The ENRICH Study

Evaluating an Innovative Approach to Increasing Use of Isoniazid Preventive Therapy to Prevent TB among People Living with HIV

PEPFAR

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Background and Rationale

People living with HIV have a greatly increased risk of developing tuberculosis (TB). In 2014, it was estimated that TB caused the death of 400,000 people living with HIV, accounting for one in four HIV-related deaths worldwide.[1] A critical, but often under-utilized medication that prevents TB among people living with HIV is isoniazid, an inexpensive drug that has been shown to reduce TB risk in this population, even in the presence of antiretroviral therapy (ART).

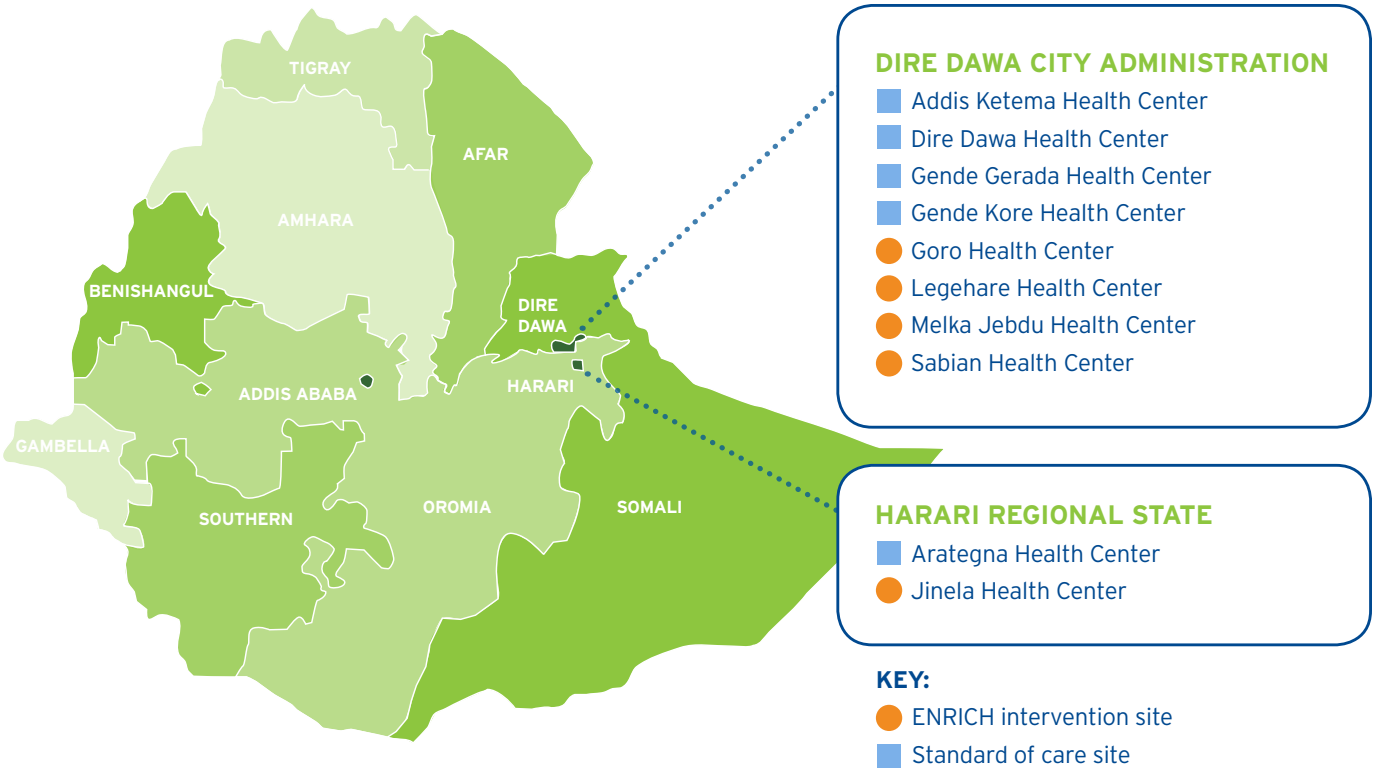
Isoniazid preventive therapy (IPT) was first recommended as a TB prevention measure for people living with HIV by the World Health Organization (WHO) in 1993—the year TB was declared a global emergency—and the scientific evidence for IPT's efficacy has continued to grow in the years since. In 2008, IPT was designated as one of three pillars of a global strategy to decrease the impact of TB on the health of people living with HIV (the "Three I's") and, in 2010, the WHO recommended that all people living with HIV who screen negative for active TB receive at least six months of IPT as part of a comprehensive package of HIV care.

Despite the scientific evidence and WHO endorsement, IPT is still not widely provided to people living with HIV in many high-burden settings. Available data also suggest that many patients who start IPT do not adhere to the full course of treatment. Barriers preventing IPT initiation and adherence include health workers with inadequate knowledge about IPT (e.g., insufficient awareness of IPT's efficacy and/or concerns about drug toxicity or drug resistance); TB programs that lack tools to sufficiently guide health workers (e.g., TB screening algorithms); patients who lack resources to cover the cost of transportation to monthly clinic visits; patients with insufficient social support (often as a result of HIV-related stigma); and a lack of systems to monitor the programmatic implementation of IPT.

Evidence-based, effective models for scaling up IPT in high-burden, resource-limited settings are urgently needed. While a small number of studies have described specific interventions to improve IPT initiation in such settings, few have rigorously assessed a combination approach that comprises programmatic, structural, and psychosocial interventions addressing the diverse barriers that exist.

A woman walks to a health facility in Dire Dawa, Ethiopia.

Figure: Location of ENRICH Study Sites



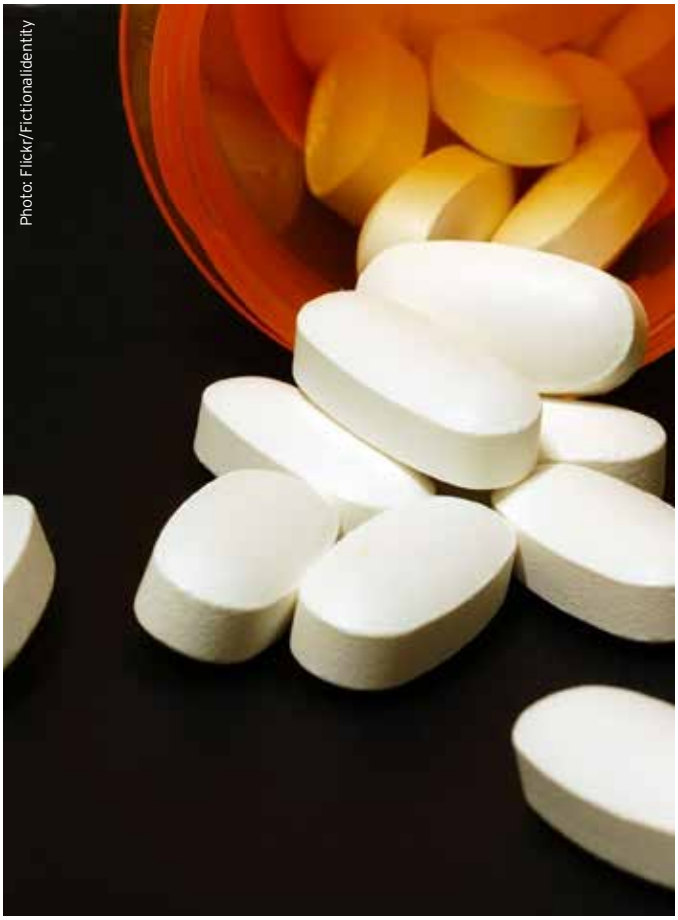


Photo: Flickr/Fictionalidentity

Study Overview

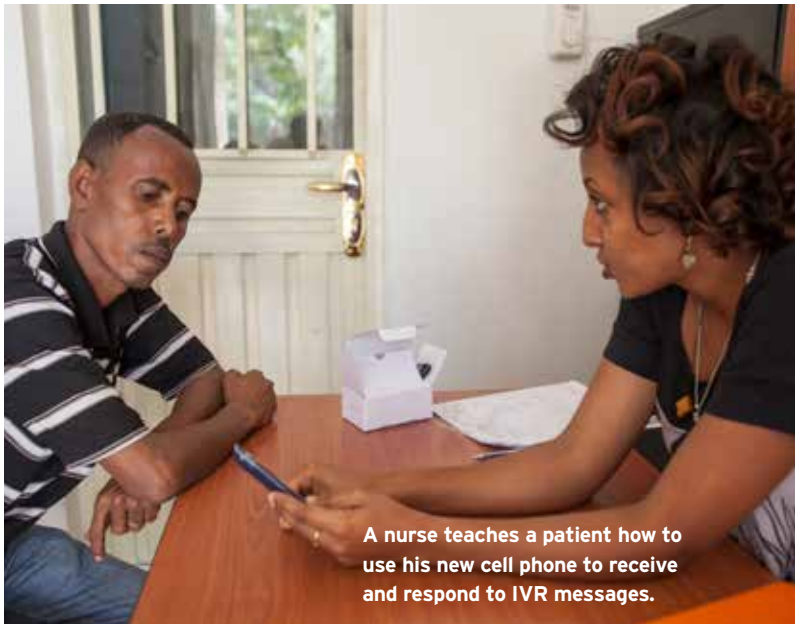
From 2013 to 2015, ICAP conducted the **En**hance Initiation and **R**etention in **I**PT **C**are for **H**IV (**ENRICH**) Study to evaluate the effectiveness and acceptability of a package of practical, scalable interventions targeting multiple barriers to IPT initiation and adherence among people living with HIV. ICAP collaborated with the Regional Health Bureaus of Harari and Dire Dawa, building on 10 years of partnership working together to scale up HIV prevention, care, and treatment services and enhance TB/HIV integration in these regions. Ethiopia—a country where approximately 800,000 people are living with HIV[2] and an estimated 200,000 people contract TB each year[3]—has recommended the use of IPT to prevent TB among people living with HIV in its national guidelines since 2007. In 2012, 18 percent of people living with HIV were receiving IPT in Ethiopia.

[1] WHO. Global Tuberculosis Report. 2015.
[2] UNAIDS. The Gap Report. 2014.
[3] WHO. Global Tuberculosis Report. 2015.

The Intervention Package

The ENRICH intervention was designed to be carried out at the health facility level and focused on providing training, mentorship, and tools to existing health workers. Facility-based peer educators were also recruited and trained to provide education and adherence support to patients, alleviating some of the counseling and follow-up work of existing health workers.

- To address **programmatic barriers**, ICAP:
  - Provided health workers with a two-day training focused on reviewing Ethiopia's IPT guidelines, discussing the importance of—and scientific evidence for—using IPT to prevent TB among people living with HIV, and introducing a new clinical algorithm. The algorithm was designed to help health workers consistently screen HIV-positive patients for TB, assess for IPT eligibility, initiate eligible patients on IPT, and provide follow-up monitoring and care. Following the training, wall charts with the clinical algorithm were provided to each health facility and a clinical mentor visited regularly to provide ongoing mentorship to health workers. Health workers were also provided with a follow-up refresher training one year after the start of the intervention.
  - Modified an existing family enrollment form, which is currently used in Ethiopia to ensure that the partners and family members of people living with HIV are offered HIV testing, to include an assessment of all HIV-positive family members of enrolled patients to determine IPT eligibility and ensure IPT is offered to those eligible.
  - Ensured that IPT monitoring and isoniazid pick-up were included as a routine part of HIV care and treatment visits.
  - Compiled summary data on IPT initiation and adherence, and worked with HIV clinic staff during monthly multidisciplinary team meetings to review IPT monitoring data, identify programmatic challenges, and develop solutions to improve the quality of care.
- To address **structural barriers**, ICAP reimbursed patients for transportation costs at the end of each monthly clinic visit.
- To address **psychosocial barriers**, people living with HIV who were enrolled in HIV care and who had themselves received IPT were recruited to serve as peer educators. A total of 10 peer educators were engaged across the five ENRICH intervention clinics. These peer educators completed a seven-day training that equipped them to provide IPT-related education and social support to newly enrolled HIV patients through individual counseling, group education sessions, and the facilitation of support groups. They were also trained to provide real-time adherence support to patients using interactive voice response (IVR) technology (see Box 1) and to make weekly phone calls to patients throughout IPT treatment. An illustrated IPT treatment literacy flipchart was developed by ICAP to help guide peer educators during individual and group education sessions.



A nurse teaches a patient how to use his new cell phone to receive and respond to IVR messages.

BOX 1: Using Interactive Voice Response (IVR) Technology to Support Patient Adherence to IPT

Recognizing that Ethiopia has relatively low rates of literacy and cell phone ownership, ICAP implemented an innovative IVR system as a way to provide real-time adherence support to patients. IVR is a phone-based technology that allows a computer to interact with humans through the use of voice responses and responses entered on a phone's keypad.

Each patient who initiated IPT at an ENRICH intervention site was provided with a cell phone and air time, and was educated on how to use the phone to receive and respond to IVR messages. Patients chose a four-digit PIN needed to access the IVR messages and indicated the time of day they preferred to receive the calls. The IVR system was used to send patients IPT adherence reminders, clinic appointment reminders, and monitoring messages to assess adherence and side effects. Calls were conducted in the patient's preferred language (Amharic, Somali, Oromiffa, or Harari) and, to protect patient confidentiality, began with a brief tune that served to prompt the patient to enter his or her PIN. Calls ended by asking if the patient had any questions or concerns, and peer educators or nurses followed up with those who responded 'yes.' Health workers also followed up with patients who did not respond to IVR messages and those who reported non-adherence or side effects.

Study Design

To evaluate the multi-component intervention, 10 public health facilities in the Dire Dawa and Harari regions of Ethiopia were randomly assigned to provide either the standard of care (i.e., to follow usual procedures, as dictated by national guidelines) or to deliver the standard of care plus the ENRICH interventions (see map on page 3 and table below). At health facilities assigned to implement the ENRICH package, relevant health providers were trained to implement the interventions as part of routine HIV care.

Table: Comparison of the Standard of Care and ENRICH Package of Interventions

	STANDARD OF CARE	ENRICH INTERVENTIONS
HIV patients **screened for TB** using a symptom questionnaire at enrollment in HIV care and at each routine clinic visit	✓	✓
Patients with negative TB screen **assessed for IPT eligibility** and, if eligible, counseled on IPT benefits, potential side effects, and adherence	✓	✓
Following IPT initiation, patients asked to return to the HIV clinic each month for **monitoring** of side effects, self-reported adherence, and IPT refill	✓	✓
Nurses provided with training and mentorship on IPT using a **clinical algorithm**		✓
Family enrollment form used by health workers to identify family members eligible for IPT		✓
Health workers supported to **review monitoring data** on IPT initiation and adherence during monthly multidisciplinary team meetings		✓
Patients provided with **health education** by peer educators using an IPT treatment literacy flipchart		✓
Patients provided with reimbursement for **transportation costs** associated with monthly clinic visits		✓
Patients provided with a **cellphone** and **airtime vouchers**		✓
Patients provided with real-time adherence support by **peer educators** and through the use of **IVR messages**		✓

Tablets were used to register patients in the IVR messaging system.

Study Methods

Clinic data were abstracted on all patients who enrolled in HIV care at the 10 study sites between January 2013 and November 2015. These data were used to measure IPT initiation, IPT completion, and retention in care across the study's two arms. A measurement cohort was also recruited, consisting of 316 HIV-positive patients newly initiating IPT across the study sites. Each participant in the measurement cohort was administered a questionnaire at seven to 10 points in time: at enrollment, at monthly intervals throughout the six-month course of IPT, and at IPT completion (if treatment was completed). These patients also received unannounced phone calls, asking them to count their remaining number of pills. Questionnaire and pill count data were used to assess adherence to IPT (and ART, if applicable) and drug-related side effects. To assess the acceptability of the intervention, key informant interviews were conducted with a sample of nurses, peer educators, and patients from ENRICH intervention sites.

Key Findings

Key characteristics of the 828 IPT-eligible patients newly enrolled in HIV care at the 10 health facilities across the study's two arms are summarized in Box 2.

Effectiveness of the ENRICH Intervention Package

- IPT initiation among patients newly enrolling in HIV care during the ENRICH study was higher than that prior to the study period; however, there was no difference in IPT initiation by study arm.
- IPT completion among ENRICH study participants was high; however, there was no difference in IPT completion by study arm.

Acceptability of the ENRICH Intervention Package among Nurses and Peer Educators

The ENRICH intervention package was well-received and deemed useful by both nurses and peer educators. They reported feeling empowered to promote IPT with patients and felt that patients' adherence to their overall care plan improved. Specific themes that emerged from the key informant interviews include:

- Both nurses and peer educators felt the trainings prepared them with comprehensive knowledge about IPT. Further, nurses reported that the training came at an opportune time because they had been encouraged to promote IPT, but did not feel they had sufficient knowledge to do so.
- Nurses and peer educators found the job aids to be very useful: nurses reported routinely referring to the laminated clinical algorithm to assess patient eligibility for IPT and monitor patients' treatment, and peer educators found the IPT patient literacy flipchart to be instrumental in guiding their patient education and counseling sessions. Many peer educators had not received such detailed information prior to taking IPT themselves, and recognized the importance of targeted patient education in promoting IPT awareness among people living with HIV.
- Both nurses and peer educators felt they had developed a positive, complementary working relationship with one another. Nurses appreciated the ability of peer educators to share their own IPT-related experiences with patients and felt relieved of some of their patient education responsibilities. Peer educators, on the other hand, embraced their new position as role models affecting positive change in the lives of their peers. They were grateful for being treated as active partners in health service delivery and felt supported and appreciated by clinic nurses.
- Health workers found that patient and provider access to cell phones facilitated the timely triage and resolution of patient questions and concerns, and made it easier to track patients at risk of being lost to follow-up.

BOX 2: Summary of Patient Characteristics

- Mean age at enrollment in HIV care was **34 years**
- **58 percent** were female and **42 percent** were male
- Among 717 patients with available data, **63 percent** had a CD4 count under 350 cells/mm^3 at enrollment

Notable challenges experienced by health workers and suggestions made to improve the intervention include:

- Nurses expressed concerns about the side effects of isoniazid and the impact concurrent administration of IPT and ART could have on patient adherence. As a result, they generally preferred to initiate patients on IPT at least one month after ART initiation to reduce the initial burden of pills and prevent the confluence of adverse effects.
- Health workers recognized that it would be difficult—due to resource constraints—to continue the provision of transportation reimbursement, phones, airtime, and IVR calls to patients on an ongoing basis. In addition, some suggested that the transportation reimbursements could create a sense of dependency among patients and negatively impact their retention in care once such reimbursements were no longer available. Some suggested that peer-based training, education, and counseling might be a more sustainable strategy over the long term.

"Patients take many medicines. They say, 'I don't have TB, why are you giving me this medicine?' So we educate them, saying that this medicine is given to patients who have no TB symptoms to prevent TB in the future. We also tell them that if you get TB, your body's ability to protect against disease will decrease. After knowing this, they decide to start [IPT]."

Nurse at a health facility
implementing the ENRICH intervention

"[Being a peer educator] has changed a lot for me. I had been hiding myself before this program, but now I am educating people."

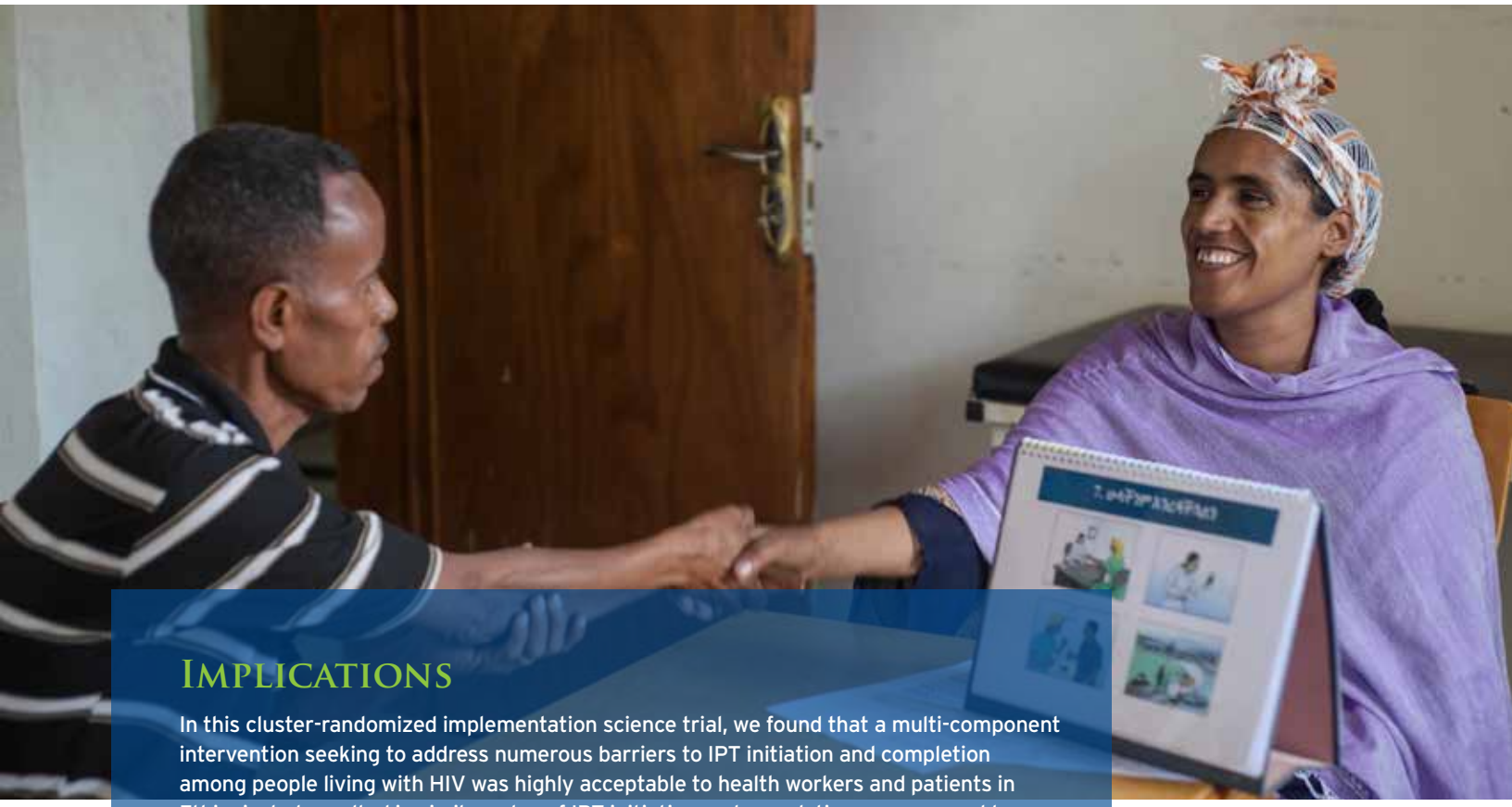
Peer educator at a health facility
implementing the ENRICH intervention

Acceptability of the ENRICH Intervention Package among Patients

Patients found the ENRICH intervention package to be highly acceptable. In particular, patients appreciated the:

- Focus on TB prevention within the context of HIV care
- Clear information provided during treatment literacy sessions, using a flipchart that provides visual reminders of key messages
- IVR messages reminding them to take their medicines each day and attend their clinic appointments each month
- Access to transport reimbursements (which alleviated some of their financial hardships) and airtime (which ensured access to ongoing health worker support)
- Empathy received from peer educators, as well as the opportunity to learn from their lived experiences
- Respectful and non-judgmental attitudes of health workers, which helped compensate for the stigmatizing attitudes and lack of social support many experienced at home

The intervention appeared to mitigate patients' experience with stigma due to the promotion of peer-based support, attention to confidentiality and empathic caregiving, and provision of phones that allowed for phone-based consultations (thus reducing patients' visibility at clinics). However, among patients who had not yet disclosed their HIV status to their partner and/or close family members, the phone and IVR calls tended to elicit unwanted attention. In these cases, patients often avoided potentially stigmatizing situations by turning the phone off for prolonged periods of time.



A peer educator begins a counseling session using the IPT treatment literacy flipchart.

Implications

In this cluster-randomized implementation science trial, we found that a multi-component intervention seeking to address numerous barriers to IPT initiation and completion among people living with HIV was highly acceptable to health workers and patients in Ethiopia, but resulted in similar rates of IPT initiation and completion as compared to standard of care study sites. It is possible that the presence of study staff—who were trained nurses—at health facilities participating in the study may have influenced health worker performance, resulting in higher rates of IPT initiation at standard of care sites than would have been seen outside of a study setting. Additionally, study staff closely followed participants in the measurement cohort, which may have resulted in increased IPT completion rates at standard of care sites. It is also possible that participants at ENRICH intervention sites did not receive sufficient exposure to the intervention package to impact IPT initiation and completion.

Based on these findings, use of enablers—including cellphones, airtime vouchers, and reimbursement of transportation costs—cannot be recommended as strategies to improve IPT initiation and completion among people living with HIV. Enhanced monitoring and evaluation of IPT implementation, however, may be sufficient to increase health worker focus on this important measure to prevent TB among people living with HIV.

ABOUT ICAP

ICAP was founded in 2003 at Columbia University's Mailman School of Public Health. Now a global leader in HIV and health systems strengthening, ICAP provides technical assistance and implementation support to governments and non-governmental organizations in more than 21 countries. ICAP has supported work at more than 5,249 health facilities around the world. More than 2.5 million people have received HIV care through ICAP-supported programs and over 1.7 million have begun antiretroviral therapy.

Online at icap.columbia.edu

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