Safe Generations

Harnessing Implementation Science to Assess the Impact of Option B+ in Swaziland

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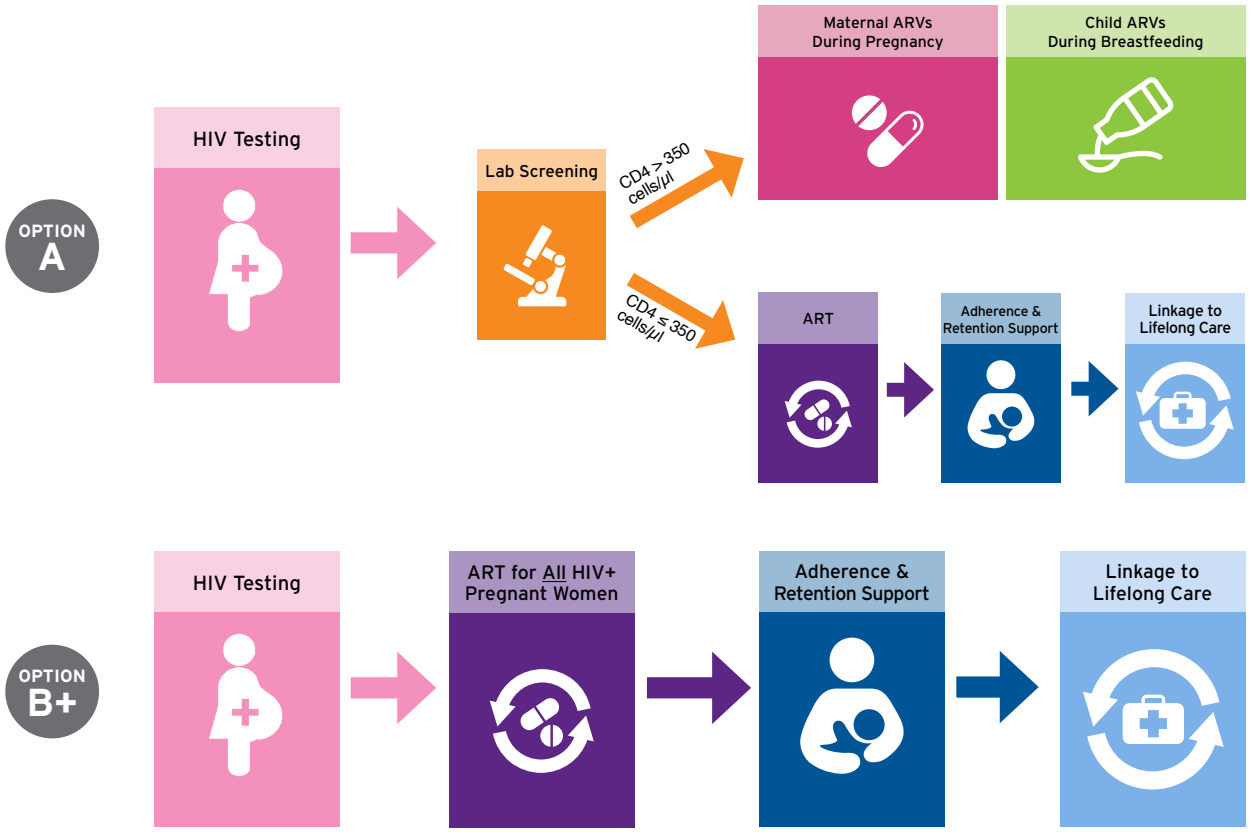
Background and Rationale

In 2015, the World Health Organization (WHO) endorsed universal treatment for all people living with HIV. Now the global community is striving to reach three ambitious targets by the year 2020: 90 percent of all people living with HIV will know their HIV status, 90 percent of those diagnosed with HIV will receive sustained antiretroviral therapy (ART), and 90 percent of people receiving ART will achieve viral suppression.

Option B+, an approach that calls for all HIV-positive pregnant women to initiate lifelong ART, was the first global effort at universal treatment, with the aim of preventing mother to child transmission of HIV (PMTCT). Recommended by WHO in 2013, the Option B+ approach represented a marked shift from treating pregnant and breastfeeding women with ART only if eligible to treating *all* HIV-positive pregnant and breastfeeding women with ART (regardless of their CD4 count).

The global shift toward Option B+ presented an opportunity for the Kingdom of Swaziland, a country at the epicenter of the HIV epidemic. Swaziland has just over 1.2 million inhabitants and, in 2013, an estimated 10,000 HIV-positive women delivered babies in the country and 1,100 children were newly infected with HIV.[1] Swaziland had been implementing a more complex PMTCT approach since 2010, Option A, which calls for HIV-positive pregnant women to receive different antiretroviral regimens before birth, during delivery, and postpartum, as well as based on their health status (with some women receiving lifelong ART and others receiving antiretroviral prophylaxis). This approach (see Figure 1) was contributing to treatment delays during a time when each week on treatment can result in substantially increased protection for the baby and mother. While 91 percent of the pregnant women who received antenatal care in Swaziland were tested for HIV in 2011, only 35 percent of those eligible for lifelong ART actually initiated treatment during pregnancy.[2] As Option B+ had the potential to streamline care and increase ART uptake for HIV-positive pregnant women, Swaziland's Ministry of Health was eager to assess the approach's impact, feasibility, acceptability, and cost-effectiveness in public health facilities. Results from a study examining these issues in Swaziland could also inform the implementation of Option B+ throughout sub-Saharan Africa and, equally important, the development of new guidance for universal treatment of *all* people living with HIV.

Figure 1: Comparison of the PMTCT Care Cascade under Options A and B+



[1] UNAIDS. The Gap Report. 2014.
[2] Swaziland Ministry of Health. PMTCT Programme Annual Report. 2011.

Figure 2: Location of Safe Generations Study Sites

Study Overview

From August 2013 to May 2016, ICAP collaborated with Swaziland's Ministry of Health and the University of Cape Town to conduct an ambitious implementation science study called Safe Generations or, in Siswati, *Sitkulwane Lesiphephile*. The study, which was supported by the United States (U.S.) President's Emergency Plan for AIDS Relief (PEPFAR) and the U.S. Agency for International Development (USAID), aimed to evaluate the impact of Option B+ on maternal retention and mother-to-child transmission of HIV, as well as the approach's feasibility, acceptability, and projected costs and cost-effectiveness.

Study Design

To study Option B+ in real-life conditions, 10 public health facilities in Swaziland's Manzini and Lubombo regions were selected to transition standard PMTCT services from Option A to B+ (see Figure 2). The transition took place over a 10-month period, with a different health facility receiving intensive support from study staff to make the transition each month (see Figure 3). This "stepped-wedge" study design allowed outcome measures to be compared before and after the transition to Option B+ at each health facility and across all study sites. Two additional health facilities, which were chosen as control sites, continued to provide standard PMTCT services according to Option A throughout the study period.

Figure 3: Stepped Transition of Study Sites from Option A to B+

	2013					2014					
	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR (1)	MAR (2)	APR	MAY
Siteki Public Health Unit	A	T	B+	B+	B+	B+	B+	B+	B+	B+	B+
Médecins Sans Frontières Matsapha Clinic	A	A	T	B+	B+	B+	B+	B+	B+	B+	B+
Lamvelase Clinic	A	A	A	T	B+	B+	B+	B+	B+	B+	B+
Siphofaneni Clinic	A	A	A	A	T	B+	B+	B+	B+	B+	B+
Raleigh Fitkin Memorial Hospital	A	A	A	A	A	T	B+	B+	B+	B+	B+
King Sobhuza II Public Health Unit	A	A	A	A	A	A	T	B+	B+	B+	B+
Mankayane Public Health Unit	A	A	A	A	A	A	A	T	B+	B+	B+
Luyengo Clinic	A	A	A	A	A	A	A	A	T	B+	B+
Family Life Association of Swaziland Manzini Clinic	A	A	A	A	A	A	A	A	A	T	B+
Mbikwakhe Clinic	A	A	A	A	A	A	A	A	A	A	T
Mbabane Public Health Unit	A	A	A	A	A	A	A	A	A	A	A
Good Shepherd Hospital	A	A	A	A	A	A	A	A	A	A	A

KEY
A: Option A approach
B+: Option B+ approach
T: Month facility transitioned from Option A to B+

The Transition Process

ICAP designed a process to support health workers at the 10 participating health facilities before, during, and after the transition from Option A to Option B+. The process included the following components:

- ICAP held a series of **community dialogues**, in collaboration with the Ministry of Health, to sensitize local communities to the introduction of Option B+. As part of this effort, easy-to-understand Option B+ pamphlets and posters were distributed at the 10 study facilities.
- ICAP provided relevant health workers at each facility with a **one-week intensive training** on the clinical procedures associated with Option B+, including same-day ART initiation, management of ART during pregnancy and breastfeeding, infant care, and early infant diagnostic testing. The training included mapping exercises to optimize the integration of HIV, ART, and maternal and child health services, and introduced a new Option B+ counseling flipchart to enhance health workers' knowledge and guide their communication of new protocols to clients.
- An **ICAP mentoring team**, made up of one nurse and one specialist in adherence and psychosocial support, worked side-by-side with each facility's health workers throughout the first month following transition to Option B+, providing continuous guidance and working collaboratively to troubleshoot issues as new clinical procedures and patient flow systems were implemented. Following this month-long period of intensive mentorship, the mentoring team visited the health facility every two weeks to support clinical staff and provided periodic refresher trainings to reinforce key concepts and address new issues as they arose.
- In April 2015, ICAP coordinated a **central review meeting** that brought together representatives from all 10 health facilities implementing Option B+ to discuss implementation challenges and successes, and to exchange ideas about what optimal implementation of Option B+ might look like (see Box 1). After the central review meeting, ICAP facilitated **follow-up workshops** at each participating health facility to review site-level data, consider findings from the central site review meeting, and discuss site-level successes, challenges, and best practices in Option B+ implementation.

Box 1. Best Practices for Implementing Option B+

Because the 10 participating health facilities varied in size, location, patient volume, and services offered, there were also variations in the way facilities implemented Option B+. Best practices identified at the central review meeting include:

- Introducing an appointment register for postnatal visit follow-up so maternal and infant visits can be scheduled concurrently
- Setting aside dedicated time to review and complete patient registers and files when client load is less intense (e.g., in the afternoon)
- Ensuring peer health workers, such as mothers2mothers Mentor Mothers, are integrated into the HIV care team to alleviate some of the counseling and follow-up work of nurses
- Fast-tracking PMTCT clients who arrive at the clinic with a male partner to increase the number of men accessing HIV services

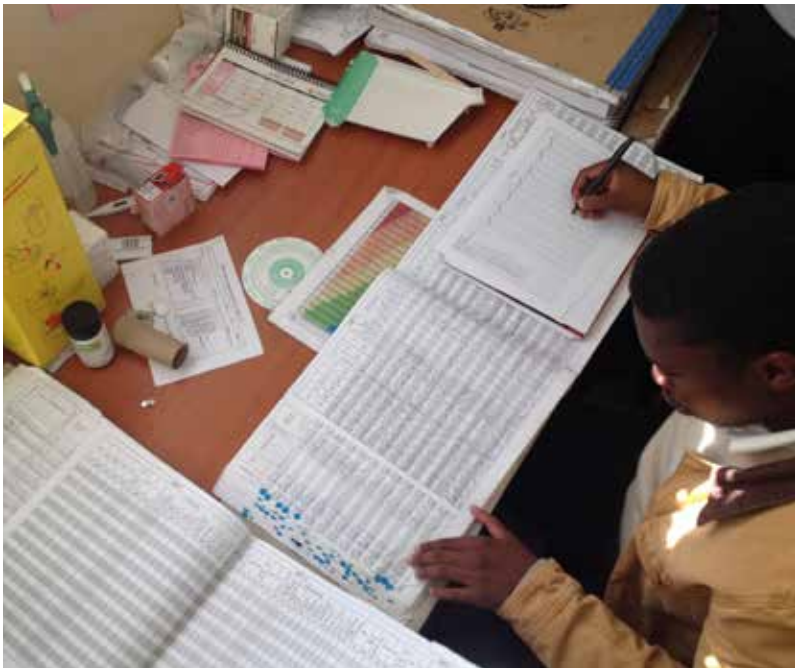
Study Methods

The Safe Generations study sought to evaluate maternal retention and mother-to-child HIV transmission outcomes as routine service delivery transitioned from Option A to B+. The study team relied primarily on routinely collected clinical data, which were abstracted from clinic registers and patient files. Clinical and laboratory data were abstracted on each woman who enrolled in PMTCT services (and her child) between August 2013 and August 2014 at the 12 participating health facilities, with abstraction beginning upon enrollment in PMTCT services and continuing through six months postpartum. The research team conducted semi-structured interviews with 50 health workers at several points in time to evaluate the acceptability and feasibility of Option B+, and six focus group discussions were held to gain even deeper insight into the acceptability—from the health worker's point of view—of the experience of transitioning to universal treatment for HIV-positive pregnant women. The study team also collected cost data from five health facilities to calculate the total cost and incremental cost-effectiveness of Option B+, compared to Option A.

Ensuring Local Ownership and Fostering Collaboration

ICAP sought to maximize local ownership of the Safe Generations study by collaborating with Swaziland's Ministry of Health to conceptualize the study's design and select the 12 health facilities that served as the study's intervention and control sites. In addition, the Ministry of Health's National PMTCT Coordinator and National ART Coordinator served as study co-investigators, guiding the study's development and implementation. In 2013, a Study Advisory Group co-chaired by ICAP and the Ministry of Health was created to bring together relevant stakeholders, including USAID and local PMTCT implementing partners, to review the study's progress each quarter and discuss implementation challenges.

ICAP also collaborated with The Elizabeth Glaser Pediatric AIDS Foundation (EGPAF), whose regional health mentors contributed to the continuous clinical mentoring of health workers throughout the study. In addition, ICAP collaborated with mothers2mothers, whose facility-based Mentor Mothers made critical contributions to counseling and tracking patients. The work was also supported in part by the donation of antiretrovirals by Merck and Gilead.



A data manager reviews a clinic register at a Safe Generations study site.

A Safe Generations researcher practices using the new Option B+ counseling flipchart.

Key Findings

Key characteristics of the 2,347 HIV-positive women who enrolled in PMTCT services at the 12 participating health facilities during the study period are summarized in Box 2.

Effectiveness of Option B+

- A significantly higher proportion of women initiated ART under Option B+ compared to Option A, resulting in more than **twice the number of women on ART.**
  - **Ninety-four percent of all pregnant women** entering PMTCT services initiated ART under Option B+, compared to only **36 percent** under Option A.
  - **Eighty-six percent** initiated ART at the first antenatal care visit under Option B+.
  - **Ninety-four percent** of women with a CD4 count ≤350 cells/μL (the national threshold for initiating ART at the time) initiated ART under Option B+, compared to **67 percent** under Option A.
- A significantly higher number of women were retained under Option B+ than under Option A, resulting in **one and a half times** as many women staying in PMTCT care from the first antenatal visit through six months postpartum.
- Overall retention in care among PMTCT clients during the **antenatal period** was sub-optimal (1,608 women or 68% retained), with a significantly higher proportion (74%, 775 women) retained under Option B+, compared with only 64 percent (833 women) retained under Option A.
  - Among women **who initiated ART**, the total number retained during the antenatal period was **more than two times** greater under Option B+, but antenatal retention was proportionally higher under Option A (342 women retained, or 89%) than under Option B+ (750 women retained, or 77%).
- Overall retention in care among PMTCT clients during the **postnatal period** was very low (41%), although it was substantially higher under Option B+ (584 women retained, or 56%) compared with only 382 women (29%) retained under Option A.
  - Among women **on ART**, over **one and a half times** as many were retained during the postnatal period under Option B+ compared with Option A. Similar to antenatal retention, the proportion of Option A women retained was modestly higher (337 women retained, or 72%) than under Option B+ (583 women retained, or 59%).
- Of the 2,347 pregnant women in the study, health workers at the study facilities were able to identify and link **1,273 infants (54%)** back to their mothers.

Box 2. Summary of Patient Characteristics

- 55% received PMTCT according to Option A and 45% received PMTCT according to Option B+
- Mean age at enrollment was 26 years
- Median gestation at enrollment was 20 weeks
- 51% were newly diagnosed with HIV
- 34% had a CD4 count of 350 cells/μL or less at enrollment
- Median CD4 count at enrollment was 404 cells/μL

As might be expected, women with linked infants were more likely to themselves be retained in care antenatally and postnatally.

- Among the 1,237 infants who received virological testing and a valid test result, 38 tests were positive (3% overall), with no differences between Options A and B+.

In response to these findings, ICAP is conducting a supplemental study called Safe Generations Plus, with funding from the U.S. National Institutes of Health. This study is actively tracing the women lost to follow-up during the Safe Generations study to determine the specific reasons they were not retained.

Acceptability of Option B+ among Health Workers

Health workers—including nurses, peer counselors, and expert clients—generally viewed Option B+ as both an acceptable and feasible approach to PMTCT. Two years after the transition, 80 percent reported that Option B+ was easy to explain and coordinate, and that immediate ART initiation reduced delays resulting from previously necessary tests and visits. Further, over half of the heath workers reported ease of patient follow-up, documentation, and counseling after two years of implementing universal ART in the maternal and child health clinic. On the other hand, health workers consistently reported increased workload under Option B+, including work associated with patient monitoring, counseling, and appointment scheduling and tracking. Health workers also reported barriers to same-day ART initiation that resulted from patient concerns about disclosing their HIV status to family members and not having enough time to prepare mentally to start lifelong ART.

"There are no criteria; as long as she is pregnant and positive, you start ART. Sometimes test results cause delay, so this makes it easier."

-Health worker at facility implementing Option B+

Economic Evaluation of Option B+

Overall, findings from the economic evaluation suggest that there is a strong economic case in favor of the Option B+ approach in Swaziland. Cost-effectiveness was estimated from the provider's perspective (which considers the cost of providing the services) in terms of the cost per woman retained in care during pregnancy and six months postpartum. Specific findings include:

- Across the five sites included in the economic evaluation, the **total cost** for PMTCT during the study period was **$868,426**[3] under Option B+ and **$680,508** under Option A.
- The **cost per woman treated per month**, which includes recurrent costs (personnel, overhead, drugs, and diagnostic tests) and capital costs (buildings, furniture, start-up costs, and training) was **$183** for a woman on ART under Option B+ (**$174** if on AZT) and **$127** and **$118** for a woman on ART and AZT, respectively, under Option A. The **weighted average cost per woman** treated under Option B+ was **$826**, compared to **$525** under Option A. The main cost drivers were the start up-costs, increased training, and staff time spent on PMTCT tasks under Option B+.
- Considering the **25 percent** difference in maternal retention between the two approaches in favor of Option B+, **the incremental cost-effectiveness ratio** was estimated at **$949**. This means that, under the Option B+ approach, it cost $949 for every additional mother retained to six months postpartum. This is well below Swaziland's 2015 per capita gross domestic product of **$3,068**, which suggests that Option B+ is highly cost-effective for Swaziland.

Implications

In this large, stepped-wedge implementation science study—the first of its kind in the Kingdom of Swaziland—ICAP found that universal ART for HIV-positive pregnant and breastfeeding women (Option B+) is an acceptable and feasible approach to preventing new child HIV infections. It also found that Option B+ results in a significantly higher proportion of HIV-positive pregnant women initiating ART and being retained in long-term HIV services. The findings from this study are particularly timely as the Kingdom of Swaziland and other countries in Africa prepare to adopt new global guidance for universal treatment of all people living with HIV.

The Safe Generations study provided a unique platform for implementing Option B+ and generated important experience regarding how best to transition PMTCT services from selective to universal treatment. Health workers found universal treatment to be easier, simpler, and faster to implement, leading to improvements along the PMTCT cascade. While overall retention rates across the antenatal and postnatal periods were suboptimal, starting women on ART was associated with improved retention, which can be expected to translate into better long-term health outcomes. At the same time, study findings suggest that rapid increases in the number of individuals on ART can result in challenges for health workers and jeopardize the quality of care. In the context of universal treatment, it will be critical to ensure that clinics are adequately resourced to manage higher patient volumes and that innovative approaches to monitoring and managing HIV disease are adopted to decrease the burden on health facilities and health workers.

The Safe Generations study identified several gaps worthy of attention. As mentioned, overall retention rates in PMTCT services were low (particularly postpartum) and understanding why women do not stay in care at the health facilities where they obtain antenatal services is an urgent concern. Additionally, linking babies and mothers at the health facility was extremely challenging, making it difficult to accurately assess HIV transmission and other health outcomes among children. This is a common phenomenon across much of sub-Saharan Africa and highlights the need to implement systems to link mothers and babies in care and monitor outcomes at the individual and national level.

Option B+ was the first intervention through which universal ART was implemented and the Safe Generations study offered a world-class opportunity to understand its implementation and impact. Findings demonstrated that a universal treatment approach leads to dramatically higher numbers of people starting treatment, but does not diminish the critical challenge of keeping clients engaged in treatment over time. As nations move toward implementing universal treatment for all people living with HIV, the focus of researchers and policymakers must shift toward identifying strategies to reliably increase patient engagement in long-term care, the next great obstacle to ending the epidemic.

[3] All costs expressed in U.S. dollars.

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 5,200 health facilities around the world. More than 2.2 million people have received HIV care through ICAP-supported programs and over 1.3 million have begun antiretroviral therapy.

Online at icap.columbia.edu

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