential impact of a moderate increase in treatment coverage from around 80% to 90% on reducing HIV transmission will be modest. Therefore, complementary prevention efforts beyond the 90-90-90 goals are believed to be vital to reaching the Ending AIDS 2030 target [13], in particular for countries that are already close to the 90-90-90 goals.

Early diagnosis of HIV infection is extremely important in preventing further transmission, as it is a gateway to the HIV care cascade and can result in behavior changes that reduce the risk of onward transmission [14]. The percentage of undiagnosed PLHIV can be reduced by increasing testing frequencies, in particular, among high-risk groups; however, there are practical limitations to what is acceptable and feasible. For example, current Australian guidelines recommend testing up to 4 times per year

for high-risk men who have sex with men (MSM; defined as MSM who have any condomless anal sex, more than 10 sexual partners in 6 months, participate in group sex, or use recreational drugs during sex [15]). A recommendation that requires more frequent testing would increase the burden to individuals as well as to the health systems that support this increase in testing demand. Moreover, the average testing frequency among high-risk MSM is currently below what is recommended (approximately 2.9 times per year [16]), meaning that programs to facilitate testing are likely to have greater impact than more stringent guidelines.

Primary prevention methods for reducing HIV transmission include condom distribution programs; needle and syringe programs; opioid substitution therapy; antenatal, childbirth, and maternal prevention of mother-to-child transmission strategies; voluntary medical male circumcision; social and behavior change communication; and community support and demand generation programs. Recently, there has been emphasis on preexposure prophylaxis (PrEP) [17] due to compelling prevention evidence from clinical trials and high levels of acceptability among high-risk populations, in particular MSM [18] who account for the majority (approximately 70%) of notified cases in Australia [4]. However, although PrEP has demonstrated clear benefits for those who are taking it, its population-level impact may be reduced by the associated increase in condomless anal intercourse reported among MSM [19–21] and increases in other sexually transmitted infections.

For this study, we used a recursive mathematical model to estimate the reduction in incidence that could be achieved in Australia if the 90-90-90 goals were reached by 2020. We then estimated the incidence reduction if these targets were expanded to 95-95-95 by 2030 [7], as well as the impact of increasing HIV testing frequencies among low- and high-risk MSM, increasing primary prevention coverage, and scaling up PrEP use among high-risk MSM.

METHODS

We used an algebraic method to link incidence to the HIV care cascade. Also, by expanding on the methods of Kelly and Wilson [8], we estimated the population-level benefits of increasing HIV testing frequencies, increasing primary prevention coverage, and scaling up PrEP coverage among MSM.

Transmission

We made the supposition that a proportion ρ of a population are at risk of either acquiring HIV (if they are not infected) or transmitting HIV (if they are infected) that is Γ times greater than the remaining proportion of the population. For example, among MSM, we can define high risk according to STIGMA testing guidelines [$(1-\rho)$ 15]. Let N be the number of HIV-positive individuals in the population and let d_1 and d_2 denote the proportions of low- and high-risk PLHIV who are diagnosed (therefore, the total proportion who are diagnosed is given by $d = d_1(1-\rho) + d_2\rho$, which represents the first "90"). We also define τ to be the proportion of those diagnosed who

have commenced treatment (the second "90") and σ to be the proportion of those on treatment who have suppressed viral load (the third "90"). For simplicity, we assume that there is a single "average" number of transmissions that result from low-risk HIV-positive individuals who have unsuppressed virus (denoted by β per person per year) and that this number is increased by a factor Γ for high-risk individuals and reduced by a factor $(1-\varphi)$ for people with suppressed virus (systematic reviews indicate that $\varphi \approx 0.96$ [22]; however, these are from clinical settings and are likely to be optimistic). This means that a proportion $d_1\tau\sigma$ of the $N(1-\rho)$ low-risk, HIV-positive individuals are virally suppressed and transmit on average $N(1-\rho)\beta(1-\varphi)$ infections per year, while the remaining proportion $(1-d_1\tau\sigma)$ of low-risk individuals are not virally suppressed and transmit on average $N(1-\rho)\beta$ infections per year. Similarly, virally supressed, high-risk individuals are assumed to transmit on average $N\rho\beta\Gamma(1-\varphi)$ infections per year, and high-risk individuals who are not virally suppressed transmit on average $N\rho\beta\Gamma$ infections per year.

These definitions allow us to construct a simple risk equation that relates the average population incidence (number of new infections per year in a population) with the average transmission rate per person per year and parameters of the HIV cascade:

$$\text{Incidece} = N\beta[(1-\rho)(1-d_1\tau\sigma\varphi) + \rho\Gamma(1-d_2\tau\sigma\varphi)] \quad (1)$$

Equation 1 can be used to calculate β for any setting and among any population or subpopulation where HIV cascade values and incidence are known. Further, if we fix the ratio $d_1/d_2 = \alpha$, we can use equation 1 to relate an increase in the first "90" or diagnosis with a decrease in incidence.

By adding the estimated new cases to the total number of PLHIV, equation 1 can also be used to recursively estimate incidence over time (see Supplementary Materials).

Preexposure Prophylaxis

Suppose that PrEP were being used by a proportion ω of the high-risk subpopulation, with an effectiveness of $\varepsilon = 0.86$ [18]. If we approximate by allowing the risk groups to interact assortatively, then the proportion of new infections occurring among the group at higher risk is $\Gamma/(1+\Gamma)$. This allows us to update equation 1 to account for the effects of PrEP:

$$I = N\beta\left[(1-\rho)(1-d_1\tau\sigma\varphi) + \rho\Gamma(1-d_2\tau\sigma\varphi)\right]\left(1 - \omega\varepsilon\frac{\Gamma}{\Gamma+1}\right)$$

$$(2)$$

Testing

If the total number of PLHIV, the proportion of PLHIV who are diagnosed, and the annual incidence are known for a population, then equation 2 can be rearranged to give the

corresponding average time from infection to diagnosis (see Supplementary Materials):

$$T = -1/\log\left(1 - \frac{dI}{I + (1-d)N}\right) \quad (3)$$

Using this relationship, as the testing frequency $(1/T)$ of the population changes, we can determine the corresponding long-term proportion of PLHIV who are diagnosed. An increase in testing in the model can result in benefits because it increases the proportion of PLHIV who are diagnosed, of which a proportion τ are assumed to initiate treatment and a proportion $\tau\sigma$ are assumed to achieve a suppressed viral load.

Primary Prevention

Australia has a concentrated HIV epidemic among MSM, and so we consider primary prevention through condom use. Currently, if condoms are used a proportion c_0 of the time and they have an effectiveness ε_c, then if usage is changed to a proportion c_1 of the time, on average this will lead to a $1 - \varepsilon_c(c_1 - c_0)$ relative reduction in incidence.

Data

Parameter values and their sources are shown in Table 1.

Scenarios

Human Immunodeficiency Virus Care Cascade Targets

We considered scenarios where diagnosis, treatment, and viral suppression were linearly scaled up to 90-90-90 by 2020 (or maintained when the "90s" have been reached prior to 2020; see Table 1). Then, between 2020 and 2030, they were (1) maintained or further linearly scaled up to (2) 95-90-90, (3) 95-95-90, or (4) 95-95-95. The resulting annual incidence was estimated from 2016 to 2030.

Preexposure Prophylaxis

Here, we improved on scenario 4 above (ie, 95-95-95) by additionally allowing PrEP to be available and scaled up among the high-risk MSM population. A 5-year period (2016–2021) was used to scale up PrEP from 0% coverage to between 10% and 70% in the high-risk MSM population, after which coverage was maintained until 2030. The resulting annual incidence was estimated for the period 2016–2030.

Testing

For the low- and high-risk MSM populations, we considered the following testing frequencies: 2 and 3, 2 and 4, 3 and 4, and 3 and 6 times per year. In each scenario, the corresponding proportion d of PLHIV who were diagnosed was determined (see Supplementary Materials), and this was modeled as scale-up to

Table 1. Data and Sources From Australia Used to Inform the Model

Parameter	Symbol	Value	Source
Estimated number of people living with HIV	N	25 313 in 2015	Kirby Institute 2015 estimate [4]
New HIV diagnoses per year	I	1043 in 2010	Kirby Institute [4]; values were unavailable for 2011 and a midpoint estimate between 2010 and 2012 was assumed
		1054 in 2011	
		1065 in 2012	
		1030 in 2013	
		1082 in 2014	
		1025 in 2015	
Proportion of MSM at high risk	ρ	40%	40% from Victorian Primary Care Network for Sentinel Surveillance [23, 24] Tested in the sensitivity analysis
Increased risk for high-risk MSM	Γ	2	Expert opinion; tested in the sensitivity analysis
Proportion of low- and high-risk who are diagnosed	d_1, d_2	0.92% / 0.87%	90% overall (Kirby Institute 2016 annual surveillance report [4]); assuming greater diagnosis rate among low risk
Proportion of all diagnosed PLHIV who are on ART	τ	83%	Kirby Institute 2016 annual surveillance report [4]
Proportion of all PLHIV on ART with suppressed virus	σ	92%	Kirby Institute 2016 annual surveillance report [4]
Testing frequency among low- and high-risk MSM	$\frac{1}{T_1}, \frac{1}{T_2}$	1.82 times per year; 2.91 times per year	New South Wales sexual health clinics [16]
Condom use with casual partners	c_0	42%	Gay Community Periodic Survey [21]
Effectiveness of preexposure prophylaxis	ε	86%	PROUD study, McCormack et al [18]
Effectiveness of condoms when consistently used	ε_c	70%	Smith et al [25]

Abbreviations: ART, antiretroviral therapy; HIV, human immunodeficiency virus; MSM, men who have sex with men; PLHIV, people who live with human immunodeficiency virus.

90-90-90 by 2020, followed by a further scale-up to "d"-95-95 by 2030. Increased testing frequency (of 2 and 4 times per year for low- and high-risk MSM) was then considered in combination with a 5-year (2016–2021) scale-up of PrEP to between 10% and 70% coverage in the high-risk MSM population, after which PrEP coverage was maintained until 2030.

Primary Prevention

This scenario considered additional primary prevention in combination with an improved HIV care cascade (90-90-90 by 2020 and 95-95-95 by 2030), increased testing frequency (2 and 4 times per year for low- and high-risk MSM), and PrEP scale-up (to 30% of high-risk MSM). These changes to the care cascade, testing frequencies, and PrEP coverage were chosen as they were believed to be feasible in Australia.

RESULTS

Reaching the UNAIDS 90-90-90 target by 2020 reduced the HIV incidence by approximately 10% that year. However, beyond this, without continued improvement to the care cascade, incidence increased due to an increasing number of PLHIV. By further scaling up to 95-95-95 between 2020 and 2030, the annual incidence was estimated to be reduced by about 17% from 2010 levels in 2030, well short of the UNAIDS 90% reduction target (Figure 1A).

When combined with 95-95-95 by 2030, every 10 percentage point scale-up in high-risk MSM PrEP coverage between 2016 and 2021 (if maintained) was estimated to provide an additional 6 percentage point incidence reduction by 2030 (Figure 1B).

However, even at high coverage, this still fell short of the HIV incidence reduction target.

Increasing HIV testing to 2 and 4 times per year for low- and high-risk MSM corresponded to approximately the same diagnosis rate as the 95-95-95 target (94.6%) and produced a 16% reduction from 2010 levels. An increase in testing frequency beyond this to 3 and 6 times per year for low- and high-risk MSM resulted in a 32% reduction from 2010 levels; however, this is unlikely to be feasible in practice and would be burdensome on the health system (Figure 2A). The combination of 95-95-95 with 2 and 4 tests per year for low- and high-risk MSM and 30% PrEP coverage reduced incidence by 34% from 2010 levels (Figure 2B).

When combined with 95-95-95 by 2030, every 10 percentage point increase in MSM condom use with casual partners (scaled up over 5 years and maintained until 2030) was estimated to provide an additional 7 percentage point incidence reduction by 2030 (Figure 3A). The combination of 95-95-95 with 2 and 4 tests per year for low- and high-risk MSM, a 5-year scale-up to 30% PrEP coverage, and an increase in condom use with casual partners from an estimated 42% to 60% reduced incidence by 45% from 2010 levels (Figure 3B).

For various combinations of PrEP and condom use scale-up, the projected 2030 HIV incidence reduction is shown by the contours in Figure 4. The model estimated that with 95-95-95, 2 and 4 tests per year for low- and high-risk MSM, 100% high-risk MSM PrEP coverage, and 100% condom use, an 80% reduction in incidence from 2010 levels was possible.
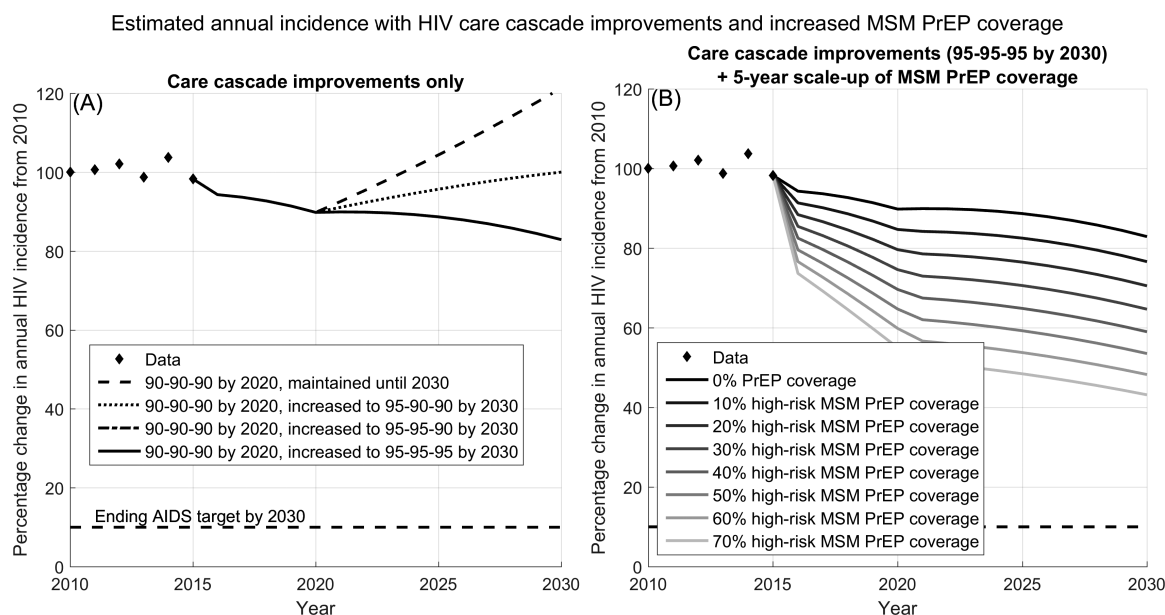

Estimated annual incidence with HIV care cascade improvements and increased MSM PrEP coverage

Figure 1. Model projections for annual human immunodeficiency virus incidence if the care cascade reached 90-90-90 by 2020. *A,* Without preexposure prophylaxis (PrEP) among men who have sex with men (MSM) and with the care cascade either maintained between 2020 and 2030 (dashed line) or further scaled up to 95-90-90 (dotted line), 95-95-90 (dash-dot line; equal to and hidden underneath solid line), and 95-95-95 (solid line) by 2030. *B,* With the care cascade scaled up to 95-95-95 by 2030 and a 5-year scale-up (2016–2021) to various levels of PrEP coverage among high-risk MSM. Abbreviation: HIV, human immunodeficiency virus.

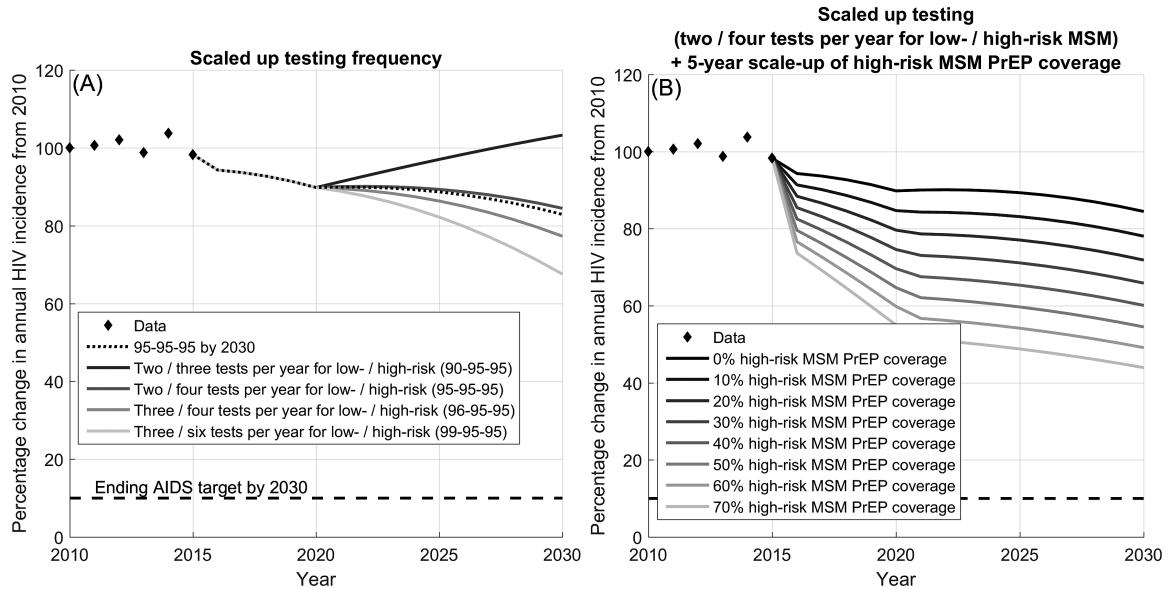Estimated annual incidence with increased HIV testing and MSM PrEP coverage

Figure 2. Model projections for annual human immunodeficiency virus incidence with the care cascade scaled up to 90-90-90 by 2020 and 95-95-95 by 2030, plus increases in testing and high-risk men who have sex with men (MSM) preexposure prophylaxis (PrEP) coverage. A, With 95-95-95 and increased testing frequencies but no PrEP coverage among MSM. B, With 95-95-95, 2 and 4 tests per year for low-and high-risk MSM and a 5-year scale-up (2016–2021) to various levels of PrEP coverage among high-risk MSM. Abbreviation: HIV, human immunodeficiency virus.

DISCUSSION

Our model shows that achieving the UNAIDS 90-90-90 target by 2020 would likely result in a 10% reduction in HIV incidence in Australia from 2010 levels. However, beyond 2020, the increasing

number of PLHIV meant that continued improvements were required to continue reducing incidence. In particular, we found that scaling up to 95-95-95 by 2030 could result in a 17% incidence reduction from 2010 levels (an additional 7% reduction),

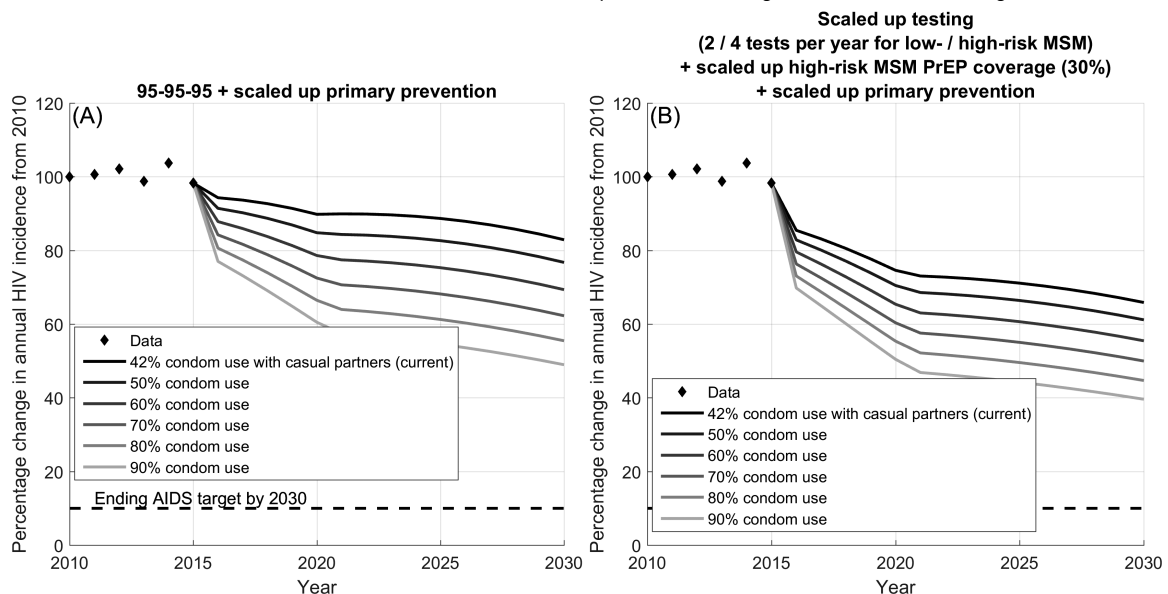Estimated annual incidence with increased HIV prevention, testing and MSM PrEP coverage

Figure 3. Model projections for annual human immunodeficiency virus incidence with the care cascade scaled up to 90-90-90 by 2020 and 95-95-95 by 2030, plus increases in primary prevention, testing, and high-risk men who have sex with men (MSM) preexposure prophylaxis (PrEP) coverage. A, With 95-95-95 and increased primary prevention among MSM but no PrEP coverage. B, With 95-95-95, 2 and 4 tests per year for low-and high-risk MSM, a 5-year scale-up (2016–2021) to 30% PrEP coverage among high-risk MSM, and increasing levels of primary prevention coverage. Abbreviation: HIV, human immunodeficiency virus.
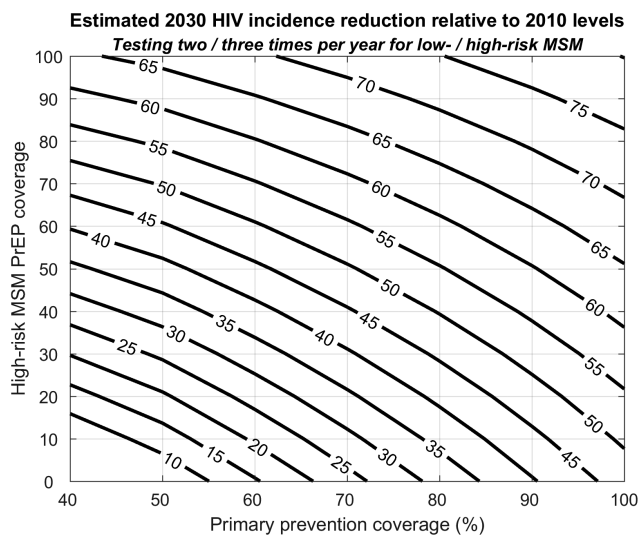
Figure 4. Estimated relative reduction in human immunodeficiency virus incidence by 2030 for various preexposure prophylaxis and primary prevention coverages. Estimates include care cascade improvements to 90-90-90 by 2020 and 95-95-95 by 2030, plus 2 and 4 tests per year for low-and high-risk men who have sex with men (MSM). Primary prevention includes condom use among MSM with casual partners. Abbreviations: HIV, human immunodeficiency virus; PrEP, preexposure prophylaxis.

with a 95% diagnosis percentage being achievable by testing low- and high-risk MSM 2 and 4 times per year, respectively. Further improvements in incidence reduction could be accrued by also including a 5-year scale-up to 30% PrEP coverage among high-risk MSM (34% incidence reduction) and by increasing condom use with casual partners from an estimated 42% to 60% (45% incidence reduction). However, achieving UNAIDS HIV elimination targets in Australia by 2030 will require enormous and, in some cases, unfeasible levels of prevention intervention scale-up. For example, with 95-95-95, 2 and 4 tests per year for low- and high-risk MSM, 100% high-risk MSM PrEP coverage, and 100% condom use, only an 80% reduction in incidence was possible by 2030.

These results apply more broadly to countries with concentrated epidemics with strong health systems and support services for PLHIV. The reliance on such high levels of PrEP and other primary prevention coverage to come close to the Ending AIDS target of a 90% reduction in incidence by 2030 suggests that in settings with relatively high HIV care cascade coverage levels (eg, France, the Netherlands, Switzerland, and the United Kingdom [5]), this is unlikely to be achieved.

Much attention has been given to countries' progress toward the 90-90-90 targets [5, 26]; however, there has been comparatively little modeling on what impact reaching these targets may have on incidence reduction. For low- and middle-income countries, compartmental modeling approaches have found that a 90% reduction in HIV incidence by 2030 may be possible [9, 10, 27]. However, even in these settings where greater marginal gains are available, this is likely to require extremely high intervention coverage, including 90% condom use [9, 10].

Although the 90-90-90 targets have been (and continue to be) a great advocacy tool for improved diagnostic and treatment services, they have also contributed to an implicit de-emphasis on harm reduction strategies and potential disinvestment or at least a stalling of program expansion in primary prevention. In this regard, biomedical prevention of HIV has usurped an emphasis on combination HIV prevention outlined in earlier UNAIDS documents [28]. Our findings suggest that while improving the care cascade will continue to be important, in particular, ensuring that hard-to-reach populations that are less engaged in existing healthcare systems are not left behind, there is an urgent need to renew focus on increasing prevention efforts that are likely to provide more significant reductions in incidence. This is supported by community-based trials of harm-reduction scale-up and indicates that primary prevention should become the focus of governments alongside global HIV cascade of care targets. There are also additional intervention delivery strategies worth exploring. For example, further benefit may be possible if responses to HIV were based on the targeting of interventions toward high-risk sexual/injecting network structures, which is something that could be investigated using agent-based models [29, 30]. Within the 2030 time frame, it is also reasonable to consider the impact that the discovery of a vaccine or cure may have. Even if only partially effective, a well-targeted vaccine could provide additional incidence reduction. If treatment were already being accessed by 95% of PLHIV, a cure could revolutionize treatment as prevention. However, with currently available interventions, our model suggests that advocates may need to temper their context-specific messages, with an understanding that although the incidence reduction target may be out of reach, significant improvements are still achievable and therefore worth pursuing.

World Health Organization guidelines currently recommend the use of PrEP for anyone at substantial risk of HIV infection [31]. In many countries, PrEP is either being considered for government subsidy or is already available [32]. Our model shows that increased coverage of PrEP in Australia can provide substantive additional incidence reduction beyond what is achievable by meeting the HIV care cascade targets. This is consistent with other modeling studies [33–35] and suggests that PrEP scale-up for high-risk populations will be a mechanism to bridge the anticipated gap in the Ending AIDS incidence-reduction target.

This study is limited in that the model has extrapolated population-level patterns over time rather than including detailed features of the key populations. This approach provides useful insight and conceptually highlights the need to reassess the care cascade as the sole or primary measure of successful HIV public health policy. Testing rates of 2 and 4 times per year for low- and high-risk MSM have been used as an optimistic upper bound for the 95-95-95 scenarios. Although consistent with current guidelines, this represents an improvement to current practice that may require additional infrastructure or policy change to

implement. No additional testing was assumed for MSM on PrEP, as 4 times per year is currently the recommendation for this high-risk group [36]. It is also unlikely that condom use and PrEP coverage could be increased simultaneously because, despite reviews that suggest minimal changes in sexual risk-behavior associated with PrEP uptake [37, 38], as trust in PrEP and normalization of use increases, evidence is emerging of reduced condom use practices [21, 39]. Therefore, the scenarios considered where both PrEP and condom use are scaled up are highly optimistic and only provided for illustrative purposes. Moreover, we assumed no changes to behavioral inhibition or condom use for men on PrEP, meaning that we are likely to have overestimated incidence reduction. This further emphasizes the need for a renewed focus on alternate prevention measures.

CONCLUSIONS

Even if UNAIDS 90-90-90 targets are met or exceeded, additional coverage of prevention programs will be required to achieve the Ending AIDS target of a 90% reduction in HIV incidence by 2030 compared to 2010 levels in countries with low HIV prevalence. While improving the care cascade beyond 90-90-90 will continue to be important, governments should renew focus on the coverage and impact of other prevention programs to achieve the greatest reduction in incidence.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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