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An evaluation of a choice architecture-based intervention on prescribing of TB preventive treatment to people living with HIV in southern Africa (the CAT study): a cluster-randomised trial

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ABSTRACT

Introduction While highly effective for reducing the risk of tuberculosis (TB) disease, TB preventive treatment (TPT) is underused among people living with HIV (PWH). We evaluated the effectiveness of a behavioural economics-based choice architecture approach to increase facility-level TPT prescribing to PWH in Malawi, Mozambique and Zimbabwe.

Methods We conducted a cluster-randomised trial within the IMPAACT4TB 3HP rollout, in which 57 healthcare facilities were randomly assigned 1:1 to choice architecture (intervention) or standard TPT prescribing (control). The aim was to link TPT to antiretroviral therapy (ART) prescribing and to make TPT prescribing the default. The intervention was supported by clinician training and a default prescribing module built into the point-of-care HIV electronic medical record in Malawi and stickers placed in clients' clinical stationery in Mozambique and Zimbabwe. Data were collected in aggregate, and the primary outcome was the facility-level percentage of clients initiating ART who initiated TPT. The CAT study was registered with clinicaltrials.gov where it is listed as completed.

Results Implementation occurred from October 2021 to September 2022 in Mozambique (20 facilities), April 2021 to March 2022 in Malawi (19 facilities) and June 2021 to May 2022 in Zimbabwe (18 facilities), for a total of 29 control arm and 28 choice architecture intervention arm facilities, respectively. Comparing control to intervention facilities, mean TPT prescribing to clients initiating ART was 70.9% vs 86.9% in Mozambique (difference: −16.0%; 95% CI: −38.3%, 6.3%; p=0.15), 56.5% vs 55.5% in Malawi (difference: 1.0%; 95% CI: −14.0%, 16.9%; p=0.89) and 56.2% vs 55.9% in Zimbabwe (difference: 0.2%; 95% CI: −25.2%, 25.8%; p=0.98).

Conclusion The choice architecture intervention did not overcome barriers to TPT prescribing. While the intervention may have led to an improvement in TPT prescribing in Mozambique, no differences were observed in the other countries. Further innovation is needed to ensure that all clients initiating ART are either prescribed TPT or started on anti-TB treatment, as appropriate.

Trial registration number NCT04466293.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ We identified no previous trials that tested a behavioural economics and/or choice architecture-based approach to tuberculosis (TB) preventive treatment (TPT) prescribing, other than a small non-randomised pilot study conducted by members of our study team in South Africa. The pilot study showed evidence for a potential increase in TPT prescribing from 68% (n=522/773) of new antiretroviral therapy (ART) initiators in the 6 months preceding the pilot to 88% (n=36/41) during the 2-week intervention period.

INTRODUCTION

Tuberculosis (TB) is the leading infectious cause of mortality globally.[1] In 2023, the WHO estimated that there were 10.8 million people who developed TB worldwide and 1.25 million deaths.[1] In the WHO African region, HIV is one of the primary drivers of the TB epidemic, with an estimated 2.55 million people who developed TB in 2023, 461 000 of whom were people living with HIV (PWH).[1] TB preventive treatment (TPT) is highly effective for reducing the risk of TB disease among PWH. The use of isoniazid preventive therapy (IPT) has resulted in an overall 32%–35% reduction

WHAT THIS STUDY ADDS

⇒ This cluster-randomised trial tested the effectiveness of a choice architecture-based intervention to increase prescribing of TPT to people living with HIV. While the overall concept of choice architecture is simple and high-level buy-in was obtained for implementing choice architecture in the study setting, we encountered important differences at the clinic level. These included the willingness of clinic staff members to adapt to choice architecture and differences in prescribing, drug dispensing and documentation. Furthermore, the approach to training varied with a combination of Ministry of Health, IMPAACT4TB and choice architecture study team training, specific to each country. While some heterogeneity was expected across countries, there was both more heterogeneity and less opportunity to improve consistency because COVID-19 travel restrictions prevented planned pre-implementation in-country visits. Thus, we did not observe consistent evidence for an effect of the intervention. We believe that our findings suggest that choice architecture may be useful in health services, such as TPT, when context-specific changes to the delivery environment can be effectively made. Our findings and experience can help guide future work in this area.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ While the prescribing of TPT to people living with HIV has increased in recent years, gaps in coverage remain. Our study adds to the evidence base of interventions tested to improve TPT prescribing in high TB and HIV burden settings, the use of behavioural economics to improve HIV-related care delivery and highlights the need for further innovation to ensure that all new ART clients are either prescribed TPT or started on anti-TB treatment, as appropriate.

in the risk of active TB disease among PWH, even in combination with antiretroviral therapy (ART).[2 3] Since the WHO first endorsed IPT for PWH in 1998, several short-course regimens have been developed, including 12 weeks of high-dose isoniazid and rifapentine given weekly (3HP).[4 5] In clinical trials conducted among PWH, 3HP has been shown to be as effective as 6–12 months of IPT with fewer adverse events.[6 7]

TPT is a cornerstone of TB control programmes and is a major component in the plan to eliminate TB. In 2018, the United Nations High-Level Meeting (UNHLM) on TB set a target to provide TPT to 6 million PWH.[8] While TPT prescribing has surpassed the UNHLM target, less than half of PWH were estimated to have been prescribed TPT between 2005 and 2022.[9] Thus, considerable increases in TPT provision must be made to achieve the End TB target of providing TPT to 90% of PWH by 2025.[10]

Multiple barriers exist to TPT prescribing at the client level (low demand), provider level (including concerns about definitively ruling out active TB disease, fears of inducing drug resistance through inappropriate TPT prescribing and a lack of knowledge of TPT benefits) and health system level (including medication stock-outs and unclear or conflicting recommendations).[11–15] Approaches to improve TPT prescribing to PWH have included training interventions for mid-level managers or clinic staff,[16 17] standardising processes for TPT eligibility screening[18] and quality improvement projects,[19 20] among others. However, success in improving TPT prescribing globally has been mixed, and new approaches are required to achieve global goals for TPT uptake.

The Increasing Market and Public health outcomes through scaling up Affordable Access models of short Course preventive Therapy for TB (IMPAACT4TB) programme supported the rollout of 3HP to PWH across 12 high TB-burden countries.[21] In this study, we tested the effectiveness of a choice architecture-based approach to facility-level TPT prescribing (the 'CAT' study) nested within the IMPAACT4TB programme in three southern African countries. Choice architecture comes from the field of behavioural economics.[22] In healthcare settings, it can be used to structure clinical operations to make a preferred action (such as TPT prescribing) the default choice for clinicians.[23]

METHODS

Study design and site selection

The CAT study was a parallel cluster-randomised trial conducted in Malawi, Mozambique and Zimbabwe (online supplemental file 1). A total of 57 healthcare facilities providing HIV-related care were included—20 in Mozambique, 19 in Malawi and 18 in Zimbabwe—and facilities were selected for inclusion in the CAT study from the IMPAACT4TB participating sites in each country. In Malawi, IMPAACT4TB supported the rollout of 3HP in five districts. Of those, two districts, with a total of 62 public-sector facilities, that were not routinely implementing TPT prior to the IMPAACT4TB programme were selected for the CAT study, and all facilities using the national HIV point-of-care electronic medical record (EMR) system at the time of facility selection were included (minus one that the team was unaware of prior to initiation of study activities). In Zimbabwe, all IMPAACT4TB participating facilities (n=20) were included in CAT, except for two that were excluded as they used a point-of-care EMR rather than the paper-based clinical stationery in use at other facilities. In Mozambique, 74 facilities participated in IMPAACT4TB, and the 20 facilities with the lowest pre-implementation (2018) TPT prescription rates (approximately 60% or less) were selected to participate in the CAT study (figure 1).

Randomisation and masking

Healthcare facilities were randomised 1:1 to either choice architecture (intervention) or standard TPT prescribing (control). The study statistician randomised facilities using the available historical data provided by each in-country study team. A constrained randomisation was conducted to balance between the two study arms, mean levels of baseline covariates that are known to be associated with the outcome.[24] This was conducted using the *cvcrand* package in R.[25] The baseline covariates used in Mozambique were the district in which the facility was located, the number of new clients starting ART and the percentage of new ART clients started on TPT.

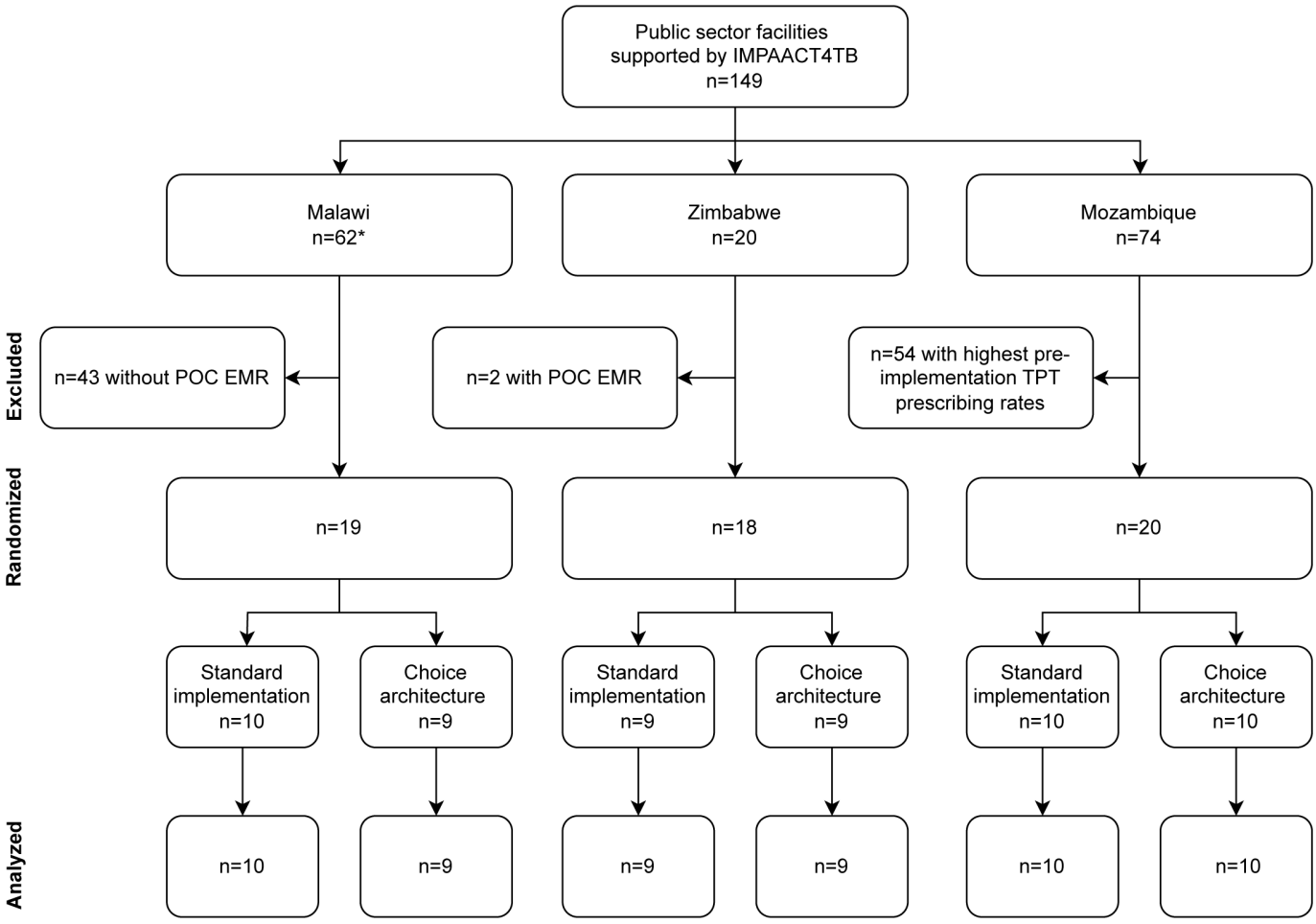

Figure 1 CONSORT diagram for clinic selection for a cluster-randomised trial of a choice architecture-based intervention on prescribing of TB preventive treatment to people living with HIV in southern Africa. *In the two selected districts that were not already implementing TPT prior to IMPAACT4TB. EMR, electronic medical record; POC, point-of-care; TB, tuberculosis; TPT, TB preventive treatment.

In Zimbabwe, the covariates were facility type, urban or rural setting, annual number of PWH attending the facility, number of nurses treating HIV/TB clients and percentage of eligible clients prescribed TPT. In Malawi, the covariates were the annual number of PWH initiating ART, the number of ART clients transferred in, the cumulative number of PWH initiating ART and the district where the facility was located.

This was an open-label trial with masking of arm allocation to the Johns Hopkins University Principal Investigators for the duration of study implementation. In-country investigators and study team members were not blinded to arm allocation for logistical purposes. Principal investigators were unblinded on a country-by-country basis on completion of implementation and data collection in each setting.

Procedures

Choice architecture is an approach rooted in behavioural economics.[22 26] The underlying principle is that choices that require less cognitive load (generally the default) are more likely to be 'chosen' at any given time.[22] Changing the way choices are presented, or framed, can change the most selected option. Changing the default is one example. The goal of the CAT intervention was to shift the need for cognitive effort from routine TPT prescribing to considerations and justification of not prescribing TPT when not appropriate (ie, receiving anti-TB treatment, under investigation for TB disease, known liver disease), through making TPT prescribing the default choice. Our intervention sought to prompt clinicians to prescribe TPT and reduce the cognitive load around a decision-making process that should most commonly lead to TPT prescribing.

The choice architecture intervention in each country included TPT prescribed as the default option linked to the ART prescription and was facilitated through a default prescribing tool (to act as an additional prescribing nudge within the choice architecture environment). Healthcare providers at intervention facilities were trained to consider TPT to be the default option for PWH, whereby all were considered eligible unless there was a clear contraindication, such as documented known liver disease or a strong clinical suspicion for TB. Default prescribing was supported by a prescribing tool

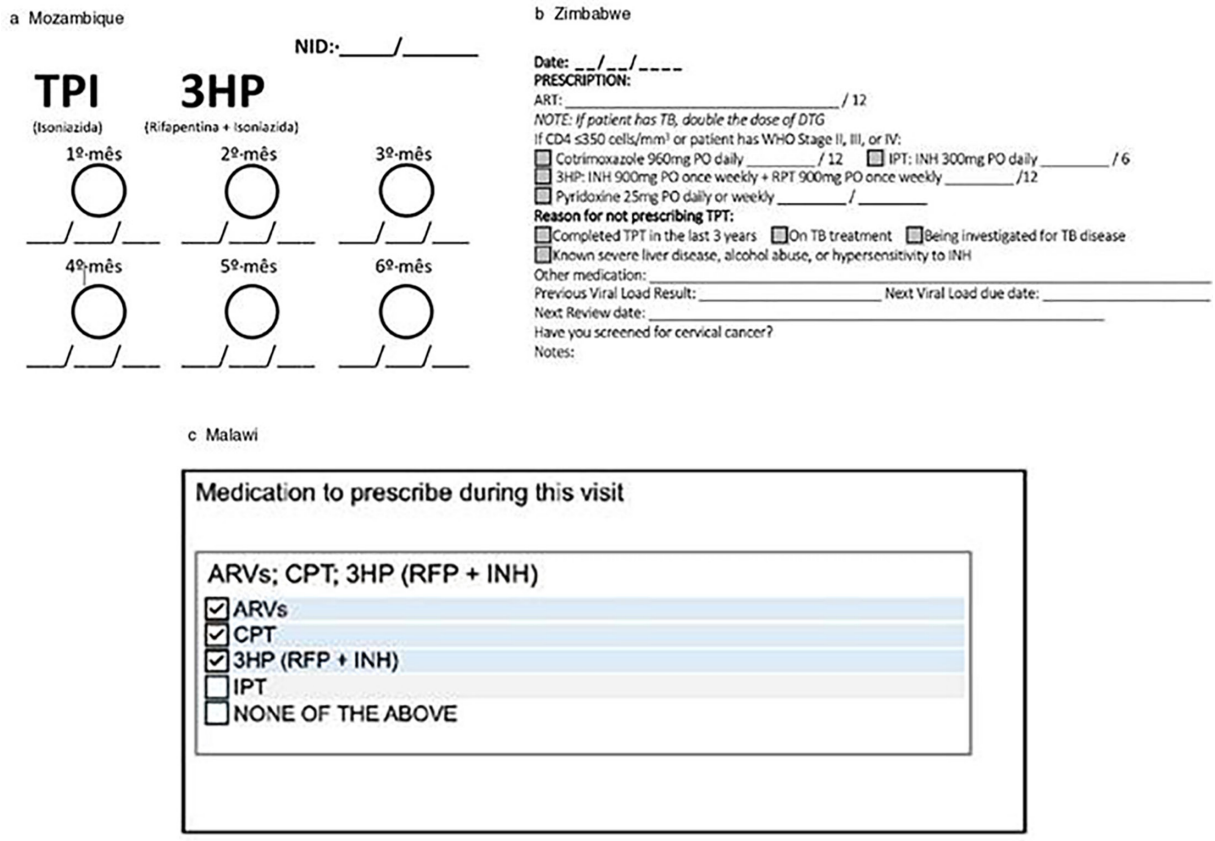

Figure 2 TPT prescribing tools to support choice architecture-based prescribing in intervention facilities by country. TB, tuberculosis; TPT, TB preventive treatment.

developed in collaboration with key stakeholders in each country, including representatives from each country's Ministry of Health, clinical providers and study team members.

In Mozambique and Zimbabwe, the choice architecture prescribing support tool was a sticker designed specifically for each country's clinical stationery. In Mozambique, the sticker was a TPT-specific prescribing sticker that clinicians placed on clients' HIV identification cards. The identification card included information regarding client appointment dates and ART prescriptions, and providers would indicate on the sticker which TPT regimen was prescribed, number of months dispensed and the dates of TPT dispensation (figure 2a). At follow-up visits, the clinician could update the sticker with additional prescribing information. If TPT was dispensed outside of the consultation room, the clinician would also complete a separate standard prescription for the client to take to the pharmacist for dispensing. In Zimbabwe, the sticker was a combined ART and TPT prescribing sticker that clinicians placed in the clients' personal carry books. Providers indicated the ART regimen prescribed, the TPT regimen (or reason for not prescribing), the most recent viral load result and next expected viral load test date and cervical cancer screening information (for female ART clients) (figure 2b). A new sticker was used at each follow-up visit to indicate prescribing information specific to that visit. Similar to Mozambique, if TPT was dispensed outside of the consultation room, a separate prescription was provided to the client to be filled at the facility pharmacy.

In Malawi, the choice architecture prescribing support tool was a default prescribing module built into the national HIV point-of-care EMR. Across intervention and control facilities in Malawi, a healthcare provider would work through standard EMR screens for each client, indicating any medication contraindications and/or side effects, whether the client was currently on TB treatment, and the presence (if any) of TB symptoms. In control facilities, the provider would then select the medications to be dispensed. In intervention facilities, the appropriate medications (including TPT) were pre-selected for the provider (figure 2c).

In support of the rollout of 3HP in each country, IMPAACT4TB conducted in-depth TPT training for participating healthcare facilities. Providers from control facilities were trained using the material developed by IMPAACT4TB. Likewise, all facilities participating in the IMPAACT4TB programme received TPT prescribing job aids and posters for use within their facilities.

Data were collected in aggregate from routine reporting data at each facility for adult PWH ages 15 and older. For the purposes of this study, clients initiating ART were defined as PWH initiating or re-initiating ART during the month, and established ART clients were those who initiated prior to the month of data abstraction. For each

month of study implementation, data were collected on the number of clients initiating ART and the number attending ART re-prescribing visits (ie, established ART clients). In addition, the number of clients started on any TPT regimen, those started on IPT (prescribed for a 6-month duration in all study countries) and those started on 3HP were collected and stratified by ART status. Indicators for completion and adverse events were also included. However, challenges with data collection occurred in all three study countries, and those results are not reported. In Malawi, study team members collected data directly at facilities from routine facility records and registers and by generating reports from the EMR. Data were collected from routine facility records and registers by nurses in Zimbabwe, with indicators validated by study team members during regular data audits. In Mozambique, data were generated retrospectively from an EMR system (OpenMRS), where available, by implementing partners responsible for oversight and management of the EMR. For facilities without the EMR (n=3), data were collected using routine paper-based facility records and registers by study team members.

Outcomes, sample size and statistical analysis

The primary outcome was the proportion of PWH initiating ART who were also prescribed TPT. Secondary outcomes included the proportion of established ART clients prescribed TPT and the proportion of all (newly initiating or re-initiating+established) ART clients prescribed TPT.

At the time of protocol development and study design, we anticipated that differences in the approach, including intervention tools and data availability, between countries would be minimal, and the study was powered for a single analysis. To determine the necessary sample size, we estimated that TPT prescribing would be 40% in control clinics and 64% (a 24% difference) in choice architecture intervention clinics. We selected a conservative coefficient of variation of 0.5, assumed a mean cluster size of at least 150 people living with HIV and an alpha of 0.05. We determined that 60 clinics would be required to achieve 90% power to detect this difference between control and intervention clinics. Thus, we sought to include 20 clinics per country.

The goal of this study was to evaluate the impact of a choice architecture-based intervention to improve TPT prescribing at the facility level. Thus, we sought to estimate cluster-averaged treatment effects. The primary analysis used an unpaired t-test of the cluster-level proportions without weighting, summing the numerator and denominator over the 12 months of study implementation within each cluster. If a facility had no new ART patients in a given month, a record for that month was considered a structural zero and was assigned to missing. The primary analysis was conducted for each country separately due to fundamental differences in each country's intervention implementation, data collection approach and data availability. We also present the prevalence ratio (PR) from a log binomial regression model applied to the data from all three countries combined, including a fixed effect for country.

The CAT study was registered with clinicaltrials.gov where it is listed as completed.

Role of the funding source

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

Patient and public involvement

This study was designed without patient participation.

RESULTS

The CAT study was implemented in 57 health facilities, 29 in the control arm and 28 in the choice architecture intervention arm, for a 12-month period in each country. Implementation occurred from October 2021 to September 2022 in Mozambique (20 clinics), April 2021 to March 2022 in Malawi (19 clinics) and June 2021 to May 2022 in Zimbabwe (18 clinics). Prior to study implementation, TPT uptake among PWH initiating ART was 34.8% (control facilities) and 31.7% (choice architecture facilities) in Mozambique, while TPT prescribing to eligible PWH in Zimbabwe was 25.6% (control facilities) and 28.5% (choice architecture facilities). As TPT was not routinely implemented prior to study implementation in the study districts in Malawi, data on TPT uptake were not available (table 1).

Primary outcomes

During the study implementation period in Mozambique, the mean number of clients initiating ART each month was 20.0 (SD: 27.0) per facility in the control arm and 19.0 (SD: 28.0) in the choice architecture arm. The cluster-averaged proportion of clients initiating ART prescribed TPT in control arm facilities was 70.9% (95% CI: 48.3%, 93.6%) compared with 86.9% (95% CI: 78.9%, 94.9%) in choice architecture facilities (difference: −16.0%; 95% CI: −38.3%, 6.3%; t-test p value: 0.15) (table 2) (figure 3). The coefficients of variation in the control and choice architecture arms were 0.44 and 0.13, respectively.

In Zimbabwe, the mean number of clients initiating ART was 14.9 (SD: 8.3) and 13.6 (SD: 6.6) in control and choice architecture facilities, respectively. Cluster-level TPT prescribing to clients initiating ART was 56.2% (95% CI: 37.2%, 75.1%) in control facilities and was 55.9% (95% CI: 35.8%, 76.1%) in choice architecture facilities (difference: 0.2%; 95% CI: −25.2%, 25.8%; t-test p value: 0.98) (table 2) (figure 3). The coefficients of variation in the control and choice architecture arms were 0.44 and 0.47, respectively.

In Malawi, the mean number of clients initiating ART was 21.5 (SD: 17.3) and 18.0 (SD: 8.7) in the control and choice architecture arms, respectively. The cluster-averaged proportion of new ART clients prescribed TPT in control arm facilities was 56.5% (95% CI: 44.7%,

Table 1 Pre-implementation characteristics

	Mozambique		Zimbabwe		Malawi	
	Standard implementation	Choice architecture	Standard implementation	Choice architecture	Standard implementation	Choice architecture
Number of facilities	10	10	9	9	10	9
Annual number of new ART clients						
Median (IQR)	184 (71, 286)	53.5 (41, 293)	248 (231, 331)	242 (111, 367)	240 (203, 491)	339 (241, 393)
Mean (SD)	326.3 (464.2)	306.1 (492.8)	289.4 (133.4)	245.4 (152.8)	389.9 (307.3)	348.2 (133.7)
Proportion of PWH on ART prescribed TPT*						
Median (IQR)	37% (19%, 51%)	35.5% (16%, 44.8%)	24% (12%, 25%)	27% (11%, 46%)	Not available	Not available
Mean (SD)	34.8% (16.9%)	31.7% (15.8%)	25.6% (19.6%)	28.5% (20.7%)	Not available	Not available
Facility location						
Urban	2 (20%)	2 (20%)	6 (67%)	5 (56%)	3 (30%)	2 (22%)
Peri-urban	1 (10%)	0 (0%)	0 (0%)	0 (0%)	2 (20%)	2 (22%)
Rural	7 (70%)	8 (80%)	3 (33%)	4 (44%)	5 (50%)	5 (56%)

*TPT uptake among new ART clients in Mozambique and among eligible PWH in Zimbabwe.
ART, antiretroviral therapy; PWH, people living with HIV; TB, tuberculosis; TPT, TB preventive treatment.

68.4%) compared with 55.5% (95% CI: 43.0%, 68.0%) in choice architecture facilities (difference: 1.0%; 95% CI: −14.0%, 16.9%; t-test p value: 0.89) (table 2). The coefficients of variation were 0.29 in both arms.

The analysis combining all 57 facilities across the three countries showed that there was no statistically significant difference between the study arms (PR: 1.1; 95% CI: 0.9, 1.2), after adjusting for country effects and in Mozambique, clients initiating ART were more likely to be prescribed TPT than in other countries (PR: 1.7; 95% CI: 1.4, 2.0).

Secondary outcomes

While established ART clients were eligible for TPT initiation in each setting, few were prescribed TPT. In Mozambique, the cluster-averaged proportion of established ART clients prescribed TPT was 1.9% (95% CI: 0%, 3.8%) in control facilities compared with 1.5% (95% CI: 0%, 3.5%) in choice architecture facilities (difference: 0.4%; 95% CI: −2.3%, 3.0%; t-test p value: 0.78). Slightly higher TPT uptake was observed in Zimbabwe where guidelines indicate clients should receive TPT every 3 years (control: 10.8% (95% CI: 5.6%, 15.9%); choice architecture: 8.7% (95% CI: 5.6%, 11.8%); difference: 2.1%; 95% CI: −3.4%, 7.6%; t-test p value: 0.42). Prescribing of TPT to all ART clients (newly initiating or re-initiating and established combined) was 4.3% (95% CI: 2.0%, 6.5%) and 4.6% (95% CI: 2.5%, 6.7%) in control and choice architecture facilities in Mozambique, respectively, (difference: 0.3%; 95% CI: −3.1%, 2.5%; t-test p value: 0.82) and was 11.9% (control; 95% CI: 6.5%, 17.3%) and 9.6% (choice architecture; 95% CI: 6.3%, 12.7%) in Zimbabwe (difference: 2.4%; 95% CI: −3.4%, 8.1%; t-test p value: 0.40) (table 2). Data on the number of established ART clients and the total number of ART clients seen each month could not be abstracted in Malawi, so results for these secondary outcomes are not available.

Regimen utilisation differed based on the client's ART status. In all study countries, 3HP was prioritised for new ART clients. Of those prescribed TPT, a median 84% (Mozambique), 75% (Zimbabwe) and 100% (Malawi) of clients initiating ART were prescribed 3HP; and 100% (Mozambique), 15% (Zimbabwe) and 92% (Malawi) of established ART clients were prescribed IPT. In Zimbabwe, 3HP was prioritised for all ART clients, while IPT was prescribed for those with a 3HP-specific contraindication or if there was a 3HP stock-out.

DISCUSSION

In this cluster randomised trial conducted in 57 facilities across three countries in southern Africa, we did not observe a consistent effect of the choice architecture intervention, as implemented, on the prescribing of TPT to adults living with HIV. Intervention facilities in Mozambique had substantially higher TPT prescription rates than control facilities, though this difference was not statistically significant. The study

Table 2 Primary and secondary outcomes

	Mozambique			Zimbabwe			Malawi		
	Standard implementation	**Choice architecture**		**Standard implementation**	**Choice architecture**		**Standard implementation**	**Choice architecture**	
Number of facilities	10	10		9	9		10	9	
Facility type									
Hospital-based facility	2 (20%)	0 (0%)		4 (44%)	4 (44%)		3 (30%)	2 (22%)	
Standalone facility	8 (80%)	10 (100%)		5 (56%)	5 (56%)		7 (70%)	7 (78%)	
Primary indicators									
Monthly number of clients initiating ART									
Median (IQR)	10.0 (3.0, 28.0)	6.0 (3.0, 12.0)		13 (9, 19)	13 (9.5, 19)		15 (10.5, 27)	18.5 (11, 23.5)	
Mean (SD)	20.0 (27.0)	19.0 (28.0)		14.9 (8.3)	13.6 (6.6)		21.5 (17.3)	18.0 (8.7)	
Monthly number of clients initiating ART prescribed TPT									
Median (IQR)	5.0 (1.0, 26.0)	6.0 (2.5, 11.0)		6 (3, 12.5)	9 (3, 12.5)		9 (4.5, 17)	8 (5, 12)	
Mean (SD)	17.9 (27.0)	18.0 (27.0)		8.4 (7.3)	8.5 (6.2)		12.4 (11.0)	9.2 (5.7)	
Primary outcome	**Standard implementation**	**Choice architecture**	**Difference (CI) p value**	**Standard implementation**	**Choice architecture**	**Difference (CI) p value**	**Standard implementation**	**Choice architecture**	**Difference (CI) p value**
Mean of cluster-level proportions of new ART clients prescribed TPT (95% CI)	70.9% (48.3%, 93.6%)	86.9% (78.9%, 94.9%)	−16.0% (−38.3, 6.3) p value=0.15	56.2% (37.2%, 75.1%)	55.9% (35.8%, 76.1)	0.2% (−25.2, 25.8) p value=0.98	56.5% (44.7%, 68.4%)	55.5% (43.0%, 68.0%)	1.0% (−14.0, 16.9) p value=0.89
Secondary indicators									
Monthly number of established ART clients									
Median (IQR)	267 (69, 932.5)	159 (84, 1074.5)		798.5 (442.5, 1058.5)	702.5 (425.5, 1017.5)		Not available	Not available	
Mean (SD)	665.1 (893.2)	724.6 (1033.1)		778.6 (430.7)	737.9 (383.3)		Not available	Not available	
Monthly number of established ART clients prescribed TPT									
Median (IQR)	0.0 (0.0, 27.5)	0.0 (0.0, 2.0)		47.0 (28.5, 96.5)	39.5 (25.0, 74.0)		2.0 (0.0, 20.0)	2.0 (0.0, 12.0)	
Mean (SD)	29.7 (67.6)	36.6 (85.1)		66.9 (52.6)	67.2 (98.6)		13.7 (22.3)	19.2 (34.4)	
Secondary outcomes	**Standard implementation**	**Choice architecture**	**Difference (CI) p value**	**Standard implementation**	**Choice architecture**	**Difference (CI) p value**	**Standard implementation**	**Choice architecture**	**Difference (CI) p value**
Mean of cluster-level proportions of established ART clients prescribed TPT (95% CI)	1.9% (0%, 3.8%)	1.5% (0%, 3.5%)	0.4% (−2.3, 3.0) p value=0.78	10.8% (5.6%, 15.9%)	8.7% (5.6%, 11.8%)	2.1% (−3.4, 7.6) p value=0.42	Not available	Not available	
Mean of cluster-level proportions of all ART clients prescribed TPT (95% CI)	4.3% (2.0%, 6.5%)	4.6% (2.5%, 6.7%)	0.3% (−3.1, 2.5) p value=0.82	11.9% (6.5%, 17.3%)	9.6% (6.3%, 12.7%)	2.4% (−3.4, 8.1) p value=0.40	Not available	Not available	

ART, antiretroviral therapy; TB, tuberculosis; TPT, TB preventive treatment.

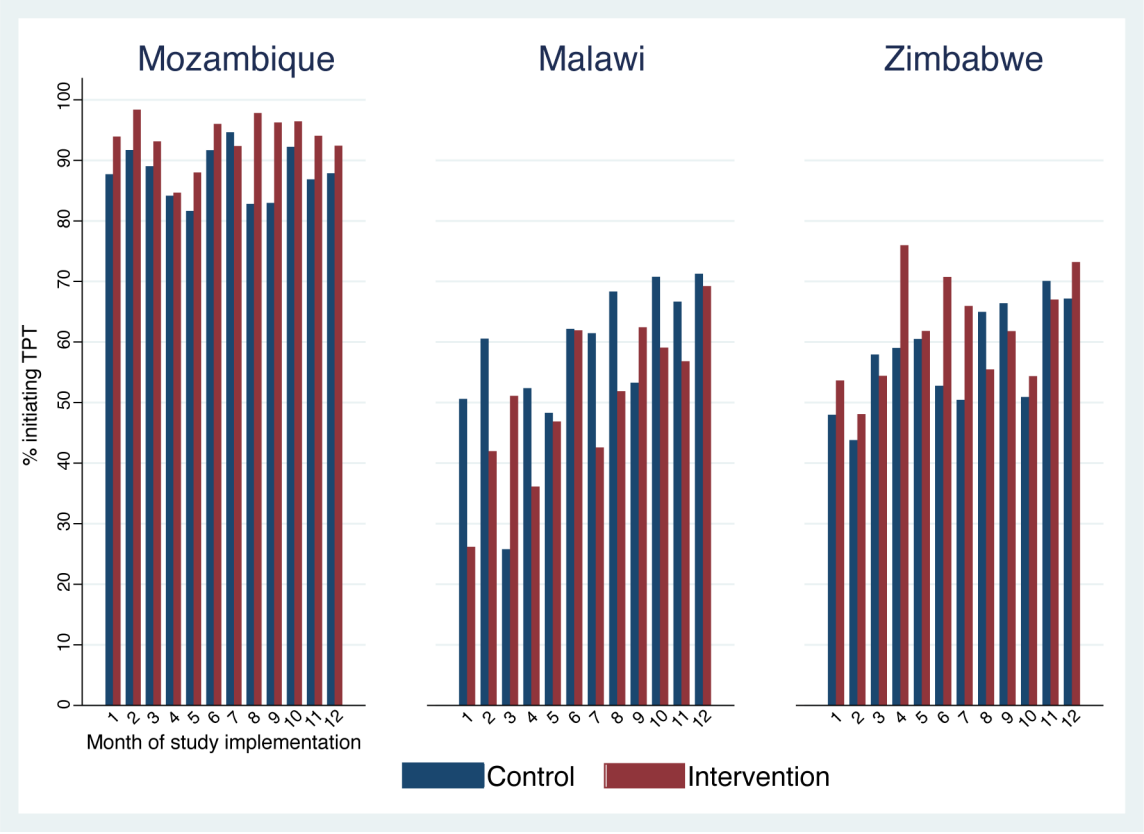

Figure 3 Mean monthly TPT prescribing to new ART clients in Mozambique, Malawi and Zimbabwe. ART, antiretroviral therapy; TB, tuberculosis; TPT, TB preventive treatment.

was originally powered to detect a large difference in TPT prescribing comparing choice architecture to control facilities based on approximately 60 facilities combined across all three countries. However, as a result of fundamental differences in study implementation in each country, we conducted country-specific analyses. Thus, while we observed evidence for a potential effect in Mozambique, our study was underpowered to demonstrate statistical significance for a change of that magnitude in just one country, and we observed no evidence for an effect in Zimbabwe or Malawi. Of note, TPT prescribing to clients initiating ART was higher in Mozambique than Zimbabwe or Malawi, irrespective of study arm. We were not able to identify specific reasons for this difference, but it may have been related to facility resources, facility-level variation in care in response to COVID-19, TPT prioritisation and the robustness of data collection. As data were collected in aggregate at each facility, we are unable to deduce reasons for non-prescribing at the individual level. We did note, however, a substantial increase in TPT provision overall when compared with pre-implementation prescribing rates that were used to inform randomisation procedures, suggesting overall success of the IMPAACT4TB programme.

Our failure to observe an effect of choice architecture-based default TPT prescribing is in contrast to other studies that have used default approaches to influence clinician decision-making in healthcare settings. In a non-randomised pilot study conducted in South Africa, a choice architecture approach was used to design a TPT prescribing intervention consisting of a brief TPT training and a prescribing stamp or sticker. In the 6 month pre-intervention period, 68% of 773 new ART clients were prescribed TPT compared with 88% of 41 new ART clients in the intervention period.[27] Likewise, opt-out approaches to HIV testing have been implemented successfully in both high- and low-resource settings. In a systematic review and meta-analysis of HIV testing approaches of 150 studies from various settings (ie, emergency departments, outpatient clinics, etc) and patient populations (hospitalised individuals, incarcerated persons, etc), including 32 from African countries and 83 from North America, HIV testing uptake was 64.3% using an opt-out approach and was 59.8% using an opt-in approach. After adjustment for rapid test availability, country-level socioeconomic status, setting and population, opt-out testing was associated with a 12% higher uptake (95% CI: 3%, 21%) compared with an opt-in approach.[28] Opt-out approaches have also increased influenza vaccination uptake in a workplace setting and HIV and syphilis testing in an urban emergency department in the USA.[29 30]

The results of this study should be viewed in light of several limitations. Study implementation was delayed due to the COVID-19 pandemic, which also hampered oversight and access to healthcare facilities by study team members. In addition, prior to study implementation in Malawi, the Ministry of Health adopted the default prescribing module (the choice architecture approach) across all health facilities with the point-of-care EMR system. For the study to proceed, facilities allocated to the control arm had to have the module deactivated. However, all facilities were exposed to the default prescribing module before study implementation began, which could have affected the results. Software updates during study implementation also led to the default prescribing module being turned off and on across arms at various time points. Qualitative research with healthcare providers revealed some distrust of the default prescribing module in accurately identifying individuals eligible to receive TPT, which could have resulted in under-prescribing.[31] Likewise, Zimbabwe expanded the use of a point-of-care EMR during study implementation, which was used in parallel to a manual register-based system in the majority of study healthcare facilities and may have affected prescriber behaviour. The effects of the challenges identified with the EMRs in Malawi and Zimbabwe could not be quantified. Finally, as all facilities included in the CAT study were also part of the IMPAACT4TB rollout of 3HP, control arm facilities received similar in-depth training on TPT prescribing (though meant to exclude the choice architecture-based framing of default prescribing that intervention clinics received), and extra support, emphasis and quality improvement regarding TPT prescribing were provided to all facilities throughout the study period.

CONCLUSION

A choice architecture intervention of default prescribing supported by a prescribing tool did not overcome barriers to TPT prescribing during an implementation period when overall TPT prescribing increased substantially through the parent project. While the intervention may have led to an improvement in TPT prescribing in Mozambique, no differences were observed in the other countries.

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Ethics approval This study involves human participants and was approved. Ethical approval was obtained from the Malawi National Health Sciences Research Committee (20/08/2589), the Mozambique National Committee on Bioethics for Health (359/CNBS/20), the Medical Research Council of Zimbabwe (MRCZ/A/2539), the Johns Hopkins University Institutional Review Board (IRB00227388) and the WHO's Ethical Review Committee (ERC.0003239). As we were evaluating strategies aimed at the health system to increase TPT prescribing that would not compromise or change overall patient care and did not collect individual-level data, individual ART clients and healthcare workers at participating health facilities did not provide written informed consent. Local, regional or national health managers were responsible for approving clinic participation in IMPAACT4TB and the CAT study.

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