








# Innovative demand creation strategies to increase voluntary medical male circumcision uptake: a pragmatic randomised controlled trial in Zimbabwe

Webster Mavhu <sup>1,2</sup>, Melissa Neuman <sup>3</sup>, Karin Hatzold <sup>4</sup>, Stephen Buzuzi,<sup>1</sup> Galven Maringwa,<sup>1</sup> Sungai T Chabata <sup>1</sup>, Collin Manganah <sup>1</sup>, Noah Taruberekera,<sup>5</sup> Ngonidzashe Madidi,<sup>5</sup> Malvern Munjoma,<sup>5</sup> Getrude Ncube,<sup>6</sup> Sinokuthemba Xaba,<sup>6</sup> Owen Mugurungi,<sup>6</sup> Cheryl C Johnson <sup>7</sup>, Elizabeth L Corbett <sup>8</sup>, Helen A Weiss <sup>3</sup>, Katherine Fielding <sup>3</sup>, Frances M Cowan <sup>1,2</sup>

**To cite:** Mavhu W, Neuman M, Hatzold K, *et al.* Innovative demand creation strategies to increase voluntary medical male circumcision uptake: a pragmatic randomised controlled trial in Zimbabwe. *BMJ Global Health* 2021;**6**:e006141. doi:10.1136/bmjgh-2021-006141

**Handling editor** Seye Abimbola

► Additional supplemental material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/bmjgh-2021-006141>).

Received 27 April 2021  
Accepted 16 June 2021



© World Health Organization 2023. Licensee BMJ.

For numbered affiliations see end of article.

## Correspondence to

Dr Webster Mavhu;  
[webster@ceshhar.co.zw](mailto:webster@ceshhar.co.zw)

## ABSTRACT

**Introduction** Reaching men aged 20–35 years, the group at greatest risk of HIV, with voluntary medical male circumcision (VMMC) remains a challenge. We assessed the impact of two VMMC demand creation approaches targeting this age group in a randomised controlled trial (RCT).

**Methods** We conducted a 2×2 factorial RCT comparing arms with and without two interventions: (1) standard demand creation augmented by human-centred design (HCD)-informed approach; (2) standard demand creation plus offer of HIV self-testing (HIVST). Interpersonal communication (IPC) agents were the unit of randomisation. We observed implementation of demand creation over 6 months (1 May to 31 October 2018), with number of men circumcised assessed over 7 months. The primary outcome was the number of men circumcised per IPC agent using the as-treated population of actual number of months each IPC agent worked. We conducted a mixed-methods process evaluation within the RCT.

**Results** We randomised 140 IPC agents, 35 in each arm. 132/140 (94.3%) attended study training and 105/132 (79.5%) reached at least one client during the trial period and were included in final analysis. There was no evidence that the HCD-informed intervention increased VMMC uptake versus no HCD-informed intervention (incident rate ratio (IRR) 0.87, 95% CI 0.38 to 2.02;  $p=0.75$ ). Nor did offering men a HIVST kit at time of VMMC mobilisation (IRR 0.65, 95% CI 0.28 to 1.50;  $p=0.31$ ). Among IPC agents that reported reaching at least one man with demand creation, both the HCD-informed intervention and HIVST were deemed useful. There were some challenges with trial implementation; <50% of IPC agents converted any men to VMMC, which undermined our ability to show an effect of demand creation and may reflect acceptability and feasibility of the interventions.

**Conclusion** This RCT did not show evidence of an effect of HCD-informed demand intervention or HIVST on VMMC uptake. Findings will inform future design and implementation of demand creation evaluations.

## WHAT IS ALREADY KNOWN?

⇒ Reaching men 20–35 years old, the age group at greatest risk of HIV, with voluntary medical male circumcision (VMMC) for HIV prevention remains a challenge.

## WHAT ARE THE NEW FINDINGS?

⇒ Demand creation intervention informed by human-centred design (HCD, fully involves intended beneficiaries in intervention design) and HIV self-testing (HIVST) trialled here did not have an impact on VMMC uptake.  
⇒ Suboptimal implementation of the HCD-informed and HIVST interventions may reflect feasibility of implementation in practice and reduced the power of the trial to show an impact.

## WHAT DO THE NEW FINDINGS IMPLY?

⇒ Demand creation using HCD-informed approach and/or HIVST did not overcome all barriers to adult men's VMMC uptake.  
⇒ Additional efforts and innovative demand creation approaches are required to overcome the opportunity costs men are likely to incur.  
⇒ Evaluations of real-world interventions continue to be affected by real life challenges to implementation including a lack of control of the manner in which interventions are implemented.

**Trial registration number** PACTR201804003064160.

## INTRODUCTION

Voluntary medical male circumcision (VMMC) is one of five key HIV prevention strategies aiming to reduce new HIV

infections by 75%.<sup>1</sup> By December 2019, nearly 27 million adolescent and adult men (≥10 years) had been circumcised and an estimated 340 000 new infections averted in 15 VMMC priority countries, including 260 000 infections among men and 75 000 among women (due to reduced secondary transmission from men).<sup>2 3</sup> However, the majority of those circumcised were adolescent boys (10–19 years); reaching adult men aged 20–35 years, who are the age group at greatest risk of HIV, remains a challenge.<sup>4–8</sup> Strategies to increase VMMC demand among adult men including financial incentives, counselling or education, involvement of influencers and novel information delivery, have had mixed results.<sup>9</sup> There have been calls for innovative and robust VMMC demand creation strategies to reach adult men.<sup>9–14</sup>

Within sub-Saharan Africa, barriers to VMMC uptake include the restricted number of service delivery sites and limited numbers of healthcare workers available to perform the procedure.<sup>15</sup> Attrition of trained staff is an additional challenge.<sup>16</sup> Men traditionally access healthcare less than women, and this might be further exacerbated by masculine norms that equate help-seeking with being ‘weak’.<sup>17–19</sup> Other barriers include poor perception of HIV risk<sup>20–22</sup> and fear of: pain, surgical complications, preoperative HIV testing<sup>20 21 23</sup> and costs (including opportunity costs).<sup>10 11</sup> Previous research suggested that preoperative HIV testing was a significant barrier to VMMC uptake as many men reported being concerned about pre-VMMC testing at a VMMC site when deductive disclosure may occur in the event they are HIV positive.<sup>20</sup> Researchers then hypothesised that if men self-tested and knew their status in advance of going to the VMMC centre, this would overcome their fear of testing for the first time at the VMMC site (even if it meant being tested again).<sup>24 25</sup> Strategies to overcome the other barriers are required if the intervention is to be brought to desired scale.

In 2015, market research was undertaken in Zimbabwe to systematically understand the journey from initial awareness of VMMC, to undergoing the procedure and in turn becoming a ‘VMMC advocate’, as well as how that journey varies across types (or segments) of men.<sup>26–28</sup> This research mapped the decision-making path men take to VMMC, identifying key triggers for demand and strategies that can be adopted to address the intend-to-action gap. It also used a hybrid psychographic-behavioural segmentation approach to profile men according to their perceptions about and orientation to VMMC.<sup>26–28</sup> Through this market research, six ‘segments’ of men were identified based on their attitudes to and motivations for VMMC. The research also identified factors driving the cognitive dissonance (conflicting attitudes, beliefs or behaviours) impeding VMMC uptake among some segments of men.<sup>26 28</sup>

Based on this market research, the largest VMMC implementer in Zimbabwe (Population Services International (PSI)) prioritised three segments of men for demand creation interventions, who represented 56% of

uncircumcised males aged 15–29 years in Zimbabwe at that time. The three prioritised segments were: VMMC *enthusiasts* (21%, have a high potential to undergo VMMC and strong commitment already—although need to overcome some dissonance in order to proceed); *neophytes* (19%, potentially enthusiastic but poor knowledge undermines their commitment—addressing this would be relatively straightforward and likely result in increased VMMC uptake) and *embarrassed rejecters* (16%, potentially interested but with little commitment and knowledge, embarrassment and fears are high—so need lots of support to undergo VMMC).<sup>26 28</sup>

Drawing on market research findings, interpersonal communication (IPC) demand creation was redesigned to encompass a human-centred design (HCD)-informed approach. IPC agents who act as community mobilisers for VMMC were trained to conduct one-on-one sessions with potential VMMC clients using three tools: a segmentation typing tool, segment-specific targeted messaging and a pain-o-metre (visual aid) to guide discussions related to pain (see online supplemental appendix for detailed descriptions).

Here, we present results of a randomised controlled trial (RCT) that assessed the effectiveness of this HCD-informed approach in motivating 15-year-old to 29-year-old men (Zimbabwe’s VMMC priority age group) to take up VMMC. In addition, we explored whether providing access to HIVST would result in increased VMMC uptake. We hypothesised that potential VMMC clients mobilised: (1) using the HCD-informed intervention would have increased circumcision uptake compared with those mobilised using standard techniques and (2) with the offer of HIVST would have increased circumcision uptake compared with those mobilised without the offer of HIVST.

## METHODS

### Study design and setting

We conducted a 2×2 factorial pragmatic RCT comparing arms with and without two interventions: (1) standard demand creation augmented by HCD-informed approach; (2) standard demand creation plus offer of HIVST.

We conducted the study in five districts (Buhera, Gokwe North, Mangwe, Mutasa, Zvimba), in 4 of 10 provinces in Zimbabwe. Neither interventions had been implemented in these districts before the trial. The interventions were implemented by IPC agents, all of whom had at least some secondary education. To guard against the risk of contamination, each IPC agent was assigned a ward (subdivision of district) and required to work within the confines of their ward.

Outcomes were measured using monthly VMMC programme outputs collected by these agents and VMMC clinics.

CONSORT guidelines for RCT<sup>29</sup> reporting were followed. Three changes were made to the trial protocol

after trial commencement. First, the intervention run-in period was extended to allow more time for the IPC agents to become comfortable with the HCD-informed approach. Second, following review of blinded interim data, the sample size was recalculated and the main analysis was changed from parallel comparisons to the two factorial comparisons, assessing outcomes with and without each intervention. Third, it was necessary to change the statistical model documented in the initial analysis plan to accommodate extremely high variability of outcomes between and within IPC agents; a more valid approach was used. These changes are summarised in detail in the online supplemental appendix.

For each study arm, training was conducted over 2 days from 1 to 8 February 2018 and implementation started straight after with a closely supervised run-in period from 20 February to 30 April 2018. By 30 April, implementers were confident that all IPC agents were able to implement demand creation as assigned. The interventions were implemented over 6 months (1 May to 31 October 2018) and counting number of circumcisions conducted over 7 months (1 May to 30 November 2018), allowing the last man enrolled on 31 October to have 1 month to be circumcised. This minimum follow-up is in keeping with the implementer's experience that men wanting to be circumcised will do so within 1 month of referral.

### Client involvement

The interventions were optimised for this setting using formative work undertaken in 2017 with VMMC clients and IPC agents. For example, during the formative work, it was observed that IPC agents did not know how to categorise men who were clearly willing to be circumcised prior to segmentation. Consequently, the implementer created an additional segment ('green'—a default segment which denoted that client was willing to be circumcised before the start of the demand creation session and therefore no proper segmentation was done).

### Randomisation and masking

IPC agents were the unit of randomisation and were assigned 1:1:1:1 to four arms, using restricted randomisation by IPC agent for sex, age and having  $\geq 12$  months of VMMC mobilisation experience. The random allocation of IPC agents to intervention arms was completed using random-number tables generated in Stata by a study statistician on 25 January 2018.

Neither IPC agents nor clients could be masked to allocation. The statistician conducting the primary analysis was masked to allocation for the planned primary and secondary analyses. Subsequent analyses were conducted on unmasked data.

### Intervention components

#### Arm 1: standard demand creation

IPC agents received basic training on how to promote VMMC, including identifying barriers, clarifying myths

and misconceptions and summarising key benefits. Men were mobilised for VMMC individually or in groups. Clients referred for VMMC either went to VMMC sites on their own or were taken there in a programme vehicle.

#### Arm 2: standard demand creation plus offer of HIVST

In addition to standard demand creation, IPC agents offered the men they mobilised a HIVST kit, with a kit use demonstration if accepted.

#### Arm 3: HCD-informed demand creation approach

IPC agents received basic training in the HCD-informed approach, including using the segmentation typing tool, to prioritise the three key segments. They then delivered messages tailored to that 'segment'. IPC agents were specifically required to address any pain-related concerns using a visual aid (pain-o-metre) to outline the VMMC procedure, healing process, as well as possible pain management techniques. Men in the non-prioritised segments received general (as opposed to tailored) messages.

As already stated, if a client was willing to be circumcised at the start of the discussion, segmentation was skipped and these men were allocated to a default 'segment' (green), which was not developed from the market research. Clients mobilised in groups at schools were also allocated to the 'green' segment.

#### Arm 4: HCD-informed demand creation approach plus offer of HIVST

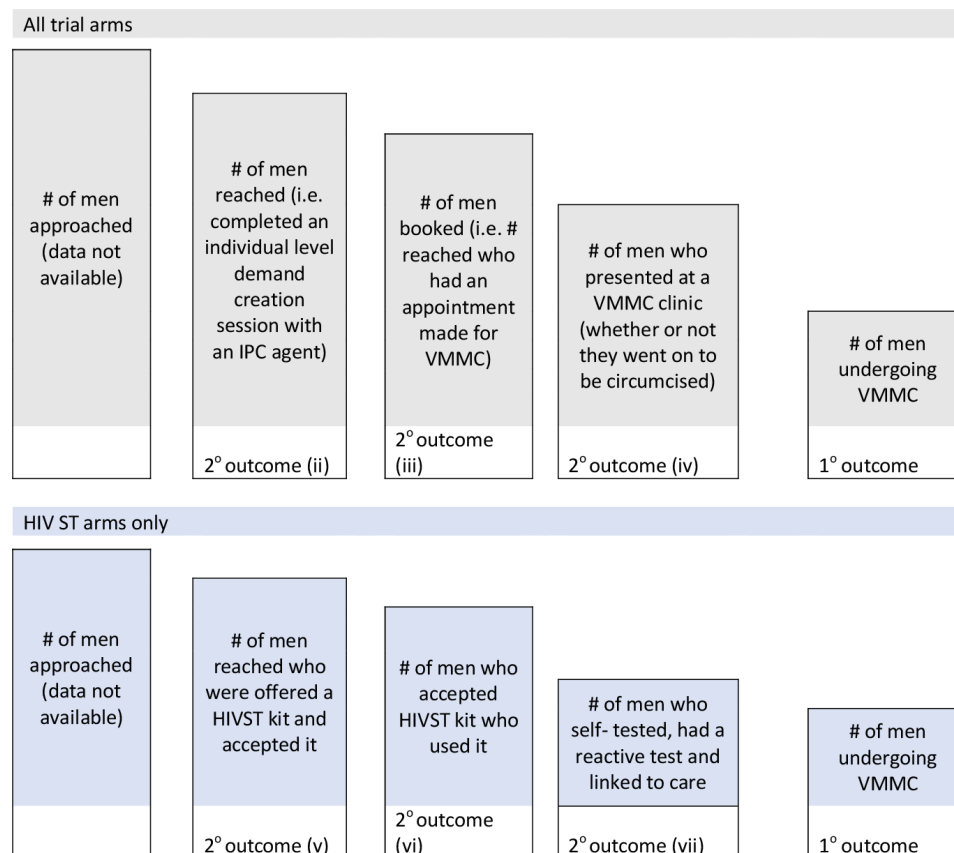
In this arm, in addition to the HCD-informed demand creation approach, IPC agents offered the men they mobilised a HIVST kit, with a kit use demonstration if accepted.

### Additional procedures—all arms

After a mobilisation session, each client was asked to provide his contact details to allow the IPC agent to provide supportive follow-up. All men who were referred for VMMC were given a referral card with a unique identifier and asked to present it when they attended for VMMC, enabling their attendance to be linked with the referring IPC agent. District Field Officers (IPC agents' supervisors) checked concordance between IPC agents and facility records, which helped curb fraud in payments to IPCs. The RCT payment structure followed that of the national VMMC programme, with IPC agents receiving US\$5 when a boy aged 10–14 years or a man  $\geq 30$  years was circumcised and US\$7 when a man aged 15–29 years was circumcised. IPCs only received an incentive if the person they reached and referred was actually circumcised.

### Process evaluation

We conducted a mixed-methods process evaluation within the trial. Data included: programme data; observations of IPC agents conducting VMMC mobilisation sessions; in-depth interviews (IDIs) and focus



**Figure 1** Primary outcome and secondary outcomes (ii)–(vii). HIVST, HIV self-testing; IPC, interpersonal communication; VMMC, voluntary medical male circumcision.

group discussions (FGDs) with IPC agents; IDIs with PSI's District Field Officers; and FGDs with men mobilised for VMMC. Iterative qualitative data collection and analysis informed a grounded thematic analytical approach.

### Outcome measures

The primary outcome was the number of men circumcised per IPC agent over the 6-month duration of the trial and compared by arm. Secondary outcomes were: (i) the mean conversion proportion (conversion proportion defined as number of men circumcised divided by the number of men reached by IPC agents); secondary outcomes (ii)–(vii) are shown in figure 1. In addition, there were three HIVST-related outcomes measured in the two HIVST arms (figure 1).

Programme data collected from IPC agents and clinic data were used to evaluate the primary outcome and secondary outcomes (i)–(iv). For ST outcomes (v)–(vii), IPC agents recorded whether the man opted to take a kit. Additional data on HIVST use were obtained from a phone-administered follow-up questionnaire with clients.

### Sample size calculation

As originally designed, this study required 35 IPC agents per arm (140 IPC agents across four arms) to have 80% power to detect a 30% proportionate difference

in VMMC uptake between any two individual arms assuming a high variability between IPC agents (coefficient of variation,  $k=0.3$ ) (see online supplemental appendix for other scenarios). A revised power calculation was completed in October 2018, using a higher  $k$  (1.0) to reflect high measured clustering within the outcome data collected to that point. This sample size calculation found that with 65 IPC agents per arm and two arms, we had 80% power to detect between 90% increase in VMMC per intervention (eg, 10.5–20). This resulted in the change from parallel comparisons to factorial-arm comparisons, assessing outcomes with and without each intervention.

### Statistical analysis

Analysis used intention-to-treat (ITT) and as-treated populations. The as-treated analysis population was based on the actual number of months each IPC agent worked, restricted to agents who reached at least one client, and included 20 IPC agents who the implementer added postrandomisation to replace 20 randomised IPC agents who declined to take part before training. The ITT analysis population was as defined based on the intended 6 months of mobilisation time each IPC agent was to work and excluded the 20 IPC agents added by the implementer postrandomisation.



The study team and the independent Technical Advisory Group (TAG) viewed the ‘as-treated’ analysis as the most appropriate for understanding the real-world effectiveness of the intervention and was therefore considered the primary analysis. This analysis compared outcomes with and without each intervention (factorial-arm analysis).

A statistical analysis plan (SAP) was developed prior to analysis; however, because the prespecified modelling approach was not valid statistically, the SAP was revised both during data collection and after the initial analysis was complete with input from the TAG. For the primary outcome, the effect of study arm was assessed at the IPC agent level using negative binomial regression. Subgroup analyses were performed to assess the differences in impact of the outcome by client age. These analyses were prespecified as 15–19 years, 20–29 years and 30+ years and then an additional post hoc analysis of 18–19 year-olds.

Conversion proportion per IPC was modelled using logistic regression. Secondary outcomes (ii)–(iv) were analysed at the same IPC agent-level data using negative binomial regression, while secondary outcomes related to self-test use were analysed using logistic regression.

All analyses were repeated using parallel-arm comparisons as well as ITT and as-treated populations. HIVST outcomes were compared by study arm 2 and 4 at the client level, using data arising from the as-treated analysis population.

Analyses were done with STATA V.15.1 software (StataCorp).

## RESULTS

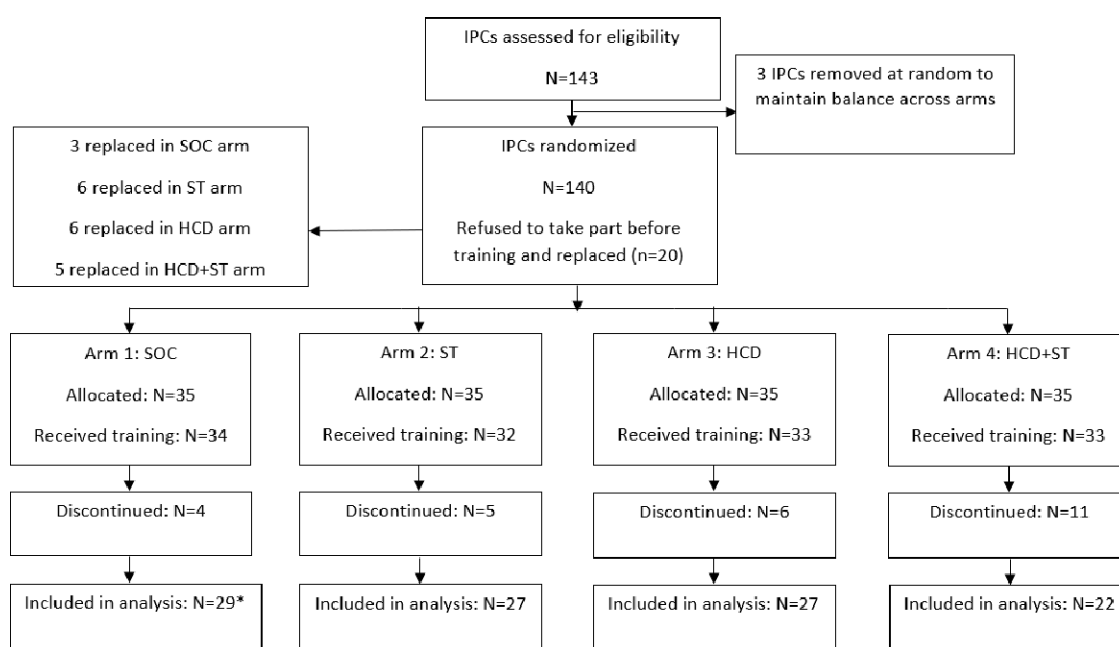
One hundred and forty-three IPC agents were identified by PSI for the trial, 140 were randomly chosen and allocated to one of four study arms. Postrandomisation, 20 declined to take part before training and were replaced with IPC agents by the implementer. One hundred and thirty-two of 140 (94.3%) attended study arm-specific training and 105/132 (79.5%) reported reaching at least one client during the trial period and were included in the ‘as-treated’ analysis. IPC agent attrition ranged from 4 (11.8%) to 11 (33.3%) by arm and was highest in arm 4 (figure 2).

### Characteristics of IPC agents

There were differences in characteristics of IPC agents by arm resulting from replacement of 20 IPCs postrandomisation and included differences in age, gender, level of education and prior VMMC mobilisation experience (table 1).

### Characteristics of clients reached

Overall, 105 IPC agents reached 8707 men with demand creation for VMMC. Arm 1 (SOC) reached the greatest number of clients (n=3105, 35.7%) while arm 4 (HCD+ST) reached the smallest (n=1542, 17.7%) (table 2). The majority of potential VMMC clients were out of school, across all the arms (table 2). Overall, 84.5% (7356/8707) of men reached were aged 15–29 years.



\*1 IPC excluded from analysis because he only had clients circumcised after the trial period

**Figure 2** CONSORT diagram for as-treated analysis population. HCD, human-centred design; IPC, interpersonal communication; SOC standard of care; ST self-testing.

**Table 1** Characteristics of IPC agents by arm (as-treated analysis population)

	Arm 1: SOC		Arm 2: ST		Arm 3: HCD		Arm 4: HCD+ST	
	n	%	n	%	n	%	n	%
IPC agents	29		27		27		22	
Total IPC mobilisation—months	126		96		101		97	
Male	8	27.6	17	63.0	15	55.6	8	36.4
District								
Buhera	6	20.7	8	29.6	2	7.4		9.1
Gokwe North	4	13.8	9	33.3	4	14.8		40.9
Mangwe	4	13.8	1	3.7	3	11.1		13.6
Mutasa	5	11.1	3	11.1	11	40.7		31.8
Zvimba	10	34.5	6	22.2	7	25.9		4.6
Age (years)								
≤19	1	3.5	1	3.7	4	14.8	1	4.6
20–29	4	13.8	12	44.5	6	22.2	5	22.7
30–39	7	24.1	8	29.6	4	14.8	2	9.1
40–49	9	31.0	5	18.5	9	33.4	13	59.0
50+	8	27.6	1	3.7	4	14.8	1	4.6
Educational level								
Primary level	8	27.6	1	3.7	1	3.7	0	0
Secondary level	15	51.7	23	85.2	25	92.6	22	100
≥Advanced level	6	20.7	3	11.1	1	3.7	0	0
IPC experience								
<12 months	22	75.9	18	66.7	21	77.8	9	40.9
≥12 months	7	24.1	9	33.3	6	22.2	3	59.1
Mean/median IPC mobilisation months	4.2/4		3.7/4		3.8/3		4.4/5	

HCD, human-centred design; IPC, interpersonal communication; SOC, standard of care; ST, self-testing.

### Effect of HCD-informed intervention on VMMC uptake (as-treated analysis population)

For the primary outcome, there was no evidence that the HCD-informed intervention increased VMMC uptake (incident

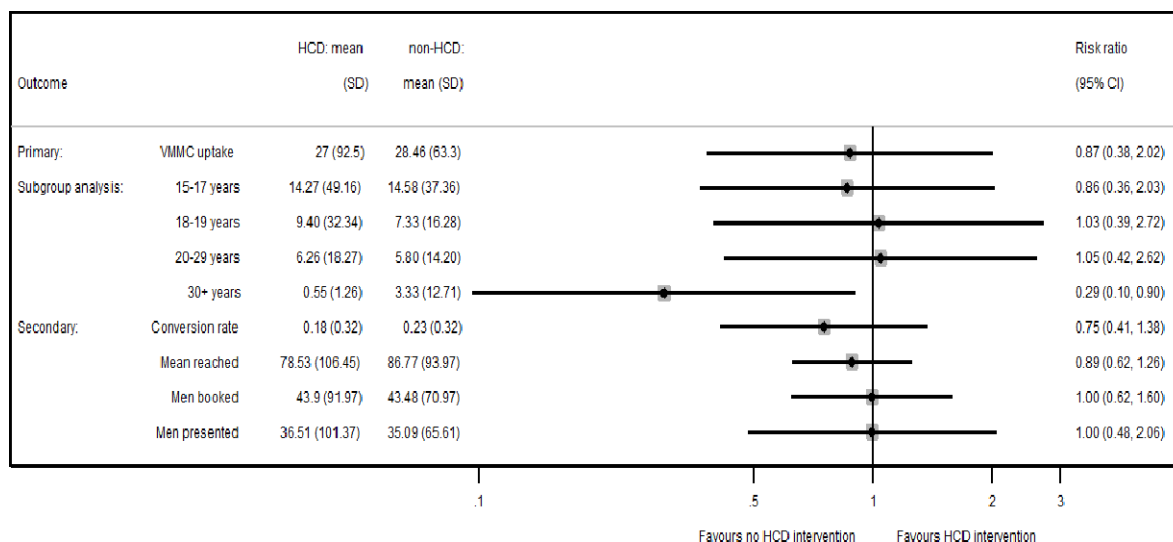
rate ratio (IRR) 0.87, 95% CI 0.38 to 2.02;  $p=0.75$ ) (figure 3 and online supplemental table 1). There was no evidence of an interaction effect between HCD-informed intervention and age for VMMC uptake ( $p=0.27$ ). The HCD-informed

**Table 2** Characteristics of ≥15-year-olds clients reached by arm (as-treated analysis population)

	Arm 1: SOC		Arm 2: ST		Arm 3: HCD		Arm 4: HCD+ST	
	n	%	n	%	n	%	n	%
Total	3105	100	1754	100	2306	100	1542	100
Age in years								
15–17	1102	35.5	592	33.8	886	38.4	509	33.0
18–19	571	18.4	318	18.1	523	22.7	278	18.0
20–29	952	30.7	440	25.1	627	27.2	558	36.2
30+	480	15.4	404	23.0	270	11.7	197	12.8
Median age (min-max), years	19.0	(15-78)	19.0	(15-87)	18.0	(15-84)	19.0	(15-83)
Education completed*								
School-going	1232	40.1	638	39.6	728	31.8	477	31.5
Out of school	1841	59.9	1041	60.4	1560	68.2	1039	68.5

\*106 missing.

HCD, human-centred design; SOC, standard of care; ST, self-testing.



**Figure 3** Effect of HCD-informed intervention—as-treated analysis population. HCD, human-centred design; VMMC, voluntary medical male circumcision.

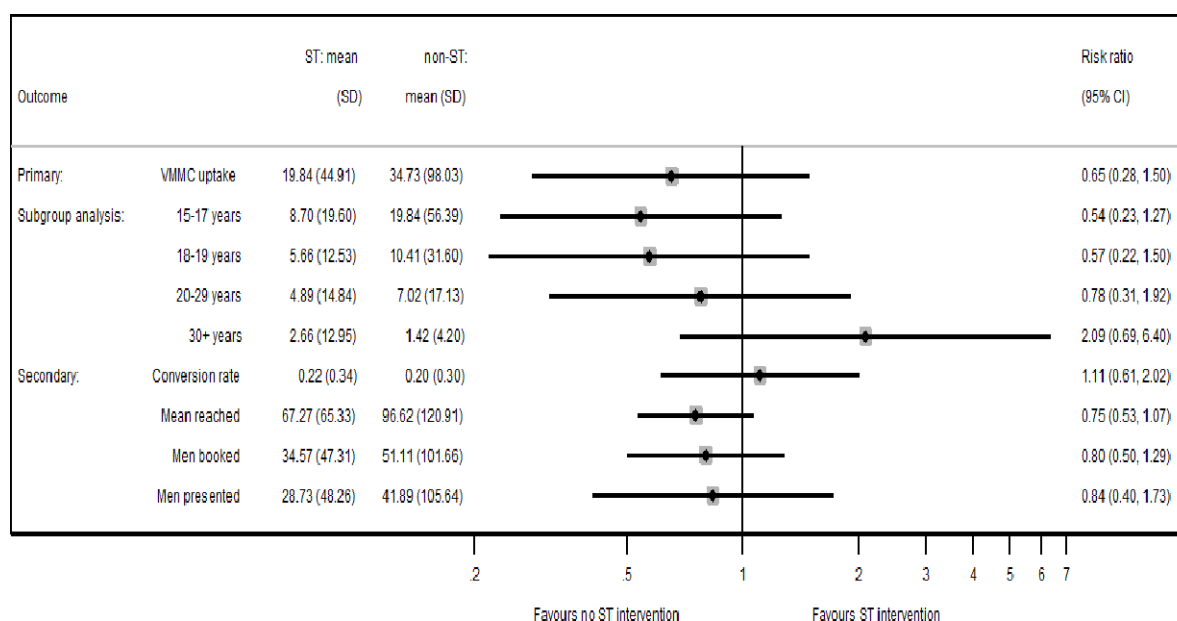
approach had no effect on secondary outcomes of: VMMC conversion proportion (risk ratio (RR) 0.75, 95% CI 0.41 to 1.38;  $p=0.36$ ), the number of men reached (IRR 0.89, 95% CI 0.62 to 1.26;  $p=0.50$ ), the number of men booked for VMMC (IRR 1.00, 95% CI 0.62 to 1.60;  $p>0.99$ ) or the number of men presenting for VMMC (IRR 1.00, 95% CI 0.48 to 2.06;  $p>0.99$ ). Overall, of all reached in the HCD arms, 12.6% (485/3848) were classified in the default 'green' segment, denoting that client was willing to be circumcised before the start of the demand creation session.

#### Effect of HIVST intervention on VMMC uptake

Offering men a HIVST kit at the time of VMMC mobilisation did not have an effect on VMMC uptake (IRR 0.65, 95% CI 0.28 to 1.50;  $p=0.31$ ) (figure 4 and online supplemental

table 1). There was also no effect of offer of a HIVST kit on secondary outcomes of: the conversion proportion (RR 1.11, 95% CI 0.61 to 2.02;  $p=0.71$ ); the number of men reached (IRR 0.75, 95% CI 0.53 to 1.07;  $p=0.11$ ), booked (IRR 0.80, 95% CI 0.50 to 1.29;  $p=0.36$ ) or presenting for VMMC at the clinic (IRR 0.84, 95% CI 0.40 to 1.73;  $p=0.63$ ). There was no evidence of an effect of an offer of HIVST on VMMC uptake in any age category although there was doubling of VMMC uptake among men over 30 years, although the CI included one (figure 4). There was no evidence of an interaction effect between HIVST intervention and age ( $p=0.21$ ).

ITT analysis also showed no evidence of an effect of HCD-informed and HIVST approaches on VMMC uptake (see online supplemental table 2).



**Figure 4** Effect of ST intervention—as-treated analysis population. ST, self-testing; VMMC, voluntary medical male circumcision.

**Table 3** Uptake of HIVST, by study arm (ST vs HCD+ST)

	Arm 2: ST		Arm 4: HCD+ST		Effect of HCD+ST vs ST	
	n/N	%	n/N	%	OR (95% CI)	P value
Men offered HIVST (% surveyed)	129/173	74.6	71/110	64.6	0.62 (0.37 to 1.04)	0.072
Men accepting HIVST (% offered)	101/129	78.3	52/71	73.2	0.76 (0.39 to 1.49)	0.420
Men using HIVST (% accepted)	91/101	90.1	50/52	96.2	2.75 (0.58 to 13.03)	0.203
Reactive HIVST (% used)	5/91	5.5	1/50	2.0	0.37 (0.04 to 3.30)	0.376 (0.072)*
Men with reactive test linked to care (% reactive)	2/5	40.0	1/1	100.0		

\*Fisher's exact test.

HCD, human-centred design; HIVST, HIV self-testing; ST, self-testing.

### VMMC cascade results—HCD-informed intervention segments

Men in the three prioritised segments (embarrassed rejecters, neophytes, enthusiasts) were more likely to be circumcised than those in the non-prioritised segments. Overall however, men in the green (default) segment were much more likely than any other segment to undergo circumcision (>70%) (see online supplemental figure 1).

### HIVST secondary outcomes

In total, 3296 men were reached by IPC agents in the HIVST arms (ST and HCD+ST arms), of whom only 8.6% (283/3296) were successfully followed by phone to ask questions about HIVST kit uptake and use. Overall, 200/283 (70.6%) men reported being offered HIVST kits. There was weak evidence that participants in the HCD+ST arm were less likely to be offered kits compared with participants in the ST arm (OR 0.62, 95% CI 0.37 to 1.04;  $p=0.07$ ). Overall, 76.5% of men who were offered a kit accepted it and 92.2% (141/153) of those accepting reported using the kit, again with no evidence of difference between arms (table 3).

### Process evaluation findings

#### Acceptability of the interventions

Most IPC agents allocated to the HCD-informed approach found it useful, noting that engaging one-on-one was more effective, resulting in more men getting quality information than was possible when using a group approach. However, all felt that some components (especially segmentation) lengthened the IPC session, resulting in fewer men 'reached' compared with using traditional IPC approaches.

Regarding HIVST, IPC agents felt that the intervention generated huge interest in the communities where HIVST had not been previously available. There was high demand for HIVST across all five districts, which appeared to be independent of intention to get circumcised.

#### Uneven performance among IPC agents and districts

There were substantial differences in the performance of IPC agents across all outcomes. Only 105 (79.5%) of

the 132 trained IPC agents reached at least one man to discuss VMMC over the course of the trial (and so were included in the 'as-treated' analysis) (see online supplemental table 3). Forty (38.1%) did not convert anyone to VMMC during the trial and 30 (28.6%) converted fewer than 6 men (one per month). Conversely, two IPC agents converted over 50 per month (one converted 553 over 6 months and the other converted 355).

In addition to variability between IPC agents, there was variability in implementation between study districts (conversion proportion ranging from 6% in Zvimba to 81% in Buhera), possibly due to contextual factors including number of men who were eligible to be circumcised. IPC agents in Buhera and Gokwe North devoted considerable time to VMMC mobilisation, perhaps reflecting the lack of employment opportunities locally. In the other districts, IPC agents were involved in additional income-generating activities. These factors likely explain some of the variability observed between study districts (online supplemental table 5).

### Implementation of the interventions

Implementation of the HCD-informed intervention was not always as intended. As segmentation lengthened the time for mobilisation, this resulted in some IPC agents resorting to traditional approaches or administering an abridged and possibly suboptimal version of the approach. IPC agents also reported they were sometimes selective about which messages they delivered to each segment (eg, they left out messages they viewed as age and sexual experience inappropriate). Of note, IPC agent gender, age and education were significantly associated with VMMC uptake (online supplemental table 4).

The HIVST intervention was similarly not implemented as intended. As IPC agents were the only source of ST kits in the RCT districts, they did not want to be seen as 'promoting HIVST' instead of VMMC, with the result that HIVST kits were not always offered by IPC agents in HIVST arms. This was in part because IPC agents sometimes reported that they felt men taking HIVST kits were not necessarily interested in VMMC. This may have been true; an appreciable proportion of the men we were able to follow-up by phone obtained ST kits and reportedly



tested but did not take up VMMC. Further, ST kits were more likely to be offered in arm 2 (HIVST arm) than in arm 4 (HCD and HIVST), where the intervention took longest to deliver and which consequently had the highest data burden. IPC agents also found it difficult to incorporate the demonstration of the HIVST kit or the demonstration video into the IPC session. Of note, IPC agents received an incentive if their clients were circumcised but not if they self-tested, which may also have reduced their enthusiasm for HIVST distribution and demonstration.

## DISCUSSION

We conducted a pragmatic randomised 2×2 factorial trial to determine the effectiveness of the HCD-informed approach and HIVST in motivating men (15–29 years) to take up VMMC. Our trial found no evidence that HCD-informed mobilisation or the offer of a HIVST kit prior to VMMC had an effect on VMMC uptake or on secondary outcomes.

The lack of detectable effect may be due to a number of factors. First, the market research conducted in 2015 identified several barriers or facilitators to VMMC uptake and recommended a set of interventions be delivered through multiple channels.<sup>26–28</sup> However, due to resource constraints, these multiple approaches were not feasible to implement in practice. The HCD-informed approach tested here only addressed a subset of barriers. For example, we know that fear of financial loss was not addressed and this could be an especially important barrier in settings where majority of men are self-employed. Recent systematic reviews<sup>9 30</sup> have found that financial incentives framed as fair compensation (rather than as lottery) appear to be the most acceptable and effective VMMC demand creation intervention found to date especially among adult men.

As stated earlier, men who were already deemed by IPC agents in HCD-informed approach arms to be highly motivated to VMMC and did not require the use of the segmentation typing tool were allocated to the ‘green’ segment. They had the highest rate of conversion to VMMC. We do not know what segment they would have been allocated to if the segmentation typing tool had been applied and so cannot determine if prioritised segments were indeed those most likely to be ‘easy to convert’. Of note, we have included the 12.6% classified in the ‘green’ category (and who therefore did not receive the intervention as planned) in the analyses, as no exclusion of men of this type in the no HCD-informed approach is possible.

It was assumed that once trained, every IPC agent would be able to implement the HCD-informed approach as intended. Field observation suggested that implementing the HCD-informed approach requires more education and skills than traditional approaches. It takes time for IPC agents to become familiar with using the tools and, indeed, some IPC agents selected for the trial never became comfortable with using the approach.

Our process evaluation found that younger, male, and better-educated IPC agents appeared more successful at creating demand for VMMC using the approach. Further, as combining the HCD-informed approach and HIVST lengthened the IPC session and resulted in a higher data collection burden, it might not be feasible for the two approaches to be rolled out simultaneously going forward.

Perhaps important is that IPC agents were incentivised according to the national incentive structure (US\$5 when a boy aged 10–14 years or a man ≥30 years was circumcised and US\$7 when a man aged 15–29 years was circumcised). IPC agents could therefore earn larger amounts by converting groups of younger boys (eg, through schools) with relatively less effort than they could by spending longer time recruiting ‘recalcitrant’ adult men using the HCD-informed approach.

The power of the trial to show an impact was likely reduced by the fact that relatively few IPC agents (75 out of 140 randomised) actually mobilised for VMMC, perhaps reflecting the acceptability and/or feasibility of delivering the interventions. Suboptimal supervision of implementation of the interventions, as indicated by a high number of inactive IPC agents, may have contributed. While the lower than anticipated VMMC conversion rate may have affected the RCT’s ability to show an impact, there is no suggestion from the effect sizes of any impact of the HCD-informed approach.

The extent of variability between IPC agents in terms of performance was greater than anticipated. In addition, there was considerable imbalance in characteristics of IPC agents by arm because of the substitution of 20 IPC agents postrandomisation and differential drop out by arm. IPC agents’ characteristics were associated with rate of VMMC conversion, and this may have undermined the ability of the trial to demonstrate an impact.

Our trial is one of the first studies to rigorously evaluate an HCD-informed intervention and as delivered in a real-world and resource-constrained setting. Moreover, rigorous procedures were used to ascertain objectively measured outcomes; the RCT was complemented by process evaluation including in-depth qualitative data collection to understand mechanisms of action. However, as with other evaluations of programmatic interventions, our trial was characterised by real life challenges to implementation including a lack of control of the manner in which interventions were implemented. Many of the challenges experienced in this trial are not unique to the interventions tested here, but are common during evaluations of real-world interventions.<sup>31</sup>

In conclusion, the RCT did not show evidence of an effect of interventions on VMMC uptake. That the majority of IPC agents referred fewer than one man a month for VMMC suggests that they may not have been motivated to use these demand creation approaches as designed, which has implications for interventions’ feasibility. Importantly, in order to appeal to adult men, other research<sup>9 30</sup> has suggested that VMMC demand creation

interventions should include financial incentives framed as fair compensation. Trial findings will inform future design and implementation of demand creation evaluations.

#### Author affiliations

<sup>1</sup>Centre for Sexual Health and HIV/AIDS Research (CeSHHAR) Zimbabwe, Harare, Zimbabwe

<sup>2</sup>Department of International Public Health, Liverpool School of Tropical Medicine, Liverpool, UK

<sup>3</sup>MRC International Statistics and Epidemiology Group, London School of Hygiene & Tropical Medicine, London, UK

<sup>4</sup>Population Services International, Washington, District of Columbia, USA

<sup>5</sup>Population Services International Zimbabwe, Harare, Zimbabwe

<sup>6</sup>Ministry of Health and Child Care, Harare, Zimbabwe

<sup>7</sup>HIV Department, World Health Organization, Geneva, Switzerland

<sup>8</sup>Department of Clinical Research, London School of Hygiene and Tropical Medicine, London, UK

**Twitter** Webster Mavhu @webstermavhu, Melissa Neuman @melneuman, Sungai T Chabata @SungaiChabata, Collin Mangenah @cmangenah01 and Cheryl C Johnson @ccasejohn

**Acknowledgements** The authors would like to thank the VMMC clients and IPC agents who made the study possible.

**Contributors** WM, FMC and KH led the trial design, with involvement from HAW, MN and KLF. WM, FMC and MN conceived and designed the study protocol. KH, NT, NM and MM developed the intervention, with support from GN, SX and OM. WM, FMC, SB and CM led the trial implementation, data collection and process evaluation. MN, GM and STC carried out the statistical analysis, with support from HAW and KLF. WM, FMC, MN, KLF, SB and CM led data interpretation with involvement from KH, GM, STC, CM, NT, NM, MM, GN, SX, OM, CJ, ELC and HAW. WM, FMC, MN and KLF wrote the paper and all authors were involved in the review of drafts. All authors have approved the final manuscript.

**Funding** Bill & Melinda Gates Foundation; Unitaid as part of the STAR Initiative. Unitaid is a hosted partnership of the World Health Organisation. The funders had no role in study design, data collection, data analysis, data interpretation or writing of the report.

**Competing interests** None declared.

**Patient consent for publication** Not required.

**Ethics approval** The trial was registered with the Pan African Trial Registry [(registration number PACTR201804003064160)]. The protocol was approved by the Medical Research Council of Zimbabwe and Research Council of Zimbabwe (#2231), Liverpool School of Tropical Medicine (#17-067) and London School of Hygiene & Tropical Medicine (#14460). Qualitative research participants provided written informed consent.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** Data are available upon request. Data from our trial will be made available upon request to the London School of Hygiene & Tropical Medicine data repository. <https://datacompass.lsh.ac.uk/>.

**Supplemental material** This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

**Open access** This is an open access article distributed under the terms of the Creative Commons Attribution IGO License (CC BY NC 3.0 IGO), which permits use, distribution, and reproduction in any medium, provided the original work is properly cited. In any reproduction of this article there should not be any suggestion that WHO or this article endorse any specific organization or products. The use of the WHO logo is not permitted. This notice should be preserved along with the article's original URL.

Disclaimer: The author is a staff member of the World Health Organization. The

author alone is responsible for the views expressed in this publication and they do not necessarily represent the views, decisions or policies of the World Health Organization.

#### ORCID iDs

Webster Mavhu <http://orcid.org/0000-0003-1881-4398>

Melissa Neuman <http://orcid.org/0000-0002-8870-6504>

Karin Hatzold <http://orcid.org/0000-0002-5117-3732>

Sungai T Chabata <http://orcid.org/0000-0001-7629-1543>

Collin Mangenah <http://orcid.org/0000-0002-0733-0622>

Cheryl C Johnson <http://orcid.org/0000-0001-5499-5523>

Elizabeth L Corbett <http://orcid.org/0000-0002-3552-3181>

Helen A Weiss <http://orcid.org/0000-0003-3547-7936>

Katherine Fielding <http://orcid.org/0000-0002-6524-3754>

Frances M Cowan <http://orcid.org/0000-0003-3087-4422>

#### REFERENCES

- UNAIDS. *Hiv prevention roadmap 2020: first progress report*, 2018. Geneva: UNAIDS, 2018.
- WHO. *Preventing HIV through safe voluntary medical male circumcision for adolescent boys and men in generalized HIV epidemics: recommendations and key considerations*. Geneva: WHO, 2020.
- UNAIDS/WHO. *Voluntary medical male circumcision: steady progress in the scaleup of VMMC as an HIV prevention intervention in 15 eastern and southern African countries before the SARS-CoV2 pandemic*. Geneva: UNAIDS and WHO, 2021.
- UNAIDS. *Global AIDS update: communities at the centre*. Geneva: Joint United Nations Programme on HIV/AIDS, 2019.
- WHO. *Voluntary medical male circumcision for HIV prevention: progress brief*. Geneva: WHO, 2018.
- Mavhu W, Hatzold K, Dam KH, *et al*. Adolescent Wound-Care self-efficacy and practices after voluntary medical male Circumcision-A multicountry assessment. *Clin Infect Dis* 2018;66:S229–35.
- Kaufman MR, Smelyanskaya M, Van Lith LM, *et al*. Adolescent sexual and reproductive health services and implications for the provision of voluntary medical male circumcision: results of a systematic literature review. *PLoS One* 2016;11:e0149892.
- Njeuhmeli E, Opuni M, Schnure M, *et al*. Scaling up voluntary medical male circumcision for human immunodeficiency virus prevention for adolescents and young adult men: a modeling analysis of implementation and impact in selected countries. *Clin Infect Dis* 2018;66:S166–72.
- Ensor S, Davies B, Rai T, *et al*. The effectiveness of demand creation interventions for voluntary male medical circumcision for HIV prevention in sub-Saharan Africa: a mixed methods systematic review. *J Int AIDS Soc* 2019;22 Suppl 4:e25299.
- Carrasco MA, Grund JM, Davis SM, *et al*. Systematic review of the effect of economic compensation and incentives on uptake of voluntary medical male circumcision among men in sub-Saharan Africa. *AIDS Care* 2018;30:1071–82.
- Choko AT, Candfield S, Maheswaran H, *et al*. The effect of demand-side financial incentives for increasing linkage into HIV treatment and voluntary medical male circumcision: a systematic review and meta-analysis of randomised controlled trials in low- and middle-income countries. *PLoS One* 2018;13:e0207263.
- Thurumurthy H, Masters SH, Rao S, *et al*. The effects of providing fixed compensation and Lottery-Based rewards on uptake of medical male circumcision in Kenya: a randomized trial. *J Acquir Immune Defic Syndr* 2016;72 Suppl 4:S309–15.
- Wambura M, Mahler H, Grund JM, *et al*. Increasing voluntary medical male circumcision uptake among adult men in Tanzania. *AIDS* 2017;31:1025–34.
- Weiss SM, Zulu R, Jones DL, *et al*. The spear and shield intervention to increase the availability and acceptability of voluntary medical male circumcision in Zambia: a cluster randomised controlled trial. *Lancet HIV* 2015;2:e181–9.
- Curran K, Njeuhmeli E, Mirelman A, *et al*. Voluntary medical male circumcision: strategies for meeting the human resource needs of scale-up in southern and eastern Africa. *PLoS Med* 2011;8:e1001129.
- MOHCC. *Zimbabwe sustainability transition implementation plan: 2019–2021 - voluntary medical male circumcision*. Harare: MOHCC, 2019.
- Mavhu W, Dauya E, Bandason T, *et al*. Chronic cough and its association with TB-HIV co-infection: factors affecting help-seeking behaviour in Harare, Zimbabwe. *Trop Med Int Health* 2010;15:574–9.

- 18 Skovdal M, Campbell C, Madanhire C, *et al*. Masculinity as a barrier to men's use of HIV services in Zimbabwe. *Global Health* 2011;7:13.
- 19 Chikovore J, Gillespie N, McGrath N, *et al*. Men, masculinity, and engagement with treatment as prevention in KwaZulu-Natal, South Africa. *AIDS Care* 2016;28 Suppl 3:74–82.
- 20 Hatzold K, Mavhu W, Jasi P, *et al*. Barriers and motivators to voluntary medical male circumcision uptake among different age groups of men in Zimbabwe: results from a mixed methods study. *PLoS One* 2014;9:e85051.
- 21 Skolnik L, Tsui S, Ashengo TA, *et al*. A cross-sectional study describing motivations and barriers to voluntary medical male circumcision in Lesotho. *BMC Public Health* 2014;14:1119.
- 22 Djimeu EW. *Scoping report on interventions for increasing the demand for voluntary medical male circumcision*. Washington DC: 3ie, 2013.
- 23 George G, Strauss M, Chirawu P, *et al*. Barriers and facilitators to the uptake of voluntary medical male circumcision (VMMC) among adolescent boys in KwaZulu-Natal, South Africa. *Afr J AIDS Res* 2014;13:179–87.
- 24 Choko AT, Corbett EL, Stallard N, *et al*. HIV self-testing alone or with additional interventions, including financial incentives, and linkage to care or prevention among male partners of antenatal care clinic attendees in Malawi: an adaptive multi-arm, multi-stage cluster randomised trial. *PLoS Med* 2019;16:e1002719.
- 25 Hatzold K, Gudukeya S, Mutseta MN, *et al*. HIV self-testing: breaking the barriers to uptake of testing among men and adolescents in sub-Saharan Africa, experiences from STAR demonstration projects in Malawi, Zambia and Zimbabwe. *J Int AIDS Soc* 2019;22 Suppl 1:e25244.
- 26 Sgaier SK, Eletskaia M, Engl E, *et al*. A case study for a psychographic-behavioral segmentation approach for targeted demand generation in voluntary medical male circumcision. *Elife* 2017;6:6.
- 27 Gomez A, Loar R, England Kramer A. The impact of market segmentation and social marketing on uptake of preventive programmes: the example of voluntary medical male circumcision. A literature review. *Gates Open Res* 2018;2:68.
- 28 Gomez A, Loar R, Kramer AE, *et al*. Reaching and targeting more effectively: the application of market segmentation to improve HIV prevention programmes. *J Int AIDS Soc* 2019;22 Suppl 4:e25318.
- 29 Schulz KF, Altman DG, Moher D, *et al*. Consort 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010;340:c332.
- 30 Kennedy CE, Yeh PT, Atkins K, *et al*. Economic compensation interventions to increase uptake of voluntary medical male circumcision for HIV prevention: a systematic review and meta-analysis. *PLoS One* 2020;15:e0227623.
- 31 Doyle AM, Mulhern E, Rosen J, *et al*. Challenges and opportunities in evaluating programmes incorporating human-centred design: lessons learnt from the evaluation of adolescents 360. *Gates Open Res* 2019;3:1472.

<b>CONSORT checklist of items for reporting pragmatic trials .....</b>	<b>3</b>
<b>Statistical Analysis Plan .....</b>	<b>5</b>
<b>SAP text dated 14 January 2019 .....</b>	<b>9</b>
<b>1. INTRODUCTION .....</b>	<b>9</b>
<b>2. TRIAL OVERVIEW .....</b>	<b>9</b>
<b>2.1. PRINCIPAL RESEARCH OBJECTIVE.....</b>	<b>9</b>
<b>2.2. TRIAL DESIGN.....</b>	<b>9</b>
<b>2.3. TRIAL ARMS, RANDOMIZATION, AND BLINDING .....</b>	<b>9</b>
<b>2.4. DURATION OF INTERVENTIONS .....</b>	<b>11</b>
<b>2.5. STUDY POPULATION AND INFORMED CONSENT .....</b>	<b>11</b>
<b>3. PRIMARY OUTCOME AND SAMPLE SIZE CALCULATION.....</b>	<b>11</b>
<b>3.1. SECONDARY OUTCOMES.....</b>	<b>12</b>
<b>4. OUTCOME EVALUATION AND DATA DESCRIPTION .....</b>	<b>12</b>
<b>4.1 RECRUITMENT AND REPRESENTATIVENESS OF SAMPLE .....</b>	<b>14</b>
<b>4.2 COMPARABILITY OF ARMS.....</b>	<b>14</b>
<b>4.3 ANALYSIS.....</b>	<b>14</b>
<b>4.4 ADJUSTED ANALYSES .....</b>	<b>17</b>
<b>4.5 PRESPECIFIED SUBGROUP ANALYSES .....</b>	<b>17</b>
<b>4.6 EXPLORATORY ANALYSIS.....</b>	<b>17</b>
<b>4.7 METHODS FOR ADDRESSING MISSING DATA .....</b>	<b>17</b>
<b>4.8 PROCESS EVALUATION .....</b>	<b>18</b>
<b>5. Six segments of men and their characteristics .....</b>	<b>31</b>
<b>6. Human centred design (HCD)-informed approach tools .....</b>	<b>32</b>
<b>6.1 Segmentation typing tool .....</b>	<b>32</b>
<b>6.2 Targeted messaging to an individual .....</b>	<b>33</b>
<b>6.3 Pain-o-meter .....</b>	<b>33</b>
<b>7. Changes to the trial protocol after trial commencement.....</b>	<b>34</b>
<b>8. Intervention components .....</b>	<b>35</b>
<b>8.1 Arm 1: Standard demand creation mobilisation .....</b>	<b>35</b>
<b>8.2 Arm 2: Standard demand creation plus offer of HIVST .....</b>	<b>35</b>
<b>8.3 Arm 3: HCD-informed demand creation approach .....</b>	<b>35</b>
<b>8.4 Arm 4: HCD-informed demand creation approach plus offer of HIVST .....</b>	<b>36</b>
<b>9. Tables of results: parallel arm and factorial analyses.....</b>	<b>37</b>
Table S1: Factorial analysis.....	37
Table S2: Parallel arm ITT analysis .....	37
Table S3: Parallel arm – as-treated analysis.....	38
<b>10. VMMC cascade results .....</b>	<b>38</b>



11. IPC agents characteristics and uptake of VMMC.....

39

Table S4: IPC agents characteristics and uptake of VMMC .....

39

Additional process evaluation findings.....

40

Table S5: Conversion proportions by district.....

40

**CONSORT checklist of items for reporting pragmatic trials**

Section	Item	Standard CONSORT description	Extension for pragmatic trials
Title and abstract	1	How participants were allocated to interventions (e.g., “random allocation,” “randomised,” or “randomly assigned”)	1-2
<b>Introduction</b>			
Background	2	Scientific background and explanation of rationale	4-5
<b>Methods</b>			
Participants	3	Eligibility criteria for participants; settings and locations where the data were collected	5-6
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered	6-7
Objectives	5	Specific objectives and hypotheses	5
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (e.g., multiple observations, training of assessors)	7-8
Sample size	7	How sample size was determined; explanation of any interim analyses and stopping rules when applicable	8-9
Randomisation—sequence generation	8	Method used to generate the random allocation sequence, including details of any restriction (e.g., blocking, stratification)	6
Randomisation—allocation concealment	9	Method used to implement the random allocation sequence (e.g., numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned	6
Randomisation—implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups	6
Blinding (masking)	11	Whether participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment	6
Statistical methods	12	Statistical methods used to compare groups for primary outcomes; methods for additional analyses, such as subgroup analyses and adjusted analyses	9
<b>Results</b>			
Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended)—specifically, for each group, report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analysed for the primary outcome; describe deviations from planned study	10

Section	Item	Standard CONSORT description	Extension for pragmatic trials
		protocol, together with reasons	
Recruitment	14	Dates defining the periods of recruitment and follow-up	6
Baseline data	15	Baseline demographic and clinical characteristics of each group	11
Numbers analysed	16	Number of participants (denominator) in each group included in each analysis and whether analysis was by "intention-to-treat"; state the results in absolute numbers when feasible (e.g., 10/20, not 50%)	11
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group and the estimated effect size and its precision (e.g., 95% CI)	12-13
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating which are prespecified and which are exploratory	13-15
Adverse events	19	All important adverse events or side effects in each intervention group	Nil
<b>Discussion</b>			
Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision, and the dangers associated with multiplicity of analyses and outcomes	15-17
Generalisability	21	Generalisability (external validity) of the trial findings	15-17
Overall evidence	22	General interpretation of the results in the context of current evidence	3 and 15-17

## Statistical Analysis Plan

### A cluster randomized controlled trial of innovative demand creation strategies to increase voluntary medical male circumcision uptake in Zimbabwe

Final version 1.9, 14 January 2019, with addendum 15 May 2019

#### Update memo, 15 May 2019 (original SAP follows)

This memo serves to update the final analysis plan with additional analysis details and proposed changes to the analysis of rate outcomes (i.e., primary outcome and secondary outcomes 2-5). The analysis and 6-8 (self-testing outcomes) will not change from the analysis plan dated 14 January 2019. The analysis of secondary outcome 1 (conversion proportion) will continue to be assessed at IPC-level, but the method of age-adjustment may change. As with the original plan, we suggested primary analyses be factorial analyses comparing arms with and without the two interventions of interest.

There are five topics covered in this memo:

1. Overview of data and description of over dispersion
2. Problems with random effect model and suggestions for modelling strategy moving forward
3. Problems with age-adjustment in initial SAP and suggestions for modelling strategy moving forward
4. As treated v. ITT analysis as primary analysis for discussion

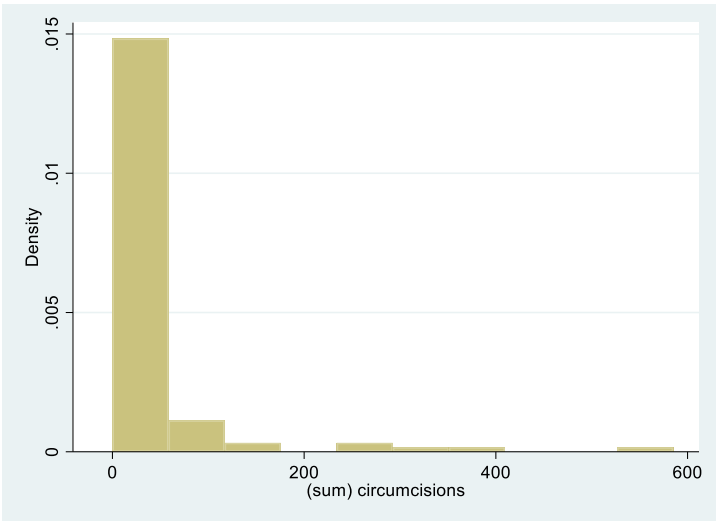
#### 1. Overview of data and description of over dispersion

The primary outcome variable, whether defined at the IPC-level or the IPC-month level, was over dispersed, or more highly variable than expected assuming the Poisson distribution. *Countfit* tests in Stata both suggest that negative binomial regression fits the outcome distribution better than Poisson, zero-inflated Poisson, or zero-inflated negative binomial models. Data summaries below show the distribution of circumcisions per IPC over the full follow-up period in tabular and graphical format, then the same information by arm for HCD-informed v. not.

#### Summary of total circumcisions/IPC across follow-up, as-treated analysis set (n=106), with histogram

(sum) circumcisions				
-----				
	Percentiles	Smallest		
1%	0	0		
5%	0	0		
10%	0	0	Obs	106
25%	0	0	Sum of Wgt.	106
50%	2.5		Mean	29.88679
		Largest	Std. Dev.	84.05637
75%	10	281		
90%	79	343	Variance	7065.473
95%	136	358	Skewness	4.343688
99%	358	585	Kurtosis	23.92946

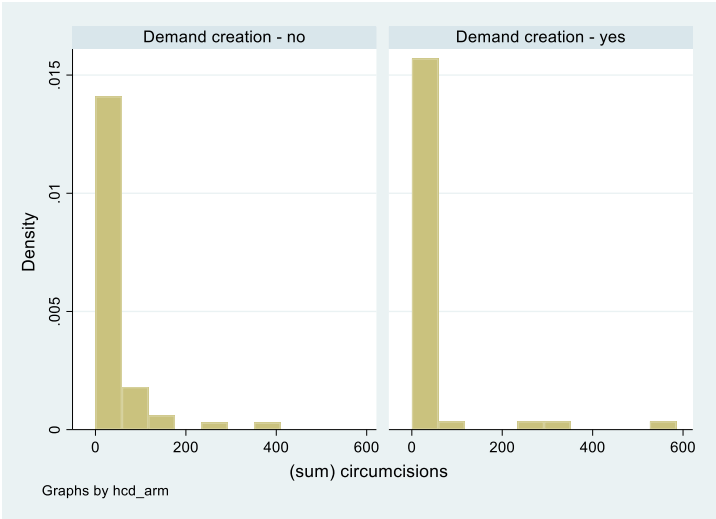




By arm

```
. table hcd_arm, c(mean circum~s sd circum~s count circum~s)
```

hcd_arm	mean(circum~s)	sd(circum~s)	N(circum~s)
Demand creation - no	29.42105	64.94997	57
Demand creation - yes	30.42857	102.6332	49



2. Problems with random effects model and suggestions for modelling strategy moving forward

The final SAP called for a random effect of IPC to be used to adjust for IPC-level differences in circumcision rates, and for Stata's *xtnbreg* command to be used. *Xtnbreg* uses a beta distribution to account for both the over dispersion parameter and the higher-level random effect ( $dispersion \sim beta(r, s)$ ). However, upon inspection the *xtnbreg* results have been difficult to interpret, and results of the model do not fit with description summaries of the data. First, the beta distribution parameters are both  $<1$ , and so standard measures used to check model fit (i.e., predicted values and deviance residuals) cannot be calculated. Second, the results vary widely if the random effect is parameterized differently (i.e., by using a mixed effect model with a dispersion parameter and a normally distributed random effect of IPC). Together, these suggest that the random-effects model is a poor fit to these data.

The poor fit of models with a random effect capturing IPC-level is likely because the bulk of the variability in the data can be found within IPCs rather than between. For example, ID Buhera-A03 had monthly totals ranging from 1-104, and A04 from 0-50 (see output). This is different from the usual pattern of variability in cluster randomized trials, with increased correlation within clusters.

### Circumcisions by month for three IPCs

clusterid	month	circum~s
Buhera-A01	5	0
Buhera-A01	6	3
Buhera-A01	9	0
Buhera-A01	10	0
Buhera-A03	5	96
Buhera-A03	6	92
Buhera-A03	7	104
Buhera-A03	8	61
Buhera-A03	9	1
Buhera-A03	10	1
Buhera-A03	11	3
Buhera-A04	5	0
Buhera-A04	6	50
Buhera-A04	7	25

We believe that the most robust solution is to conduct all analyses on aggregated cluster-level data, i.e. at IPC-level, using standard negative binomial regression. This is a standard method often used in the analyses of cluster-randomized trials (see Hayes and Moulton), and will make minimal assumptions about the distribution of circumcisions by month within IPCs. Thus, rate based models will be of the general form:

$$circumcisions_i = \beta_0 + \beta_1 arm_i$$

Where circumcisions are measured over  $i$  IPCs as the sum over the full follow-up period, and are assumed to have a negative binomial distribution with variance  $\mu + \alpha\mu^2$  (NB2). No random effect will be used. The as-treated analysis will also include an offset term with the logged number of months of follow-up included in the model with coefficient constrained to 1.

### 3. Problems with age-adjustment in initial SAP and suggestions for modelling strategy moving forward

Across arms, IPCs were believed to use standard group recruiting for young men, and this group recruiting was likely to result in large numbers of circumcisions per month across all arms. For this reason, the original SAP called for including an age-adjusted result, not to

adjust for baseline imbalance by age, but to add a fixed parameter to capture the variability in the outcome by client age. In the final SAP (dated 14 January 2019), age was adjusted at client level. However, based on discussions with the team it seems increasingly likely that age of client recruited was not a nuisance variable, but was substantially affected by the interventions themselves.

For this reason, we suggest that unadjusted rate ratios be the primary analysis, and to drop age-adjustment and to only present unadjusted rate ratios, as was suggested in earlier versions of the SAP. Differences in the impact of the outcome would be identified by analysing age-specific subgroups, including the pre-specified subgroups of 15-19 years, 20-29 years, 30+ years, and an additional post-hoc analysis of 18-19 years. These subgroup analyses will take the following form:

$$\text{circumcisions of 15 – 17 year old clients}_i = \beta_0 + \beta_1 \text{arm}_i$$

They will have similar assumptions to the main model – i.e., the outcome will be the sum of all circumcisions in the follow-up period among this age group, and the outcome has a negative binomial distribution. Post-hoc subgroup analyses assessing impact among in-school v. out of school persons using similar models.

Additional post-hoc analyses could seek to explore differences in effectiveness over the follow-up period, by separately estimating impact earlier and later in the intervention. Specific dates of interest would have to be decided with input from PSI and CeSHHAR.

However, if there is a strong desire to adjust for age, the method for doing so should be at the level of the IPC not the level of the client, with the interpretation being that some IPCs were more likely to target younger clients. (This is the same method used to adjust for client age in the analysis of secondary outcome 2 (IPC conversion proportion, measured at IPC-level) as specified in the final SAP

The approximate model would then be:

$$\text{Rate outcome}_i = f(\text{allocation}_i, \text{proportion clients circumcised by IPC who were 18-19 years}_i, \text{proportion 20-29 years}_i, \text{proportion 30+}_i).$$

Where  $i$  IPCs are measured across the follow-up period. The predicted exponentiated parameter on allocation is thus the rate ratio comparing the intervention and comparison among IPCs who circumcised only clients in the 15-17 year age group (i.e., with all other age groups = 0). This is a methodological improvement but still a very cumbersome interpretation, especially as we are aware that one of the effects of the intervention seemed to be to affect the age of clients reached

#### 4. As treated v. ITT analysis as primary analysis for discussion

During the TAG meeting, there was some concern about using the as-treated analysis as the primary analysis for reporting. However, we believe that this is appropriate, given the pragmatic nature of this trial and the fact that ITT results will be reported simultaneously. It is particularly important to report ITT results given that IPCs were added to the trial after randomization. While we believe these added “at random” from a practical perspective, the work of these IPCs cannot be included in an ITT analysis because they were not randomized by the research statistician. However, we also believe that the information contributed by these IPCs is important and will be useful for understanding the impact of the interventions.

**SAP text dated 14 January 2019****1. INTRODUCTION**

Voluntary medical male circumcision (VMMC) has been recommended by the World Health Organization as a strategy for preventing HIV transmission in high-prevalence countries. VMMC clients are recommended to test for HIV pre-operatively, making VMMC services an opportunity for men to receive HIV testing services (HTS). Studies on VMMC uptake have identified several key barriers inhibiting men from taking up VMMC; these include fear of pain and complications, pre-operative testing, and lack of awareness of HIV risk.

This study evaluates a community-based VMMC demand creation tool designed to address concerns around VMMC and focused VMMC demand creation among high risk populations. This tool was developed by PSI and the Zimbabwe Ministry of Health and Child Care (MOHCC) based on robust market research data provided by IPSOS Healthcare. This research is funded by the Bill and Melinda Gates Foundation through PSI. The study also evaluates the effectiveness of distributing HIV self-testing for use as a pre-operative HIV test on VMMC uptake, and evaluates whether there is a synergistic effect of combining the VMMC demand creation tool with ST distribution on VMMC uptake. HIV self-testing is supported by the UNITAID/PSI STAR (Self-Testing Africa) Initiative.

**2. TRIAL OVERVIEW****2.1. PRINCIPAL RESEARCH OBJECTIVE**

The aim of this trial is to assess the effectiveness of two new community-based demand creation models (a demand creation tool and HIVST, respectively), in motivating men to take up VMMC.

**2.2. TRIAL DESIGN**

The study is a four-arm parallel-arm cluster-randomized trial of two interventions to promote VMMC – a community-based demand creation model and HIV self-test distribution. This design allows for estimation of a synergistic (greater than multiplicative) effect of combined behaviour change communication and self-testing on VMMC uptake.

However, we will additionally analyse this trial as a factorial trial, estimating the independent impact of ST intervention and the demand creation intervention on the primary and secondary outcomes. More detail on this is in **section 2.3** (trial arms, randomization, and blinding) and **section 4.3** (data analysis). (Please also see **appendix A**, which summarizes the post-hoc power calculation conducted in September 2018, and recommends a factorial analysis be conducted on these data due to power concerns.)

**2.3. TRIAL ARMS, RANDOMIZATION, AND BLINDING**

**Trial arms.** Interpersonal communication agents (IPCs) were randomized using restricted randomization to four arms at a ratio of 1:1:1:1. The four arms include:

- **Arm 1:** To undertake standard community based demand creation for VMMC.
- **Arm 2:** To undertake standard community based demand creation for VMMC with the ability to offer HIV self-test kits to potential VMMC clients.



- **Arm 3:** To undertake community based demand creation using the new IPC demand creation approach (informed by human-centred design (HCD) and the market research)
- **Arm 4:** To undertake community-based demand creation using the new IPC demand creation approach with the ability to provide HIV self-test kits to potential VMMC clients.

Analyses will be completed using programme or survey data. Analyses will use principles for analysis of clustered RCTs with a large number of clusters (>20) per arm (1).

For the analysis as parallel arm trial, the following comparisons will be undertaken for the primary outcome and 3 secondary outcomes on VMMC uptake (Specific outcomes are listed in **section 3**):

- Effect of ST kits v. SOC (Arm 2/Arm 1)
- Effect of new IPC demand creation approach v. SOC (Arm 3/Arm 1)
- Effect of new IPC demand creation plus ST v. SOC (Arm 4/Arm1)
- Effect of new IPC demand creation plus ST v. ST kits only (Arm 4/Arm 2)

For the analysis as factorial trial, the following comparisons will be undertaken:

- Effect of ST kits (Arm 2 and arm 4 v. arm 1 and arm 3);
- Effect of IPC demand creation approach (Arm 3 and arm 4 v. arm 1 and arm 2).

Three outcomes related to the uptake of HIVST will be evaluated by comparing arms 4 and 2 only.

**Randomization.** 143 IPCs were in the original sample, with 3 removed at random to allow for equal numbers of IPCs per arm. There were 140 IPCs assigned 1:1:1:1 to four arms of 35 IPCs each. Randomization was restricted by age and sex of IPC agent, and mobilization experience.

- **Age.** The mean age in the sample was 35.27 years (SD: 11.37). We restricted such that the mean age in each arm is within +/- 5 years of the sample mean (i.e. between 30.27 and 40.27 years).
- **Gender.** There are 80 male IPCs (56%) in the sample. We restricted such that the proportion of male IPCs per arm is within +/- 15 percentage points of the total, so arms will have between 40.9-70.9% male IPCs.
- **Experience level.** 28.7% of IPCs had at least 12 months of experience. We restricted such that the proportion with ≥12months experience is between 18.7-38.7% in each arm.

The randomization was completed on 25 January 2018 by MN.

**Blinding.** Due to the nature of the intervention, neither the IPCs nor the clients can be blinded to allocation. The statistician conducting the primary analysis (GM) will be blinded to allocation. Analyses of uptake of VMMC (primary outcome and secondary outcomes 2-5) will be completed first and using a dataset that does not include any self-testing data. A second dataset blinded to IPC demand creation tool allocation but including all self-testing arms will be prepared for analysis of the self-testing outcomes.

## 2.4. DURATION OF INTERVENTIONS

Both interventions will be implemented for 6 months. The initial timeline for the trial included a trial data collection from 20 February – 31 August 2018, with data collected on uptake of circumcision until 30 September 2018. After review of early process evaluation data which indicated that it was taking longer than expected for IPCs to become comfortable with the new IPC demand creation tool, the study team and TAG decided to add a run-in period from 20 February-30 April 2018, and shift the trial start date to 1 May 2018 and end date to 31 October 2018, with data collected on uptake of circumcision until 30 November 2018.

## 2.5. STUDY POPULATION AND INFORMED CONSENT

This trial was designed as a pragmatic trial of the effectiveness of two VMMC mobilization tools under usual programme conditions in the field. For this reason, there were no age restrictions for clients in this study beyond those usually used in programmatic conditions. However, both the demand creation tool and the HIV self-test are likely to appeal to older adolescents and adults. The demand creation tool was designed for use with men ages 15 years and older, and HIV self-testing distribution is limited to men ages 16 years and older. For this reason, we will conduct the factorial and parallel arm analyses on the population 15 years and older for the primary analysis of VMMC outcomes (primary and secondary outcomes 1-5), and 16 years and older for ST outcomes (secondary outcomes 6-8).

Because the interventions are being evaluated under field conditions and in a routine programmatic context, and because the interventions pose minimal risk to IPC agents or clients, written informed consent has not been obtained from men contacted by IPC agents.

Ethical approval for the study has been obtained from the London School of Hygiene and Tropical Medicine (ID: 14460, approved on 14 February 2018); the Liverpool School of Tropical Medicine (ID: 17-067, approved on 15 December 2017); and the Medical Research Council of Zimbabwe (ID 2231, approved on 29 November 2017). The trial is registered with the Pan-African Clinical Trials Registry as PACTR201804003064160.

## 3. PRIMARY OUTCOME AND SAMPLE SIZE CALCULATION

The primary outcome is the number of men circumcised per IPC-month of follow-up. Analysis will be by intention-to-treat (ITT) and per-protocol. There was substantial attrition among IPCs, including between randomization and initial training, the “as-treated” analysis will

In the ITT analysis, IPCs randomized to each arm assumed to contribute 6 full months of follow-up to the analysis. An “as-treated”-analysis of VMMC outcomes will also be conducted – this will account for the actual number of months of follow-up time contributed by IPCs. For the as-treated analysis, an IPC will be assumed to be active in a given calendar month if s/he has recorded reaching at least one client during that calendar month.

The study sample size was calculated to detect differences across arms in the primary outcome. To account for multiple comparisons across arms, the sample size was calculated to  $\alpha=0.05/4$  (2)

This study requires 35 IPCs per arm, 140 IPCs across 4 arms to have 80% power to detect a 30% proportionate difference in VMMC uptake between any two arms even if variability between IPCs is high ( $k=0.3$ ). It would also provide 90% power to detect a proportionate

30% difference in VMMC uptake between arms if variability between IPCs is less ( $k=0.25$ ) and over 90% power to detect a 40% proportionate difference between arms if variability between IPC agents is higher ( $k=0.3$ ).

### Sample size and potential power of the trial

1-type I	power	z_a	z_b		rate_0	%	rate_1	# of	cluster	person	k	# clusters
						increase		months	size	months		per arm
0.9875	0.8	2.497705	0.841621	11.1511	12	30%	15.6	6	1	6	0.25	25.79
0.9875	0.8	2.497705	0.841621	11.1511	12	40%	16.8	6	1	6	0.25	16.22
0.9875	0.8	2.497705	0.841621	11.1511	12	50%	18	6	1	6	0.25	11.61
0.9875	0.8	2.497705	0.841621	11.1511	12	30%	15.6	6	1	6	0.3	34.95
0.9875	0.8	2.497705	0.841621	11.1511	12	40%	16.8	6	1	6	0.3	21.89
0.9875	0.8	2.497705	0.841621	11.1511	12	50%	18	6	1	6	0.3	15.60
0.9875	0.9	2.497705	1.281552	14.28278	12	30%	15.6	6	1	6	0.25	32.75
0.9875	0.9	2.497705	1.281552	14.28278	12	40%	16.8	6	1	6	0.25	20.49
0.9875	0.9	2.497705	1.281552	14.28278	12	50%	18	6	1	6	0.25	14.59
0.9875	0.9	2.497705	1.281552	14.28278	12	30%	15.6	6	1	6	0.3	44.49
0.9875	0.9	2.497705	1.281552	14.28278	12	40%	16.8	6	1	6	0.3	27.76
0.9875	0.9	2.497705	1.281552	14.28278	12	50%	18	6	1	6	0.3	19.69

1-type 1 = 1 - (0.05/4) to account for multiple comparisons												
Power = 0.8 or 0.9 (varied as requested by PSI/Gates in an earlier round)												
Rate 0 = average of output per IPC agent per month in SOC (see data from PSI sheet)												
% increases as requested by PSI												
# months - 6 month trial												
cluster size = 1 because rate is per IPC time, and there is 1 IPC/cluster												
k = 0.25 or 0.3 (varied as requested by PSI/Gates in an earlier round)												

### 3.1. SECONDARY OUTCOMES

- **Secondary outcome 1.** The mean conversion proportion by trial arm (conversion proportion defined as number of men who are circumcised divided by the number of men reached by IPC agent per month).
- **Secondary outcome 2.** The number of men spoken to by IPC agents (not included in final analysis plan because data were not collected.)
- **Secondary outcome 3.** The number of men reached per IPC-month. A potential VMMC client is considered "reached" once they have been enrolled and have completed an individual-level demand creation session with an IPC agent.
- **Secondary outcome 4.** The number of men booked for VMMC per IPC-month.
- **Secondary outcome 5.** The number of men who present for VMMC per IPC-month.
- **Secondary outcome 6.** Proportion of men offered HIV self-test kits who accepted the test. (Self-testing arms only [arm 4/arm 2]).
- **Secondary outcome 7.** Proportion of men who obtain HIV self-test kits and go on to self-test. (Self-testing arms only [arm 4/arm 2]).
- **Secondary outcome 8.** Proportion of men with a reactive HIV self-test result who link to post-test services (Self-testing arms only [arm 4/arm 2]).

### 4. OUTCOME EVALUATION AND DATA DESCRIPTION

The primary outcome and secondary outcomes 1-5 will be measured using programme data collected by PSI Zimbabwe. Data on the number of men reached and followed up by IPCs will be collected using electronic data capture and uploaded to the DHIS2 server.

Each IPC agent will conduct community mobilization and collect client data using an allocated tablet. Client data collected will include (at most) the information below depending on the arm:

1. Personal details that will include
  - a. Name, surname, date of birth
  - b. Other demographic characteristics such as level of education, marital status, employment status and religion
2. Contact numbers
3. Geographical location; Urban, Rural or Peri Urban
4. State whether group or one-on-one session
5. Record whether client opted to take a self-test kit or not. **(Note: Those men who are given self-test kits should be asked to bring the used self-test kit when they take up services at VMMC centres)**
6. Reasons for refusing to take self-test kit
  - a. Tested recently/already tested (ask where, what type of test)
  - b. Not interested
  - c. Scared of known risk behaviour
  - d. Prefer testing at health centre or VMMC site
  - e. Other specify
7. Client segment/Colour code of the client
8. Agreed date for circumcision
9. Client referral card number/Unique identifier number
10. Date for follow up visit
11. Client follow-up details where applicable (number of times contacted after reach)
  - a. 1<sup>st</sup> follow up visit
  - b. 2<sup>nd</sup> follow up visit
  - c. 3<sup>rd</sup> follow up visit
12. Date of circumcision

District Field Officers (DFO) and District Field Assistants (DFA) will supervise the IPC agents during implementation and will be responsible for checking consistency and completeness of data collected and ensure that it is uploaded to the DHIS2 server. The DFO will accompany the IPC agent in the field once a month to evaluate the IPC agent's effectiveness based on session adequacy of content, articulation of key VMMC benefits, ability to address questions with regards to VMMC, facilitation skills, use of segmentation tool, pain-o-meter and key messages, HIVST offer (for relevant arms) and ability to identify the barriers to MC from the client and to subsequently address them.

Secondary outcomes 6-8 will be measured using a follow-up survey administered by CeSHHAR researchers to clients reached by PSI 4 weeks after the clients were reached. The follow-up survey will be administered by telephone.

Data captured in the survey data include:

- Prior HIV testing
- Whether IPC offered ST kit and whether kit was used
- Confirmatory testing and treatment uptake for respondents with reactive HIVST
- VMMC uptake

## STATISTICAL METHODS



All analyses will use methods appropriate for CRTs randomized at the community level with a large number of clusters (1). Reporting will conform to the 2010 Consort statement as applicable to cluster randomized trials (3).

#### 4.1 RECRUITMENT AND REPRESENTATIVENESS OF SAMPLE

The trial flow chart will follow principles of CONSORT guidelines for CRTs, and will show the process of recruitment of clients (**figure 1**).

#### 4.2 COMPARABILITY OF ARMS

We will first summarize client data by arm and IPC to detect imbalances by the following characteristics.

- Client age in years and in 5-year age bands
- Client in or out of school
- Client past HIV testing history for self-testing arms only using survey data

The study team will identify substantial differences between arms in terms of the above factors. This assessment will not be completed using statistical tests, and p-values will not be shown, as any difference will be due to chance if the randomisation was correctly performed. **Table 1** presents a sample analysis of comparability across arms.

#### 4.3 ANALYSIS

Sample analysis tables are presented in **table 2a** (VMMC outcomes - parallel arm), **table 2b** (VMMC outcomes - factorial), and **table 3** (self-testing outcomes).

**Primary outcome – parallel arm analysis.** The primary outcome is comparison of the number of men circumcised per IPC-month of follow-up by trial arm. The numerator is the number of clients circumcised per IPC-month.

Using programme data, the variables *eventdate* and *agent\_code* will be used to identify the months each IPC agent was active for the as-treated analysis. *Client\_circum* will be used to count the number of circumcisions, and *service\_date* used to measure the date of circumcision. *Study\_arm* will be used to allocate IPCs by study arm. Note that, for the last month of the trial, outcome measures will continue to be collected, and these outcomes will be included in the analysis as part of the last month of implementation.

The primary outcome will be modelled as a circumcision rate per IPC month using negative binomial regression, and will use a random effect of IPC to account for clustering of outcomes by IPC.

**Unadjusted:**  $\log(Circ_{it}) = \beta_0 + \beta_1 arm2_i + \beta_2 arm3_i + \beta_3 arm4_i + \log(person\ time_{it}) + u_i$

**Age-adjusted:**  $\log(Circ_{it}) = \beta_0 + \beta_1 arm2_i + \beta_2 arm3_i + \beta_3 arm4_i + \Sigma B\ ageband_i + \log(person\ time_{it}) + u_i$

In the above equation, *circ<sub>it</sub>* represents a circumcision associated with IPC agent *i* during month *t*. This equation calculates estimates of effect comparing arms 2, 3, and 4 to arm 1. To calculate the estimate of effect of arm 4 compared with arm 2, we will rerun the same equation using arm 2 as the reference category.

As a sensitivity analysis, we will also calculate p-values for the primary outcome comparisons using a permutation test accounting for the restrictions used in randomization (1). We will adjust p-values for multiple comparisons in the main (non-exploratory) analysis using this Benjamini-Hochberg procedure for controlling the false discovery rate (4).

**Primary outcome – factorial analysis.** The definition of the primary outcome is the same in the factorial analysis.

The primary outcome will be modelled as a circumcision rate per IPC month using negative binomial regression, and will use a random effect of IPC to account for clustering of outcomes by IPC:

Comparison of self-testing arms (arms 2/4 v. arms 1/3)

**Unadjusted:**  $\log(Circ_{it}) = \beta_0 + \beta_1 STarm_i + \log(person\ time_{it}) + u_i$

**Age-adjusted:**  $\log(Circ_{it}) = \beta_0 + \beta_1 STarm_i + \Sigma B\ ageband_i + \log(person\ time_{it}) + u_i$

Comparison of IPC demand creation arms (arms 3/4 v. arms 1/2)

**Unadjusted:**  $\log(Circ_{it}) = \beta_0 + \beta_1 DCarm_i + \log(person\ time_{it}) + u_i$

**Age-adjusted:**  $\log(Circ_{it}) = \beta_0 + \beta_1 DCarm_i + \Sigma B\ ageband_i + \log(person\ time_{it}) + u_i$

**Secondary outcome 1 – parallel arms analysis.** The mean conversion proportion by trial arm (conversion proportion defined as number of men who are circumcised divided by the number of men reached by IPC agent per month). Men are reached if they have completed the IPC session.

The numerator is the total number of circumcisions associated with an IPC over the total follow-up period.

The denominator is the total number of clients reached by an IPC over the total follow-up period.

*Cilent\_circum* will be used to measure the numerator for this outcome, and the count of client records entered for each IPC will be used to generate the number of clients reached by each IPC.

This will be analysed at the IPC level using logistic regression analysis:

The parallel arm analysis will be completed as follows:

**Unadjusted:**  $\log odds\left(\frac{Circ_i}{Reached_i}\right) = \beta_0 + \beta_1 arm2_i + \beta_2 arm3_i + \beta_3 arm4_i$

**Age-adjusted:**  $\log odds\left(\frac{Circ_i}{Reached_i}\right) = \beta_0 + \beta_1 arm2_i + \beta_2 arm3_i + \beta_3 arm4_i + \Sigma B\ ageband_i$

This equation calculates estimates of effect comparing arms 2, 3, and 4 to arm 1. To calculate the estimate of effect of arm 4 compared with arm 2, we will rerun the same equation using arm 2 as the reference category. Odds ratios will be converted to risk (proportion) ratios and 95% confidence intervals using the *margins* post-estimation command in Stata 15.1.

**Secondary outcome 1 – factorial analysis.** The definition of secondary outcomes will be the same in the factorial analysis. This outcome will be analysed at the IPC level using logistic regression analysis.

Comparison of self-testing arms (arms 2/4 v. arms 1/3)

**Unadjusted:**  $\log \text{odds} \left( \frac{\text{Circ}_i}{\text{Reached}_i} \right) = \beta_0 + \beta_1 \text{STarm}_i$

**Age-adjusted:**  $\log \text{odds} \left( \frac{\text{Circ}_i}{\text{Reached}_i} \right) = \beta_0 + \beta_1 \text{STarm}_i + \Sigma B \text{ageband}_i$

Comparison of IPC demand creation arms (arms 3/4 v. arms 1/2)

**Unadjusted:**  $\log \text{odds} \left( \frac{\text{Circ}_i}{\text{Reached}_i} \right) = \beta_0 + \beta_1 \text{DCarm}_i$

**Unadjusted:**  $\log \text{odds} \left( \frac{\text{Circ}_i}{\text{Reached}_i} \right) = \beta_0 + \beta_1 \text{DCarm}_i + \Sigma B \text{ageband}_i$

**Secondary outcome 2** will not be analysed as these data have not been collected. (See **section 4** for details).

**Secondary outcome 3 – parallel arm and factorial analysis.** The number of men reached per IPC-month. The count of client records entered for each IPC will be used to generate the number of clients reached by each IPC, and the *event\_date* (or earliest *event\_date* for each client if more than one event associated with this client) will be used to determine the date of the event.

The method of analysis will be similar to the primary outcome.

**Secondary outcome 4 – parallel arm and factorial analysis.** The number of men booked for VMMC per IPC-month. The variable *client\_booked* will be used to indicate whether or not a client was booked for VMMC. Clients are considered booked if they have agreed to VMMC and set an appointment for the procedure.

The method of analysis will be similar to the primary outcome.

**Secondary outcome 5 – parallel arm and factorial analysis.** The number of men who present for VMMC per IPC-month. The variable *has\_client\_turned\_up* will be used to indicate whether or not a client was present for VMMC.

The method of analysis will be similar to the primary outcome.

#### **Additional outcomes for self-testing arm comparisons only (arm 4/arm 2)**

These analyses use responses from the HIVST follow-up questionnaire administered by CeSHHAR.

**Secondary outcome 6.** Proportion of men offered HIV self-test kits who accepted the test.

- Numerator: ST taken (2a = yes)
- Denominator: ST offered (2 = yes)

This will be analysed using logistic regression of data at the client level. A random effect of IPC will be used to adjust for study design. Clients will be identified using PSI data, and the IPC and arm associated with each client will be allocated based on PSI data.

**Secondary outcome 7.** Proportion of men who obtain HIV self-test kits and go on to self-test.

- Numerator: (2b = yes)
- Denominator: ST taken (2a = yes), among respondents offered a test.

**Secondary outcome 8.** Proportion of men with a reactive HIV self-test result who link to post-test services

- Numerator: Respondents confirming reactive result (4 = yes)
- Denominator: Respondents with reactive result on HIVST (3 = positive/reactive, among respondents testing with ST [2b = yes]. Exclude respondents who had a previous HIV diagnosis [4d = no].)

#### 4.4 ADJUSTED ANALYSES

Both unadjusted and age-adjusted analyses will be conducted for all outcomes. Age-adjusted analyses will include parameters for age, grouped into 5 levels: under 15 years, 15-17 years, 18-19 years, 20-29 years, and 30 years and older. Before conducting the final analyses, the statistician will confirm that there are sufficient numbers in the each age band to complete the analysis, and will adjust the number of age bands if needed.

The primary analysis for presentation will be the age-adjusted as-treated analysis using the factorial design.

#### 4.5 PRESPECIFIED SUBGROUP ANALYSES

**Subgroup analysis by age:** In addition to the analyses described above, we will also conduct subgroup analyses estimating the impact of the ST distribution and the impact of the demand creation interventions on the primary outcome (VMMC conversions/IPC-month), secondary outcome 1 (conversion proportion), and secondary outcome 3 (number of men reached/IPC-month) among men 15-19 years, 20-29 years and 30 years and older. These will be conducted using the factorial analysis only, and will include both ITT and as-treated analyses. We will test for effect modification between age and each of the two interventions by fitting a model including parameters estimating the interaction effect of age and each intervention and testing the significance of these using likelihood ratio tests. **Table 4** presents subgroup analyses by age.

#### 4.6 EXPLORATORY ANALYSIS

In addition to the main analysis conducted on the population 15 years and older, we will conduct exploratory analyses of VMMC outcomes (primary and secondary outcomes 1-5; see section 3.1) for all clients (regardless of age) entered into the VMMC client database will be compared by arm. This analysis will estimate the effectiveness of the two VMMC mobilization tools in increasing VMMC uptake among all men

#### 4.7 METHODS FOR ADDRESSING MISSING DATA

Missing data will be examined for each variable and for each individual participant. A systematic assessment of missingness will be conducted to ascertain the reason and possible mechanism for missing data by identifying the quantity of missing data and patterns

within the data. Missingness will be particularly examined by IPC and between randomised arms to assess for systematic biases.

In cases where a client's circumcision date is missing, we will conduct a sensitivity analysis substituting the most recent event date for the client in the dataset for the date of circumcision.

#### **4.8 PROCESS EVALUATION**

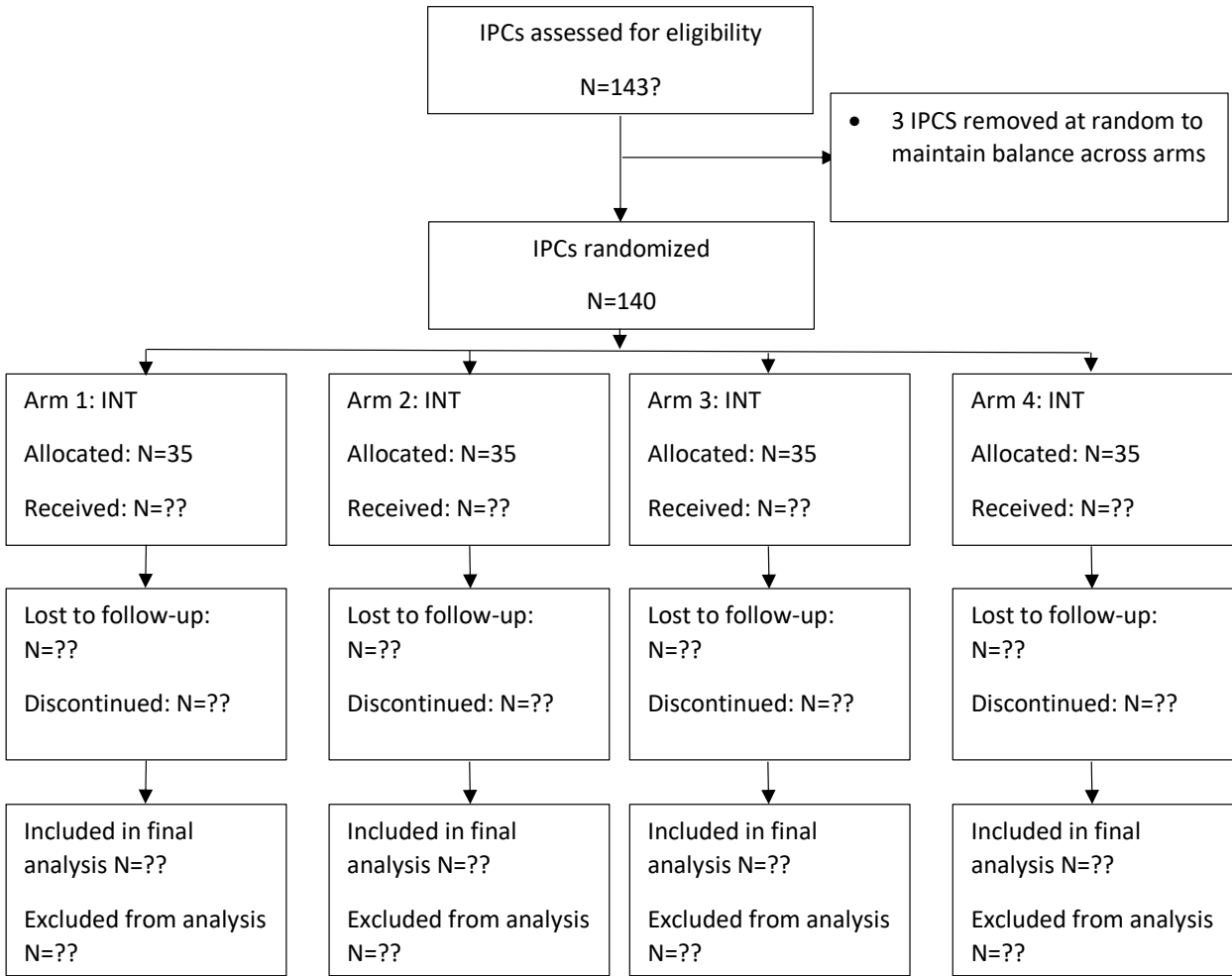
A mixed methods process evaluation was conducted within the trial to provide an understanding of if, why and how the interventions were impacting VMMC uptake. We analysed programme data and conducted two rounds of monitoring visits at different time points, during which we observed 100 IPC agents (n=25 per arm) conducting VMMC mobilisation sessions. We held 24 in-depth interviews (IDIs) and four focus group discussions (FGDs) with purposively selected IPC agents (n=36) and IDIs with PSI's District Field Officers (n=5; 1 from each trial district). We conducted eight FGDs with men mobilised for VMMC (n= 40 who took up VMMC; n=40 who did not). Iterative qualitative data collection and analysis informed a grounded thematic analytical approach.



**WORKS CITED**

1. Hayes R, Moulton L. Cluster randomised trials. 2009.
2. Bland JM, Altman DG. Multiple significance tests: the Bonferroni method. *Bmj*. 1995;310(6973):170.
3. Campbell MK, Piaggio G, Elbourne DR, Altman DG. Consort 2010 statement: extension to cluster randomised trials. 2012.
4. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *Journal of the royal statistical society Series B (Methodological)*. 1995:289-300.
5. Hayes R, Moulton L. Cluster Randomised Trials. Boca Raton: CRC Press; 2009.

**Figure 1. CONSORT flow diagram for full population analysis.**  
(Additional row added to bottom of diagram will present numbers included in 15 years and older analysis by arm and numbers excluded).



**Table 1. Characteristics of clients by arm – parallel arm and factorial analysis**

(Note: complete for both full population and 15 years and older analyses separately)

	Standard of care		Demand creation only		Self-test only		Demand creation and self-test		Total	
	Freq.	Pct.	Freq.	Pct.	Freq.	Pct.	Freq.	Pct.	Freq.	Pct.
IPCs (no.)	#		#		#		#		#	
Total IPC-months	#		#		#		#		#	
Male IPCs (% IPCs)	#	%	#	%	#	%	#	%	#	%
<b>Reached client characteristics</b>										
Total	#	100	#	100	#	100	#	100	#	100
Age in years (% total)										
<15	#	%	#	%	#	%	#	%	#	%
15-19	#	%	#	%	#	%	#	%	#	%
20-24	#	%	#	%	#	%	#	%	#	%
25-29	#	%	#	%	#	%	#	%	#	%
30-34	#	%	#	%	#	%	#	%	#	%
35-39	#	%	#	%	#	%	#	%	#	%
40-44	#	%	#	%	#	%	#	%	#	%
45-49	#	%	#	%	#	%	#	%	#	%
50+	#	%	#	%	#	%	#	%	#	%
Education completed?										
School-going	#	%	#	%	#	%	#	%	#	%
Out of school	#	%	#	%	#	%	#	%	#	%
Type of location of recruitment	#	%	#	%	#	%	#	%	#	%
Rural	#	%	#	%	#	%	#	%	#	%
Peri-urban	#	%	#	%	#	%	#	%	#	%
Urban	#	%	#	%	#	%	#	%	#	%

**Table 2a. Effect of demand creation and HIV self-testing interventions on primary and secondary outcomes – parallel arm analysis**

(Note: complete for both full population and 15 years and older analyses separately)

	SOC		Demand creation only		ST only		Demand creation and ST		Effect of demand creation (v. SOC)		Effect of ST (v. SOC)		Effect of demand creation + ST v. SOC		Effect of demand creation + ST v. ST only	
	n/N	Rate or %	n/N	Rate or %	n/N	Rate or %	n/N	Rate or %	Rate/risk ratio (95% CI)	p-value	Rate/risk ratio (95% CI)	p-value	Rate/risk ratio (95% CI)	p-value	Rate/risk ratio (95% CI)	p-value
<b>Primary outcome</b> : VMMC uptake per IPC-month	###/##	###	###/##	###	###/##	###	###/##	###	###	###	###	###	###	###	###	###
	#		#		#		#		(###,###)		(###,###)		(###,###)		(###,###)	
<b>Primary outcome as-treated:</b> VMMC uptake per active IPC-month	###/##	###	###/##	###	###/##	###	###/##	###	###	###	###	###	###	###	###	###
	#		#		#		#		(###,###)		(###,###)		(###,###)		(###,###)	
<b>Secondary outcomes</b> Conversion	###/##	###%	###/##	###%	###/##	###%	###/##	###%	###	###	###	###	###	###	###	###
	#		#		#		#		#	#	#	#	#	#	#	#

proportion								(#.##,## #)	(#.##,## #)	(#.##,## #)	(#.##,## #)
Men reached per IPC-month	##/## #	#.##	##/## #	#.##	##/## #	#.##	##/## #	#.## (#.##,## #)	#.## (#.##,## #)	#.## (#.##,## #)	#.## (#.##,## #)
Men booked per IPC-month	##/## #	#.##	##/## #	#.##	##/## #	#.##	##/## #	#.## (#.##,## #)	#.## (#.##,## #)	#.## (#.##,## #)	#.## (#.##,## #)
Men presenting for VMMC per IPC-month	##/## #	#.##	##/## #	#.##	##/## #	#.##	##/## #	#.## (#.##,## #)	#.## (#.##,## #)	#.## (#.##,## #)	#.## (#.##,## #)



**Table 2b. Effect of demand creation and HIV self-testing interventions on primary and secondary outcomes – factorial analysis**

(Note: complete for both full population and 15 years and older analyses separately)

	ST - yes		ST - no		Effect of ST		Demand creation – yes		Demand creation – no		Effect of demand creation	
	n/N	Rate or %	n/N	Rate or %	Rate/risk ratio (95% CI)	p-value	n/N	Rate or %	n/N	Rate or %	Rate/risk ratio (95% CI)	p-value
<b>Primary outcome:</b> VMMC uptake per IPC-month	##/##	#.##	##/##	#.##	#.## (#.##,#.##)	#.###	##/##	#.##	##/##	#.##	#.## (#.##,#.##)	#.###
<b>Primary outcome as-treated:</b> VMMC uptake per active IPC-month	##/##	#.##	##/##	#.##	#.## (#.##,#.##)	#.###	##/##	#.##	##/##	#.##	#.## (#.##,#.##)	#.###
<b>Secondary outcomes</b>												
Conversion proportion	##/##	##.##%	##/##	##.##%	#.## (#.##,#.##)	#.###	##/##	##.##%	##/##	##.##%	#.## (#.##,#.##)	#.###
Men reached per IPC-month	##/##	#.## #.##	##/##	#.## #.##	#.## (#.##,#.##)	#.###	##/##	#.## #.##	##/##	#.## #.##	#.## (#.##,#.##)	#.###
Men booked per IPC-month	##/##	#.## #.##	##/##	#.## #.##	#.## (#.##,#.##)	#.###	##/##	#.## #.##	##/##	#.## #.##	#.## (#.##,#.##)	#.###
Men presenting for VMMC per IPC-month	##/##	#.## #.##	##/##	#.## #.##	#.## (#.##,#.##)	#.###	##/##	#.## #.##	##/##	#.## #.##	#.## (#.##,#.##)	#.###

Table 3. HIVST secondary outcomes among clients ages 16 years and older

	ST only		Demand creation and ST		Effect of demand creation + ST v. ST only	
	n/N	%	n/N	%	Risk ratio (95% CI)	p-value
Men accepting HIVST	###/###	##.##%	###/###	##.##%	### (###, ###)	####
Men using HIVST	###/###	##.##%	###/###	##.##%	### (###, ###)	####
Men with reactive tests linked to HIV care	###/###	##.##%	###/###	##.##%	### (###, ###)	####

**Table 4. Planned subgroup analyses by age**

(Note: include all age [including men under 15 years])

	ST - yes		ST - no		Effect of ST		Demand creation – yes		Demand creation – no		Effect of demand creation	
	n/N	Rate or %	n/N	Rate or %	Rate/risk ratio (95% CI)	p-value	n/N	Rate or %	n/N	Rate or %	Rate/risk ratio (95% CI)	p-value
<b>Primary outcome: VMMC uptake per IPC-month</b>												
<b>Under 15 years</b>	###/##	#.##	###/##	#.##	#.##	#.###	###/##	#.##	###/##	#.##	#.##	#.###
<b>15-17 years</b>	###/##	#.##	###/##	#.##	(#.##,#.##) #.##	#.###	###/##	#.##	###/##	#.##	(#.##,#.##) #.##	#.###
<b>18-19 years</b>	###/##	#.##	###/##	#.##	(#.##,#.##) #.##	#.###	###/##	#.##	###/##	#.##	(#.##,#.##) #.##	#.###
<b>20-29 years</b>	###/##	#.##	###/##	#.##	(#.##,#.##) #.##	#.###	###/##	#.##	###/##	#.##	(#.##,#.##) #.##	#.###
<b>30+ years</b>	###/##	#.##	###/##	#.##	(#.##,#.##) #.##	#.###	###/##	#.##	###/##	#.##	(#.##,#.##) #.##	#.###
					(#.##,#.##)						(#.##,#.##)	
<b>Primary outcome as-treated: VMMC uptake per IPC-month</b>												
<b>Under 15 years</b>	###/##	#.##	###/##	#.##	#.##	#.###	###/##	#.##	###/##	#.##	#.##	#.###
<b>15-17 years</b>	###/##	#.##	###/##	#.##	(#.##,#.##) #.##	#.###	###/##	#.##	###/##	#.##	(#.##,#.##) #.##	#.###
					(#.##,#.##)						(#.##,#.##)	

	ST - yes		ST - no		Effect of ST		Demand creation – yes		Demand creation – no		Effect of demand creation	
	n/N	Rate or %	n/N	Rate or %	Rate/risk ratio (95% CI)	p-value	n/N	Rate or %	n/N	Rate or %	Rate/risk ratio (95% CI)	p-value
<b>18-19 years</b>	###/##	#.##	###/##	#.##	#.##	#.###	###/##	#.##	###/##	#.##	#.##	#.###
					(#.##,#.##)						(#.##,#.##)	
<b>20-29 years</b>	###/##	#.##	###/##	#.##	#.##	#.###	###/##	#.##	###/##	#.##	#.##	#.###
					(#.##,#.##)						(#.##,#.##)	
<b>30+ years</b>	###/##	#.##	###/##	#.##	#.##	#.###	###/##	#.##	###/##	#.##	#.##	#.###
					(#.##,#.##)						(#.##,#.##)	
<b>Secondary outcome: Conversion proportion</b>												
<b>Under 15 years</b>	###/##	#.##	###/##	#.##	#.##	#.###	###/##	#.##	###/##	#.##	#.##	#.###
					(#.##,#.##)						(#.##,#.##)	
<b>15-17 years</b>	###/##	#.##	###/##	#.##	#.##	#.###	###/##	#.##	###/##	#.##	#.##	#.###
					(#.##,#.##)						(#.##,#.##)	
<b>18-19 years</b>	###/##	#.##	###/##	#.##	#.##	#.###	###/##	#.##	###/##	#.##	#.##	#.###
					(#.##,#.##)							
<b>20-29 years</b>	###/##	##.##%	###/##	##.##%	#.##	#.###	###/##	##.##%	###/##	##.##%	#.##	#.###
					(#.##,#.##)						(#.##,#.##)	
<b>30+ years</b>	###/##	##.##%	###/##	##.##%	#.##	#.###	###/##	##.##%	###/##	##.##%	#.##	#.###
					(#.##,#.##)						(#.##,#.##)	

	ST - yes		ST - no		Effect of ST		Demand creation – yes		Demand creation – no		Effect of demand creation	
	n/N	Rate or %	n/N	Rate or %	Rate/risk ratio (95% CI)	p-value	n/N	Rate or %	n/N	Rate or %	Rate/risk ratio (95% CI)	p-value
Secondary outcome: Men reached per IPC-month												
Under 15 years	###/###	#.##	###/###	#.##	#.##	#.###	###/###	#.##	###/###	#.##	#.##	#.###
15-17 years	###/###	#.##	###/###	#.##	(#.##,#.##) #.##	#.###	###/###	#.##	###/###	#.##	(#.##,#.##) #.##	#.###
18-19 years	###/###	#.##	###/###	#.##	(#.##,#.##) #.##	#.###	###/###	#.##	###/###	#.##	(#.##,#.##) #.##	#.###
20-29 years	###/###	#.##	###/###	#.##	(#.##,#.##) #.##	#.###	###/###	#.##	###/###	#.##	#.##	#.###
30+ years	###/###	#.##	###/###	#.##	(#.##,#.##) #.##	#.###	###/###	#.##	###/###	#.##	(#.##,#.##) #.##	#.###



## Appendix A: Summary of sub analysis for VMMC trial, 1 October 2018

(Prepared by HW and MN)

### Design:

4 armed trial comparing SoC, SoC plus HIVST, SoC plus HCD, SoC plus HCD and HIVST

Original sample size calculations assumed SoC arm would circumcise **12 men/month/IPC agent with 6 month follow up**

80% power to observe an increase of 30% per arm with 35 IPCs per arm with  $k=0.3$

**Number of IPC agents randomized 140.** Number of IPC agents active 121

**Rationale:** Process evaluation suggested variability between how quickly IPC agents in different arms became proficient in delivering intervention assigned to that arm. SoC arm were proficient straight away but other arms appeared to take 2-3 months to become proficient. Suggestion was to increase run in (training) period, but to maintain 6 month follow up period so that IPC agents in all arms were assessed at similar levels of proficiency.

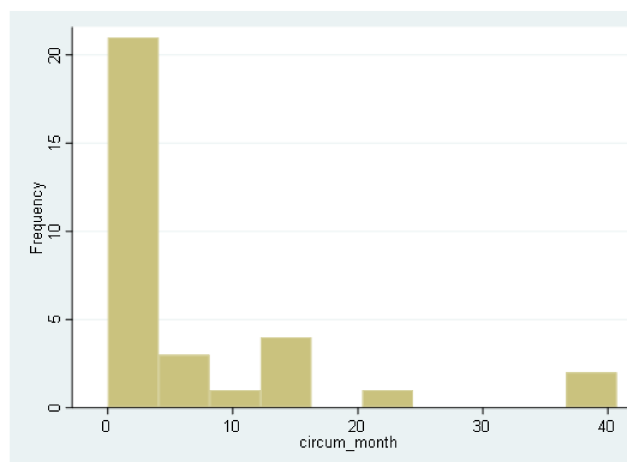
Sub-analysis conducted to explore power of trial if we shifted follow up from Feb to Sep to May to Dec.

**Results:** Examining data in SoC arm reveals a highly skewed distribution and hence a large degree of variability between IPC agents – overall monthly circumcision rate is 10.5 but varies between 0-239 (Figure) – such that  $k=1.2$  (instead of 0.3)

This maybe in part be explained because VMMC are being attributed to IPC agents in some settings differently than others – e.g. attribution during campaigns may be done differently or IPC agents in some settings operate very different. So we need to examine the reason for the variability.

If we take out extreme outliers,  $k$  falls to 0.88. (and the average rate falls to 5.4 VMMC/month/IPC agent)

Importantly there is no indication that  $k$  in the SoC arm is greater during the run-in period (Feb to May). While this may not be case for the other arms, the  $k$  included in analysis will be an average of  $k$  from SoC and other arms and so any reduction in  $k$  in the intervention arms will be influenced by the large  $k$  in SoC.



With this unanticipated variability in  $k$ , the power of the trial is diminished (and this cannot be overcome by extending length of trial – size of  $k$  swamps any benefit from increasing duration).

With 10.5 VMMC/month/IPC agent we have 80% power to detect a 160% increase (i.e. to 27.3 VMMC/month/IPC agent) by arm at 6 months (assuming  $k=1$  i.e. slightly smaller than in the SoC due to smaller  $k$  in the intervention arms) – can show interactively in the spreadsheet at the meeting.

In practice we can legitimately analyse as a factorial design by combining intervention arms (will not have power to detect interaction between arm) giving us 65 IPC agents per arm.

**Summary: With 65 IPC agents per arm we have 80% power to detect between 90% increase in VMMC per intervention (e.g. 10.5 to 20).** (See table 5).

Table 5. Revised power calculations, 1 October 2018.

1- type l	pow er	z_a	z_b		rate _0	% incre ase	rate _1	# of mon ths	clus ter size	pers on mon ths	k	# cluste rs per arm
<b>0.98 75</b>	<b>0.8</b>	2.497 705	0.841 621	11.15 11	<b>10. 5</b>	<b>30%</b>	13. 65	<b>6</b>	<b>1</b>	6	<b>1</b>	338.8 2
<b>0.98 75</b>	<b>0.8</b>	2.497 705	0.841 621	11.15 11	<b>10. 5</b>	<b>40%</b>	14. 7	<b>6</b>	<b>1</b>	6	<b>1</b>	209.9 5
<b>0.98 75</b>	<b>0.8</b>	2.497 705	0.841 621	11.15 11	<b>10. 5</b>	<b>50%</b>	15. 75	<b>6</b>	<b>1</b>	6	<b>1</b>	147.7 3
<b>0.98 75</b>	<b>0.8</b>	2.497 705	0.841 621	11.15 11	<b>12</b>	<b>30%</b>	15. 6	<b>6</b>	<b>1</b>	6	<b>0. 3</b>	34.95
<b>0.98 75</b>	<b>0.8</b>	2.497 705	0.841 621	11.15 11	<b>12</b>	<b>40%</b>	16. 8	<b>6</b>	<b>1</b>	6	<b>1</b>	209.6 2
<b>0.98 75</b>	<b>0.8</b>	2.497 705	0.841 621	11.15 11	<b>12</b>	<b>50%</b>	18	<b>6</b>	<b>1</b>	6	<b>1</b>	147.5 1
<b>0.98 75</b>	<b>0.8</b>	2.497 705	0.841 621	11.15 11	<b>10. 5</b>	<b>160%</b>	27. 3	<b>6</b>	<b>1</b>	6	<b>1</b>	35.05
<b>0.98 75</b>	<b>0.8</b>	2.497 705	0.841 621	11.15 11	<b>10. 5</b>	<b>90%</b>	19. 95	<b>6</b>	<b>1</b>	6	<b>1</b>	65.10
<b>0.98 75</b>	<b>0.9</b>	2.497 705	1.281 552	14.28 278	<b>10. 5</b>	<b>50%</b>	15. 75	<b>6</b>	<b>1</b>	6	<b>1</b>	188.9 4
<b>0.98 75</b>	<b>0.9</b>	2.497 705	1.281 552	14.28 278	<b>12</b>	<b>30%</b>	15. 6	<b>6</b>	<b>1</b>	6	<b>1</b>	432.9 7
<b>0.98 75</b>	<b>0.9</b>	2.497 705	1.281 552	14.28 278	<b>12</b>	<b>40%</b>	16. 8	<b>6</b>	<b>1</b>	6	<b>1</b>	268.2 1
<b>0.98 75</b>	<b>0.9</b>	2.497 705	1.281 552	14.28 278	<b>12</b>	<b>50%</b>	18	<b>6</b>	<b>1</b>	6	<b>1</b>	188.6 6

## 5. Six segments of men and their characteristics

Segment Name*	Segment Color*	Characteristics
VMMC Enthusiasts	Orange	Large potential (21% of uncircumcised men) and high commitment already; need to overcome some dissonance issues
VMMC Champions	Purple	Low potential (6% of uncircumcised men), but easy conversion to action and highly likely to act as advocates for other men after VMMC
VMMC Neophytes	Yellow	Large potential (19% of uncircumcised men), but lack of knowledge is key to informing their commitment – addressing knowledge gap is relatively easy
Embarrassed Rejecters	Gray	Moderate potential (16% of uncircumcised men) but commitment is rather low and knowledge, embarrassment and fears are high – need a lot of support
Scared Rejecters	Brown	Moderate potential (17% of uncircumcised men) but commitment is very low and fears / dissonance are strong barriers
Highly Resistant	Maroon	Large potential (21% of uncircumcised men), but hard to crack; knowledgeable and little fear about VMMC; but do not recognize the need; commitment very low

\* These were names assigned by the market researchers for each of the segments identified through the quantitative approach. They were later reassigned as colours for use in the field.

Based on the market research, VMMC program implementers decided to prioritize particular segments to target with an initial set of interventions. PSI prioritized three segments of men to target with demand creation interventions developed using human-centred design (HCD) methods. The three segments representing 56% of uncircumcised males 15-29 years are: VMMC *Enthusiasts* (orange), *Neophytes* (yellow), and *Embarrassed Rejecters* (grey). This decision was based on the following factors:

5. Size of the segment (21%, 19% & 16% of uncircumcised men, respectively for each of the segments)
6. High level of commitment to get circumcised in the future
7. High risk sexual behaviour and risk perception
8. Potential for advocating for VMMC among other men post circumcision

## 6. Human centred design (HCD)-informed approach tools

### 6.1 Segmentation typing tool

The segmentation tool helps IPC agents identify the segment within which each potential VMMC client falls in order to improve targeting and to ensure appropriate and specific segment messages are delivered. IPC agents ask the client a series of questions to which he responds by choosing his response from seven Likert scale options. The tool is designed in such a way that a sequence of responses will determine a client's segment (See Figure 1). In order for a client to be appropriately segmented, both the IPC agent and the client need to have a clear understanding of the questions and their response options. Otherwise, a client will be wrongly segmented.

**Figure 1: Copy of paper-based segmentation tool**



To facilitate user-friendliness, each of the segmentation tool's six segments is represented by a unique colour (Table 6).

**Table 6: VMMC segments and their corresponding colours**

Segment	Color	
VMMC enthusiasts	Orange	
VMMC champions	Purple	
VMMC neophytes	Yellow	
Scared rejecters	Brown	
Embarrassed rejecters	Gray	
Highly resistant	Maroon	

Initially, the segmentation tool was paper-based but it is now in an electronic form and has been uploaded onto a tablet.

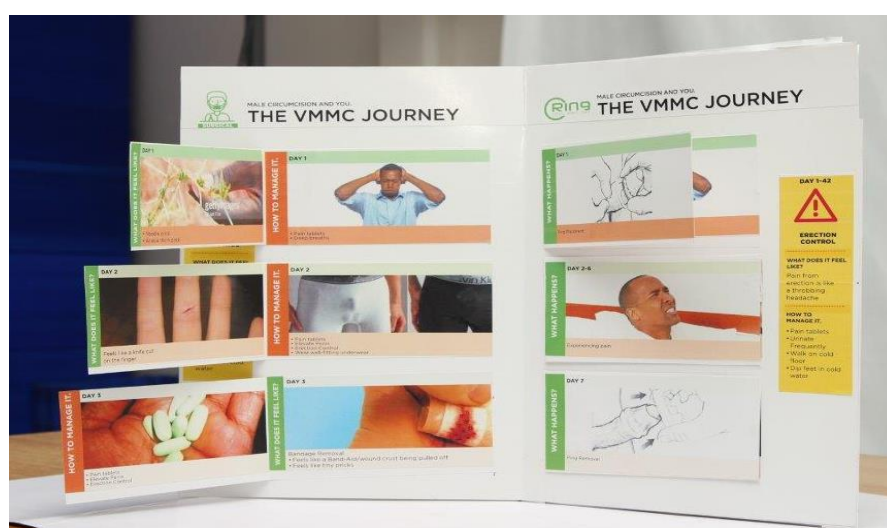
## 6.2 Targeted messaging to an individual

IPC agents have been trained to deliver tailored messages to men based on which segment they fall into and that segment's perceived information needs (as highlighted by the IPSOS research). If a client prefers a specific message instead of all messages in a catalogue of messages relevant to their segment, the IPC agent proceeds to provide the message and refer the client without having to deliver all messages. The segment for each client is recorded by the IPC agent. The client also gives the IPC agent his contact details during that session to allow the IPC agent to follow him up and encourage linkage to VMMC services.

## 6.3 Pain-o-meter

IPC agents have been trained to use a pain-o-meter - a job aid that was developed using Human-centred design (HCD) in response to IPSOS research findings indicating that men want honest communication on pain and procedure. The tool outlines the healing process (days 1 to 3 for surgical, days 1 to 7 for PrePex procedure) together with an analogy of the pain as well as the pain management techniques available in the VMMC program (based on experiences of circumcised men e.g. surgical VMMC pain on days 1 and 2 is likened to a thorn prick and knife cut on finger, respectively) (Figure 2). The tool is designed to help IPC agents communicate honestly about pain during IPC to prepare men to anticipate the MC pain better, thereby improving clients' overall VMMC experience.

**Figure 2: Copy of pain-o-meter illustrating pain of surgical and PrePex VMMC**



## 7. Changes to the trial protocol after trial commencement

**Change of timeline to allow for additional run-in period.** The initial timeline for the trial was 20 February-31 August 2018, with data collected on uptake of circumcision until 30 September 2018. After review of early process evaluation data, which indicated that it was taking longer than expected for IPC agents to become comfortable with the HCD-informed approach, a run-in period from 20 February-30 April 2018 was added, and the trial dates shifted to 1 May-31 October 2018. Data were collected on uptake of circumcision until 30 November 2018.

**Change in primary analysis from parallel-arm to factorial.** The trial was originally conceived as a parallel-arm design to identify synergistic effects between the two interventions under consideration. However, an analysis of blinded data in September 2018 indicated that the clustering of outcomes as measured by the cluster coefficient of variation was much greater than the assumptions used in the power calculation, leading to reduced power to detect differences between four parallel arms. Consequently, the primary analysis was changed from a parallel-arm to a 2x2 factorial analysis comparing arms with and without each of the two interventions. The parallel-arm analysis was conducted as a secondary analysis (see appendix A).

**Outcome measures used.** The protocol specified that the primary outcome - completed circumcisions - and secondary outcomes, be measured as the number of events per month of IPC agent activity and analysed as Poisson-distributed clustered data with months of work nested within IPC agents. This assumed that IPC agents would have varying activity throughout the evaluation period, but that their outcomes would be similar and correlated across months. However, the preliminary review of data in September 2018 found that there was extremely high variability both between and within IPC agents making it difficult to estimate and interpret mixed effect models as planned. We therefore changed the analysis strategy to combine outcomes across IPC agents into a cluster-level analysis, a robust approach to departures from distributional assumptions.<sup>(5)</sup> We also used a negative binomial model to account for greater than expected variability. Separately, the number of men spoken to by IPC agents was included in the protocol, but programme data were not collected on this outcome and it was not included in the final analysis.



## 8. Intervention components

### 8.1 Arm 1: Standard demand creation mobilisation

IPC agents randomised to the standard demand creation arm received basic training on how to promote VMMC, including identifying barriers, clarifying myths and misconceptions, and summarising key benefits. Thereafter, they mobilised men and boys for VMMC either as individuals or in groups. Those men expressing willingness to undergo VMMC had appointments booked. Subsequently, these VMMC referees either went to VMMC sites on their own or were taken there in a PSI vehicle.

### 8.2 Arm 2: Standard demand creation plus offer of HIVST

In addition to standard demand creation, IPC agents in Arm 2 offered men they mobilised access to an oral-fluid-based HIVST kit. These IPC agents were trained to demonstrate use of the kit and demonstrated HIVST kit use if required. IPC agents recorded whether or not VMMC referees opted to take a kit.

### 8.3 Arm 3: HCD-informed demand creation approach

IPC agents randomised to this arm received basic training and were also trained to use the segmentation typing tool to identify the segment within which each potential VMMC client fell. They would then deliver messages tailored to that 'segment' addressing the specific information needs identified by the market research. If a client appeared to be interested in one specific message rather than hearing about all messages relevant to their segment, the IPC agent concentrated on that message. For each potential client mobilised, the segment was recorded. For this arm, IPC agents were specifically required to address any pain-related concerns using a visual aid (pain-o-meter) to outline the VMMC procedure, healing process (together with an analogy of the degree of pain that might be experienced at each stage of the VMMC process up to wound healing), as well as possible pain management techniques.

If a client was willing to be circumcised at the start of the discussion, IPC agents did not segment or deliver targeted messages. They allocated these men to a default 'segment' (green), which was not one of those included in the market research but which was added subsequently when IPC agents reported there were men who did not require more intensive demand creation approaches. Clients mobilised in groups at schools were also allocated to the 'green' segment.

#### **8.4 Arm 4: HCD-informed demand creation approach plus offer of HIVST**

In this arm, in addition to the HCD-informed demand creation approach, IPC agents offered the men they mobilised a HIVST kit and if they accepted it, they demonstrated how to use the kit.

## 9. Tables of results: parallel arm and factorial analyses

**Table S1: Factorial analysis**

	Circumcisions/IPC					Circumcisions/IPC				
	Not HCD- HCD-informed	informed	IRR	(95% CI)	p-value	ST	No ST	IRR	(95% CI)	p-value
<b>Primary trial outcome: VMMC uptake per IPC</b>										
Mean	27	28.46	0.87	(0.38.2.02)	0.75	19.84	34.73	0.65	(0.28.1.50)	0.313
Std deviation	92.5	63.3				44.91	98.03			
<b>Secondary trial outcomes</b>										
Conversion rate (circumcisions per men reached, not adj)			<b>RR</b>					<b>RR</b>		
Mean	0.18	0.23	0.75	(0.41.1.38)	0.36	0.22	0.2	1.11	(0.61.2.02)	0.71
Std deviation	0.32	0.32				0.34	0.3			
Men reached per IPC-month			<b>IRR</b>					<b>IRR</b>		
Mean	78.53	86.77	0.89	(0.62.1.26)	0.498	67.27	96.62	0.75	(0.53.1.07)	0.115
Std deviation	106.45	93.97				65.33	120.91			
Men booked per IPC-month										
Mean	43.29	43.48	1.00	(0.62.1.60)	0.987	34.57	51.11	0.8	(0.50.1.29)	0.362
Std deviation	91.97	70.97				47.31	101.66			
Men presenting for VMMC per IPC-month										
Mean	36.51	35.09	1.00	(0.48.2.06)	0.985	28.73	41.89	0.84	(0.40.1.73)	0.632
Std deviation	101.37	65.61				48.26	105.64			

**Table S2: Parallel arm ITT analysis**

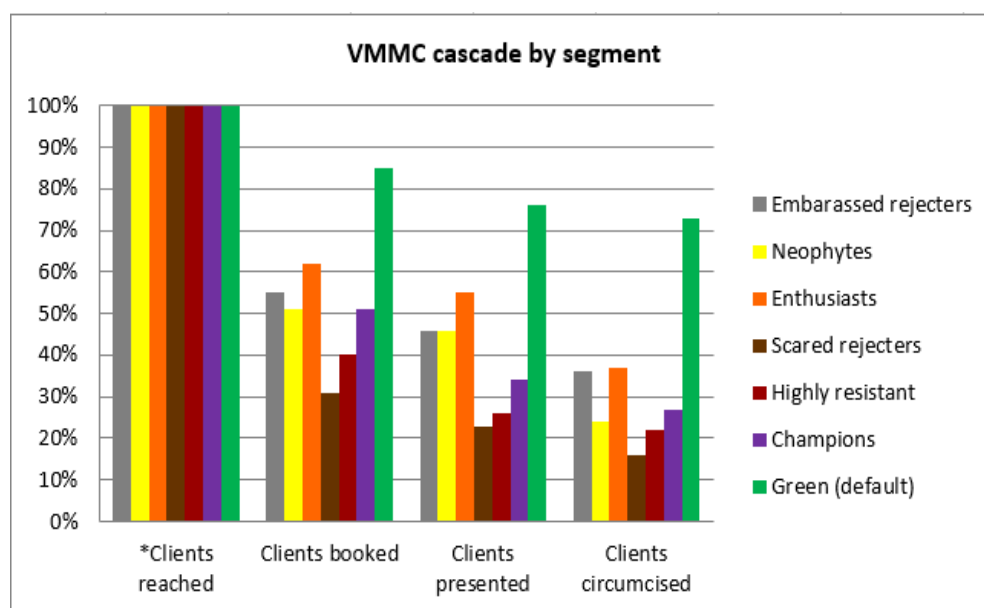
		SOC	ST	HCD	HCD+ST	Effect of ST vs SOC			Effect of HCD vs SOC			Effect of ST+HCD vs SOC			Effect of ST+HCD vs ST		
						IRR	(95% CI)	p-value	IRR	(95% CI)	p-value	IRR	(95% CI)	p-value	IRR	(95% CI)	p-value
Primary trial outcome: VMMC uptake per IPC-month																	
	Mean	27,74	13,77	26,94	10,29	0,61	(0.16,2.40)	0,484	1,20	(0.31,4.69)	0,791	0,57	(0.133,2.41)	0,443	0,92	(0.20,4.20)	0,917
	Std deviation	74,11	33,3	102,44	42,14												
Secondary trial outcomes																	
Conversion proportion*																	
	Mean	0,22	0,21	0,19	0,14	0,96	(0.44,2.11)	0,937	0,88	(0.37,2.07)	0,767	0,66	(0.24,1.79)	0,413	0,62	(0.17,2.25)	0,473
	Std deviation	0,28	0,31	0,33	0,27												
Men reached per IPC-month																	
	Mean	81,42	38,26	54,17	38,11	0,58	(0.30,1.13)	0,11	0,82	(0.42,1.60)	0,567	0,72	(0.35,1.45)	0,354	1,23	(0.59,2.58)	0,582
	Std deviation	113,1	56,73	118,15	65,41												
Men booked per IPC-month																	
	Mean	41,31	20,14	35,09	19,40	0,60	(0.26,1.40)	0,238	1,05	(0.46,2.43)	0,906	0,72	(0.29,1.75)	0,466	1,19	(0.47,3.02)	0,715
	Std deviation	83,28	39,67	103,64	45,26												
Men presenting for VMMC per IPC-month																	
	Mean	29,83	18,51	33,60	16,17	0,77	(0.23,2.55)	0,667	1,39	(0.42,4.62)	0,586	0,83	(0.23,2.96)	0,773	1,08	(0.28,4.09)	0,911
	Std deviation	74,98	37,78	113,51	45,78												

**Table S3: Parallel arm – as-treated analysis**

	SOC	ST	HCD	HCD+ST	Effect of ST vs SOC			Effect of HCD vs SOC			Effect of ST+HCD vs SOC			Effect of ST+HCD vs ST		
					IRR	(95% CI)	p-value	IRR	(95% CI)	p-value	IRR	(95% CI)	p-value	IRR	(95% CI)	p-value
Primary trial outcome: VMMC uptake per IPC-month																
Mean	34.14	22.37	35.37	16.73	0.76	(0.24,2.37)	0.634	0.98	(0.32,3.07)	0.979	0.51	(0.15,1.69)	0.271	0.67	(0.20,2.28)	0.523
Std deviation	80.18	38.45	115.78	52.54												
Secondary trial outcomes																
Conversion proportion (circumcisions per man reached)					Odds ratio			Odds ratio			Odds ratio			Odds ratio		
Mean	0.2	0.27	0.19	0.16	0.64	(0.20,2.05)	0.448	0.25	(0.08,0.80)	0.019	0.46	(0.14,1.53)	0.205	0.72	(0.22,2.32)	0.585
Std deviation	0.27	0.36	0.34	0.31												
Men reached per IPC-month					IRR			IRR			IRR			IRR		
Mean	107.07	64.96	85.41	70.09	0.69	(0.43,1.12)	0.135	0.82	(0.51,1.32)	0.405	0.68	(0.41,1.13)	0.133	0.98	(0.59,1.64)	0.933
Std deviation	113.05	62.95	130.02	69.52												
Men booked per IPC-month																
Mean	53.55	32.67	48.48	36.91	0.75	(0.40,1.44)	0.393	0.94	(0.49,1.78)	0.843	0.81	(0.41,1.60)	0.537	1.07	(0.53,2.14)	0.85
Std deviation	88.87	43.74	115.51	52.31												
Men presenting for VMMC per IPC-month																
Mean	39.9	29.93	44.04	27.27	0.91	(0.34,2.46)	0.857	1.07	(0.40,2.88)	0.896	0.81	(0.28,2.31)	0.689	0.88	(0.30,2.57)	0.822
Std deviation	82.00	42.57	127.89	55.45												

**10. VMMC cascade results**

Men in the prioritised segments (embarrassed rejecters, neophytes, enthusiasts) were more likely to be circumcised than those in the non-prioritised segments. Overall however, men in the green (default) segment were much more likely than any other segment to undergo circumcision (>70%) (Figure S 1).



\*Embarrassed rejecters (n=969:25.4%), Neophytes (n=849:22.3%), Enthusiasts (n=600:15.7%), Scared rejecters (n=282:7.4%), Highly resistant (n=410:10.8%), Champions (n=222:5.8%), Green (n=480:12.6%)

**Figure S1: VMMC cascade by segment**

## 11. IPC agents characteristics and uptake of VMMC

In the univariable model, gender, age, education and district were significantly associated with VMMC uptake while in the adjusted model age and district remained significantly associated with VMMC uptake (Table S4).

**Table S4: IPC agents characteristics and uptake of VMMC**

Factor	N (%) N=105	IRR (univariable) (95% CI)	p-value	IRR (Adjusted) (95% CI)	p-value
<b>IPC gender</b>			0.002		0.221
Female	57(54%)	1		1	
Male	48(46%)	3.53(1.58 - 7.86)		1.47(0.51 - 4.25)	
<b>IPC age</b>			<0.001		0.050
18-34 years	42(40%)	1		1	
35+ years	63(60%)	0.21(0.09 - 0.46)		0.46(0.21 - 1.07)	
<b>IPC education level</b>			0.044		0.121
Primary level (ref)	10(10%)	1		1	
Secondary level +	95(90%)	4.28(1.04 - 17.64)		0.34(0.06 - 2.04)	

<b>IPC mobilizing experience</b>					
<12 months (ref)	71(68%)	1	0.969		
At least 12 months	34(32%)	0.98(0.40 – 2.40)			
<b>IPC district</b>			0.049		0.001
Buhera (ref)	18(17%)	1		1	
Gokwe North	26(25%)	0.54(0.18 – 1.59)		0.67(0.22 – 2.01)	
Mangwe	11(10%)	0.05(0.01 – 0.20)		0.11(0.02 – 0.63)	
Mutasa	26(25%)	0.08(0.03 – 0.24)		0.17(0.04 – 0.75)	
Zvimba	24(23%)	0.07(0.02 – 0.22)		0.08(0.02 – 0.28)	

### Additional process evaluation findings

Uneven performance among IPC agents and districts: there were substantial differences in the performance of IPC agents across all outcomes. In Mangwe for example (where VMMC coverage was already high at the start of the trial), young men often travel to Botswana and South Africa and so were largely unavailable for mobilisation. IPC agents in Buhera and Gokwe North devoted considerable time to VMMC mobilisation, perhaps reflecting the lack of employment opportunities locally. In the other districts, IPC agents were involved in additional income-generating activities. These factors likely explain some of the variability observed between study districts (Table S5).

**Table S5: Conversion proportions by district**

District	Clients reached	Clients circumcised	Conversion proportion
Buhera	1717	1390	81%
Gokwe North	2925	1177	40%
Mangwe	423	44	10%
Mutasa	1474	169	11%
Zvimba	2168	137	6%