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Costs and outcomes of routine HIV oral pre-exposure prophylaxis implementation across different service delivery models and key populations in South Africa: a retrospective cohort study

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Summary

Background Despite several service delivery models that aim to improve uptake and persistence of pre-exposure prophylaxis (PrEP) in sub-Saharan Africa, the full costs of daily oral PrEP provision in routine care settings remain largely unknown. We aimed to evaluate outcomes and costs of daily oral PrEP delivery among key and priority populations at in-facility and community outreach programmes in South Africa.

Methods This retrospective cohort study was done at seven urban sites across South Africa with in-facility or community outreach PrEP service delivery models. We did top-down and bottom-up microcosting, from the provider perspective, of routine oral PrEP provision in programmes focusing on men who have sex with men (MSM), female sex workers, and adolescent girls and young women (aged 15–24 years) who initiated oral PrEP between March 12, 2018, and Aug 13, 2019. The primary outcome was PrEP in-hand at 6 months, defined as having sufficient PrEP drug dispensed at the last visit to have the drug available 6 months after PrEP initiation. A subset of enrolled participants with sufficient potential follow-up were included in a 12-month outcome analysis. We report the cost per client initiated on PrEP in 2021 US dollars.

Findings We enrolled 1281 people aged at least 15 years who initiated oral PrEP in either in-facility or community outreach programmes between March 12, 2018, and Aug 13, 2019. The proportion of participants with PrEP in-hand at 6 months varied from 41·8% (95% CI 31·9–52·2; 41 of 98 participants) at one MSM-focused clinic to 0% (0–6·7; 0 of 53 participants) in an MSM-focused outreach programme. Among 633 clients receiving oral PrEP with the potential for 12 months follow-up, 86 (13·6%) had PrEP in-hand at 12 months. The mean average 6-month costs per client initiating oral PrEP ranged from US$29 (95% CI 26–31) to $590 (488–692), with higher costs generally observed for in-facility programmes ($152, 140–164) than for outreach programmes ($84, 79–88). The mean average monthly cost per client with PrEP in-hand at 6 months ranged from $18 (15–21) to $160 (126–194).

Interpretation Costs and outcomes of daily oral PrEP provision across several populations and service delivery models in real-world settings show substantial variability. Policy makers should consider this variability when planning further scale-up of oral PrEP programmes in South Africa and the sub-Saharan Africa region to maximise opportunities to improve efficiency based on local context.

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Introduction

The HIV epidemic continues to affect millions of people globally, particularly in sub-Saharan Africa, which incurred almost 50% of new global infections in 2023.[1] South Africa is especially affected, with an estimated 140 000 new HIV infections and an HIV incidence of 4·55 per 1000 population in 2023.[2] Progress in HIV prevention has been slow, with global annual new infections declining by only 38% between 2010 and 2023, far short of the 2016 UN General Assembly target of a 75% reduction by 2020.[1,3] This slow decline is despite the introduction of pre-exposure prophylaxis (PrEP), a highly effective biomedical HIV prevention tool that can reduce the risk of HIV-1 acquisition by more than 95%.[4]

South Africa adopted the WHO recommendation to offer PrEP to those at substantial risk of HIV infection in 2016, beginning oral PrEP roll-out to select key populations at pilot sites and expanding nationally thereafter.[5] However, uptake has been slow, with only around 106 400 people at risk of HIV infection receiving PrEP at least once in 2020.[6] Although these numbers did

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Research in context

Evidence before this study

Although several modelling studies have investigated the cost and cost outcomes of pre-exposure prophylaxis (PrEP) in sub-Saharan Africa, evidence for real-world costs of providing PrEP in this region is scarce. We searched PubMed using the terms "PrEP" AND "cost analysis" AND "sub Saharan Africa" for studies published in English between Jan 1, 2016, and June 30, 2024. After excluding publications that were not relevant or derived results from models, we found only 14 studies covering seven countries that calculated the primary costs of providing PrEP in sub-Saharan Africa. These studies generally focused on one population group, costed interventions in a research setting, or used only ingredients-based methods without analysing associated outcomes.

Added value of this study

We include cost and cost outcomes from a large cohort of individuals who initiated PrEP through in-facility and community outreach service delivery models in seven distinct geographical locations in South Africa. Costs are based on actual individual resource utilisation data and programme expenses, differentiating this study from modelling and ingredients-based costing studies that identify and value resource requirements but do not consider the use of resources at the individual-client level. Such individual-level costs, which can be used as inputs in future PrEP models, have been called for in at least two large systematic reviews. This study provides evidence needed to inform scale-up of PrEP service delivery models. Using a microcosting approach across several sites that provide PrEP to different target populations, we cost the real-world implementation of in-facility and outreach models, contributing to the evidence required for HIV prevention scale-up and budget planning in South Africa and the wider sub-Saharan Africa region. These results add to the growing body of evidence on the outcomes and associated costs of routine implementation of PrEP programmes in the sub-Saharan Africa region and can be used to strengthen budget impact analyses, which will, in turn, assist policy makers in decisions regarding programme scale-up.

Implications of all the available evidence

Cost estimates for providing large-scale, routine, effective PrEP-delivery platforms that consider economies of scale, changes in marginal costs as programmes expand, and differences in costs and benefits for different populations and risk groups will be essential to the success and sustainability of PrEP programmes in sub-Saharan Africa.

increase, with almost 350 000 people receiving oral PrEP in 2021,[7] uptake is still suboptimal, representing only a small fraction of those estimated to be at high risk of HIV infection.[8] As South Africa continues to scale up oral PrEP provision, data are needed to inform the total cost and affordability of the various service delivery models. However, little information is available to support evidence-based resource allocation decisions in the public sector and, as funding responsibility for the South Africa PrEP programme shifts to the South African Government from international funders, such data are greatly needed.

Several modelling studies have investigated the cost-effectiveness of oral PrEP provision in sub-Saharan Africa, finding large variations in assumed costs.[9–12] Similarly, modelling studies in South Africa show cost-effectiveness only under particular conditions, such as population-targeted programmes in which PrEP clients self-select or have high assumed rates of uptake and persistence. These results are largely dependent on the cost estimates used and the assumptions around oral PrEP uptake and persistence.[13–15] Although modelled estimates provide useful approximations, the most accurate cost estimates are based on actual client resource usage in routine implementation and are crucial to calculating true cost-effectiveness.

An understanding of true resource utilisation, cost, and outcomes of different oral PrEP service delivery models in South Africa is currently lacking. We did a cost outcomes study to evaluate the cost and associated outcomes of delivering daily oral PrEP to various populations via different service delivery models in South Africa. These results could inform the expansion of PrEP programmes within both South Africa and the greater sub-Saharan Africa region, inform the optimisation of service delivery to improve cost-effectiveness, and provide data for budget impact analyses to inform future policy decisions and implementation strategies in HIV prevention programming.

Methods

Study design

In this retrospective cohort study, we did top-down and bottom-up microcosting of oral PrEP service delivery through in-facility and community outreach service delivery models in seven distinct geographical locations (henceforth termed sites) in Gauteng and KwaZulu-Natal provinces in South Africa. These sites included public, multiservice clinics; specialised clinics; and community outreach programmes (appendix p 1). Most sites had both in-facility and outreach models of PrEP provision, although some had only a single model. The selected sites were either run by, or had PrEP services provided by, implementation partners who were funded to focus on reaching specific populations considered to be at increased risk of HIV acquisition: female sex workers, men who have sex with men (MSM), and adolescent girls and young women. We intentionally selected sites that,

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before data collection, had been routinely providing PrEP for at least 9 months and had initiated at least 25 people on PrEP who had at least 6 months of potential follow-up. All PrEP service delivery was provided in accordance with South African national guidelines, which, at the time of data collection, included only daily oral PrEP, with 1 month's worth of tablets supplied at initiation followed by 3 months' supply thereafter (appendix p 3).[16] Data were collected between Sept 15, 2020, and Aug 31, 2021. This study was approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand (M190621) and the Boston University Institutional Review Board (H-39120).

Participants

The retrospective cohort comprised clients aged at least 15 years who started oral PrEP at one of the study sites between March 12, 2018, and Aug 13, 2019, allowing for at least 6 months of potential follow-up by February, 2020, when the cohort was censored. We excluded PrEP clients if they had missing files or incomplete data or if they had been transferred out of care at the selected site within 6 months of PrEP initiation. Although sites focused on specific populations, we did not limit enrolment on the basis of target population. For example, a programme focused on MSM could have provided services to a man who did not identify in this way, and this man would have been eligible for inclusion in the costing cohort provided he met other inclusion criteria. For each site, we obtained a list of clients who initiated PrEP on or before Aug 13, 2019. We used convenience sampling and began by enrolling the most recently initiated PrEP clients, working backwards until either our target sample size had been reached or there were no more eligible clients to include. The target enrolment per study population and service delivery model was 200, based on a *t* test for sample means using modelled results of cost estimates for PrEP service delivery in South Africa.[14] As this was a retrospective medical record review that involved no interaction with clients, we obtained a waiver of consent from the ethics review boards that approved the study.

Procedures

Routinely collected client-level data from clients' medical records, including hard-copy client files and both hard-copy and electronic client registers, were retrospectively extracted and managed using REDCap electronic data capture tools hosted at the University of Witwatersrand.[17] These data provided information on individual resource utilisation, such as number of clinic visits, services and medications provided, and laboratory tests done. Facility-level data, such as client headcounts (ie, the number of visits by clients during the study period), were extracted from clinic registers. Client-level data for the period March 12, 2018, to Feb 12, 2020, were collected from Sept 15, 2020, to March 31, 2021. Facility-level data for the 2019 calendar period were collected from Feb 16 to Aug 31, 2021.

We estimated the economic costs of PrEP provision from the provider's perspective following recommended guidance from the Global Health Cost Consortium.[18] We used routine client records to estimate resource utilisation for each client over the study period, calculated from date of PrEP initiation, and then multiplied this by unit cost. Resources considered were drugs, diagnostic and laboratory tests, clinical staff time, buildings, equipment, supplies, and other shared services such as

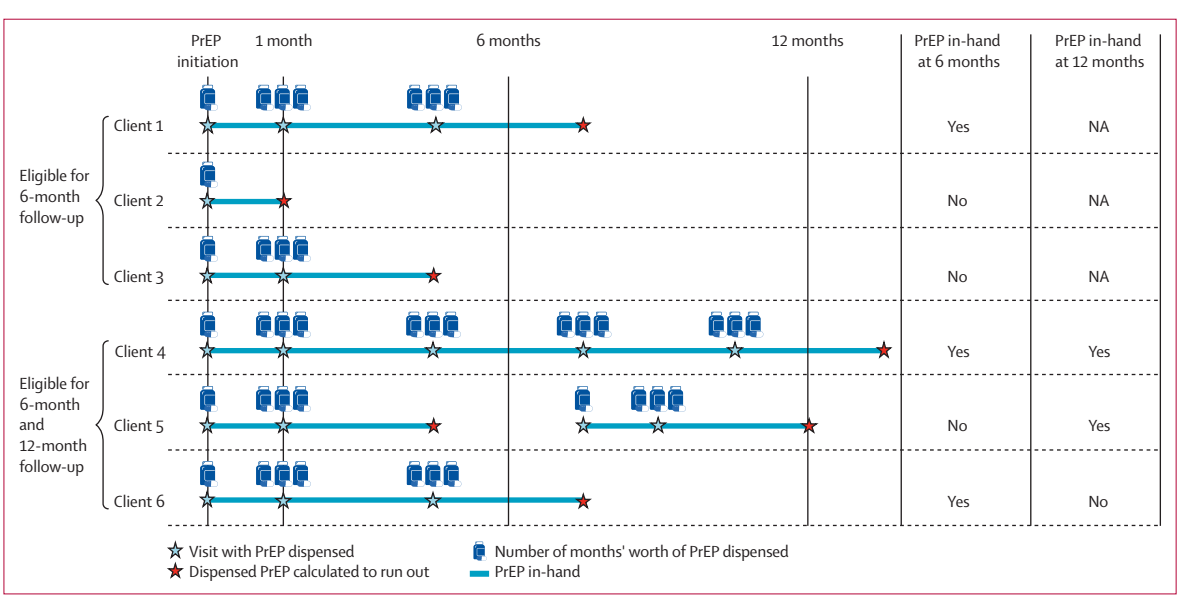


Figure: **Examples of PrEP in-hand outcomes**
NA=not applicable. PrEP=pre-exposure prophylaxis.

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utilities and non-clinical staff time; specific methods and sources for determining the costs for these resources are shown in the appendix (p 4). We obtained shared resource costs from facility-level financial records and price lists from suppliers, and these were proportionally allocated according to the fraction of total visits that were dedicated to PrEP provision. Resources shared between a site's in-facility and outreach service delivery models were proportionally allocated according to either the level of effort (for staff costs) or the client headcounts for each model. Staff salaries for positions above site-level management were excluded from the main analysis. We collected all costs in South African rand (ZAR) and inflated the costs to 2021 prices (where necessary) using the South African Consumer Price Index.[19] Costs are reported in US dollars using the average 2021 exchange rate of ZAR14·78 to US$1 and we assumed a useful life of 5 years for all capital items.[20]

Outcomes

The primary outcome, PrEP in-hand at 6 months, was defined as having sufficient PrEP drug dispensed at the last clinic visit to have the drug available 6 months after PrEP initiation. This outcome was calculated for each enrolled participant by use of recorded visit dates and dispensing records. Because PrEP outcomes are not a standard outcome metric within a clinic file, we measured outcomes with available data (such as visit dates, services received, and medications dispensed) to reflect individual engagement with PrEP care. To gain further insight into each programme, we reported several additional outcomes (PrEP initiation on the same day as a negative HIV test, engagement in care, and time in care) at various timepoints, if available (figure, table 1). 9-month and 12-month outcomes were reported for only the subset of participants with 12 months of follow-up.

Data analysis

We describe baseline characteristics and outcomes across study sites, service delivery models, and study population. We also estimated average PrEP-client resource utilisation over the 6-month study period and average cost per PrEP client by site, target population, service delivery model, and primary outcome and disaggregated by cost category (drugs, laboratory testing, visit costs and fixed costs). We also estimated production cost, calculated by dividing the costs of services to all clients by the number of participants who reached the primary outcome of PrEP in-hand at 6 months after PrEP initiation, as a way to incorporate effectiveness into the cost estimates. To assess the effect of varying assumptions on the average cost per day with PrEP in-hand, we did one-way sensitivity analyses for total clinic visits per year, staff cost per visit, and days with PrEP in-hand. We estimated best-case and worst-case scenarios using parameters yielding the lowest and highest average cost per day with PrEP in-hand, respectively. We also used two post-hoc mixed-effects regression models to analyse the factors influencing the cost per client for PrEP, accounting for clustering across different geographical locations: cost per day with PrEP in-hand is a function of age, sex, key population group, model type, PrEP in-hand at 6 months; and 6-month cost per person is a function of age, sex, key population group, model type, PrEP in-hand at 6 months; for further details, see appendix (p 8). All analyses were done in Excel (Microsoft Office Standard 2019), using the Healthcare Cost and Outcomes Model to estimate the cost per patient,[21] and RStudio version 1.4.1106.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

We collected data on 1281 people aged at least 15 years who initiated PrEP between March 12, 2018, and Aug 13, 2019, across seven sites in South Africa, about half (633, 49·4%) of whom had potential for 12 months of

	Definition	Notes	Timepoints
Same-day initiation (%)	Participant initiated PrEP on the day of presentation for their HIV test	Participants who did not initiate on the same day would have had separate visits for HIV testing and PrEP initiation.	Singular
Engaged in care after PrEP-initiation visit (%)	Participant attended at least one visit after PrEP initiation within the follow-up period	This is a measure of short-term persistence: many studies report rapid attrition after initiation, which is measured by this outcome.	Singular
Time in care (days)	Total number of PrEP tablets dispensed during the follow-up period	We excluded any tablets dispensed at the last visit that would have covered time outside the follow-up period: for example, if a participant has five visits in 12 months, with a total of 300 tablets dispensed over the first four visits and 90 tablets dispensed at visit five (day 330), only 35 tablets from the final visit count towards time in care; time in care for this participant is therefore 335 days at 12 months.	6 and 12 months
PrEP in-hand (%)	At client's last visit in follow-up, they were dispensed sufficient PrEP drug to still have the drug available at the end of the follow-up period	For example, if a participant came back 4 months after initiation and was dispensed 3 months' worth of PrEP drug at that visit and did not come back again before the 6-month period was reached, they were counted as having PrEP-in-hand at 6 months; however, if a participant came for a visit 4 months after initiation and was dispensed 1 month's worth of tablets at that visit and did not come back again before 6-months, they were counted as not having PrEP in-hand at 6 months (figure)	3, 6, 9, and 12 months

PrEP=pre-exposure prophylaxis.

Table 1: **Outcome definitions**

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	MSM site 1		MSM site 2		FSW site 1		FSW site 2		FSW site 3	AGYW site 1		AGYW site 2	All sites
	In-facility (n=98)	Outreach (n=139)	In-facility (n=102)	Outreach (n=53)	In-facility (n=96)	Outreach (n=98)	In-facility (n=42)	Outreach (n=99)	Outreach (n=96)	In-facility (n=168)	Outreach (n=90)	In-facility (n=200)	All models (n=1281)
Potential for 12-month follow-up	97 (99·0%)	71 (51·1%)	0	0	93 (96·9%)	98 (100%)	41 (97·6%)	99 (100%)	0	68 (40·5%)	66 (73·3%)	0	633 (49·4%)
Age at PrEP initiation, years													
Mean (SD)	35·6 (11·5)	30·4 (8·0)	32·1 (9·5)	31·6 (8·3)	30·3 (6·1)	29·5 (5·5)	30·7 (7·6)	29·7 (6·7)	28·9 (6·2)	23·1 (7·5)	23·3 (5·3)	25·1 (6·9)	28·5 (8·4)
Median (IQR)	34 (26–42)	29 (25–35)	30 (25–36)	31 (25–36)	30 (26–35)	29 (26–33)	30 (26–34)	29 (25–34)	28 (25–32)	21 (17–26)	22 (21–25)	24 (19–29)	27 (23–33)
Sex													
Male	98 (100%)	139 (100%)	101 (99·0%)	53 (100%)	16 (16·7%)	7 (7·1%)	0	4 (4·0%)	0	27 (16·1%)	16 (17·8%)	4 (2·0%)	465 (36·3%)
Female	0	0	1 (1·0%)	0	80 (83·3%)	91 (92·9%)	42 (100%)	95 (96·0%)	96 (10%)	141 (83·9%)	74 (82·2%)	196 (98·0%)	816 (63·7%)
Population*													
MSM	92 (93·9%)	61 (43·9%)	94 (92·2%)	10 (18·9%)	6 (6·2%)	4 (4·1%)	0	4 (4·0%)	0	0	0	1 (0·5%)	272 (21·2%)
FSW	0	0	0	0	66 (68·8%)	86 (87·8%)	40 (95·2%)	93 (93·9%)	96 (100%)	0	0	2 (1·0%)	383 (29·9%)
AGYW	0	0	0	0	2 (2·1%)	0	0	2 (2·0%)	0	111 (66·1%)	51 (56·7%)	110 (55·0%)	276 (21·6%)
PWID, SDC, TGW, TGM, or MSW	2 (2·0%)	0	3 (2·9%)	1 (1·9%)	0	3 (3·1%)	0	0	0	0	1 (1·1%)	0	10 (0·8%)
General population, males aged ≥15 years†	1 (1·0%)	40 (28·8%)	2 (2·0%)	0	2 (2·1%)	0	0	0	0	19 (11·3%)	5 (5·6%)	3 (1·5%)	72 (5·6%)
General population, females aged ≥25 years†	0	0	0	0	1 (1·0%)	0	0	0	0	30 (17·9%)	17 (18·9%)	84 (42·0%)	132 (10·3%)
Not indicated	3 (3·1%)	38 (27·3%)	3 (2·9%)	42 (79·2%)	19 (19·8%)	5 (5·1%)	2 (4·8%)	0	0	8 (4·8%)	16 (17·8%)	0	136 (10·6%)
Year of PrEP initiation													
2018	61 (62·2%)	57 (41·0%)	0	0	52 (54·2%)	19 (19·4%)	34 (81·0%)	8 (8·1%)	0	0	55 (61·1%)	1 (0·5%)	287 (22·4%)
2019	37 (37·8%)	82 (59·0%)	102 (100%)	53 (100%)	44 (45·8%)	79 (80·6%)	8 (19·0%)	91 (91·9%)	96 (100%)	168 (100%)	35 (38·9%)	199 (99·5%)	994 (77·6%)
Indication for PrEP													
Scored as at-risk on risk assessment by health-care worker‡	34 (34·7%)	6 (4·3%)	81 (79·4%)	9 (17·0%)	42 (43·8%)	65 (66·3%)	9 (21·4%)	33 (33·3%)	77 (80·2%)	120 (71·4%)	52 (57·8%)	165 (82·5%)	693 (54·1%)
Requested by client§	62 (63·3%)	132 (95·0%)	16 (15·7%)	29 (54·7%)	31 (32·3%)	30 (30·6%)	33 (78·6%)	65 (65·7%)	13 (13·5%)	48 (28·6%)	27 (30·0%)	34 (17·0%)	520 (40·6%)
No reason provided	2 (2·0%)	1 (0·7%)	5 (4·9%)	15 (28·3%)	23 (24·0%)	3 (3·1%)	0	1 (1·0%)	6 (6·2%)	0	11 (12·2%)	1 (0·5%)	68 (5·3%)
Risk assessment completed before or at PrEP initiation	95 (96·9%)	120 (86·3%)	100 (98·0%)	29 (54·7%)	81 (84·4%)	85 (86·7%)	42 (100%)	99 (100%)	95 (99·0%)	168 (100%)	78 (86·7%)	199 (99·5%)	1191 (93·0%)

Data are n (%) unless otherwise indicated. AGYW=adolescent girls and young women. FSW=female sex workers. MSM=men who have sex with men. MSW=male sex worker. PrEP=pre-exposure prophylaxis. PWID=person who injects drugs. SDC=serodiscordant couple. TGM=transgender man. TGW=transgender woman. *MSM includes eight participants who indicated that they are bisexual. †General population comprises individuals who did not identify as one of the listed priority populations. ‡PrEP was not explicitly indicated as the reason for the client's visit to the clinic; however, the risk assessment indicated high risk, and the client went on to initiate PrEP. §PrEP initiation was explicitly indicated as the client's reason for the clinic visit, regardless of the results of the risk assessment.

Table 2: **Characteristics of 1281 PrEP clients at PrEP initiation by site type and service delivery model**

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	MSM site 1		MSM site 2		FSW site 1		FSW site 2		FSW site 3	AGYW site 1		AGYW site 2
	In-facility (n=98)	Outreach (n=139)	In-facility (n=102)	Outreach (n=53)	In-facility (n=96)	Outreach (n=98)	In-facility (n=42)	Outreach (n=99)	Outreach (n=96)	In-facility (n=168)	Outreach (n=90)	In-facility (n=200)
Visits and health-care worker interactions												
Number of visits												
Mean (SD)	2·7 (1·1)	1·0 (0·2)	3·0 (1·5)	1·0 (0·1)	1·6 (1·0)	1·9 (1·0)	3·1 (2·0)	2·2 (1·5)	1·7 (1·0)	2·1 (1·7)	1·3 (0·7)	2·2 (1·9)
Median (IQR)	3 (2–3)	1 (1–1)	3 (2–4)	1 (1–1)	1 (1–2)	2 (1–2)	3 (2–5)	2 (1–3)	1 (1–2)	1 (1–3)	1 (1–1)	1 (1–3)
Number of nurse interactions												
Mean (SD)	2·7 (1·1)	1·1 (0·2)	3·0 (1·5)	1·1 (0·3)	1·6 (1·0)	1·9 (1·0)	2·9 (1·6)	2·2 (1·5)	1·7 (1·)	2·1 (1·7)	1·3 (0·7)	2·2 (1·9)
Median (IQR)	3 (2–3)	1 (1–1)	3 (2–4)	1 (1–1)	1 (1–2)	2 (1–2)	3 (2–4)	2 (1–3)	1 (1–2)	1 (1–3)	1 (1–1)	1 (1–3)
Number of counsellor interactions												
Mean (SD)	2·6 (1·1)	1·1 (0·2)	2·6 (1·2)	0·9 (0·5)	1·5 (0·8)	1·8 (1·0)	2·7 (1·6)	2·2 (1·3)	1·7 (1·0)	1·3 (1·7)	1·0 (0·8)	1·7 (1·6)
Median (IQR)	3 (2–3)	1 (1–1)	3 (2–4)	1 (1–1)	1 (1–2)	2 (1–2)	2 (2–4)	2 (1–3)	1 (1–2)	1 (0–1)	1 (0–1)	1 (1–2)
Drugs, medications, or devices dispensed												
Days of PrEP dispensed												
Mean (SD)	130·0 (62·8)	32·9 (16·9)	119·0 (59·6)	30·6 (4·12)	68·3 (58·9)	79·6 (63·1)	79·6 (54·1)	66·0 (44·3)	57·8 (42·5)	65·2 (65·3)	37·4 (19·7)	64·5 (55·3)
Median (IQR)	120 (120–186)	30 (30–30)	120 (60–163)	30 (30–30)	30 (30–120)	59 (30–120)	60 (30–120)	60 (30–90)	30 (30–90)	30 (30–90)	30 (30–30)	30 (30–90)
PrEP clients who had STI medication dispensed,* n (%)	4 (4·1%)	0	15 (14·7%)	2 (3·8%)	18 (18·8%)	19 (19·4%)	10 (23·8%)	14 (14·1%)	32 (33·3%)	7 (4·2%)	0	0
PrEP clients who had any other medication dispensed,† n (%)	5 (5·1%)	0	20 (19·6%)	2 (3·8%)	26 (27·1%)	41 (41·8%)	21 (50·0%)	42 (42·4%)	53 (55·2%)	9 (5·4%)	2 (2·2%)	0
Laboratory tests conducted, mean (SD)												
HIV test	2·0 (1·0)	1·0 (0·2)	2·6 (1·2)	1·0 (0·2)	1·4 (0·7)	1·7 (1·0)	2·2 (1·2)	1·9 (1·1)	1·6 (1·0)	1·9 (1·5)	1·3 (0·6)	1·6 (1·1)
Creatinine test	1·2 (1·0)	1·0 (0·2)	1·0 (0·7)	0·2 (0·5)	1·2 (0·6)	1·2 (0·6)	1·6 (0·7)	1·4 (0·7)	0·8 (0·5)	1·0 (0·4)	0·8 (0·5)	1·0 (0·3)
Hepatitis B surface antigen test	0·0 (0·0)	0·0 (0·0)	0·2 (0·5)	0·0 (0·1)	0·0 (0·1)	0·0 (0·1)	0·1 (0·4)	0·0 (0·2)	0·0 (0·0)	0·7 (0·5)	0·5 (0·5)	0·0 (0·1)
Hepatitis B antibody to surface antigen test	0·0 (0·0)	0·0 (0·0)	0·9 (0·6)	0·1 (0·3)	0·8 (0·6)	0·9 (0·4)	0·9 (0·5)	0·8 (0·4)	0·8 (0·5)	1·0 (0·3)	0·7 (0·4)	1·0 (0·2)
Syphilis rapid test	0·0 (0·2)	0·0 (0·0)	0·5 (0·9)	0·1 (0·4)	0·5 (0·5)	0·5 (0·5)	0·9 (0·4)	0·8 (0·5)	0·0 (0·1)	0·9 (0·3)	0·7 (0·4)	0·9 (0·3)
Pregnancy test	0·0 (0·0)	0·0 (0·0)	0·0 (0·0)	0·0 (0·0)	0·1 (0·4)	0·3 (0·8)	0·5 (0·9)	0·4 (0·9)	1·2 (0·9)	1·3 (1·4)	0·7 (0·8)	0·9 (0·4)
Other‡	0·2 (0·4)	0·0 (0·0)	0·5 (0·7)	0·2 (0·4)	0·2 (0·5)	0·1 (0·4)	0·2 (0·4)	0·1 (0·3)	0·0 (0·0)	0·0 (0·2)	0·1 (0·3)	0·0 (0·0)

AGYW=adolescent girls and young women. FSW=female sex workers. MSM=men who have sex with men. PrEP=pre-exposure prophylaxis. STI=sexually transmitted infection. *STI medications dispensed were ceftriaxone, cefuroxime, metronidazole, doxycycline, azithromycin, benzathine benzylpenicillin, flucloxacillin, and aciclovir. †Other medications were paracetamol, ibuprofen, diclofenac, amlodipine, amoxicillin/clavulanic acid, ciprofloxacin, co-trimoxazole, chlorpheniramine maleate, amoxicillin, oxymetazoline hydrochloride, combined oral contraceptives, progesterone injection, and saline nasal spray. ‡Other laboratory tests conducted were the measurement of aspartate aminotransferase, alanine aminotransferase, and haemoglobin concentrations; the use of urine dipstix (primarily used to screen for urinary tract infections, kidney problems, diabetes, haematuria, and pregnancy); cervical screening; screening for the presence of hepatitis A IgM and hepatitis C antibody; and the GeneXpert test.

Table 3: **6-month resource utilisation in the 6-month cohort (n=1281) by site and service delivery model**

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follow-up across four of the sites (table 2). These data included 1281 initiation visits and 1245 follow-up visits, amounting to 3086 months of PrEP dispensed. Most participants (994, 77·6%) initiated PrEP in 2019, with the remainder (287, 22·4%) initiating in 2018. On average, participants were young: median age was 27 years (IQR 23–33) in the whole cohort, and 22 years (21–25) in programmes focused on adolescent girls and young women. 465 (36·3%) of 1281 participants were male and 816 (63·7%) were female, with the sex distribution largely influenced by the population on which the site focused; however, 74 (8·3%) of 889 participants starting in the programmes focused on female sex workers or adolescent girls and young women were male.

In general, the sites and service delivery models largely served the population on whom they were focusing (ie, an MSM-focused programme mostly initiated MSM on PrEP); however, we observed variability within sites and service delivery models. The MSM-focused outreach programmes reported that 40 (20·8%) of 192 individuals who initiated PrEP identified as heterosexual men; by comparison, the in-facility MSM programmes reported only three (1·5%) heterosexual men among 200 clients. Other sites and service delivery models showed more heterogeneity in their PrEP-client populations: among the 368 participants at in-facility sites focusing on adolescent girls and young women, 221 (60·1%) were from this target population, whereas 114 (31·0%) were older women (aged ≥25 years), two (0·5%) were female sex workers, and 22 (6·0%) were heterosexual men, with one (0·3%) MSM. The outreach sites for adolescent girls and young women were similar, with the majority (51, 56·7%) of the 90 participants initiating PrEP belonging to this population; however, 17 (18·9%) were women aged at least 25 years and five (5·6%) were heterosexual men. In these outreach sites, 16 (17·8%) participants did not indicate which population group they belonged to. The sites focused on female sex workers largely initiated people from this population (106 [76·8%] of 138 people at in-facility sites and 275 [93·9%] of 293 people at outreach sites); however, a few adolescent girls and young women, MSM, and transgender women also initiated PrEP on these programmes.

In general, resource utilisation was higher in the in-facility models than in the outreach models (table 3). The mean number of visits per client initiated on PrEP was 2·3 (SD 1·7) for the in-facility models and 1·5 (1·0) for the outreach models. Across all population groups, the mean number of days of PrEP dispensed was higher in the in-facility models (83·2, 65·3) than in the outreach models (50·8, 42·1); this difference was greatest among the MSM-focused programmes (outreach 32·3, 14·7; in-facility 124·3, 60·7). Over the 6-month follow-up period after the initiation of PrEP, 121 (9·4%) of 1281 participants were dispensed treatment for sexually transmitted infections and 221 (17·3%) received other medication. The proportions of participants receiving treatment for sexually transmitted infections were higher in models focusing on female sex workers (14·1–33·3%) than among models focused on adolescent girls and young women (0–4·2%). The mean number of HIV tests administered over the 6 months after PrEP initiation was 1·87 (1·22) for in-facility models and 1·43 (0·84) for outreach models.

Among 1281 PrEP clients, 1191 (93·0%, 95% CI 91·4–94·3) initiated PrEP on the same day as their negative HIV tests; one notable exception was an MSM-focused clinic at which only 32 of 98 clients (32·7%, 23·5–42·9) initiated on the same day (table 4). The proportion of PrEP clients returning for at least one follow-up visit varied greatly, from only 1·9% at one MSM-focused outreach programme to 83·7% at another clinic focused on MSM. Similarly, time in care at 6 months ranged from a mean of 28·9 days (SD 8·2) to 125·9 days (61·2) across sites. Our primary outcome, PrEP in-hand at 6 months, varied greatly across sites, populations, and service delivery models, but was low overall: the highest proportion was at an MSM-focused in-facility programme (41·8%, 31·9–52·2), whereas an MSM-focused outreach programme had no clients with PrEP in-hand at 6 months. In general, in-facility models had higher PrEP in-hand coverage at 6 months than outreach models, with the exception of one of the programmes focused on female sex workers, in which the outcome was higher in the outreach model (22·4%, 14·6–32·0) than in the in-facility model (13·5%, 17·4–22·0). Programmes focused on adolescent girls and young women had low proportions of participants with PrEP in-hand at 6 months, ranging from 4·4% to 15·5%. Three clients (two at a clinic focused on female sex workers and one at a clinic focused on adolescent girls and young women) acquired HIV during the 6-month follow-up period.

Similar patterns were observed among the 633 PrEP clients with 12 months of potential follow-up, with a mean average time in care ranging from 41·2 days (SD 42·1) to 221·0 days (127·3). Across all included programmes, PrEP in-hand at 12 months was 13·6% (86 of 633 participants), with variability across sites and models. For the MSM-focused clinic, PrEP in-hand at 12 months was 35·1% for the in-facility programme, whereas no clients had this outcome in the outreach programme. For the two clinics focused on female sex workers, PrEP in-hand at 12 months ranged from 9·7% to 19·5%, both for in-facility models, whereas the site focused on adolescent girls and young women had 4·4% of clients with PrEP in hand at 12 months in the in-facility programme and 6·1% in the outreach programme.

When considering all clients initiated on PrEP, mean 6-month cost per client ranged from $29 (95% CI 26–31) for an MSM-focused outreach programme to $590 (488–692) for an in-facility programme focused on female sex workers, with higher average costs generally

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	MSM site 1		MSM site 2		FSW site 1		FSW site 2		FSW site 3	AGYW site 1		AGYW site 2	Overall	
	In facility	Outreach	In facility	Outreach	In facility	Outreach	In facility	Outreach	Outreach	In facility	Outreach	In facility	In facility	Outreach
Clients in 6-month cohort (N=1281), n	98	139	102	53	96	98	42	99	96	168	90	200	706	575
Same-day PrEP initiation, n (%)	32 (32·7%)	135 (97·1%)	100 (98·0%)	50 (94·3%)	92 (95·8%)	97 (99·0%)	42 (100%)	98 (99·0%)	96 (100%)	164 (97·6%)	89 (98·9%)	196 (98·0%)	626 (88·7%)	565 (98·3%)
At least one follow-up visit, n (%)*	82 (83·7%)	6 (4·3%)	82 (80·4%)	1 (1·9%)	35 (36·5%)	53 (54·1%)	33 (78·6%)	58 (58·6%)	38 (39·6%)	68 (40·5%)	16 (17·8%)	76 (38·0%)	376 (53·3%)	172 (29·9%)
Time between PrEP initiation and first follow-up, days†														
Mean (SD)	31·2 (21·6)	71·8 (56·5)	32·0 (18·1)	NA	59·1 (45·4)	67·3 (51·4)	48·4 (32·2)	49·6 (36·6)	62·0 (36·3)	36·6 (25·4)	55·2 (49·0)	36·8 (17·4)	37·5 (26·3)	58·8 (43·7)
Median (IQR)	25·0 (21·0–29·8)	48·5 (43·5–83·5)	28·0 (27·0–29·0)	NA	35·0 (28·0–74·0)	29·0 (28·0–115·0)	32·0 (28·0–59·0)	28·0 (28·0–77·8)	58·5 (28·0–83·5)	28·0 (28·0–33·0)	34·5 (28·0–55·8)	28·0 (28·0–37·0)	28·0 (27·0–34·0)	33·0 (28·0–84·5)
Time in care at 6 months, days‡														
Mean (SD)	132 (57·4)	36·1 (25·0)	128 (59·8)	32·3 (9·88)	97·0 (54·7)	108 (60·9)	121 (63·3)	90·3 (63·9)	78·3 (60·9)	72·5 (61·4)	47·4 (44·2)	70·1 (59·5)	94·3 (64·6)	66·2 (56·6)
Median (IQR)	142 (104–183)	30·0 (30·0–30·0)	146 (67·3–183)	30·0 (30·0–30·0)	90·0 (30·0–144)	116 (30·0–183)	143 (58·3–183)	58·0 (30·0–166)	30·0 (30·0–136)	30·0 (30·0–118)	30·0 (30·0–30·0)	30·0 (30·0–92·5)	88·0 (30·0–182)	30·0 (30·0–90·0)
PrEP in-hand at 6 months, n (%)§	41 (41·8%)	1 (0·7%)	38 (37·3%)	0	13 (13·5%)	22 (22·4%)	9 (21·4%)	13 (13·1%)	9 (9·4%)	22 (13·1%)	4 (4·4%)	31 (15·5%)	154 (21·8%)	49 (8·5%)
Reason for not reaching PrEP in-hand at 6 months, n (%)¶														
Death	0	0	0	0	0	0	0	0	0	0	0	0	0	0
HIV seroconversion	0	0	0	0	0	0	2 (4·8%)	0	0	1 (0·6%)	0	0	3 (0·4%)	0
Reported as having stopped PrEP	2 (2·0%)	1 (0·7%)	1 (1·0%)	5 (9·4%)	1 (1·0%)	3 (3·1%)	2 (4·8%)	5 (5·1%)	1 (1·0%)	1 (0·6%)	1 (1·1%)	7 (3·5%)	14 (2·0%)	16 (2·8%)
Reason unknown	96 (98·0%)	138 (99·3%)	101 (99·0%)	48 (90·6%)	95 (99·0%)	95 (96·9%)	38 (90·4%)	94 (94·9%)	95 (99·0%)	166 (98·8%)	89 (98·9%)	193 (96·5%)	689 (97·6%)	559 (97·2%)
Clients in 12-month cohort (N=633), n	97	71	0	0	93	98	41	99	0	68	66	0	299	334
Same-day PrEP initiation, n (%)	32 (33·0%)	68 (95·8%)	..	..	90 (96·8%)	97 (99·0%)	41 (100%)	98 (99·0%)	..	66 (97·1%)	66 (100%)	..	229 (76·6%)	329 (98·5%)
At least one follow-up visit, n (%)*	83 (85·6%)	6 (8·5%)	..	..	37 (39·8%)	58 (59·2%)	37 (90·2%)	59 (59·6%)	..	27 (39·7%)	14 (21·2%)	..	184 (61·5%)	137 (41·0%)
Time between PrEP initiation and first follow-up, days†														
Mean (SD)	32·3 (30·1)	71·8 (56·5)	..	..	79·3 (75·0)	80·5 (68·9)	79·4 (78·9)	52·1 (41·0)	..	49·5 (50·5)	102 (114)	..	53·7 (59·8)	70·1 (66·1)
Median (IQR)	25·0 (21·0–29·5)	48·5 (43·5–83·5)	..	..	41·0 (28·0–111)	29·5 (28·0–127)	34·0 (29·0–96·0)	28·0 (28·0–83·5)	..	29·0 (28·0–37·5)	35·0 (28·0–149)	..	29·0 (25·0–49·3)	31·0 (28·0–106)
Time in care at 12 months, days‡														
Mean (SD)	220 (133)	41 (42)	..	..	122 (126)	155 (129)	221 (127)	137 (128)	..	88 (104)	69 (95)	..	160 (136)	108 (118)
Median (IQR)	201 (113–365)	30 (30–30)	..	..	30 (30–209)	118 (30–262)	227 (114–352)	58 (30–259)	..	30 (30–98)	30 (30–30)	..	114 (30–320)	30 (30–146)

(Table 4 continues on next page)

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	MSM site 1		MSM site 2		FSW site 1		FSW site 2		FSW site 3		AGYW site 1		AGYW site 2	Overall	
	In facility	Outreach	In facility	Outreach	In facility	Outreach	In facility	Outreach	Outreach		In facility	Outreach	In facility	In facility	Outreach
(Continued from previous page)															
PrEP in-hand at 12 months, n (%)§	34 (35·1%)	0	..	..	9 (9·7%)	15 (15·3%)	8 (19·5%)	13 (13·1%)	..		3 (4·4%)	4 (6·1%)	..	54 (18·1%)	32 (9·6%)
Reason for not reaching PrEP in-hand at 12 months, n (%)¶															
Death	0	0	..	..	0	0	0	0	..		0	0	..	0	0
HIV seroconversion	0	0	..	..	0	0	2 (6·1%)	0	..		1 (1·5%)	0	..	3 (1·2%)	0
Reported as having stopped PrEP	1 (1·6%)	1 (1·4%)	..	..	1 (1·2%)	4 (4·8%)	4 (12·1%)	4 (4·7%)	..		1 (1·5%)	1 (1·6%)	..	7 (2·9%)	10 (3·3%)
Reason unknown	96 (98·4%)	70 (98·6%)	..	..	92 (98·8%)	94 (95·2%)	35 (81·8%)	95 (95·3%)	..		66 (97·0%)	65 (98·4%)	..	289 (95·9%)	324 (96·7%)

AGYW=adolescent girls and young women. FSW=female sex workers. MSM=men who have sex with men. NA=not applicable. PrEP=pre-exposure prophylaxis. *In addition to the PrEP-initiation visit, the PrEP client had at least one additional visit within the 6-month or 12-month time period. †Among those who had at least one follow-up visit within the 6-month or 12-month time period. ‡Total number of PrEP tablets dispensed, excluding any overdispensing at the last visit (capped at the maximum follow-up period; 180 or 365 days). §At the PrEP client's last visit in the follow-up period, they were dispensed sufficient PrEP drug to still have the drug available at the end of the follow-up period. ¶Among those who were not dispensed sufficient PrEP drug to still have the drug available at the end of the follow-up period.

Table 4: **6-month and 12-month outcomes by site and service delivery model**

observed for the in-facility programmes (table 5). This wide range in part reflects the high variation in the proportion of clients with PrEP in hand at 6 months (range 0–42%). When estimating costs for only those clients who reached this outcome, the average cost per client ranged from $108 ($92–125) at one of the outreach programmes focused on female sex workers to $959 ($753–1164) at an in-facility programme focused on the same population. The high cost at the in-facility programme was driven largely by staffing, which accounted for $744 (78%) and was attributed to the high staff-to-client ratio during the study period, which, although distorting the cost per client interaction, accurately reflects the cost of sites with low client numbers. Overall, the in-facility programmes had higher average costs per PrEP client than the accompanying outreach programmes. This pattern held when considering the average cost per PrEP client among those with PrEP in-hand at 6 months, with the in-facility programme costs ranging from $170 (160–181) to $959 (753–1164) and the outreach programme costs ranging from $108 (92–125) to $276 (231–320) over 6 months. Although the average costs were lower for outreach than for in-facility programmes, the production costs (ie, the 6-month costs to produce one client with PrEP in-hand at 6 months) were, on average, much higher, with the exception of outreach programmes for female sex workers, which had lower production costs than the corresponding in-facility programmes. The cost per day with PrEP in-hand ranged from $0·93 (0·85–1·01) for an MSM outreach model to $5·95 (5·22–6·68) for an in-facility programme for female sex workers. Considering all participants, the cost per day with PrEP in-hand was $1·80 (1·73–1·86).

We did two preliminary analyses, using mixed-effects regression models, to understand drivers of costs. After controlling for site location (which accounted for a large proportion of the variation in the cost estimate), having PrEP in-hand at 6 months, initiating at an outreach programme, and identifying as MSM lowered the estimate of cost per client per day with PrEP in-hand compared with our base case: a 28-year-old female, who was not identified as a female sex worker, an adolescent girl or young woman, or MSM, and who received services in a fixed facility and did not have PrEP in-hand at 6 months. Being in an outreach model and being an adolescent girl or young woman decreased the total 6-month cost, whereas having PrEP in-hand increased this total cost compared with the same base case (appendix p 8).

Average costs remain robust under these varying parameters (appendix p 12). Compared with a cost for the base case of $1·75, the average costs after increasing or decreasing the number of days with PrEP in-hand by 20% were $1·50 and $1·90, respectively. Increasing or decreasing the annual clinic patient volume by 20% yielded costs of $1.65 and $1.89, respectively, whereas

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	MSM site 1		MSM site 2		FSW site 1		FSW site 2		FSW site 3	AGYW site 1		AGYW site 2
	In-facility	Outreach	In-facility	Outreach	In-facility	Outreach	In-facility	Outreach	Outreach	In-facility	Outreach	In-facility
Proportion of clients with PrEP in-hand at 6 months, n/N (%)	41/98 (41·8%)	1/139 (0·7%)	38/102 (37·3%)	0/53	13/96 (13·5%)	22/98 (22·4%)	9/42 (21·4%)	13/99 (13·1%)	9/96 (9·4%)	22/168 (13·1%)	4/90 (4·4%)	31/200 (15·5%)
Average 6-month cost per PrEP client												
All PrEP clients	$228 (208–248)	$76 (73–79)	$191 (175–208)	$29 (26–31)	$125 (111–140)	$75 (68–83)	$590 (488–692)	$105 (93–117)	$131 (116–147)	$84 (76–92)	$61 (55–68)	$73 (66–80)
PrEP clients with PrEP in-hand at 6 months*	$312 (293–332)	$140	$248 (236–262)	..	$236 (204–268)	$108 (92–125)	$959 (753–1164)	$220 (190–250)	$276 (231–320)	$179 (155–203)	$132 (43–220)	$170 (160–181)
Average cost per person-month per PrEP client†												
All PrEP clients	$58 (53–63)	$71 (70–73)	$53 (49–58)	$28 (26–31)	$68 (62–74)	$32 (29–34)	$182 (159–204)	$44 (41–47)	$66 (62–70)	$47 (42–52)	$48 (45–51)	$37 (36–39)
PrEP clients with PrEP in-hand at 6 months	$52 (49–55)	$23	$42 (39–44)	..	$39 (34–45)	$18 (15–21)	$160 (126–195)	$37 (32–42)	$46 (39–53)	$30 (26–34)	$22 (7–39)	$28 (27–30)
Cost breakdown for PrEP clients with PrEP in-hand at 6 months												
Drugs	$26 (24–28)	$5	$24 (23–26)	..	$13 (13–13)	$18 (14–22)	$20 (13–26)	$21 (17–25)	$16 (11–21)	$24 (17–31)	$10 (1–19)	$24 (22–26)
Laboratory tests	$16 (14–19)	$12	$35 (30–39)	..	$31 (24–38)	$26 (21–30)	$32 (28–37)	$33 (27–39)	$28 (23–34)	$43 (38–49)	$35 (6–63)	$28 (25–30)
Clinic staff visit cost	$133 (124–142)	$47	$127 (120–135)	..	$89 (77–102)	$15 (13–17)	$744 (573–915)	$60 (51–69)	$23 (19–28)	$69 (56–82)	$45 (17–73)	$61 (57–65)
Fixed costs (ie, buildings, equipment, management, and administration)	$136 (128–146)	$75	$63 (58–67)	..	$103 (89–117)	$50 (43–57)	$163 (130–196)	$107 (90–124)	$208 (170–245)	$42 (37–48)	$42 (16–67)	$58 (54–62)
Production cost of PrEP in-hand at 6 months‡	$545	$10 537	$514	..	$929	$336	$2754	$780	$1403	$643	$1379	$470
Cost per day with PrEP in-hand§	$1·91 (1·75–2·07)	$2·34 (2·29–2·39)	$1·74 (1·60–1·89)	$0·93 (0·85–1·01)	$2·24 (2·04–2·43)	$1·03 (0·95–1·12)	$5·95 (5·22–6·68)	$1·46 (1·36–1·55)	$2·17 (2·03–2·30	$1·55 (1·39–1·71)	$1·58 (1·49–1·67)	$1·23 (1·19–1·26)

Data are mean (95% CI) unless otherwise stated. Costs reported in 2021 US dollars (95% CI). AGYW=adolescent girls and young women. FSW=female sex workers. MSM=men who have sex with men. PrEP=pre-exposure prophylaxis. *Calculated by summing the 6-month costs for each client who reached the outcome (PrEP in-hand at 6 months) and then finding the average across those clients. †Total cost per month divided by the total number of PrEP tablets dispensed, excluding any overdispensing at the last visit (capped at the maximum for the 6-month follow-up period [180] × 30·5). ‡Calculated by summing the costs of services to all clients and dividing this value by the number of clients reaching the primary outcome of PrEP in-hand 6 months after PrEP initiation. For example, for the MSM site 1 in-facility programme, the total costs are $228 × 98=$22 344. This value is then divided by 41 to yield a production cost of $545. §The total cost for each person divided by the total number of PrEP tablets dispensed during the 6-month period, excluding any tablets dispensed at the last visit, which would have covered time outside of the follow-up period (ie, time in care; see table 1 for full definition).

Table 5: **Estimated costs per PrEP client of 6 months of PrEP provision by site and service delivery model**

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varying the staff cost per visit up and down by 20% resulted in costs of $1.87 and $1.62, respectively. The multivariate best-case scenario, involving a 20% decrease in staff cost per visit and 20% increases in both annual clinic volume and days with PrEP in-hand, resulted in a reduced cost of $1.31. The worst-case scenario, involving a 20% increase in staff cost per visit and 20% decreases in both annual clinic volume and days with PrEP in-hand, yielded an increased cost of $2·19.

Discussion

In this microcosting study, we estimated the real-world outcomes and costs of PrEP provision across seven sites in South Africa that provided either in-facility or community outreach service delivery models or both, focused on MSM, female sex workers, or adolescent girls and young women. The costs of 6 months of PrEP provision varied widely across sites and service delivery models, ranging from $29 to $590 per client initiated and from $108 to $959 among those who reached the primary outcome of PrEP in-hand at 6 months. These costs were largely driven by clinic personnel and fixed costs, as was observed in other studies in the region.[22–24] Meyer-Rath and colleagues[25] used an ingredients-based approach relying on expert opinion, available literature, and several assumptions to estimate the cost per client-year for the first year on PrEP for young women in South Africa, obtaining an estimate of approximately $124; no specific service delivery model was indicated. This estimate is generally lower than those obtained through the costing of real-world service delivery, highlighting the importance of microcosting in providing a more granular view of costs and associated outcomes of PrEP provision, which is key for future programme, intervention, and budget planning. When compared with published costs of providing PrEP obtained from other microcosting studies in the region, the costs observed in the service delivery models reported on here are generally higher, with annual costs ranging from $92 to $943 per year.[22,24,26–31] Two possible explanations for these differing results are more extensive inclusion of programmatic costs and relatively low PrEP-client volumes in service delivery models with particularly high costs. Some service delivery models were still within their first year or two of PrEP provision, which could have contributed both to low client volumes and to low PrEP persistence, as the services were still learning how to effectively promote PrEP among those who might benefit from it. In this study, one site had particularly low client volumes and high staff numbers, which can distort costs, highlighting the importance of considering expected client volumes and required staff numbers to provide services when setting up a new PrEP-delivery site.

Overall, in-facility programmes had a higher cost per client initiated on PrEP than did outreach programmes; however, they generally had higher numbers of clients with PrEP in-hand at 6 months, resulting in lower production costs. A notable exception to this finding were outreach programmes focused on female sex workers, which had lower production costs than in-facility programmes, highlighting the need for differentiated programmes that focus on PrEP-client needs (in this case, PrEP service delivery offered at the client's places of work). Some of the high costs observed at some sites within our cohort can be attributed to low PrEP-client volume, and we observe patterns of lower costs with higher client volumes, indicating potential for economies of scale for these programmes. The mobile outreach programmes tended to have a high proportion of clients initiate PrEP on the same day as their negative HIV test; however, the rates of return for a follow-up visit and the average times to return were lower than for in-facility programmes. This finding could indicate that, in general, these mobile programmes might not be reaching people who find it more difficult to remain in consistent care for structural reasons, or who do not see a personal benefit in consistent care and are therefore less motivated to be on daily oral PrEP.

Across all sites and service delivery models we observed low proportions of clients with PrEP in-hand at 6 months, ranging from 0% to 41·8%; these findings are in line with those of other studies in the region.[24,32] These low proportions are concerning given that the populations on which we focused are disproportionally affected by HIV. Despite comprising only 10% of the population of sub-Saharan Africa, adolescent girls and young women accounted for 25% of new HIV infections in the region in 2020, with an estimated 4200 infections each week.[6] Additionally, in 2020, key populations (sex workers and their clients, gay men and other MSM, people who inject drugs, and transgender people) and their sexual partners accounted for 65% of HIV infections globally and 39% of new HIV infections in sub-Saharan Africa.[6] The costs associated with PrEP delivery presented in this study could help service delivery planners to set realistic expectations around daily oral PrEP continuation figures and costs when budget planning. Furthermore, these outcomes and costs are valuable as inputs for existing and future models aimed at assisting with strategic and tactical decision making, and could assist in planning for interventions aimed at improving low PrEP continuation rates among populations at risk of HIV acquisition in the sub-Saharan Africa region.[9]

This study has several limitations. First, differences within service delivery model design and implementation (including facility type, client volume, and the type and quality of services delivered) are likely to affect PrEP uptake and persistence. Drawing associations between these factors and outcomes is challenging and outside the scope of this study. Future research should focus on elucidating these details to enable a more granular understanding of these associations to be reached. Second, the little information available regarding ongoing risk in the PrEP cohort limits any conclusions

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about which clients are persisting on or discontinuing PrEP. Risk assessments were not captured at all visits, so changes in risk and the reasons for stopping PrEP cannot be established. Therefore, apart from three clients who seroconverted during the 6-month follow-up period, whether changes in outcomes for PrEP clients were due to changes in risk, adoption of other HIV-prevention mechanisms, or simply discontinuation of PrEP with no change in the risk of HIV acquisition is not known. The documentation of risk or reason for PrEP initiation at first visit was not standardised and, as such, we are unable to say whether these programmes were initiating the people who would most benefit from being on PrEP. We were also unable to trace the movement of clients from one site or model to another, so cannot accurately distinguish between transfer of PrEP care to another facility and loss to follow-up. Furthermore, we could not define an outcome for individuals with missing files who were not included in our analysis, and so cannot establish with certainty whether discrepancies in outcomes exist between those included and those excluded from analysis. With regards to costing, demand creation efforts (eg, community events, advertising, and social media promotion) were not captured in a systematic and measurable way, so we are unable to differentiate those costs from the broader fixed costs of the programme. Additionally, we captured resource utilisation only from the point of PrEP initiation, so cannot attribute any costs associated with PrEP demand creation and screening at the individual level. It is becoming increasingly clear that such activities are important components of PrEP provision programmes that need to be included when considering PrEP programme scale-up. Finally, since these costs were collected, the monitoring guidelines for PrEP clients have changed; tests such as creatinine clearance are no longer mandatory at each visit and instead are requested only for particular age and risk groups and on a less frequent basis than previously. These changes should be considered when reviewing the costs presented here.

Despite these limitations, our study is an important addition to the literature on the costs of PrEP in sub-Saharan Africa, providing outcome and unit-cost data on real-world PrEP provision in South Africa across a diverse set of service delivery models and populations. These data could be used to strengthen budget impact and cost-effectiveness analyses, providing crucial information for further scale-up of the oral PrEP programme in South Africa and the greater sub-Saharan Africa region.

Contributors

CH and LCL led the conception and design of the study, drafting of the manuscript, and data analysis and interpretation with contributions from KH, CM, MB, and BEN. KH, CM, and MB acquired the data. RB, JM, and CS provided site and resource utilisation data. All authors had full access to the client-level resource utilisation data; CH and MB verified these data. CH, KH, MB, CM, BEN, and LCL had full access to the cost and financial data; CH and KH verified these data. KH, CM, MB, and BEN contributed to the critical revision of the manuscript. All authors reviewed and approved the final version of the manuscript and had final responsibility for the decision to submit for publication.

Declaration of interests

We declare no competing interests.

Data sharing

Individual de-identified participant data that underlie the results reported in this Article are available upon request from the corresponding author after receipt of a valid research proposal from interested researchers. We will also make available the study protocol upon request. Data will be available from 3 months to 5 years after Article publication. To gain access, data requestors will need to sign a data access agreement and show evidence that the proposed use of the data has been approved by an independent local ethical review committee identified for this purpose.

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