**Objectives of the cost analysis**

The overall objectives of this costing component are:

* To construct and validate mathematical models to estimate the impact of PrEP on HIV transmission at population level in South Africa
* To assess the incremental costs of PrEP combined with adherence support interventions
* To estimate the cost-effectiveness and budget impact of targeted PrEP initiation and compare standard practice to the following three strategies for adherence support:
  + Through group-based community health clubs
  + Through individual-based one-on-one counseling
  + Through medication provision only (control arm)

**Study Location and Description**

This study will be conducted in King Williams town (rural site) and East London (urban site) in Buffalo City Municipality, Eastern Cape Province. Buffalo City Municipality has approximately 700,000 inhabitants. The general population HIV prevalence in the districts is 14% and antenatal HIV prevalence of 31.2%, above the national average of 29.7%[*SOURCE 2 IN PROTOCOL*]. The Foundation for Professional Development (FPD) implemented its Community-Based Counselling and Testing (CBCT) programme in the district; from October 2015-September 2016, FPD tested 49,911 individuals (68.5 per 1000 population) in Buffalo City Municipality.

FPD’s Community-Based Counselling and Testing (CBCT) platform is currently being implemented in 22 high-burden sub-distracts/local municipalities in South Africa. The CBCT program targets priority populations in the identified sub-districts through strategic mobilization efforts and targeted HIV testing and counselling (HTC) interventions. The programme achieves this by providing HIV testing services through mobile units, systematic door-to-door home-based, workplace, index patient training, key population (KP) outreach (a.k.a twilight) and the provision of self-testing kits. PrEP initiation nurses and research assistants will be integrated into these CBCT teams for the recruitment and enrollment of participants into the study.

The sample of enrolled participants may be divided into three sub-groups: *Immediate PrEP Acceptors, Early PrEP Acceptors, and Delayed PrEP acceptors.* Immediate PrEP Acceptors will enroll in the study immediately upon consenting to participation in the study. Early PrEP Acceptors will return within 14 days of initial offering and will be enrolled in the study following another confirmed negative HIV test. Delayed PrEP acceptors will return after 14 days and will be enrolled in the study following another confirmed negative HIV test, as well as a repeat of the baseline survey.

The study consists of two intervention arms, group-based Community Health Clubs (GCHCs) and Individual Adherence Support (IBAS), and a control arm consisting of passive adherence support. The study leverages extensively researched theory for improving medication adherence and incorporates these principles into both group and individual learning sessions. These learning sessions will provide participants with information about PrEP, define problems impacting adherence, generate alternative solutions, make decisions about the alternatives, and collaboratively decide on a plan regarding how to implement the solution.

Young women will remain in the study for a maximum of 24 months from the date of enrolment.

**Measuring Costs**

This evaluation is intended to influence the delivery of such health services from the perspective of the Department of Health in South Africa, thus will incorporate costing information specific to scaling up the program nationally. This cost analysis will include the financial costs for all activities and inputs used to implement the study, as well as include an economic component that incorporates costs of resources that may have been either donated or shared with existing government health services that were leveraged in the implementation of this study. Overhead costs and expenses that have been spent and used for research such as building infrastructure, maintenance, and building expense will be omitted from the total costs. This analysis will particularly focus on the value of all resources used to achieve the project outputs and health outcomes.

Activity-based costing will be used to identify the main activities, resources, and specific inputs used to support each main activity from all sources contributing to the intervention (project and government). Data collection will begin by listing all of the main activities associated with each component from the Manual of Procedures (MOP) and listing the specific resources and inputs used at different stages of implementation of the study.

This analysis will account for costing data through both expenditure and ingredients approaches. The expenditure approach utilizes budgetary and expense reports from implementing agencies. As these reports are limited in their costing breakdown, the ingredients approach is a useful supplement. The ingredients approach will meticulously outline the quantities and prices of all inputs. For specific labor components, follow-up interviews and/or surveys will be used to estimate the amount of time personnel devoted to the project.

Some components of the time and motion study can be captured using the REDCap software. REDCap has the capacity to provide crude reports of the time each patient survey takes. Staff surveys and interviews will complement this data, offering insight as to what portions of services are applicable only to the research component of the study. For example, time-intensive components such as obtaining consent for research and communication with project managers can be accounted for in REDCap data following this supplemental data collection.

While certain budgetary components for this study are not relevant to the costing objective of providing data for scaling-up this intervention (i.e. international travel fees, research unit overhead), not all this information is omitted. This analysis will function as a comprehensive costing report of all research activities. Additionally, costs relevant only to components of the intervention that may be scaled up will be stratified out as well.

**Sampling strategy**

**\*Needs to be developed**

*Cost data collection: time and motion*

During the project implementation stage, we will conduct visits to oversee each unique component of the study, of which there are six separate components. In this study, PrEP initiation may result from four unique services: systematic home-based HTC, index patient HTC, mobile HTC, and workplace HTC. Time and motion data collection will be conducted for each of these services. Additionally, time and motion data collection will be conducted during the group-based community health club and individual-based one-on-one counseling adherence support phases of the study.

***Start-up costs***: This section will include program development costs. These include (but are not limited to) costs necessary to mobilize efforts within the community, interviewing, hiring, and training of staff and advertisements

***Materials and Supplies:*** This section will include computers and technological supplies, specimen collection and testing kits, medications, and printing, and refreshments (for participants taking part in the in-depth interview portion of the study). A more detailed breakdown of these costs can be found in TABLE 1.

**Travel Costs:**

*International Travel:* This section will include costs from each year of the project for research personnel to travel to project sites and to advise on study development and review progress. Costs will include international airfare, lodging, and taxi allowance.

*Local Travel:* This section will include the vehicle rental, vehicle purchases, and costs associated with fuel consumption.

***Contact Costs***: This section will include health worker time that is both directly and indirectly involved with this costing analysis. This will be done through defining the number of health workers involved in specified activities and obtaining an estimate of their time for each activity. Their time will be valued by obtaining information on their salaries and getting a common measure of cost per unit. Information on time allocation will be obtained primarily through time and motion studies conducted in the field. Secondary measures will include interviews with staff to determine full time equivalent time that is used in each phase of the intervention. Alternatively, the survey software, REDCap, provides data on the time spent per study unit/ patient. Such data will supplement the recall of the workers as well as data from the time and motion studies.

***Training Costs*:** This section will include project-specific training that will be provided to the team members working on the project at project initialization and whenever a need arises. . These costs include rental of venues, light catering for the training events, and printing materials. The *Contact Costs* for research staff salary grade/time is not counted in this section.

***Other Direct Costs*:** This section will include a range of miscellaneous costs that may be incurred during startup, the intervention, or both. These costs include participant reimbursements, ADP/ computer services, office rental and renovations, translation and transcription, specimen transport, and report writing and dissemination.

Expenditure reports will be obtained from project expense reports. In addition, data collection tools will be developed for capturing resources and costs incurred at various points of implementation.

**TABLE 1**

|  |  |  |
| --- | --- | --- |
| **Data Type** | **Source** | **Collection Methods** |
| **Start-up Costs (*Intervention specific)***   * Project/program micro-planning * Hiring staff * Development of training materials * Development of project documents (Protocol, MOP, etc.) * Software development * Clinic arrangements and meetings * Hiring advertisements * PrEP awareness advertisement campaign | FPD budgets and GLs  Facility level data  Organization level data | Interviews with facility staff  Interviews with FPD staff  Budget expense reports  Project Expense reports |
| **Start-up Costs *(Research Specific)***  -Program development  -Software development | FPD budget and GLs  Organization level data | Interviews with FPD staff  Budget expense reports  Project expense reports |
| **Contact Costs1(*Intervention specific)***  -Salary grade/time of PrEP Initiation Nurses  - Salary grade/time of PrEP Initiation Research Assistants  - Salary grade/time adherence support nurses  - Salary grade/time adherence support counselors  *-*Salary grade/time of FPD staff | FPD budgets and GLs    Organization level data | Budget expense reports  Project Expense reports  Interviews with FPD staff  Time and motion observations |
| **Contact Costs (*Research Specific)***  - -Salary grade/time of FPD staff | FPD budget and GLs  Organization level data | Interviews with FPD staff  Budget expense reports  Project expense reports |
| **Travel Costs (*Intervention Specific)***  -Car Rentals  -Petrol | FPD budgets and GLs    Facility level data | Budget expense reports  Project Expense reports  Facility level interviews |
| **Travel Costs *(Research Specific)***  -Accommodation  -Per Diem for key personnel  -Air travel (including return)  -Taxi fare | FPD budgets and GLS | Budget expense reports  Project Expense reports |
| **Materials & Supplies Costs (*Intervention specific)***  -Computer tablets  -Voice recorders  -Fingerprint scanners  -Handheld barcode scanners  -Earphones  -Specialized backpacks  -Qualitative analysis software  -Filing cabinets  -HIV test kits  -Pregnancy test kits  -STI testing kits  -Creatine Clearance Testing (CrCL) testing kits  -Medications  -Printing of questionnaires, project materials | FPD budgets and GLs | Budget expense reports  Project Expense reports |
| **Materials & Supplies Costs *(Research Specific)***  **-**Office supplies  -Printing of office supplies | FPD budgets and GLs | Budget expense reports  Project Expense reports |
| **Training Costs (*Intervention specific)***  -Venue rental  -Venue catering  -stationary and printing  \*FPD training time in Contact Costs | FPD budgets and GLs  Facility level data | Budget expense reports  Project Expense reports |
| **Training costs *(Research Specific)*** |  |  |
| **Other Direct Costs (*Intervention Specific****)*  -Participant reimbursement vouchers  -ADP/ Computer services (Airtime and 3G for staff cell phones)  -Office rental and renovations (including furniture)  -Translation of participant questionnaires  -Transcription of recorded interviews and focus groups  -Specimen Transport  -Fingerprint scanner registration  -Medical Waste Collection | FPD budgets and GLs  Facility level data | Interviews with FPD staff  Budget expense reports  Project Expense reports |
| **Other Direct Costs *(Research Specific)***  -Consultant Fees | FPD budgets and GLs  Facility level data | Budget expense reports  Project Expense reports |
| **Patients:**  Travel time  Financial burden (Transportation time, child care, and out-of-pocket expenses) | Client interviews  Literature estimates | Surveys and key informant interviews |

**Measuring Impact:**

Measuring impact

The outcome measurement of the project is the number of infections averted through the program interventions; the difference in the number of infections that occurred during the program and the number of infections that would have occurred without the intervention. The benefits of the intervention are expected to come through 1) an increase in coverage of PMTCT due to community activities and also from POC CD4 testing; and 2) use of a more effective treatment regimen of Option A in lieu of sdNVP for women with CD4>350. The estimated infections averted will be based on a number of assumptions regarding project coverage and uptake of the PMTCT service cascade.. The measurement of intervention effectiveness will be by DNA PCR testing of infants at six weeks of age and HIV rapid tests at 9 months for those who tested negative at 6 weeks and may have seroconverted during this time and for newborns that missed the DNA PCR test at 6 weeks. The project will provide PCR testing to all infants born to HIV positive mothers who turn up for the six weeks immunization visit and will prove antibody testing at 9 months to all infants that show up for the 9 month immunization visit.

***Estimating number of infections without intervention:***

This highlights low coverage along the PMTCT cascade and treatment consisting of sdNVP only through labor. This will be estimated using MOHCW records prior to the program initiation for expected number of pregnancies in the program cachment area, historical coverage at ANC, and ANC HIV prevalence rates. The calculation will use World Health Organization (WHO) transmission rates of infants born to mothers with no PMTCT treatment and the rate of transmission of those who received sdNVP including transmission that would occur through 9 months of breastfeeding as Zimbabwe has a high rate of breastfeeding.

*Number of expected births to HIV positive women =# of expected births in cachment area\*Provincial HIV prevalence*

*Expected # of infants infected by women without PMTCT = # of expected births to HIV+ women\*(1-previous coverage of ANC)\*transmission rate of no PMTCT with breastfeeding through 9 months.*

*+*

*Expected # of infants infected by women with sdNVP = # of expected births to HIV+ women\*(previous coverage of ANC)\*(1-rate on ART)\*transmission rate of sdNVP with breastfeeding through 9 months.*

*+*

*Expected # of infants infected by women on ART = # of expected births to HIV+ women\*(previous coverage of ANC)\*(rate on ART)\*transmission rate of ART with breastfeeding through 9 months.*

***Estimating number of infection with intervention:***

This will incorporate a difference in coverage of PMTCT and the additional benefit of a more effective PMTCT regimen of Option A through breastfeeding and prophylaxis for the infants. The number of infant infections with the intervention will use a mix of results found in the data from the program and modeling. We will then use the WHO transmission rate corresponding to no PMTCT to estimate the number of HIV infants in the out of coverage group. Transmission rates for infants will be calculated through analysis of infant test results. Sample sizes for different arms of treatment were calculated using EPI Info STATCALC and are as follows – sdNVP (n=239), Option A (n=129) and ART triple therapy (n=34). Expected number of pregnancies in the cachment will be the same as the estimate without intervention, and the HIV prevalence resulting in an equal number of expected HIV+ pregnancies.

Increase in ANC coverage of HIV positive women will measured by the difference in the expected number of women who would receive PMTCT without the intervention and the number of patients who received PMTCT from the data registers.

*Expected # of infants infected by women without PMTCT-will be calculated as the without intervention arm (coverage rate is anticipated to be higher)*

*+*

*Expected # of infants infected by women with sdNVP = # of expected births to HIV+ women\*(previous coverage of ANC)\*(1-rate on ART)\*(1-rate receiving OptionA)\*transmission rate of sdNVP with breastfeeding through 9 months.*

*+*

*Expected # of infants infected by women with OptionA = # of expected births to HIV+ women\*(previous coverage of ANC)\*(1-rate on ART)\*(rate receiving Option A)\*transmission rate of sdNVP with breastfeeding through 9 months.*

*+*

*Expected # of infants infected by women on ART = # of expected births to HIV+ women\*(previous coverage of ANC)\*(rate on ART)\*transmission rate of ART with breastfeeding through 9 months.*

***Estimating the number of infections without intervention:***

***Estimating the number of infections with intervention:***

**Cost analysis**

Data will be entered and analyzed in Excel to provide the total incremental costs of each intervention.

**Measuring program impact**

The goal of the program is to avert HIV infections through both increased PrEP initiation and adherence. This costing analysis will focus on the incremental costs incurred as a result of each intervention, beginning with the Community-Based Counseling and Testing and culminating at the primary endpoints outlined in the main study protocol. These endpoints will test for PrEP adherence using tenofovir diphosphate (TFV-DP) levels assessed among arms and compared at 3, 6, 12, 18, and 24 months.

Modeling of these program results will help to depict the difference in estimated number of HIV infections that would occur without the intervention, and/or that would occur with each unique arm of the intervention.

**Measuring cost effectiveness**

The cost effectiveness analysis will compare the incremental costs and benefits of the intervention compared to the status quo of current HTC in South Africa. The incremental cost effectiveness ratio (ICER) will be measured by the additional costs incurred through the intervention divided by the additional number of infections averted through the intervention (compared to the number of infections averted through no intervention).

This cost analysis will also provide information on the cost per young women initiated on PrEP, the cost per young women adhering to PrEP treatment at the 3, 6, 12, 18, and 24-month endpoints. Finally, we will provide information on the cost profiles of total costs by cost category.

**Timeline**

|  |  |  |  |
| --- | --- | --- | --- |
| **No** | **Activities** | **Expected Outputs** | **Timeline** |
| **1** | Finalize the economic evaluation protocol | Protocol developed | July 2018 |
| **1.1** | Finalize methodological approach | Methods described and approved | August 2018 |
| **1.2** | Modify interview guidelines or cost data questionnaires for both start up activities and on-going project activities | Guidelines and forms developed and/or revised | July-September2018 |
| **2.** | Collection information form project reports and project expense reports on start-up activities and costs. | Start-up cost data collected from project expense reports and entered into excel spreadsheet files. | July 2018-September 2018 |
| **3.** | Collect information from project report, project expense reports and facilities on recurrent operational costs | Information on recurrent operational costs collected | October 2018 |
| **3.1** | Collect time and motion information on PrEP initiation from each of the 4 HTC modes | Data collected at HTC phase | October  2018 |
| **3.1** | Collect time and motion information on PrEP adherence from each adherence support mode | Data collected at adherence support phase | October 2018 |
| **4.0** | Follow up on missing or necessary supplementary data | Self-reported surveys from staff in East London (or if return trip possible, self-observed data) | November 2018 |
| **5.** | Enter cost data into excel | - | October-November 2018 |
| **6.** | Conduct cost data analysis | Summary costs using spreadsheet-based cost model | October-November 2018 |