

HIV Preexposure Prophylaxis Cascades to Assess Implementation in Australia: Results From Repeated, National Behavioral Surveillance of Gay and Bisexual Men, 2014–2018

Martin Holt, PhD,^a Evelyn Lee, PhD,^{a,b} Toby Lea, PhD,^{a,c} Benjamin Bavinton, PhD,^d Tim Broady, PhD,^a Limin Mao, PhD,^a James MacGibbon, MAppLing,^a Phillip Keen, BA,^d Dean Murphy, PhD,^{d,e} Brandon Bear,^f David Crawford, MPH,^g Jeanne Ellard, PhD,^h Johann Kolstee, MPH,^d Cherie Power, MPH,ⁱ Garrett Prestage, PhD,^d Andrew Grulich, PhD,^d Rebecca Guy, PhD,^d and John de Wit, PhD^{a,j}

Background: HIV prevention cascades can assist in monitoring the implementation of prevention methods like preexposure prophylaxis (PrEP). We developed 2 PrEP cascades for Australia's primary HIV-affected population, gay and bisexual men.

Methods: Data were drawn from 2 national, repeated, cross-sectional surveys (the Gay Community Periodic Surveys and PrE-

PARE Project). One cascade had 3 steps, and the other had 7 steps. Trends over time were assessed using logistic regression. For the most recent year, we identified the biggest drop between steps in each cascade and compared the characteristics of men between the 2 steps using multivariate logistic regression.

Results: Thirty-nine thousand six hundred and seventy non-HIV-positive men participated in the Periodic Surveys during 2014–2018. PrEP eligibility increased from 28.1% (1901/6762) in 2014 to 37.3% (2935/7878) in 2018 ($P < 0.001$), awareness increased from 29.6% (563/1901) to 87.1% (2555/2935; $P < 0.001$), and PrEP use increased from 3.7% (21/563) to 45.2% (1155/2555; $P < 0.001$). Of 1038 non-HIV-positive men in the PrEPARE Project in 2017, 54.2% ($n = 563$) were eligible for PrEP, 97.2% (547/563) were aware, 67.6% (370/547) were willing to use PrEP, 73.5% (272/370) had discussed PrEP with a doctor, 78.3% (213/272) were using PrEP, 97.2% (207/213) had recently tested, and 75.8% (157/207) reported reduced HIV concern and increased pleasure because of PrEP. The break point analyses indicated that PrEP coverage was affected by geographical availability, education level, employment, and willingness to use PrEP.

Conclusions: PrEP eligibility, awareness, and use have rapidly increased among Australian gay and bisexual men. The cascades identify disparities in uptake by eligible men as a result of socioeconomic factors and PrEP's acceptability.

Key Words: preexposure prophylaxis, prevention cascade, men who have sex with men, Australia, implementation, disparities

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From the ^aCentre for Social Research in Health, University of New South Wales, Sydney, New South Wales, Australia; ^bCentre for Economic Impacts of Genomic Medicine, Macquarie University, New South Wales, Sydney, Australia; ^cGerman Institute on Addiction and Prevention Research, Catholic University of Applied Sciences, Cologne, Germany; ^dThe Kirby Institute, University of New South Wales, Sydney, New South Wales, Australia; ^eDepartment of Gender and Cultural Studies, the University of Sydney, Sydney, New South Wales, Australia; ^fACON, Sydney, New South Wales, Australia; ^gPositive Life NSW, Sydney, New South Wales, Australia; ^hAustralian Federation of AIDS Organisations, Sydney, New South Wales, Australia; ⁱNew South Wales Ministry of Health, Sydney, New South Wales, Australia; and ^jDepartment of Interdisciplinary Social Science, Utrecht University, Utrecht, Netherlands.

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Correspondence to: Martin Holt, PhD, Centre for Social Research in Health, UNSW Sydney, Sydney, NSW 2052, Australia (e-mail: m.holt@unsw.edu.au).

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methods.⁶ Researchers have suggested cascades to assess factors that may influence the implementation of preexposure prophylaxis (PrEP), the regular use of antiretroviral drugs to prevent HIV acquisition.^{7–10} As Australia has recently embraced PrEP, particularly for gay and bisexual men (GBM) at risk of HIV,^{11,12} we developed 2 different PrEP cascades from existing monitoring systems that can assess change over time and factors affecting implementation.

As with the development of any HIV monitoring system, it is desirable for HIV prevention cascades to use common measures, so different settings can be compared.⁴ However, many monitoring systems are developed in response to local epidemics,¹³ are conducted infrequently, or collect limited information.^{6,14} This results in “scarcity of data and standard indicators” and a need for pragmatism in how prevention cascades are fashioned.⁴ That said, most HIV prevention cascades feature common elements or stages, with the first steps defining the eligible or at risk population, the next steps assessing awareness or willingness to use the prevention method, and subsequent steps focusing on access and use and, if relevant, adherence and retention in care.^{2–4} These stages can be derived from or inform models of behavior change.^{4,8} A key feature of cascades is that each step in the cascade is a subset of the preceding step.

A number of cascades have been published about PrEP use by GBM, mainly from North America.^{7–10} None of these publications assessed change over time or progress in addressing gaps in the cascades. They also illustrate a number of issues. It is not always obvious in which order to place different measures in a cascade. Researcher- or clinician-defined eligibility for PrEP, for example, has been placed early in some cascades to define the target population,^{8,10} while others have placed it near the end of the cascade as an indicator of a participant’s likelihood of receiving a prescription.⁷ There are tensions between top-down or researcher-driven measures and participant or user perceptions of HIV risk, which may not match.⁹ If a PrEP cascade has a lot of steps, it illustrates more points of intervention that may influence PrEP use, but longer cascades are also more likely to show a “drop-off” throughout the cascade (as fewer people meet additional criteria).^{9,10} Existing monitoring systems may not collect sufficient indicators to construct multistep cascades and may not be repeated regularly enough to assess change over time. It has been recommended that PrEP cascades should be drawn from population-level data, to include the widest range of people at risk of HIV and those currently disengaged from services.² However, in some settings, only service- or clinic-level data may be available, which may bias estimates of PrEP uptake.

Since April 2018, PrEP can be prescribed by any doctor in Australia. Before its public listing, early PrEP use was driven by the personal importation of generic drugs, then by large implementation projects from 2016 onward.^{11,12,15} PrEP use continues to increase, but there are concerns about disparities in PrEP access, because of geography, socioeconomic, and cultural factors.¹⁶ We constructed 2 different PrEP cascades from ongoing, national studies of GBM. Our aims were to assess progress in increasing PrEP use in Australia, and identify drop-off points in the cascades to guide future

implementation.¹⁷ We also assessed the utility of the 2 cascades for ongoing monitoring.

METHODS

Participants and Procedures

Data were drawn from 2 national, repeated, cross-sectional studies: the Gay Community Periodic Surveys (GCPS), HIV behavioral surveillance of GBM, and the PrEPARE Project, an online survey of GBM’s attitudes to biomedical HIV prevention.

The GCPS methods have been previously described.¹⁸ The GCPS target Australia’s most HIV-affected population, GBM in metropolitan areas.¹⁹ Recruitment occurs at gay venues and festival events, supplemented by online recruitment. Eligible participants are male (cisgender or transgender), aged 18 years or older (face-to-face recruitment), 16 years or older (online recruitment), resident in Australia, identified as gay or bisexual or have had sex with a man in the previous 5 years. The questionnaire assesses demographics, recent sexual behavior, testing history, drug use, and the use of different HIV prevention methods. Identifying information is not collected; return of the questionnaire is taken as evidence of consent. The GCPS are conducted in 7 states and territories with annual recruitment in the 3 most populous states and biennial recruitment elsewhere. The study was approved by the UNSW Human Research Ethics Committee (refs. HC13366 and HC180903).

The PrEPARE Project methods have been previously described.¹² Since 2011, a national online survey of GBM has been conducted every 2 years, assessing attitudes to biomedical HIV prevention. Recruitment is conducted online, driven by paid Facebook advertising. Eligible participants are male (cisgender or transgender), aged 18 or older, resident in Australia, and identified as gay or bisexual. The questionnaire assesses demographics, attitudes to and experience of using biomedical HIV prevention methods, recent sexual behavior with male partners, HIV and sexual health testing, and drug use. The study was approved by the UNSW Human Research Ethics Committee (ref. HC16954).

Measures

The denominator for the GCPS cascade was all HIV-negative, untested, and unknown status men in the sample (non-HIV-positive men), excluding previously diagnosed HIV-positive men. It consisted of the following steps:

1. Eligible for PrEP
2. Aware of PrEP
3. Using PrEP.

Participants in steps 2 and 3 met the criteria for the preceding steps. Eligibility for PrEP was adapted from Australian prescribing guidelines²⁰ and operationalized as shown in Table 1, Supplemental Digital Content, <http://links.lww.com/QAI/B404>.

Awareness of PrEP was assessed with the question, “What do you know about preexposure prophylaxis (PrEP)?.”

Participants who answered “It’s available now” were classified as aware. PrEP use was assessed with the question, “In the last 6 months, did you take anti-HIV medication regularly to protect yourself from HIV (PrEP)?” Participants who answered “Yes, I was prescribed anti-HIV medication to take every day” were classified as using PrEP.

The denominator for the PrEPARE cascade was non-HIV-positive men, excluding previously diagnosed HIV-positive men. It consisted of the following steps:

1. Eligible for PrEP
2. Aware of PrEP
3. Willing to use PrEP
4. Discussed PrEP with a doctor
5. Using PrEP
6. Recently tested for HIV/sexually transmitted infections (STIs) (in the last 3 months)
7. Reduced HIV concern and increased pleasure because of PrEP.

To be included in step 2 onward, participants had to meet the criteria for the preceding steps. Based on items available in the PrEPARE questionnaire, eligibility for PrEP was operationalized as shown in Table 1, Supplemental Digital Content, <http://links.lww.com/QAI/B404>.

Awareness of PrEP was assessed with the question, “How much have you heard about pre-exposure prophylaxis (PrEP)?” with men who answered “A little” or “A lot” classified as aware. Willingness to use PrEP was assessed with a previously validated 7-item scale (Cronbach $\alpha = 0.78-0.86$) scored from 1 to 5.^{12,21} Participants who scored ≥ 4 on the scale were classified as willing. Participants who answered “Yes” to the question “Have you ever discussed pre-exposure prophylaxis (PrEP) with a doctor?” were included in step 4. PrEP use was assessed with the question, “Are you currently taking PrEP?” (Yes/No). It was assumed that all PrEP users were aware of PrEP, willing to use it, and had discussed PrEP with a doctor (they were not shown questions about these topics). Only PrEP users who were classified as eligible for PrEP were included in the cascade. PrEP users were classified as recently tested if they indicated they had been tested for both HIV and STIs in the previous 3 months. PrEP users were classified as having reduced HIV concern and increased pleasure if they scored ≥ 4 on a 4-item scale ($\alpha = 0.78$) scored from 1 to 5.¹²

Analyses

Analyses were conducted using Stata version 15. The GCPS and PrEPARE samples were compared using multivariate logistic regression.

For the GCPS cascade, we included data collected between 2014 and 2018 in every participating jurisdiction. The sample was divided into the cascade steps for each year, and trends over time in each category were assessed using logistic regression. We also report trends in PrEP eligibility criteria. For the break point analysis (the biggest drop between cascade steps by absolute proportion $\geq 10\%$),¹⁷ we included data from the most recent survey round (2017 or 2018, depending on jurisdiction) and compared the character-

istics of men between the 2 steps using multivariate logistic regression.

For the PrEPARE cascade, we only included data collected in the 2017 survey round, which allowed the construction of a more complex cascade. We divided the sample into the cascade steps, then we conducted a break point analysis using multivariate logistic regression.

For multivariate logistic regression models, variables that had a statistically significant relationship at a bivariate level ($P < 0.05$) were block entered into the multivariate model. For the logistic regression models, we report crude and adjusted odds ratios, 95% confidence intervals, and P values.

RESULTS

Participant Characteristics

In the GCPS, there were 39,670 non-HIV-positive participants between 2014 and 2018. Their mean age was 35.2 years, 70.7% were born in Australia, 51.4% had a university degree, and 64.3% were in full-time employment. The majority of participants were from New South Wales (33.0%), Victoria (31.1%), and Queensland (20.9%), with 15.0% from the other states and territories. Most participants self-identified as gay (88.4%) or bisexual (6.8%). Current gender identity and gender assigned at birth were only collected in 2018. Of 7878 participants in 2018, 94.1% were cisgender men, 1.0% transgender men, 1.1% nonbinary, and 3.8% did not report their gender identity. All were included in these analyses, as long as they met the other inclusion criteria.

In the PrEPARE Project, there were 1038 non-HIV-positive participants in 2017. Their mean age was 36.3 years, 80.3% were born in Australia, 45.5% had a university degree, and 64.5% were in full-time employment. The majority of participants were from New South Wales (30.7%), Victoria (32.5%), and Queensland (16.8%), with 20.0% from the other states and territories. Most participants were identified as gay (94.8%) or bisexual (3.7%). Most participants were cisgender men (96.7%), and 3.3% were transgender men.

The characteristics of participants from the GCPS (in 2017–2018) and PrEPARE Project were compared in Table 2, Supplemental Digital Content, <http://links.lww.com/QAI/B404> using variables common to both studies. The multivariate analysis showed that GCPS participants were slightly younger, more likely to be recruited from the Australian Capital Territory or South Australia or have a degree. GCPS participants were less likely than PrEPARE participants to be born in Australia, to be gay identified, report condomless sex, or have recently tested for HIV.

PrEP Cascade, GCPS

Table 1 and Figure 1 show the cascade derived from the GCPS. There were between 6762 and 9032 non-HIV-positive participants each year. The proportion of participants who were classified as eligible for PrEP increased from 28.1% in 2014 to 37.3% in 2018, with the largest increase between 2016 and 2017. Table 2 shows trends in PrEP eligibility

TABLE 1. PrEP Cascade for Non-HIV-positive Men in the GCPS, 2014–2018

	2014 n (%)	2015 n (%)	2016 n (%)	2017 n (%)	2018 n (%)	P trend
Eligible for PrEP	1901 (28.1)	2079 (28.3)	2678 (29.7)	3096 (35.8)	2935 (37.3)	<0.001
Eligible and aware that PrEP is available	563 (8.3)	845 (11.5)	1406 (15.6)	2491 (28.8)	2555 (32.4)	<0.001
Eligible, aware, and using PrEP	21 (0.3)	44 (0.6)	219 (2.4)	914 (10.6)	1155 (14.7)	<0.001
Non-HIV-positive men	6762 (100)	7360 (100)	9032 (100)	8638 (100)	7878 (100)	

criteria. Very few were eligible because of condomless anal intercourse (CAI) with HIV-positive regular partners not on treatment or with a detectable viral load. Eligibility because of recent methamphetamine use declined, whereas eligibility because of receptive CAI with casual male partners or STI diagnoses increased, particularly between 2016 and 2017.

Returning to Table 1 and Figure 1, we can see that PrEP awareness increased over time and was reported by 29.6% (563/1901) of eligible participants in 2014 and 87.1% (2555/2935) of eligible participants in 2018 (note that unlike in Table 1, the denominators here are the previous step in the cascade, not all non-HIV-positive participants). PrEP use among eligible and aware participants increased from 3.7% (21/563) in 2014 to 45.2% (1155/2555) in 2018. In the earlier years (2014–2015), the biggest absolute drop in the cascade was between steps 1 and 2 (eligibility and awareness). By 2018, the largest drop in the cascade was between steps 2 and 3 (awareness and use).

The break point analysis is shown in Table 3, Supplemental Digital Content, <http://links.lww.com/QAI/B404>. This compares eligible and aware participants in 2017–2018 who were and were not using PrEP. Focusing on the outcomes of the multivariate analysis, non-PrEP users were more likely to be from the Australian Capital Territory or Western Australia and less likely to be Anglo-Australian, have a university degree or be in full-time employment. Non-PrEP users were less likely to have met partners at sex venues, to report CAI with regular or casual partners, or have recently engaged in group sex. Non-PrEP users were less

likely to be recently tested for HIV and STIs, have a recent STI diagnosis, or have used postexposure prophylaxis. Although non-PrEP users were generally less likely to have used illicit drugs, they were more likely than PrEP users to report recent crystal methamphetamine use.

PrEP Cascade, PrEPARE Project

Figure 2 shows the cascade derived from the PrEPARE Project. Of 1038 non-HIV-positive men in 2017, 563 (54.2%) were classified as eligible for PrEP. The primary reasons for eligibility were recent CAI with casual male partners (n = 473, 45.6%), STI diagnoses (n = 248, 23.9%), and methamphetamine use (n = 121, 11.7%). Only 2 men (0.2%) were eligible because of CAI with HIV-positive regular male partners who were not on treatment or had a detectable or unknown viral load. Nearly all eligible participants were aware of PrEP (547/563 = 97.2%). Most eligible and aware participants were willing to use PrEP (370/547 = 67.6%); this was the largest absolute drop in the cascade. Most eligible, aware, and willing participants had discussed PrEP with a doctor (272/370 = 73.5%), and most men who had discussed PrEP with a doctor were using PrEP (213/272 = 78.3%). Of PrEP users, nearly all had been tested for HIV and STIs in the previous 3 months (207/213 = 97.2%), and most of these recently tested men reported reduced HIV concern and increased sexual pleasure because of PrEP (157/207 = 75.8%).

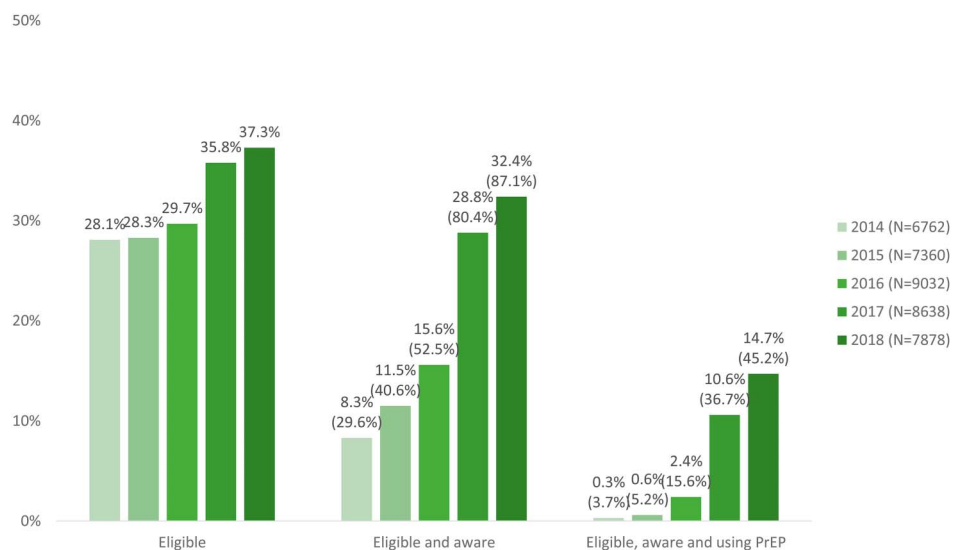


FIGURE 1. PrEP cascade for non-HIV-positive participants in the GCPS, 2014–2018. Percentages in parentheses are calculated with the previous cascade step as the denominator.

TABLE 2. Trends in Eligibility Criteria for PrEP Among Non-HIV-positive Men in the GCPS, 2014-18

	2014 n (%)	2015 n (%)	2016 n (%)	2017 n (%)	2018 (%)	P trend
Receptive CAI with casual male partners*	966 (14.3)	1049 (14.3)	1492 (16.5)	1964 (22.7)	1954 (24.8)	<0.001
CAI with a HIV-positive regular male partner not on treatment or with detectable viral load*	17 (0.3)	14 (0.2)	15 (0.2)	17 (0.2)	9 (0.1)	0.09
Diagnosis with any STI other than HIV†	729 (10.8)	893 (12.1)	1249 (13.8)	1680 (19.5)	1654 (21.0)	<0.001
Any crystal methamphetamine use*	668 (9.9)	651 (8.9)	731 (8.1)	682 (7.9)	559 (7.1)	<0.001
Non-HIV-positive men	6762 (100)	7360 (100)	90,32 (100)	8638 (100)	7878 (100)	

*In the previous 6 months.

†In the previous 12 months.

The break point analysis is shown in Table 4, Supplemental Digital Content, <http://links.lww.com/QAI/B404>. It compares eligible and aware participants who were and were not willing to use PrEP. Focusing on the multivariate analysis, willingness to use PrEP was less likely among men aged 40 years and older and more likely among men who had CAI with casual partners and those who were recently tested for HIV. Willingness to use PrEP was not independently related to the other variables, although we note that being born in Australia and knowing other people using PrEP were associated with greater willingness to use PrEP at a bivariate level.

DISCUSSION

We constructed 2 cascades assessing PrEP use by Australian GBM. The first cascade, from national, repeated behavioral surveillance, shows dramatically increasing eligibility for awareness and use of PrEP, particularly after 2016 when large implementation projects were initiated.^{11,12,15} In this cascade, PrEP use by eligible and aware men reached 45% in 2018, a considerably higher level of coverage than that shown in previous cascades from North America.⁷⁻¹⁰ This cascade suggests that initial rollout of PrEP in Australia has been successful, particularly in increasing awareness of PrEP among GBM. However, more than half of eligible participants (based on “high risk” prescribing criteria) were not using PrEP in 2018,²⁰ suggesting considerable room for improvement in promoting uptake. Our second cascade showed a similar level of recent PrEP coverage to the first cascade but suggested that a lack of willingness to use PrEP may be a critical barrier to uptake among eligible GBM.

The first cascade demonstrates the advantage of using a simple set of measures that can be repeated in routine behavioral surveillance.² The cascade suggests that poor awareness of PrEP may have been an impediment to PrEP use in 2014–2016, after which the main barrier became uptake of PrEP among those who were already aware of it. This cascade seems suitable for routine monitoring, but as a simple, 3-step cascade, it highlights fewer points of intervention, and it is more difficult to explain gaps in the cascade. For example, the break point analysis we conducted on this cascade largely confirms what was known from other studies: PrEP users are more sexually active and report more condomless sex and drug use than nonusers.^{12,22,23} PrEP use was also more common in the eastern states of Australia

where the largest implementation projects were conducted.^{11,12,15,22} The fact that PrEP use was less likely among GBM who had not been to university and who were not in full-time employment does, however, suggest some socioeconomic barriers, despite a public subsidy for PrEP.^{12,16}

The second PrEP cascade drew on acceptability research, allowing a cascade with 7 steps and potential points of intervention. The survey from which this was drawn is conducted every 2 years, so this cascade may not be as useful for routine monitoring, although comparing the 2 cascades seems fruitful. This cascade suggests that the gap between awareness and use in the first cascade may be the result of limited willingness to use PrEP, with only one-third of eligible and aware GBM expressing willingness to use PrEP. This level of willingness is similar to that found in Australian and international research.^{12,24} The break point analysis found that older men were less willing and men who had condomless sex with casual partners were more willing to use PrEP, echoing international research.^{21,24-26} Concerns about taking medication and side effects, perceptions of low risk, and cost are among the main barriers to willingness to use PrEP.^{21,24-26} Although willingness to use PrEP has increased and concern about its use has fallen among Australian GBM,¹² it is unclear to what extent “demand-side interventions” can be used to “improve risk perception and awareness and acceptability of prevention approaches” like PrEP,³ particularly among GBM who have concerns about taking medication.

The second cascade also illustrates the potential to monitor retention in care (using recent HIV and STI testing as a proxy for retention) and also some aspects of quality of life. We operationalized this using a scale that measures reduced HIV concern and increased sexual pleasure as a result of PrEP.¹² By including this measure, we were responding to some criticisms of the HIV cascade of care, which does not assess quality of life after treatment.²⁷

We acknowledge the limitations of our analyses. As recommended,² both cascades drew on population-level surveys of GBM rather than service-level data, but neither data source is representative. Representative samples of Australian GBM would feature a broader age range, more men from regional areas, and bisexual men.²⁸ However, our surveys are targeted at GBM at higher risk of HIV, who are overrepresented in metropolitan areas.¹⁸ Both surveys contained slightly different questions, so we had to

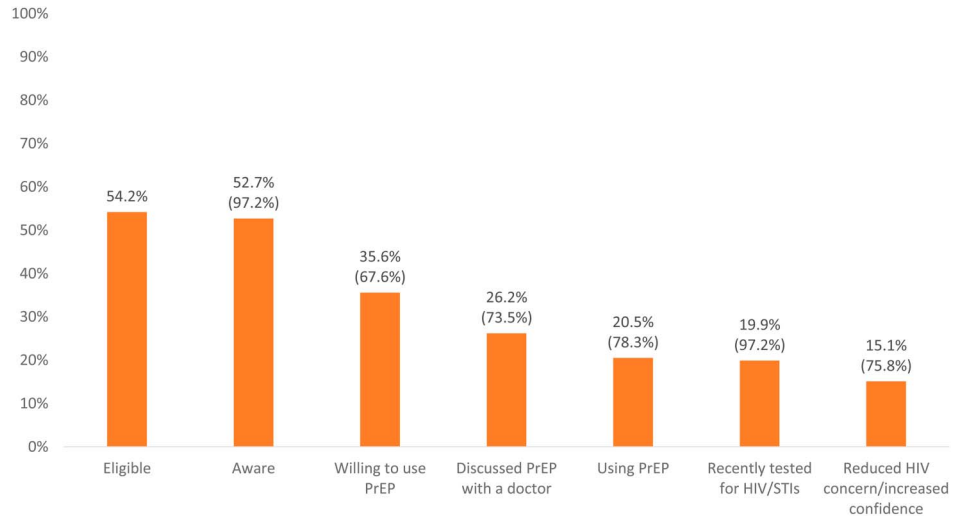


FIGURE 2. PrEP cascade for non-HIV-positive participants in the PrEPARE project, 2017 (N = 1038). Percentages in parentheses are calculated with the previous cascade step as the denominator.

operationalize PrEP eligibility differently for each cascade, with a more generous definition for the PrEPARE cascade. Other cascade steps (like PrEP awareness) were also measured differently. This highlights one of the difficulties of using existing systems to create PrEP cascades when this was not an original aim of either study. The GCPS function as routine behavioral surveillance of GBM and do not ask detailed questions about attitudes to PrEP, although our results suggest if there was room, a measure of willingness to use PrEP would be useful. The PrEPARE Project assesses the acceptability of PrEP in detail, but is a much smaller study than the GCPS, and may be less reliable in assessing national PrEP coverage. PrEPARE may over-recruit GBM who have heard of or are using PrEP, and the survey sample was more gay identified and reported more risk behavior than the GCPS. We have fashioned cascades from the data sources we had available, but they may overlook a range of influences on PrEP uptake,⁴ over-estimate eligibility, or give the misleading impression that PrEP uptake always proceeds in a linear fashion.^{29,30} However, in contrasting 2 different cascades, we have highlighted the strengths and weaknesses of using existing data sources to monitor PrEP uptake by GBM in Australia.

The PrEP cascades we developed can be updated periodically to monitor PrEP uptake by Australian GBM. Many other countries cannot develop similar cascades because they do not conduct regular behavioral surveillance.¹⁴ Contrasting the 2 cascades reveals their strengths and weaknesses. Shorter cascades may be easier to construct and repeat but may highlight fewer points of intervention. Longer cascades require more measures, which may only be possible in specialized studies, but they highlight more points of intervention. We believe that we are the first to construct a PrEP cascade showing change over time, including the rapid increase in PrEP use among eligible Australian GBM between 2016 and 2018. Comparing the 2 cascades suggests that coverage has been affected by the availability of PrEP in different states, socioeconomic factors, and willingness to use PrEP among GBM. These will need to be addressed to encourage further uptake among GBM.

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