Comprehensive HIV risk reduction interventions for 2020 and beyond: product choices and effective service-delivery platforms for individual needs and population-level impact

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Purpose of review
This review summarizes key HIV prevention strategies in the 2020 toolkit and discusses opportunities to maximize the public health impact of these prevention interventions at a population level.

Recent findings
HIV prevention has relied on counseling, HIV testing, and condom distribution for the past three decades. Recent exciting work has provided evidence on effective HIV prevention interventions, including antiretroviral therapy for HIV prevention, expanding preexposure prophylaxis modalities, and voluntary medical male circumcision which all reduce individual-level HIV risk. Efficient service-delivery approaches are necessary to deliver these products at scale while addressing population-specific needs. These approaches include: making it easier to get individuals HIV tested and linked to prevention services; de-medicalization to increase access to prevention products; creating welcoming clinic service-delivery environments; and integrating HIV prevention products into existing clinical platforms to support ongoing care engagement.

Summary
The 2020 HIV prevention toolkit includes powerful HIV prevention options, and product choice will be increasingly imperative. Meeting ambitious global HIV reduction targets in the next decade will require improved service-delivery platforms to get prevention choices to persons at risk while layering prevention coverage to achieve population-level impact.

Keywords
antiretroviral therapy, HIV prevention, HIV testing, preexposure prophylaxis, voluntary medical male circumcision

INTRODUCTION

During first three decades of the HIV epidemic, HIV prevention relied on a limited package of interventions: behavior change counseling, distribution of condoms and clean injection equipment, treatment of sexually transmitted infections (STIs), and HIV testing. Those foundational interventions remain as important as ever, but the past decade has also seen rapid advancement in the development of novel, highly-effective, biomedical interventions, some of which have the ability to eliminate HIV risk at the individual level. In the next decade, we will be challenged with taking these new approaches to scale to deliver them to populations at greatest HIV risk.

In 2014, UNAIDS released an ambitious 'fast-track' strategy to end the HIV/AIDS epidemic worldwide by 2030 [1]. This strategy calls for rapid increases in HIV testing and diagnosis, antiretroviral treatment (ART), and viral suppression (shorthanded as the '90–90–90 targets') by 2020 and even higher targets ('95–95–95 targets') by 2030 [1]. At the same time, ambitious 2020 targets have been set for voluntary medical male circumcision (VMMC, 25 million young men) and preexposure prophylaxis (PrEP, 3 million individuals) [1]. Combining primary and secondary prevention at the population level has the potential to massively decrease the global burden of new infections; however,

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KEY POINTS

- The 2020 HIV prevention toolbox includes exciting and effective approaches such as universal testing and treatment with ART, PrEP modalities, and VMMC.
- To maximize the public health benefit from these approaches, service-delivery platforms must: make it easier for individuals to get HIV tested and link to prevention services; de-medicalize prevention services; create safe and welcoming service-delivery environments that address individuals' HIV prevention needs as well as their broad health concerns; and integrate HIV prevention services with existing clinic infrastructure.
- The HIV prevention toolbox in 2020 and beyond can leverage and layer prevention approaches, encouraging HIV prevention product choices and building off of existing service-delivery infrastructure as new prevention products and vaccines enter the market.

these targets may fail to match realities of service access on the ground or capture granular trends in HIV incidence among marginalized, highest-risk groups [2▪].

There is no 'one-size-fits-all' HIV prevention solution. HIV prevention in 2020 and beyond will be about providing choices in prevention products and delivering these products through platforms that efficiently and effectively reach those at greatest risk, thus aiming for population-level impact. This review will summarize the current state of HIV prevention options, with a particular focus on recent findings around products, populations, and platforms.

TEXT OF REVIEW

Products: recent work on HIV prevention options for the 2020 toolkit

New studies continue to expand today's HIV prevention toolkit, with exciting recent work on ART for HIV prevention, expanding PrEP modalities, and continued learning about the VMMC's prevention benefits (Table 1) [3].

Table 1. Recent findings for products in the 2020 HIV prevention toolkit

HIV prevention strategy	2020 toolkit products	Key findings from recent individual randomized trials, subgroup analyses, and observational studies[a]	Key findings from recent demonstration, implementation, and community-based studies[b]	Potential barriers to future intervention delivery
Universal testing and treatment	ART	~0 HIV infections observed in heterosexual and MSM serodiscordant couples in which the partner living with HIV had a suppressed viral load [6,7▪▪,8▪▪]	Community-based UTT approaches result in increased rates of HIV testing, linkage to care, and viral suppression [39▪▪,40,41▪▪,42▪▪,43▪▪,44▪▪] Two studies report improvements in population-level HIV incidence because of community-based approaches that include UTT [43▪▪,44▪▪]	Nonadherence limits product effectiveness Gaps in delivering ART to men and younger individuals Delayed linkage to care after testing
Preexposure prophylaxis	Daily oral FTC/TDF; On-demand FTC/TDF; Daily oral FTC/TAF; Monthly dapivirine vaginal ring	Daily FTC/TDF >90% effective at reducing HIV incidence when taken with high adherence [11–14] 'On-demand' FTC/TDF dosing is efficacious among MSM [28] FTC/TAF appears to provide comparable protection as FTC/TDF [30▪▪] Dapivirine ring is safe and acceptable; randomized trials show a ~30% reduction in HIV incidence and effectiveness may be ~50% or greater when used with high adherence [31,32]	Oral PrEP is highly acceptable and effective as an HIV prevention option in real-world delivery settings in the United States, Europe, Asia, and sub-Saharan Africa [16,17,20,21▪▪] Women find oral PrEP to be an empowering, female-initiated approach [49,51▪,78▪] Women find the dapivirine ring easy to use and acceptable as a monthly prevention option, particularly after counseling and peer support [33▪▪,34▪▪]	Nonadherence limits product effectiveness Need to better align delivery and adherence counseling to at-risk periods Drug concentrations may be more sensitive to missed doses in vaginal than rectal tissue Concerns around pill storage and community stigma around PrEP particularly in settings in which less is known about it Concerns around ring size, appearance, and partner reactions
Voluntary medical male circumcision	Surgical and nonsurgical VMMC methods	Results in ~60% reduction in HIV transmission [36▪]	VMMC has reached 15 million people [38▪] Results in 40% reduction in HIV transmission in MSM from low and middle-income countries (20% reduction overall) [36▪]	Hesitations related to side-effects and cultural norms Need to reach men in high incidence cohorts to achieve population impact

ART, antiretroviral therapy; FTC, emtricitabine; MSM, men who have sex with men; PrEP, preexposure prophylaxis; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; UTT, universal test and treat; VMMC, voluntary medical male circumcision.
[a]Data in this column reflect findings from blinded and open-label individual randomized controlled trials, prospective cohort studies, and post hoc subgroup analyses conducted with samples of high adherers.
[b]Data in this column reflect findings from community randomized trials and more 'real-world' implementation and demonstration projects.

Viral suppression from effective ART eliminates sexual HIV transmission risk in heterosexual partnerships [4], confirming earlier observational data [5]. The last few years have also seen clear evidence, from large and carefully conducted observational cohort studies, that transmission risk is similarly eliminated with ART for men who have sex with men (MSM) over thousands of years of follow-up [6,7▪▪,8▪▪]. Evidence of the clinical and prevention benefits of ART in 2015 prompted a global 'universal test and treat' (UTT) standard, in which ART is recommended for all persons living with HIV [9]. In the past year, there has been an evolution in messaging about the prevention benefits of ART with new, clear, and correct statements from scientists and normative agencies that viral suppression eliminates HIV sexual transmission risk (colloquially branded as 'undetectable equals untransmittable' or 'U=U') [10].

The evidence that PrEP is effective for HIV prevention was established first for oral emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) in pivotal clinical trials [11–13] and demonstration studies [14]. A global PrEP recommendation followed in 2015. As of 2018, FTC/TDF PrEP has regulatory approval in over 40 countries [15]. Open-label and demonstration projects have reported markedly low HIV incidence and frequent willingness and desires to take daily oral PrEP in real-world delivery settings [16,17,18,19,20,21▪▪]. Only a handful of PrEP breakthrough infections worldwide have been seen (almost all of which seemingly reflect transmitted resistance to the PrEP medications), confirming analyses from the clinical trials showing nearly-complete HIV protection when PrEP was taken with good adherence [22▪,23,24,25]. Recent PrEP research has grappled with defining long-term adherence goals for PrEP, better aligning PrEP use with individuals' dynamic sexual behavior, and improving adherence counseling to maximize PrEP effectiveness during periods of high HIV risk [26,27▪].

A single clinical trial tested FTC/TDF PrEP dosing around sex events ('on-demand dosing') among MSM [28], demonstrating HIV protection seemingly comparable to daily dosing. On-demand PrEP appears workable in real-world delivery settings, with about as many MSM choosing on-demand as daily when both options are offered [29▪], suggesting that there is appetite for continued product development of new on-demand PrEP agents.

New oral PrEP agents are also on the horizon. Recently, a combination daily dose of emtricitabine and tenofovir alafenamide (FTC/TAF) was compared to FTC/TDF, finding very low HIV incidence for both regimens (<0.5% per year), despite high rates of concurrent STIs [30▪▪]. Statistically, FTC/TAF was noninferior to FTC/TDF, with nearly all infections occurring in the absence of PrEP use; FTC/TAF may also have properties that result in improved long-term safety (compared to FTC/TDF which already has an excellent safety profile) [30▪▪].

The monthly dapivirine vaginal ring was recently reported to be a safe, acceptable, and efficacious longer-term primary HIV prevention option in two pivotal trials [31,32]. Open-label extension studies from these trials suggest reasonable uptake, use, and HIV protection [33▪▪,34▪▪]. Although not yet available outside of research settings, when the dapivirine ring becomes included with other HIV intervention packages it will offer an important additional primary prevention choice which may be particularly appealing for individuals who have difficulty taking a daily PrEP pill. Barriers to ring use include concerns about ring appearance, side-effects, and male partner reactions [31,35]. The ring is about 5–7 years behind oral PrEP and lessons from the oral PrEP efficacy-to-implementation pipeline may help improve product framing and counseling approaches and prepare for widespread ring delivery in the near future.

VMMC significantly decreases HIV acquisition risk in heterosexual men [36▪]. Recent meta-analyses have explored the HIV prevention benefit of VMMC among MSM and report a 20% reduced HIV risk across over 40 observational cohort studies [36▪] and a nearly 40% reduction in risk when data were limited to men from low and middle-income countries [37].

Populations: uptake and use of HIV prevention products to achieve impact at scale

ART, oral PrEP, and VMMC are currently being delivered to general populations in high-prevalence areas and to key populations including adolescent girls and young women (AGYW), pregnant women, female sex workers, transgender women (TGW), HIV serodiscordant couples, MSM, and injection drug users. Each of these populations has unique prevention needs and product preferences. Key populations also face social and legal barriers to service utilization including criminalization of HIV and sex work, stigma, and marginalization [3].

VMMC programs have reached over 15 million men in high HIV prevalence countries in sub-Saharan Africa [3,38▪]. However, more work is needed to increase the number of circumcised men from high HIV incidence cohorts to improve the population-level impact on HIV incidence [3,38▪]. Although conventional healthcare communication messaging may reach early adopters of

VMMC, behavioral economics and marketing research have highlighted the importance of community-wide initiatives that target social and sexual networks and create broader community demand for VMMC to appeal to hard-to-reach populations [38▪]. ART, PrEP, and other HIV prevention strategies can learn from the successes and trials of VMMC roll-out, particularly around community engagement, demand creation, and service-delivery models, to more efficiently deliver prevention tools at scale [38▪].

Five community-based trials were recently conducted to understand the population-level effects of UTT on progress toward 90–90–90 targets and community-level HIV incidence [39▪▪,40,41▪▪,42▪▪,43▪▪,44▪▪]. These trials have reported that community-based HIV prevention and treatment approaches, including UTT alongside improved testing services and community mobilization activities, resulted in improved rates of HIV testing, linkage to care, and viral suppression and helped move countries toward (and above) 90–90–90 targets. Two of these trials found statistically significant, although modest, reductions in HIV incidence in communities receiving community-based testing, linkage, and universal treatment [43▪▪,44▪▪], emphasizing that HIV testing delivered at scale and coupled to universal ART access is both absolutely necessary but also insufficient to eliminate HIV transmission at the population scale. Indeed, three of the trials achieved 90–90–90 goals but had persistent HIV incidence far in excess of what is predicted to be necessary for epidemic control [2▪]. In all of these studies, important barriers to testing and viral suppression included relatively lower testing and ART uptake for men and younger populations and challenges in rapidly linking individuals to HIV care [39▪▪,41▪▪,42▪▪].

Currently, only about 500 000 individuals have enrolled in PrEP demonstration studies, implementation projects, and service delivery programs worldwide [14]. In the United States, where the largest number of PrEP users reside, less than 17% of the 1.2 million individuals with a PrEP indication have ever taken PrEP, with gaps in PrEP availability and uptake greatest for racial and ethnic minorities, younger individuals, and those with lower education levels [15,45,46]. Low and middle-income countries also face substantial gaps in PrEP coverage for key populations. In Kenya, 10% of eligible high-risk individuals initiated PrEP by the end of 2017 [27▪]. In South Africa, only 12% of sex workers reported PrEP use during 2017, although PrEP uptake was encouragingly higher among MSM (43%) during the same period [47,48]. For key populations accessing PrEP services, improved counseling and engagement for medication refill visits may help boost continued use but will not address gaps in product uptake and demand creation [49,50▪]. High-risk women who are pregnant, breastfeeding, or planning to become pregnant also face barriers to PrEP use related to provider and community stigma, lack of provider training, and busy antenatal and postnatal clinic settings, which prevent countries from implementing World Health Organization recommendations about PrEP use during peri-conception, pregnancy, and breastfeeding periods [51▪,52].

Platforms: improving HIV prevention service delivery

With effective prevention options now available, great attention in the last few years has gone into developing strategies to improve their delivery. Several recent studies have seen improved ART, oral PrEP, and VMMC coverage and effectiveness using four key service-delivery approaches, either alone or in combination (Fig. 1).

The first service-delivery approach focuses on making it easier for individuals to get HIV tested, as the starting point for linkage to treatment and prevention services and demand creation around HIV prevention products. Self-testing and home and community-based testing models remove HIV testing from often overcrowded and stigmatizing clinic waiting rooms and bring it directly to populations. HIV self-testing programs in Uganda and Zambia have reported increases in HIV testing frequency and successful integration with ART and PrEP services [53▪,54▪,55]. Self-tests do experience a low, but measurable, frequency of user error in execution or interpretation which may delay linkage to HIV treatment and prevention services in individuals with less knowledge about correct self-test use [53▪,54▪]. Mobile van-based HIV testing (e.g., 'Tutu Teen Tester') has also been successfully used to bring testing, along with ART and PrEP, into communities and may be particularly useful for male populations who would not regularly access clinic-based services [56,57]. Although community outreach testing approaches are important to reduce the number of undiagnosed individuals, they may be less cost-effective than more targeted testing campaigns and should be primarily used to find those who are missing from traditional clinic-based testing services [58]. Individuals who receive HIV testing are primed for thinking about their HIV risk and testing provides an important window for demand creation around engagement with ART, PrEP, and VMMC services [38▪,59]. Importantly, HIV counselors and service providers should emphasize U=U messaging as part of HIV testing and regular clinical care to reduce HIV-related stigma, improve community

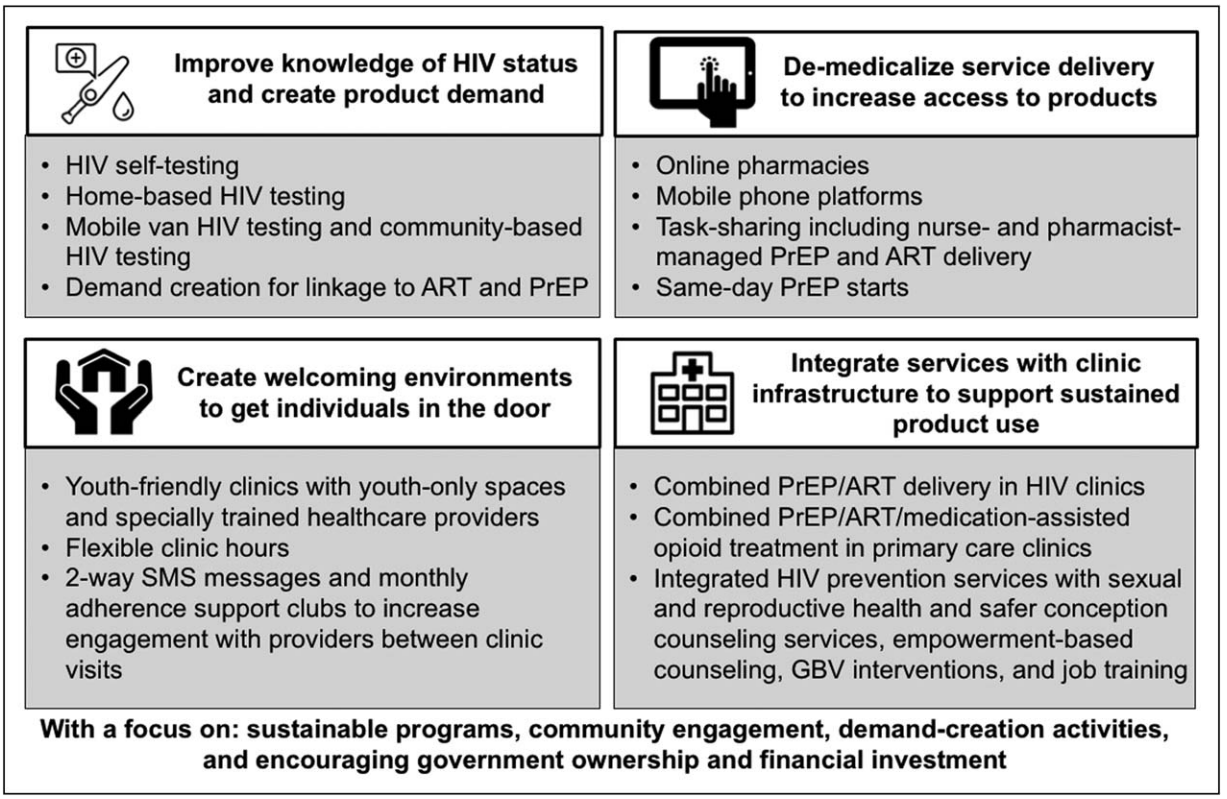

FIGURE 1. Four key service-delivery approaches for HIV prevention product delivery. ART, antiretroviral therapy; GBV, gender-based violence; PrEP, preexposure prophylaxis; SMS, short message service.

knowledge and awareness of the benefits of ART, and increase service uptake [60].

The second approach involves improving access to HIV prevention services through task-shifting and de-medicalized approaches to HIV prevention service delivery. For example, online oral PrEP pharmacies have been rolled out in the United States and the United Kingdom to facilitate online PrEP ordering and pill pick-up (e.g., 'Nurx', 'iwantPrEP now'), allowing individuals to leapfrog clinic appointments [61,62▪]. Mobile technologies (e.g., SMS messages, smart phone applications) can create demand for PrEP, support individual decision-making around PrEP use, and help people identify clinics in which they can access PrEP [63–66]. PrEP implementation studies have highlighted the importance of reducing geographic barriers and streamlining PrEP access which could be achieved through pharmacist and nurse-managed PrEP delivery and same-day PrEP starts [62▪,67▪,68▪,69▪]. These task-shifting and de-medicalized approaches have been tried and scaled successful for ART delivery [70], and could also be used for future roll-out of the dapivirine ring and other novel HIV prevention products coming down the pipeline.

The third approach focuses on creating safe and welcoming service-delivery environments which can get individuals through the clinic door and improve interactions with HIV service providers who are understanding and responsive to their specific needs. Youth-friendly healthcare clinics, including youth-only spaces, internet and computer access, flexible hours, and specially trained healthcare providers, facilitate regular HIV testing, ART, PrEP, and hormonal contraception uptake among adolescents particularly in sub-Saharan Africa [71▪,72▪,73]. Extended clinic hours and shifted opening times have been helpful for increasing PrEP coverage among MSM in London as well [62▪]. Two-way SMS messages with healthcare providers and monthly in-person adherence clubs with other PrEP or ART users and a staff facilitator may also increase positive interactions with clinic staff and improve engagement with HIV prevention services in-between routine clinic visits [49,50▪].

The fourth approach integrates HIV prevention product delivery and counseling into existing clinical platforms to support ongoing engagement in HIV prevention services, while leveraging the strengths of clinic settings. Synergies between HIV prevention services and other healthcare programs can maximize the public health potential of HIV prevention products while also improving other health outcomes. Female-centered PrEP

implementation projects have begun to integrate HIV prevention with sexual and reproductive healthcare services, safer conception counseling, gender-based violence services, and job and career training to improve PrEP uptake and persistence, while addressing broader societal issues that interfere with PrEP pill-taking over time [74–77,78▪,79]. Studies with HIV serodiscordant couples have successfully delivered integrated PrEP with ART and behavioral counseling in busy HIV clinic settings in East Africa, resulting in significant reductions in HIV transmissions within couples, high levels of ART and PrEP uptake and sustained adherence, and secondary benefits on safer conception outcomes, improved monitoring of sexually transmitted infections, and reduced vertical HIV transmissions [16,17]. PrEP delivery has also been successfully integrated into antenatal and postnatal care settings in Kenya [51▪]. HIV treatment programs have seen improvements in ART adherence and engagement in care outcomes by integrating mental health, microfinance services, and medication-assisted opioid treatment with ART provision [80▪,81,82]. Both ART and VMMC services were introduced as vertical programs, but successful PrEP integration may be more wide-reaching. PrEP has found a home within existing sexual and reproductive health delivery spaces in several cities worldwide [74,77,78▪,79], and continued integration could help to revitalize sexual and reproductive health services. Current work on PrEP integration will also build critical service-delivery infrastructure for the roll-out of future HIV prevention products.

Although these four delivery approaches have the potential to more efficiently provide PrEP to high-risk individuals, successful HIV prevention service delivery will also require sustainable programs, government ownership and community engagement, and financial investments to ensure adequate supply of drugs, personnel, and resources in the face of competing health issues and government priorities (Fig. 1). In the United States and some European countries, only high-cost, branded PrEP is currently available but lower price generic versions are on the market in many lower resource settings and financial resources to develop and provide generic PrEP options will increase cost-effectiveness, while minimizing financial burdens for the individual [38▪]. Integrated and de-medicalized PrEP delivery approaches have the potential to reduce costs to the healthcare system, but local and national government buy-in is required to develop these programs, generate demand for them, and deliver PrEP at scale. Programmatic data and mathematical models can be used to inform cost-effective PrEP delivery and to convince policymakers of affordable PrEP delivery avenues in the future.

Putting it together: choice and the case for a layered HIV prevention model

None of our HIV prevention options are one-size-fits all approaches for individuals or at the population level. Indeed, the mantras for prevention for the next decade will emphasize the importance of individual choice among prevention options and layering coverage of those options at the population level to achieve impact. Hints that such integrated HIV prevention approaches can work are already emerging. The New South Wales Expanded PrEP Implementation in Communities (EPIC-NSW) program built upon existing widespread test-and-treat infrastructure to rapidly expand targeted PrEP delivery among MSM communities in Sydney and nearby areas. The program exceeded expectations with respect to PrEP uptake (9714 people were enrolled on PrEP over a 2-year period) and showed an approximately 50% reduction in new HIV infections over a period of a year in gay suburbs in which HIV testing and ART delivery were already assumed to be delivered at scale [69▪,83▪▪]. These data show that layering in a new primary prevention intervention for targeted delivery still had an incidence effect particularly in high-risk populations when delivered alongside HIV testing and ART programs, which emphasizes how layered interventions, even with imperfect coverage of each component, can amplify prevention effects. Similar declines in new HIV infections have been reported in Seattle and San Francisco [46,84▪▪,85], two cities that have had test-and-treat and same-day starts for some time now, with the greatest declines seen once scale-up of PrEP reaching 20–40% of high-risk MSM, was achieved [46,84▪▪,85]. These cities highlight that better testing coverage, reduced barriers to treatment, and rapid PrEP integration, in combination, can result in bigger population-level gains in HIV control than any of these strategies alone.

Looking forward: the 2025 toolbox and beyond

We can look forward to the arrival of promising new HIV prevention products by 2025 and beyond, including new oral, injectable, implantable, and topical delivery approaches in the preclinical to phase 3 pipeline. Broadly neutralizing antibodies (essentially a large biologic molecule as PrEP, instead of a small molecular antiretroviral) may offer another prevention option during the same time period, and several prophylactic HIV vaccine

candidates are under investigation as well. Importantly, none of these new options will be one-size-fits-all either – each will carry cost, convenience, side-effect, and acceptability pros and cons, emphasizing how the idea of choice for prevention will become increasingly important. Experience from the contraception field teaches that individuals want a range of prevention options to meet their needs at different times in their lives and the availability of choice actually expands the proportion of persons accessing effective prevention [86,87▪,88,89]. Notably, it is likely that there may be a range of HIV prevention efficacies seen for these new products. For example, the dapivirine ring appears to have a ceiling of protection less than 90% even with evidence of good use and new vaccine trials are aiming for ~50% reductions in HIV risk; like contraception, there may be interest by individuals for HIV prevention tools that offer convenience, privacy, or other characteristics even if protection is less than for other products on the market. Platforms for delivery of these new prevention strategies will continue to be refined as individuals are tasked with returning multiple times each year for an injection, infusion, or vaccine booster and we will need to develop new delivery approaches with minimal burden on a large scale for healthy, HIV-uninfected persons. Thus, we can take some of the lessons learned about service-delivery and layered intervention approaches to deliver these novel biomedical HIV prevention and vaccine approaches within the context of a wide range of existing, highly effective prevention options.

CONCLUSION

The 2020 HIV prevention toolkit includes exciting and powerful prevention options, with more on the way. What works for some may not work for all. Product delivery platforms are evolving, removing barriers to product use by bringing interventions to the communities, integrating and de-medicalizing HIV prevention services, and meeting broader client needs. At a population-level, layered HIV prevention approaches can have tremendous benefit, supporting individual choice and product preferences, and improving service-delivery strategies. This integrated, community-based HIV prevention approach is necessary to meet the ambitious global HIV reduction targets in the next decade.

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Conflicts of interest

There are no conflicts of interest.

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- ▪ of special interest
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This manuscript describes an intervention-centric cascade for defining metrics around PrEP uptake and coverage for AGYW. It also emphasizes the need to reframe definitions of 'low uptake' to focus on delivering oral PrEP to AGYW during periods of HIV risk when they most need PrEP.

28. Molina JM, Capitant C, Spire B, *et al.* On-demand preexposure prophylaxis in men at high risk for HIV-1 infection. N Engl J Med 2015; 373:2237–2246.
29. ■ Noret M, Balavoine S, Noret M, *et al.* Daily or on demand oral TDF/FTC for HIV preexposure prophylaxis: experience from an hospital-based clinic in France. AIDS 2018. (e-pub). doi: 10.1097/QAD.0000000000001939.

This open-label, prospective cohort study describes the real-world use of on demand oral TDF/FTC PrEP among men who have sex with men in France. Of 1069 eligible individuals, 98.1% started PrEP, most opted for on demand PrEP, and HIV incidence was low, indicating high acceptability and effectiveness of on demand oral PrEP.

30. ■■ Hare CB, Coll J, Ruane P, *et al.* The phase 3 Discover Study: daily F/TAF or F/TDF for HIV preexposure prophylaxis. Abstract #104. Conference on Retroviruses and Opportunistic Infections (CROI) 2019; 2019 March 4-7; Seattle, WA, USA.

This randomized controlled trial compared daily FTC/TAF to FTC/TDF among 5387 adults in 11 countries. FTC/TAF was not inferior to FTC/TDF and both drugs were well-tolerated, indicating that FTC/TAF could be an additional efficacious and safe oral PrEP option.

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This open-label trial of the monthly dapivirine ring built off of prior work from Phase III randomized controlled trials. The study found high rates of ring uptake and consistent use and HIV incidence was half of what was expected in the absence of the dapivirine ring, indicating that the ring may offer an important additional HIV prevention modality for high-risk women.

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This open-label trial of the monthly dapivirine ring built off of prior work from Phase III randomized controlled trials. The study reported high rates of consistent ring use and HIV incidence was half of what was expected in the absence of the dapivirine ring, indicating that the ring may offer an important additional HIV prevention modality for high-risk women.

35. Montgomery ET, van der Straten A, Chitukuta M, *et al.* Acceptability and use of a dapivirine vaginal ring in a phase III trial. AIDS 2017; 31:1159–1167.
36. ■ Sharma SC, Raison N, Khan S, *et al.* Male circumcision for the prevention of human immunodeficiency virus (HIV) acquisition: a meta-analysis. BJU Int 2018; 121:515–526.

This meta-analysis incorporated data from 49 studies to assess the HIV prevention benefit of VMMC among heterosexual and homosexual men. VMMC was found to be protective for heterosexual and homosexual men, showing strong evidence that VMMC can effectively reduce HIV risk for men.

37. Pintye J, Baeten JM. Benefits of male circumcision for MSM: evidence for action. Lancet Glob Health 2019; 7:e388–e389.
38. ■ Reed JB, Patel RR, Baggaley R. Lessons from a decade of voluntary medical male circumcision implementation and their application to HIV preexposure prophylaxis scale up. Int J STD AIDS 2018; 29:1432–1443.

This commentary highlights critical lessons learned during VMMC roll-out (e.g., demand creation, government and key stakeholder involvement) to inform oral PrEP implementation efforts.

39. ■■ Iwuji CC, Orne-Gliemann J, Larmarange J, *et al.* Universal test and treat and the HIV epidemic in rural South Africa: a phase 4, open-label, community cluster randomised trial. Lancet HIV 2018; 5:e116–e125.

This phase 4 cluster randomized controlled trial examined the effect of a UTT approach on HIV incidence in 22 communities in South Africa. There was no statistically significant difference in HIV incidence observed between intervention and control clusters, which was likely explained by poor linkage to care rates. UTT approaches must also focus on improving linkage to care rates to see population-level impacts.

40. Petersen M, Balzer L, Kwarsiima D, *et al.* Association of implementation of a universal testing and treatment intervention with HIV diagnosis, receipt of antiretroviral therapy, and viral suppression in East Africa. JAMA 2017; 317:2196–2206.
41. ■■ Havlir D, Charlebois E, Balzer L, *et al.* SEARCH community cluster randomized study of HIV test and treat using multi disease approach and streamlined care in rural Uganda and Kenya. Abstract #WEAX0106LB. The 22nd International AIDS Society Conference (IAS 2018) 2018; Amsterdam, the Netherlands.

This phase 4 cluster randomized controlled trial examined the effect of a UTT approach on HIV incidence, compared with HIV testing and linkage to care according to national guidelines, in Uganda and Kenya. HIV incidence did not statistically significantly differ between intervention and control communities, but the intervention group had improved mortality and other disease outcomes pointing to other health benefits of UTT. The intervention also resulted in achievement of 90-90-90 targets.

42. ■■ Khan S, Spiegelman D, Walsh F, *et al.* Universal test and treat (UTT) versus standard of care for access to antiretroviral therapy in HIV clients: The MaxART stepped-wedge randomized controlled health systems trial in Swaziland. Abstract #WEAX0102LB The 22nd International AIDS Society Conference (IAS 2018); 2018; Amsterdam, the Netherlands.

This stepped wedge randomized controlled trial examined the effect of a UTT approach on HIV incidence in 14 health facilities in Swaziland. UTT importantly improved retention in care and viral suppression rates, but there was no statistically significant difference in HIV incidence between intervention and control groups.

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This community randomized trial examined the effect of a UTT approach on HIV incidence in 30 communities in Botswana. There was a statistically significant difference in HIV incidence in the intervention versus standard of care communities, indicating the importance of UTT in reducing population-level HIV transmission.

44. ■■ Hayes RJ, Donnell DJ, Floyd S, *et al.* Impact of universal testing and treatment in Zambia and South Africa: HPTN 071 (PopART). Abstract #92 Conference on Retroviruses and Opportunistic Infections (CROI 2019); 2019; Seattle, WA, USA.

This cluster-randomized trial examined the effect of a UTT approach on HIV incidence in 21 communities in Zambia and South Africa. The study found statistically significantly lower HIV incidence rates in intervention arms compared with the control arm. Rates were lowest in the arm receiving PopART intervention activities with ART initiation according to current national guidelines, although guidelines changed to UTT partway through the study.

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47. Kenya National AIDS & STI Control Programme (NASCOP). Implementation of PrEP in Kenya. 19th Annual International Conference on AIDS and STIs in Africa (ICASA); 2017 Dec 4; Abidjan, Cote D'Ivoire

48. South African National Department of Health (NDoH). Preexposure prophylaxis implementation in South Africa. 19th Annual International Conference on AIDS and STIs in Africa (ICASA); 2017 Dec 4; Abidjan, Cote D'Ivoire

49. Gill K, Dietrich J, Gray G, *et al.* Pluspills: an open label, safety and feasibility study of oral preexposure prophylaxis (PrEP) in 15-19 year old adolescents in two sites in South Africa. Abstract #TUAC0207LB. 9th International AIDS Society Conference on HIV Science; 2017 July 23-26; Paris, France

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This work presents baseline statistics from a cohort of 434 young women enrolled in the HPTN 082 randomized controlled trial of PrEP adherence support approaches. PrEP uptake was very high and HIV risk behaviors and STI prevalence were also high in this cohort indicating that the study successfully delivered PrEP to an at-risk population.

51. ■ Pintye J, Kinuthia J, Roberts DA, *et al.* Integration of PrEP services into routine antenatal and postnatal care: experiences from an implementation program in Western Kenya. J Acquir Immune Defic Syndr 2018; 79:590–595.

This manuscript describes the operationalization of PrEP implementation within antenatal and postnatal care services in Kenya. PrEP counseling and initiation added approximately 15 min to clinic visits, but this time will likely decrease with additional community awareness about PrEP, and findings support future integrated PrEP delivery within existing healthcare infrastructure in Kenya.

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Results from two self-testing randomized controlled trials in Zambia and Uganda found that self-testing was preferred to clinic-based testing and self-testing participants were very interested in PrEP. Future PrEP delivery programs could include self-testing to reduce clinic HIV testing burden.

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A majority of 104 self-testing participants in Uganda reported difficulty with at least one step in self-testing and misinterpretation of results was common. Training on the use of self-test kits is necessary to prevent errors in kit use and interpretation of self-test results.

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The Dean Street Express clinic was developed to support PrEP initiations via community education initiatives and PrEP information and screening on clinic touch screens. The community-based services enabled enrollment and follow-up of 17 000 participants in 3 months, emphasizing the importance of informational campaigns and mHealth approaches to support rapid PrEP delivery in busy urban locations.

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The Princess PrEP program involved PrEP delivery to MSM and TGW by trained key population community health workers. The program successfully delivered PrEP to MSM and TGW with high levels of adherence reported over time and future scale-up of key population PrEP programs could follow a similar model to reach MSM and TGW.

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This article describes an evaluation of a Seattle-based pharmacy-managed PrEP program. Of 714 patients evaluated, 97.3% initiated PrEP, most began medications the same day as their appointment, and there were no seroconversions observed. Pharmacy-managed PrEP may provide a successful alternative model of PrEP care to clinic-based PrEP delivery.

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The EPIC-NSW program points to the success of nurse-led PrEP delivery to facilitate rapid expansion of PrEP delivery in public health clinics. No serious adverse events were reported and over 8000 participants were initiated on PrEP in under 2 years.

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AGYW randomized to attend youth-friendly healthcare services in Malawi were more likely to receive HIV testing, condoms, and hormonal contraception than those in standard of care services. Youth-friendly healthcare services may improve access to health resources for AGYW.

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This manuscript highlights results from focus group discussions with South African adolescents who were asked about their preferences in sexual and reproductive health service (SHRS) delivery. Adolescents wanted appropriately tailored information, flexible hours, and youth-friendly providers, providing guidance for improving future SRHS to meet adolescents' needs.

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This presentation provides results from a safer conception intervention delivering integrated ART and PrEP to HIV serodiscordant couples with immediate fertility desires in Kenya. Pregnancy rates were high in this pilot study, zero HIV transmissions were observed, and integrated PrEP, ART, and safer conception service delivery was feasible in this context.

79. Narasimhan M, Celum C, Askew I, *et al.* Supporting people living with HIV in serodiscordant partnerships to attempt a desired pregnancy by integrating sexual and reproductive health and HIV interventions. J Int AIDS Soc 2017; 20(Suppl 1):21829.

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This manuscript reports the findings from a randomized controlled trial delivering ART and medication-assisted treatment to people living with HIV who also injected drugs. The intervention increased both ART and medication-assisted treatment use and points to future directions for integrated HIV prevention and substance use services.

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83. ■■ Grulich AE, Guy R, Amin J, *et al.* Population-level effectiveness of rapid, targeted, high-coverage roll-out of HIV preexposure prophylaxis in men who have sex with men: the EPIC-NSW prospective cohort study. Lancet HIV 2018; 5:e629–e637.

Rapid PrEP implementation, as part of a combination HIV prevention approach, was associated with significant declines in HIV incidence in New South Wales and increased coverage of prevention options. Such integrated approaches with rapid PrEP scale-up may be necessary to decrease population-level HIV incidence.

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The article presents findings on temporal trends in HIV diagnosis, linkage to care, ART initiation, viral suppression, and clinical outcomes in the 'Getting to Zero' era. New HIV diagnoses declined and care indicators improved in recent years. Future successes will require increased attention to hard-to-reach populations.

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Results from a discrete choice experiment with 536 women in Kenya and South Africa emphasize desires for multipurpose HIV and pregnancy prevention technologies that address young women's different needs at different periods in their lives.

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