

**RAPID POINT OF CARE TESTING FOR SEXUALLY
TRANSMITTED DISEASES AND BACTERIAL VAGINOSIS IN
SOUTH AFRICA: COST ESTIMATION & BUDGET IMPACT
ANALYSIS**

By

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PART 0: PREAMBLE

PLAGIARISM DECLARATION

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DEDICATION

I dedicate my thesis to my parents and three sisters who have shown me great support and encouragement throughout this journey, to all my friends for their words of encouragement, and to God for making everything possible.

Abstract

Sexually transmitted infections (STIs) remain a global public health concern. Together with bacterial vaginosis (BV), the association with HIV acquisition through genital inflammation in women poses a challenge towards the control of HIV/AIDS, more so in asymptomatic cases. Diagnosis of asymptomatic women using a genital inflammation screening tool, the cytokine biomarker rapid test, reduces the cases of untreated women. However, as a newly developed screening tool, there are no prior cost estimates to advocate for its funding and implementation. This study estimated the costs of genital inflammation screening of women (15-49 years) and, assessed the budget impact of providing this screening service in primary health facilities in South Africa in 2016. This thesis is a sub-study of the GIFT project (Genital Inflammation Test for HIV Prevention) whose main objective is HIV prevention through improved control of sexually transmitted infections (STIs). The micro-costing approach was used to calculate the unit cost per patient screened from a provider's perspective at the Desmond Tutu HIV Foundation youth clinic (DTHF), and, the University of Cape Town Student Wellness Service (UCT SWS), over a 1 year period. The unit cost estimates were used to analyse the budget impact of scaling-up and providing the screening service in primary health facilities countrywide. Sensitivity analyses were carried out to determine the robustness of the study findings.

The results demonstrated that the cost per woman screened for genital inflammation was \$24.26 at DTHF and \$14.32 at UCT SWS. The scaled-up costs ranged from \$107,183,655 to \$183,062,066 in South Africa. The screening intervention accounted for a significant amount of the available funds. The cost estimates were sensitive to the personnel costs, clinic utilization rates and population coverage rates.

According to this study, it can be concluded that, the cost estimates of screening are high, and its implementation may not be affordable within the current budget. However, this screening

tool will increase the cases detected, contributing towards better STIs management and control.

Additionally, it will reduce the risk of HIV acquisition among women.

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List of Abbreviations

Abbreviation	Description
AIDS	Acquired Immune Deficiency Syndrome
BIA	Budget impact analysis
BV	Bacterial Vaginosis
CEA	Cost-effectiveness analysis
CRT	Chlamydia rapid tests
CSIR	Council for Scientific and Industrial Research
DTHF	Desmond Tutu HIV Foundation
FP	Family planning
GIFT	Genital Inflammation Test
HIV	Human Immunodeficiency Virus
NAAT	Nucleic acid amplification test
NGO	Non-governmental Organization
PID	Pelvic Inflammatory Disease
POC	Point of care
SA	South Africa
STIs	Sexually Transmitted Infections
TB	Tuberculosis
UCT	University of Cape Town
UCT SWS	University of Cape Town Student Wellness Service
USA	United States of America
USD	United States Dollar
WHO	World Health Organization
ZAR	South African Rand

PART A: PROTOCOL

1 INTRODUCTION

1.1 Background Information

Sexually transmitted infections (STIs) are a common cause of acute illness especially in developing countries. In the era of Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS), the prevalence of STIs has greatly increased. Worldwide, over 1 million sexually transmitted diseases are acquired each day. Annually, an estimated 499 million new cases of curable STIs (gonorrhoea, chlamydia, syphilis, trichomoniasis) occur in individuals aged 15 to 49 years (World Health Organization, 2013). STIs disease burden has become a major public health concern in a bid to control the HIV epidemic. Over the years, studies have explored the association between curable STIs and HIV, their role in the transmission of HIV infection and, as a result increased HIV prevalence. Among women, Bacterial Vaginosis (BV) is associated with STIs and other reproductive health complications (Woodman, 2016). The presence of STIs and BV has been found to increase the susceptibility of HIV acquisition. Among one of the causes for this is genital tract inflammation in women. STIs and BV cause genital tract inflammation in women putting them at high risk of HIV infection (Fleming and Wasserheit, 1999, Mayer and Venkatesh, 2011, Masson et al., 2015b).

In most developing countries like South Africa, STIs are diagnosed using a syndromic approach based on presumptive clinical diagnosis by a clinician and, through laboratory testing. Laboratory testing is both costly and dependent on skilled personnel. Due to resource constraints, most STIs are managed based on clinical diagnosis of STIs syndromes. Resource constraint settings are characterized by inadequate funds to cover for health care costs both at individual and societal levels, leading to limited availability and access to medical equipment and supplies, personnel, medication, and, less developed infrastructure. Recent literature has shown that numerous women with STIs/BV are asymptomatic and therefore left untreated. As a result, many new cases of HIV infection are largely attributed to STIs (Wilkinson et al., 1999,

World Health Organization, 2013). An alternative diagnostic tool such as rapid point of care (POC) test is an essential strategy for effective STIs management. Various rapid POC tests for STIs diagnosis have been researched over time. This has yielded POC tests which are currently used for STIs diagnosis (Mayaud and McCormick, 2001, Bowden et al., 2002, Eden and Johnson, 2016). Based on recent research that established the association between genital tract inflammation, STIs, and HIV acquisition in women, the Genital Inflammation Test (GIFT) for HIV prevention project has developed a cytokine biomarker rapid POC test to detect genital inflammatory markers in women (Masson et al., 2014, Masson et al., 2015a, Masson et al., 2015b). This screening will ensure early detection of infection reducing their susceptibility to HIV acquisition and eventual control of HIV/AIDS.

The availability of this newly developed test in South Africa will provide genital inflammation screening. Therefore, for the provision of this service, a cost estimation of screening with this test is necessary. In addition, a budget impact analysis of the costs is beneficial to enable the South African government avail these services at primary level health care facilities.

1.2 Problem Statement

In developing countries with populations at high risk of HIV infection, the prevalence of STIs and BV is high (Kamb et al., 2008b). In South Africa, women are mostly affected and account for the greater proportion. In most cases, not all women who have STIs are symptomatic. Wilkinson et al (1999) found that in women aged 15-49 years, 24.9% were infected with at least trichomoniasis, gonorrhoea, chlamydia or syphilis and 48% of the investigated were asymptomatic. STIs and BV have been proven to cause female genital tract inflammation which is associated with increased susceptibility to HIV infection (Wilkinson et al., 1999). Both women with asymptomatic and symptomatic STIs have similar levels of genital inflammation compared to uninfected women. Therefore, numerous women are likely to have

unresolved STI-related genital inflammation, increasing their risk of HIV acquisition and reproductive complications (Masson et al., 2015a).

In resource constraint settings such as South Africa, most cases are diagnosed using the syndromic approach because laboratory testing is expensive and labour intensive. The gold standard for STIs diagnosis is laboratory based nucleic acid amplification tests (NAATs). This requires specialised equipment and experienced laboratory personnel, both of which are often scarce in such settings. Moreover, the test results are not immediate and STIs or HIV transmission may occur during the waiting period (Masson et al., 2015a). Over the years, the use of rapid POC tests has evolved, and these are especially vital in areas with limited access to health care, or with poor return rates of patients for follow-up management.

POC diagnostic tests are rapid, simple and can be availed to most public health facilities. Their use for detection of infection prevents overtreatment, and identifies asymptomatic infected women, enabling effective syndromic management of STIs. Thus far, the tests developed do not detect genital tract inflammation in women. Identification of genital inflammation and STIs diagnosis of asymptomatic women at high risk of HIV infection, will result in effective and prompt STI management of many untreated women. Not only will this reduce the burden of disease, but also decrease their susceptibility to HIV infection and prevent reproductive health complications.

With the recent developments of the association of genital inflammation with HIV acquisition, the lack of a cytokine biomarker rapid POC test and screening for genital inflammation in women poses a drawback in STIs management in South Africa. Establishing the affordability of these services is an essential step towards better STIs management to augment the fight against HIV infection.

1.3 Rationale

Genital tract inflammation screening in women has not yet been introduced in South Africa, and no published study has assessed the costs associated with providing this health care service for patients with STIs and BV.

Based on a cost-effectiveness study on rapid POC diagnostic tests for STIs conducted in Benin, evidence suggests that POC testing is a cost-effective strategy and reduces inappropriate STIs treatment with syndromic management (Vickerman et al., 2006). Being a developing country, this study could be generalized to the South African context as cost effectiveness is majorly linked to available resources. However, cost data is country and setting specific and so accessibility to financial data and financial practices impacts on the results (Drummond et al., 2015). Therefore, this study aims to collect and analyze primary data so as to estimate the costs and budget implications from a provider's perspective, specific to the South African context.

As this newly developed rapid POC diagnostic test for STIs is yet to be implemented, no cost estimates are available for genital inflammation screening in women. It would be beneficial to compare cost estimates of providing genital inflammation screening in two or more clinics providing reproductive health services.

STIs have a substantial impact on sexual and reproductive health and may lead to fetal and neonatal deaths, cervical cancer, infertility, and increased risk of HIV infection. In addition, the social and psychological consequences of STIs have an impact on the quality of life (World Health Organization, 2013). The most affected are young women whose reproductive and sexual health determines the continuity of future generations. The age range of 15 to 49 years represents women of reproductive age who support families and are economically active. Identification of genital tract inflammation for effective STIs management would have

socioeconomic benefits for the country, and so it is necessary to determine the affordability of such a program.

Genital tract inflammation screening in women emphasizes on the detection and treatment of asymptomatic cases of STIs and BV. In support of the World Health Organization (WHO) STIs prevention and control strategies, the cytokine rapid POC test would not only allow screening for asymptomatic infections and better targeted treatment and interruption of onwards STIs transmission, but also would make integration of STIs services into primary healthcare, family planning, antenatal, and HIV-care settings simpler and more feasible (World Health Organization, 2013). This is in line with WHO's goal to end sexually transmitted infections as a major public health concern, through 90% reduction of STI incidence by 2030 (World Health Organization, 2016). Also, the results of this study will contribute towards research for innovation and policy, and social and public health research, which are two of the streams that support the goals of the government's national strategic plan (NSP) (Council, 2012). Furthermore, this innovative test device targets women, and so will ensure universal access to diagnosis and early treatment for STIs for a key population in support of the Western Cape Department of Health strategic objective of sustaining health and wellness (Government, 2012). Lastly, the results of this study in terms of the cost component would be beneficial for cost-effectiveness analysis studies in the future.

This research is a sub-study of the Genital Inflammation Test (GIFT) for HIV prevention research project, carried out by UCT researchers, who have developed a cytokine biomarker rapid POC test which will be used to improve syndromic management of STIs and BV in South Africa. Hence, this study will estimate the cost of the newly developed test, and the budget impact of its implementation in the primary health care clinics in South Africa.

1.4 Theoretical and Empirical Literature

1.4.1 STIs/BV and genital inflammation

Sexually transmitted infections (STIs) are among the most common cause of acute illness worldwide. These infections have extensive health, psychological, and social consequences that profoundly impact on sexual and reproductive health. To date, over thirty bacterial, parasitic and viral pathogens are known to be transmitted sexually. However, globally most of the STIs are caused by eight infections (gonorrhoea, syphilis, chlamydia trachomatis, HIV, genital herpes, hepatitis B [HBV] and human papilloma virus [HPV]). According to WHO, over a million people acquire an STI every day with the largest disease burden in developing countries (Kamb et al., 2008b). Bacterial vaginosis (BV) has been found to be a highly prevalent vaginal infection especially in high HIV prevalent countries. It is the commonest type of vaginitis in women of aged 15 to 49 years, and is caused by an imbalance in the ecology of the normal vaginal flora. BV increases the risk of obstetric and gynaecological outcomes such as pelvic inflammatory disease (PID), preterm delivery, and upper genital tract infections (Atashili et al., 2008).

STIs and BV cause inflammation in the female genital tract that leads to, recruitment of immune cells to the genital mucosa and inflammatory cytokine up-regulation, but also down-regulation of some cytokines in BV infections. This process is necessary to control and clear the infection and is sustained by cytokine production in response to pathogen recognition. Despite this, it may destroy infected epithelial layers, enabling access of STI-associated microbes to deeper tissues. Genital inflammation influences susceptibility to HIV infection. Increased cytokine levels in the genital tract results in “recruiting and activation HIV target cells, reduction of epithelial barrier integrity, and promotion of HIV replication” through NF- κ B activation, which may facilitate HIV infection (Masson et al., 2014).

South Africa's STIs disease burden is one of the largest worldwide. These STIs pose a significant threat as a common cause of adverse pregnancy outcomes and infertility, but also increase the risk of HIV transmission. In 2000, a study done established that the STI disease burden is 20% greater in women than in men (Johnson et al., 2007). In addition, bacterial vaginosis (BV) is also prevalent in South African women at high risk of HIV infection. STIs and BV cause female genital tract inflammation. Women are at high risk of HIV acquisition and the continual transmission of HIV infection among young women poses a challenge towards achieving an AIDS free generation (Masson et al., 2015b).

1.4.2 Screening and diagnosis of STIs/BV

Currently, diagnosis of STIs and BV is based on two approaches which are: aetiological diagnosis through laboratory testing and syndromic diagnosis. Aetiological diagnosis based on laboratory testing is the most accurate but also costly approach. The gold standard diagnostic test for BV is Gram stained smears of genital fluid interpreted using the Nugent scoring; while that of STIs is laboratory based nucleic acid amplification tests (NAATs) (Kettler et al., 2004). The expense of this approach is attributed to diagnostics, infrastructure, and maintenance, and often leads to delays in diagnosis and treatment. Furthermore, resource constraint areas do not have access to reliable laboratory facilities. As a result, clinicians make presumptive clinical diagnosis or refer patients for specialized treatment leading to further delay. To address these limitations the WHO developed the syndromic management approach (Mayaud and McCormick, 2001).

Syndromic diagnosis involves presumptive diagnosis by health care professionals, based on identifiable clinical syndromes caused by STIs, with the aim to provide treatment for the most common infections linked to a specific cluster of symptoms. Despite this being relatively simple to use and easily incorporated into all levels of health care systems, it has two limitations (Kettler et al., 2004). First is the additional cost of over diagnosis and treatment of uninfected

patients which includes the direct costs of medication, as well as indirect costs such as adverse drug reactions. Second is the poor specificity and sensitivity of detection for asymptomatic STIs such as gonorrhoea and/or chlamydia. This has prompted the urgent need for simple, rapid and cheap diagnostic tests to identify asymptomatic infected women in family planning, antenatal, and maternal and child health clinics (Mayaud and McCormick, 2001).

Point of care testing has gradually developed over the years. POC tests are rapid, simple and can be easily availed in resource limited settings. These tests permit screening of women reducing false diagnosis, overtreatment, and enable diagnosis and treatment in a single visit. Because of their use in resource limited settings, the benefits should outweigh the costs. Herbst de Cortina et al (2016) conducted a systematic review of 33 studies on point of care testing for STIs. The study involved an evaluation of test performance, cost effectiveness, acceptability and feasibility and concept articles introducing new tests. Most of these studies were set in developed countries. The review established that sensitive and specific POC test are available for curable STIs but with room for further improvement. These tests were acceptable to patients and providers and were also cost-effective (Herbst de Cortina et al., 2016).

Some of the tests in current use include the Chlamydia Rapid Test (CRT) which has been found have 41% sensitivity in a recent study. Moreover, its utilization is a complex process that is time consuming (van der Helm et al., 2012). *Neisseria gonorrhoea* diagnosis with immunochromatographic and leukocyte esterase tests have shown sensitivities and specificities widely ranging between 54% to 70% and, 89% to 97% respectively for the former. Similarly, sensitivities and specificities for the leukocyte esterase test range between 23% to 86%, and 30% to 99% respectively (Smith et al., 2012). Rapid antigen test for *Trichomonas vaginalis* has been found to be highly sensitive and specific at 90% to 95% and 100% respectively, but involves numerous steps to complete (Campbell et al., 2008). Also, for detection of BV, the BV Blue test has shown a high specificity of 92.7%, but poor sensitivity of 38.1% (Madhivanan

et al., 2014). This indicates that there is still need for a rapid POC diagnostic test which is simple and with improved specificity and sensitivity.

The newly developed genital inflammation test by the UCT research team, detects cytokines IL-1B and IP-10 which were found to predict an active STI, with 77% sensitivity, 72% specificity, 82% positive predictive value (PPV), and 65% negative predictive value (NPV). Compared to the sensitivity of clinical signs (19%), the two cytokine biomarkers considerably improved sensitivity, detecting 58% additional women with laboratory diagnosed STIs and BV (Masson et al., 2015a).

1.4.3 Cost-effectiveness studies on POC testing for STIs

Research on cost-effectiveness of rapid point of care tests is gradually evolving (Vickerman et al., 2006, Rydzak and Goldie, 2008, Huang et al., 2013). Some of these studies have been based in developing countries with focus on developing accurate and affordable POCs for STIs and BV.

An evaluation of a rapid diagnostic kit (FemExam) for BV in Gambia revealed that the cheapest diagnostic test would be the gold standard procedure (Gram stain) at a cost per patient of US\$1.39, but may not be available in all clinical settings. The most affordable strategy was presumptive treatment of all women with vaginal discharge for BV which would only cost US\$ 0.50 per patient and US\$ 1.04 per true case treated. However, FemExam was sensitive detecting 70% of the cases, but with a cost range of US\$4.52 to US\$8.72. Based on a hypothetical price for developing countries at US\$1, FemExam would comparatively reduce overtreatment costs given its specificity. Together with syndromic management it would improve clinical management and reduce medication use and costs (West et al., 2003). These research findings build on evidence of POC tests as a cost-effective strategy.

Huang et al (2013) conducted a cost–effectiveness and comparative study on a rapid POC test for Chlamydia and the laboratory nucleic acid amplification (NAAT) testing for women in an STD clinic. The base case scenario of POC testing predicted more cases of pelvic inflammatory disease (PID) that would be averted and more cost savings compared to the NAAT strategy. Sensitivity analyses showed that changes in the proportion of women receiving treatment, disease prevalence and PID rate among untreated infected women affected the magnitude of the outcomes, but the POC testing dominated the NAAT strategy. The proportion of women willing to wait for the POC test results affected its sensitivity increasing its effectiveness close to that of NAAT strategy. Cost savings of POC testing outweighed those of NAAT (Huang et al., 2013). As such, this lays further emphasis on the cost-effectiveness of POC tests.

1.4.4 Budget impact analysis

Budget impact analysis (BIA) is a vital component of a complete economic evaluation for a health care program. Along with cost-effectiveness analysis (CEA), there is an increasing recognition of its importance at start of a new health care program. BIA assesses the financial consequences of implementing and expanding a new healthcare intervention particularly within resource limited health care settings. BIA is beneficial for forecasting and budget planning. It predicts how a change in the intervention will influence the trajectory of expenditure on that condition (Mauskopf et al., 2007).

Budget impact analysis is complementary to CEA and should not be considered as a replacement. It is mainly used by individuals managing and planning health-care budgets in national health care programs, health-care delivery organizations and private insurance plans. BIA addresses the financial outcomes relating to the adoption of new health care intervention to evaluate their affordability. Both CEA and BIA use similar data and methodological requirements but vary in how they are integrated into models as their intended use differs (Mauskopf et al., 2007).

BIA synthesizes knowledge available at a specific time to approximate the likely financial consequences of a decision for a health care system. It provides a computing framework that allows application of input values and viewing of financial estimates specific to the setting. The outcomes represent scenarios consisting of data inputs and specific assumptions of interest to the decision maker instead of the generally applicable normative case. The analytic framework design is important and should consider relevant features of the health care system, the anticipated uptake of the new intervention, possible access restrictions, and the use and effects of the current and new interventions (Sullivan et al., 2014).

A limited number of BIA studies have been published more so those estimating the financial and health-care service impact of a new intervention for a defined national health plan. The results generated from these studies have demonstrated significant financial implications of certain health interventions on government budgets. Martin et al (2010) conducted a study on the expansion of the Human Immunodeficiency Virus (HIV) screening program in the United States of America (USA) forecasting on the impact of testing programs, discretionary treatment programs and entitlement programs on government budgets, establishing that although the financial burden of expanded screening would disproportionately fall on discretionary programs that funded care of newly identified patients, this represented a small proportion of the total budget. Hence, decision-makers were informed about which government programs required sufficient budgets to achieve early treatment goals (Martin et al., 2010).

Gidwani et al (2012) assessed the budget impact of implementing a new HIV testing program which was found to be cost-effective but not cost-saving, in comparison to the financial impact of following standard care in a veteran health administration emergency department. The results demonstrated the relationship between both alternatives and provided evidence that the screening program was not a significant cost burden, and, provided a new component of support for HIV screening. Such findings may benefit decision-makers in integrated systems

and exhibit the practical actual effect of implementing evidence-based policies (Gidwani et al., 2012).

2 AIMS AND OBJECTIVES

2.1 Aim

The aim of the study is to estimate the cost of genital inflammation screening using the cytokine biomarker rapid POC test recently developed by UCT researchers, and the budget impact for the health service provision in primary healthcare facilities.

2.2 Objectives

To identify, quantify and value the resources required for the provision of genital inflammation screening for detection of STIs/BV infections at primary care level health facilities in order to:

1. Estimate the total and unit cost of screening using the cytokine biomarker rapid POC test device.
2. To determine the budget impact of nationally scaling-up genital inflammation screening.

3 METHODOLOGY

3.1 Study design

The study design will be a cost and budget impact analysis, centred on the collection of primary cost data, and will be conducted from the provider's perspective. This is a prospective study and the cost data will be obtained from healthcare facilities where the GIFT project will be piloted. The most relevant costs will be related to the resources required for cytokine rapid POC testing. Costs of resources will be valued and presented in 2016 South African Rand.

3.2 Setting and population

The target population for the study is women of reproductive age, ranging from 15 to 49 years of age attending family planning clinics (World Health Organization, 2006). The study will be undertaken at two primary health care facilities in the Western Cape, South Africa.

Reproductive health services (family planning) will be part of the health care provision of these facilities. Alternatively, the cost data will be sourced from published literature.

3.3 Cost analysis

Costs of providing health interventions are the value of the resources used to avail the intervention. The resources include capital costs such as equipment, vehicles, and building space, and, recurrent costs such as consumables like medical supplies, labour, and overhead costs (Gray et al., 2010). The costs for performing genital inflammation screening in women will be identified, measured and valued.

The approaches of estimating costs could be gross-costing which identifies costs in bundles or micro-costing that involves identifying and costing all resources related to the health intervention (Drummond et al., 2015). Being a new health intervention with no cost estimates available on genital tract inflammation screening in the public sector, a micro-costing approach will be used. Table 1 and 2 (on pages 17 and 18) present a summary of the categories of resources that will be considered and the methods that will be used to collect, measure and value these costs.

In order to estimate the costs of providing genital inflammation screening services at the patient and facility level, a costing spreadsheet will be designed on Microsoft Excel. The unit cost per patient screened will be estimated by calculating the cost per clinic visit, which is inclusive of the cost of diagnostic test per patient screened. The total costs of screening will be estimated by calculating the product of the unit cost per patient screened and an estimate of the number of patients attending the clinic for reproductive health services.

3.4 Budget impact analysis

Firstly, an expenditure-based model will be developed in Microsoft Excel. Initially using the available demographic and contraception coverage rates data, the size of the population group

for which the intervention is designed to reach, will be determined. This potential target group will comprise women of reproductive age (15 to 49 years), attending family planning clinics in South Africa.

Secondly, the patient-level unit cost estimated under objective 1 will be used to scale-up and provide national estimates under various coverage scenarios. These levels of coverage can assist with the adoption of the most feasible level of implementation given the current levels of infrastructure and capacity development.

3.5 Sensitivity analyses

The most relevant uncertainties in the study include the test price, the staff/personnel costs, and the number of women attending family planning clinics. For the budget impact analysis, the population coverage rate will be varied to determine the total annual cost of screening. Univariate sensitivity analyses will be performed on the test price, the personnel costs, the clinic utilization rates and the population coverage rates, by varying the values over a plausible range. This study will assume that the contraception coverage rates are representative of the number of women aged 15 to 49 years attending FP clinics; this would be a once-off screening for every woman per year; the overall service framework within which the scaling up of the screening program is modelled to occur at primary care level; and the screening intervention would be made available as part of the routine FP service provision.

Table 1 Methods and data used in estimating costs: identifying and measuring CAPITAL costs

TYPE OF COST	IDENTIFICATION	Costing method	MEASUREMENT		VALUATION	
			Related information for allocation purposes	Source of data	Valuation method	Source of data
Capital costs	Categories	Costing method	Related information for allocation purposes	Source of data	Valuation method	Source of data
Building	Consulting room, waiting room, toilet	Current replacement cost (CSIR building costs per m ² x square meter of facility). 20-year life span. 3% discount or annuitization	Space (square metres). Number of consultations and type of service	Observation and record reviews	Replacement and contract prices or rent	Department of Public Works, building contractors
Medical equipment	Weighing scale, blood pressure machine, stethoscope, examination couch, bed screen, trolley.	Actual current replacement cost. 5-year life span. 3% discount rate for annuitization	Resources used by each cost centre. Number of consultation and type of service	Observation and record reviews	Replacement and contract prices, rental fees for equipment	Supply Chain Management: records and contracts, clinic expenditure records, commercial price lists
Furniture and other equipment	Tables, chairs, cabinets	Actual current replacement cost. 15-year life span for furniture and 5-year life span for equipment 3% discount rate for annuitization	Resources used by each cost centre. Number of consultation and type of service	Observation and record reviews	Replacement and contract prices, rental fees	Department of Public Works, Supply Chain Management: records and contracts
Vehicles		Actual current replacement cost. 6-year life span. 3% discount rate for annuitization	Number of consultations per type of service Log books/time spent travelling for different types of services	Transport records	Replacement and contract prices, rental charges	Transport contracts and records
In service-training	Personnel; doctors and nurses	Actual current cost of training. 5-year life span. 3% discount rate for annuitization	Number of staff trained Time spent on different services by these staff	Management, training records	Course fees; for in-house training – staff remuneration	Training Providers, remuneration packages

Table 2 Methods and data used in estimating costs: identifying and measuring RECURRENT costs

TYPE OF COST	IDENTIFICATION		MEASUREMENT		VALUATION	
Recurrent cost	Categories	Costing method	Related information for allocation purposes	Source of data	Valuation methods	Source of data
Administration & management	Management staff (human resource and other) Administration staff (stock control and drug ordering; other records staff, reception area staff)	Document staff time on these activities Total remuneration package costs. Any external costs	Number of consultations per type of service Record reviews	Observation, record reviews	Gross salary per month, including benefits (Cost to company)	Government salary packages
Overheads	Electricity, water and other utilities Rent (where applicable) Telephones, faxes & postage Stationery, computer consumables & photocopies Support staff (all staff not classified as clinical, admin. and management, or maintenance)	Actual costs from facility records In case of support staff, total remuneration package 	Number of consultations per type of service Space (square meters) used by each cost centre for utilities and rent	Procurement records, observation, patient records	Tender contracts and expenditure records	Tender contracts and expenditure records
Clinical personnel:	Doctors PHC nurses Other nurses Other clinical staff	Total remuneration costs (salary and all benefits, including 'free housing' for which rent must be included) Calculate separately for each category of personnel listed in previous column	Number of consultations per type of service Time spent on different types of services	Observation and record reviews	Gross salary per month, including benefits (Cost to company)	Government salary packages
Medical and surgical supplies:	Pharmaceutical products All other medical and surgical supplies	Actual costs from facility/ service records (where 'internal') Unit costs to be obtained from supplier (e.g. provincial depot) where 'external'	Detailed list of types, quantities and unit costs of all pharmaceutical products and other supplies required	Observation and patient records reviews	Tender contract prices and expenditure records	Supply Chain Management: records, contracts; Pharmacy Services: contracts, records
Diagnostic tests	Laboratory tests (for STIs/BV diagnosis)	Actual costs from facility (consumables and relevant technical staff) where 'internal' Price charged where 'external'	Number of consultations per type of service Record reviews	Procurement records, observation and patient record reviews	Tender contract prices and expenditure records	Supply Chain Management: records, contracts, clinic expenditure records, suppliers
Transport/ Vehicle running costs		Number of kilometers travelled in a year AA rate per kilometer	Number of consultations per type of service Log books/time spent travelling for different types of services	Observation, transport records	Expenditure records	Transport contracts and records
Maintenance		Actual costs of supplies related to maintenance activities Total remuneration costs of maintenance staff External costs	Number of consultations per type of service	Observation, record reviews	Tender contract prices and expenditure records	Department of Public Works, Supply Chain Management: records and contracts, clinic expenditure records
Other (all other costs including cleaning material etc.)		Actual costs from facility or service records	Number of consultations per type of service	Observation, record reviews	Tender contract prices and expenditure records	Supply Chain Management: records and contracts, clinic expenditure records

4 DATA ANALYSIS AND MANAGEMENT

The costs will be estimated using Microsoft Excel. These costs will include the unit cost of genital inflammation screening in women using:

1. The cytokine biomarker POC test device.
2. Total costs of screening for the study population.

Data will be stored in password protected folders and a back-up system maintained. The data will be entered, cleaned and changes made will be captured in the database.

5 ETHICAL CONSIDERATIONS

5.1 Ethical approval

Ethical approval for this study will be sought from the University of Cape Town Human Research Ethics Committee. Amendments to the protocol will be submitted for approval prior to implementation. The protocol will also be submitted to the relevant Provincial Department of Health (DoH) authorities for review and permission to obtain data in areas of their jurisdiction.

5.2 Potential benefits and risks

This study involves cost data, therefore, poses no potential risk or harm to any individual. The study is unlikely to have direct benefits to individuals. As an indirect benefit of the study, the information generated may augment STIs/BV testing and diagnosis contributing towards better STIs/BV management.

5.3 Autonomy and informed consent

This study does not involve human subjects; therefore, no major ethical conflicts are anticipated. Cost data will be obtained from health facility records, financial records and published literature.

5.4 Confidentiality and privacy

Confidentiality and privacy will be assured. Information will not be linked to individuals. No names will appear in the database or on the forms. No identifiers will appear in any report or publication. All electronic data will be password protected with accessible only by the study team. Paper forms will be filed and stored in a locked cabinet.

6 PUBLICATION AND DISSEMINATION POLICY

Upon completion, the study will be submitted for the Masters in Public Health: Health Economics Degree. Also, the results will be submitted to the Medical Research Council (MRC) South Africa, the relevant Department of Health Officials in the Western Cape, the Strategic Health Innovations Partnerships, and the Health Economics Unit- UCT. An article will be drafted for publication in a peer reviewed journal.

7 LOGISTICS

The study will be carried over a 12-month period. Table 3 shows the activities and timelines.

Table 3: Study activities and timeline

Activity	Sept	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	July	Aug
Finalize protocol	X	X										
Obtain approval: GSH, DOH, Ethics		X	X									
Finalize data capture forms				X	X							
Collect data: Observation & interview						X	X					
Collect data: Review records, tender docs, etc.						X	X					
Capture data on database								X	X			
Analyze & clean data								X	X			
Write up										X		
Complete dissertation											X	
Submission												X

8 BUDGET

The study will be funded by the Medical Research Council of South Africa.

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PART B: STRUCTURED LITERATURE REVIEW

2.0 Introduction

Sexually Transmitted Infections (STIs) remain a major public health concern globally. Annually, 499 million new cases of curable STIs (chlamydia, gonorrhoea, trichomoniasis and syphilis) occur, with developing countries accounting for eighty six percent of the disease burden. There has been an increased focus on the control of STIs, which together with bacterial vaginosis (BV), have been associated with increased risk of HIV acquisition (Fleming and Wasserheit, 1999, Mayer and Venkatesh, 2011). One of the prominent strategies is effective management of STIs and BV through prompt diagnosis using rapid point of care (POC) testing and treatment, more so in asymptomatic women who are left untreated, and highly susceptible to HIV infection (Wilkinson et al., 1999, World Health Organization, 2013).

Rapid point of care tests defined as tests that are performed near the patient, provide results within a short time period, and ensure testing and treatment occur within the same clinic visit. This has the potential to improve STIs and BV management especially in developing countries that have limited health resources. (Drain et al., 2014). The increasing development of new rapid POC tests gives rise to the need for evaluations in regards to their effectiveness and efficiency. Similar to other healthcare interventions, STIs and BV management interventions need financial resources, and this necessitates their economic evaluation together with the assessment of budget allocation. This will inform policy makers on how to best use and maximize the scarce resources available, and, to the benefit of large populations in need of effective STIs management towards the global fight against HIV/AIDS. Hence, the subject of this literature review is economic evaluation and budget impact analysis of rapid POC tests for STIs and BV.

This study sought to estimate the costs of STIs and BV screening using a cytokine biomarker rapid POC test and the budget impact of this health service in order to reduce the risk of HIV

infection among asymptomatic women in developing countries. Therefore, the objectives of the literature review were to identify information on:

- The interaction between STIs/BV and HIV through genital inflammation, and the impact of STIs and BV on HIV control;
- Current screening and diagnostic tools for STIs and BV;
- The methodology of economic evaluation of health care services, budget impact analysis and similar approaches taken for rapid point of care tests for STIs and BV.

Literature was sourced through an exploratory search of PubMed, EBSCO host database and Google scholar based on identified keywords. The references cited in the articles identified were manually searched, and Google was employed to search for grey literature. The literature reviewed included studies on the disease evolution and diagnosis of STIs and BV, as well as the costs and cost-effectiveness of the different diagnostic tools. Due to the vast amount of literature on the disease evolution and diagnosis, and limited studies on the costing of STI diagnostic tools, relevant studies were included despite the time frame, ranging from the years 2006 to 2016. The studies of primary focus were those done in low and middle-income countries. However, few relevant studies in high income countries were also included. Additionally, books and articles about methods of economic evaluation and budget impact analysis were included.

The literature review contributed to an understanding of the impact of STIs and BV on the control of HIV, the challenges facing effective STIs and BV management, and informed on the utilization of newly developed screening and diagnostic tools for STIs and BV that are both efficient and cost-effective.

The first section is a brief overview of the epidemiology of STIs and BV globally and in South Africa. This is followed by a detailed description of STIs and BV, their association

with HIV acquisition and the challenges in addressing STIs control; and the impact on affected individuals. The second section addresses the current screening and diagnostic tools for STIs and BV, with a detailed discussion of rapid point of care testing focusing on developing countries. The third section is a brief theoretical overview of cost analysis as a component of health economic evaluations, and its role in rapid point of care testing for STIs and BV through cost-effectiveness studies. It also discusses aspects of budget impact analysis for health care economic evaluations and its role in decision making. Lastly, the conclusion summarizes the findings from the literature review, and identifies gaps that justify conducting a costing study for rapid point of care testing for STIs and BV in South Africa.

2.1 Epidemiology of Sexually Transmitted Infections and Bacterial Vaginosis

Globally, sexually transmitted infections (STIs) are among the major causes of acute illness and represent a large burden of disease. Over the years, STIs continue to be a public health concern, with serious medical complications such as increased HIV risk, infertility, foetal and neonatal deaths, long term disability and death. The medical and psychological consequences of STIs on sexual and reproductive health exert a significant economic and social burden on individuals and their families (Sonko et al., 2002, World Health Organization, 2013, World Health Organization, 2014).

In 2013, World Health Organization (WHO) estimated that over a million people are infected with an STI every day. Presently, over thirty viral, bacterial, and parasitic pathogens have been identified to be transmitted sexually (World Health Organization, 2013). However, most of the STIs worldwide are caused by eight infections namely: chlamydia trachomatis, HIV, gonorrhoea, syphilis, trichomoniasis vaginalis, hepatitis B (HBV), genital herpes, and human papilloma virus (HPV). Of these, 499 million new cases of curable STIs (chlamydia, gonorrhoea, trichomoniasis and syphilis) occur annually (Kamb et al., 2008a, World Health Organization, 2013). In the developing world, STIs account for eighty six percent of the

worldwide disease burden. The largest burden is among countries within Sub-Saharan Africa with populations at high risk of HIV infection. In South Africa it is estimated that around 11 million cases of STIs occur, with women accounting for a large proportion of the infections (Sonko et al., 2002, Kamb et al., 2008a). Moreover, among women, bacterial vaginosis is associated with sexually transmitted infections and other reproductive health complications (Woodman, 2016).

Bacterial vaginosis (BV) is a common vaginal condition in women of reproductive age. BV is characterized by an imbalance in the ecology of the normal vaginal flora, leading to loss of lactobacilli, elevated vaginal pH, and an increase in other predominant anaerobic flora. An increased vaginal pH facilitates the growth of sexually transmitted disease agents, and this increases the susceptibility to HIV infection in women (Taha et al., 1998).

BV is estimated to mostly occur in high HIV prevalent areas, especially in developing and resource-poor countries. Among the African population, the prevalence of BV in women ranging from 20% to 50% could be an important contributor to the prevalence of HIV infection in Sub-Saharan Africa. Additionally, BV increases the risk of obstetric and gynaecological outcomes such as preterm delivery, pelvic inflammatory disease (PID), and upper genital infections (Myer et al., 2005, Atashili et al., 2008, Cohen et al., 2012, Woodman, 2016).

2.2 The Association between STIs, BV and HIV Acquisition

Over the years, various studies have established the association between STIs, BV and their role in the transmission of HIV infection, negatively contributing towards HIV control. STIs and BV are associated with increased risk of HIV acquisition, more so in women. One of the causes for this is genital tract inflammation. STIs and BV cause genital tract inflammation, putting women at high risk of HIV infection (Fleming and Wasserheit, 1999, Mayer and Venkatesh, 2011, Cohen et al., 2012, Masson et al., 2015a, Masson et al., 2014).

STIs and BV cause an inflammatory response in the female genital tract that leads to recruitment of immune cells to the genital mucosa and inflammatory cytokine up-regulation, but also down regulation of some cytokines in BV infections. This process is necessary to control and clear the infection and is sustained by cytokine production in response to the pathogen recognition. Despite this, it may destroy infected epithelial layers, enabling access of STI-associated microbes to deeper tissues. This influences the susceptibility to HIV infection. Increased cytokine levels in the genital tract results in “recruitment and activation of HIV target cells, reduction of epithelial barrier integrity and promotion of HIV replication” through NF- κ B activation, which may facilitate HIV infection. Generally, STIs and BV infections may either be asymptomatic or symptomatic in women (Masson et al., 2014, Masson et al., 2015a). In most cases, women are asymptomatic. Wilkinson et al (1999) found that in South African women aged 15-49 years, 24.9% were infected with at least trichomoniasis, gonorrhoea, chlamydia or syphilis and, 48% of the investigated were asymptomatic (Wilkinson et al., 1999). Similarly, a recent study established that 90% of BV cases in South Africa were asymptomatic (Mlisana et al., 2012). Compared to uninfected women, both women with asymptomatic and symptomatic STIs have similar levels of genital inflammation. Therefore, numerous women are likely to have unresolved STIs-related genital inflammation putting them at high risk of HIV acquisition and reproductive complications (Masson et al., 2014). This poses a major challenge in the effective control of STIs, BV and ultimately the control of HIV infections and AIDS.

In addition, the occurrence of STIs and BV has been found to be more common in the HIV infected women compared to the HIV negative women. Numerous studies have demonstrated that HIV infected women have high prevalence of STIs or BV compared to uninfected women (Imade et al., 2014, Acquaro et al., 2012, Watts et al., 2006, Helfgott et al., 2000). Although

there are no studies that look at the simultaneous association of STIs and BV in HIV infected women, this evidence further shows the association between STIs, BV and HIV infection.

South Africa's STIs disease burden is one of the largest worldwide. These STIs pose a significant threat as a common cause of adverse pregnancy outcomes, cervical cancer and infertility, but also increase the risk of HIV transmission (Johnson et al., 2012). Moreover, the social and psychological consequences of STIs impact on the quality of life, more so in women of reproductive age. This age range represents women who are economically active, support families, but also determine the continuity of future generations (World Health Organization, 2013).

In 2000, a study in South Africa established that the STI burden of disease is 20% greater in women than in men (Johnson et al., 2007). In addition, bacterial vaginosis (BV) is also prevalent in South African women who are at high risk of HIV infection. STIs and BV cause female genital tract inflammation. Women have an increased risk of HIV acquisition and the continued transmission of HIV infection among young women poses a challenge towards achieving an AIDS free generation (Masson et al., 2015a). As such, genital tract inflammation screening in women for effective STIs and BV management especially for asymptomatic cases would not only benefit the reproductive and sexual health of women, but also have a positive impact on the social and economic status of the country. The effective control and management of STIs and BV requires the use of accurate and efficient diagnostic tools and treatment.

2.3 Current tools for screening and diagnosis of STIs and BV

The diagnosis of STIs and BV is dependent upon different approaches which are often complementary. There are two standard approaches used to diagnose STIs namely; aetiological approach through laboratory testing and syndromic approach based on clinical diagnosis (Kettler et al., 2004).

2.3.1 Aetiological Approach (Laboratory Testing)

Aetiological diagnosis approach involves laboratory testing which identifies the causative agents of infections. Laboratory testing is performed by trained personnel and is a thorough and time-consuming process, which often requires hours or days to obtain results. This approach needs a secondary level facility and multiple appointments for the patients to be tested and obtain results (Eden and Johnson, 2016).

The common curable STIs (gonorrhoea, trichomoniasis and chlamydia) typically require a wet mount preparation and gram stain to be examined by a trained laboratory technician, a culture that needs 72 hours to obtain results, and special incubation demands. The current gold standard laboratory test for gonorrhoea and chlamydia is the laboratory based nucleic tests (NAATs) specific to the causative organism (Gaydos and Hardick, 2014). NAAT uses the replication of the genetic material of bacteria, in which detection of target bacteria is made easier by increasing the quantity of bacteria within the testing matrix. NAATs have greatly improved detection and diagnosis of STIs, but the time limitations and costs results in their limited use in resource constraint settings. Resource constraint settings are characterized by inadequate funds to cover for health care costs both at individual and societal levels, leading to limited availability and access to medical equipment and supplies, personnel, medication, and, less developed infrastructure. Therefore, NAATs laboratory testing may have limited contribution to the STIs public health burden in such settings (Gaydos and Hardick, 2014). Trichomonas is manually cultured using a special medium that needs a trained eye to observe for several days to confirm a negative result. It can also be identified from urine microscopy and wet mounts which inexperienced laboratory personnel can find difficult to do so (Eden and Johnson, 2016). The gold standard laboratory test for BV is Gram stained smears of genital fluid interpreted using the Nugent score (Kettler et al., 2004).

However, there are multiple accurate laboratory tests available for the different STIs and BV. The choice of appropriate laboratory test to use is made difficult by the numerous STIs and the different potential tests for each STIs. Despite this, the choice of laboratory test is based on the purpose of the testing which may be for surveillance, quality assurance, antimicrobial susceptibility testing, screening of asymptomatic individuals, diagnosis of individuals with symptoms and signs of possible STI, and for validation of syndromic management (Kettler et al., 2004, Unemo et al., 2013, Eden and Johnson, 2016).

Commonly, the precise diagnosis of STIs and BV may be difficult as most symptoms tend to overlap or are non-specific, and have various potential causative agents which may need different treatments. Therefore, for purposes of accurate diagnosis and the aforementioned reasons, laboratory testing is necessary. With laboratory testing, the time needed for results to be obtained is an important consideration in the choice of tests, as transmission of infection may occur between persons during this interval, or the loss of follow up of these patients between the testing time and notification of the test results (Gift et al., 1999, Geisler et al., 2008). Hence, monitoring the interval between the time the test is performed and the treatment of individuals with positive results as a measure of quality of care, is beneficial when the clinical service involves laboratory testing (Unemo et al., 2013).

Additionally, screening is a vital element of STIs and BV control strategies for optimal management, and its contribution adds to that of laboratory testing and syndromic diagnosis in treatment of patients. STIs and BV infections may be unknown to infected persons or occur asymptotically. With the absence of symptoms, infected persons are at risk for transmission to others and, to developing complications. As such, screening that involves testing of at-risk individuals who may be asymptomatic, will diagnose infected individuals, and hence reduce the risk of transmission of infections and complications. Similar to laboratory testing, the interval the time of testing and treatment and also proportion of treated individuals in relation

to loss of follow up, are useful measures for quality of care. Screening of STIs and BV that targets at-risk population groups could be cost-efficient (Unemo et al., 2013).

The main advantage of laboratory testing is the precision of diagnosis. Aetiological approach is commonly used in developed countries for screening and diagnosis of asymptomatic infections. However, in middle and low-income countries, laboratory testing is not easily accessible especially in resource constraint areas, as this requires adequate laboratory infrastructure and trained personnel, both of which are seldom available at primary health care facilities. Aetiological diagnosis of STIs and BV is expensive and the delayed time in receiving results often leads to loss to follow up and delayed diagnosis and treatment (Kettler et al., 2004, World Health Organization, 2013, Unemo et al., 2013). Consequently, clinicians make a presumptive diagnosis or refer patients for specialized treatment leading to further treatment delays. Based on these limitations, the WHO developed the syndromic management approach (Mayaud and McCormick, 2001).

2.3.2 Syndromic Approach (Clinical Diagnosis)

Syndromic diagnosis approach involves the use of signs and symptoms to identify clinical syndromes caused for STIs. Various sexually transmissible pathogens produce a limited number of these syndromes. This approach relies on presumptive diagnosis by healthcare professionals based on the identifiable STIs clinical syndromes. The signs and symptoms are matched to a particular STI syndrome resulting in a syndromic diagnosis. The aim is to provide treatment for the most common infections linked to a specific cluster of symptoms. With the guide of internationally used standard algorithms, health care workers are able to correctly implement syndromic management of STIs. Syndromic management entails the use of a treatment plan for each syndrome that addresses the pathogens most likely to cause the syndrome. Generally, with syndromic management, the antimicrobial therapy is effective

against the multiple pathogens that cause the syndrome (Kettler et al., 2004, Lewis and Maruma, 2009).

Within South Africa, STI syndromic management approach was introduced into primary healthcare in the 1990s (Lewis and Maruma, 2009). This approach remains the most appropriate one within South Africa and for the South African Development Community (SADC) because of the inadequate laboratory facilities that are necessary for laboratory testing of STIs in primary health care facilities, and, also to reduce the risk in the loss of follow up of patients (Sonko et al., 2002).

In general, the benefits of syndromic approach include the relative ease of use, the provision of complete STIs care at first visit and it can be easily incorporated into all levels of health care systems. Moreover, within primary health care settings, the integration of STI syndromic management can be at primary care, family planning and maternal and child health clinics. This improves accessibility, reduces costs and the social stigma associated with specialised STI clinics (Mayaud and McCormick, 2001, Kettler et al., 2004).

On the contrary, this approach has limitations. First is the additional cost of over diagnosis and treatment of patients which includes direct costs of medication as well as indirect costs such as adverse drug reaction, potential for increased drug resistance, and alteration of the vaginal flora. Second is the reliance of algorithms or flowcharts for diagnosis, which requires trained service providers to use the algorithm to evaluate the patient's signs and symptoms, determine the clinical syndrome, and to identify the correct method of treatment and for management. This does not only include establishing a diagnosis, but also non-medication management for example, behavioural modifications. Thirdly, there is poor sensitivity and specificity for the detection of asymptomatic STIs such as *Chlamydia trachomatis* and/or *Neisseria gonorrhoea* (Mayaud and McCormick, 2001, West et al., 2003, Kettler et al., 2004). Francis et al (2014)

conducted a study among women with increased HIV risk which demonstrated that there was a high prevalence of curable STIs mainly due to missed infections with syndromic management. As a result, rapid POC tests would be beneficial in reduction of STIs disease burden (Francis et al., 2014).

2.3.3 Performance of Syndromic Approach

The diagnostic performance of syndromic approach and laboratory testing has a significant impact on the incidence and prevalence of STIs. In Sub-Saharan Africa, information regarding the profiles of STIs largely relies on clinician-diagnosed STIs or self-reporting. Over the years, various studies in the developed world and Sub-Saharan African countries have reported varying results on the diagnostic performance of syndromic approach. A study in South Africa conducted on women attending a sexually transmitted disease (STD) clinic, established the sensitivity of STIs symptoms in detecting different infections ranged from 0% to 88% (Mathews et al., 1998). In India and Egypt, studies among women attending family planning, antenatal and primary government clinics reported low specificity and high sensitivity of STI symptoms (Ray et al., 2009, Elkhwsky et al., 2007). Mukenge-Tshibaka et al (2002) conducted a study on female sex workers in Benin that reported poor sensitivity of the STIs symptoms (Mukenge-Tshibaka et al., 2002). Studies in Peru and China reported low sensitivity and high specificity of self-reported STIs (Clark et al., 2009, Yin et al., 2008). Overall, the information derived from relevant studies could potentially influence the strategies developed to control STIs and BV, but the variation of findings could pose a challenge. Laboratory testing would be ideal in view of its accuracy, but this is limited by the inadequate laboratory facilities and trained personnel. With the aim to improve STIs diagnosis and treatment, point of care (POC) testing has been widely implemented as a control strategy for STIs and BV.

2.3.4 Point of care testing

Point of care testing (POC) has gained great focus as a diagnostic tool in the standard care of STIs and BV. A POC test can be defined as any diagnostic tool that provides prompt precise results, and facilitates treatment within the same clinic visit as the testing (Pai et al., 2015). In 2002, the World Health Organization (WHO) Special Program for Research and Training in Tropical Disease identified POC testing as priority for controlling curable STIs. The WHO developed a guideline called ASSURED to assist in developing and utilizing POC diagnostics for STIs beneficial to both developing and developed countries. The ASSURED criteria defines a POC tests as: “Affordable by at-risk persons; Sensitive, with very few false negatives; Specific, with very few false positives; User friendly, simple to use with minimal steps and minimal training needed; Rapid and Robust, enabling treatment within the same visit and does not require refrigeration storage; Equipment-free, non-invasive and easily collected specimen; and Deliverable, to end users” (Kettler et al., 2004, Peeling et al., 2006).

The recent advancements in the use of POC tests for detection of STIs and BV has enabled health facilities accurately treat patients, speed up turn around patient times, and reduce the number of patient clinic visits, especially in resource limited areas. Most of these tests can negatively identify or detect STIs within an hour or less (Eden and Johnson, 2016). POC testing aims to enable individuals to receive treatment on the same clinic visit as the testing and reduce the number of patients who do not receive results or are lost to follow up (Gift et al., 1999).

As demonstrated by mathematical models, POC tests with 63% sensitivity would ensure improved treatment rates as opposed to tests with high sensitivity but a poor patient return rate (Gift et al., 1999). Additionally, a direct comparison of the accuracy between POC and laboratory tests can be misleading. A comprehensive assessment of the trade-off between accuracy and usefulness of the test that includes the effect on patient outcomes such as retention to care or treatment initiation is more beneficial (Drain et al., 2014). In resource constraint

areas, this addresses some of the limitations of aetiological diagnosis. In United States, a study that evaluated and compared different methods of detection of chlamydia trachomatis in women reported using POC testing together with a treatment algorithm that determines empiric treatment without testing is useful and a cost-effective strategy that ensures same-day treatment, and contributed to improved STIs management (Swain et al., 2004).

Furthermore, POC testing could complement the syndromic approach, and similarly, addressing its limitations. Syndromic management ensures that patients receive treatment within the same visit, however, this approach misses infections by curable STIs because most are asymptomatic cases. POC tests are rapid, simple and can be easily availed in resource limited settings (Herbst de Cortina et al., 2016). The recent advances in POC testing have made it possible to perform quick preliminary screening for infectious pathogens, through integration of external and internal controls within the test kits, which provide results in 20 minutes or less (Eden and Johnson, 2016). A systematic review conducted by Herbst de Cortina et al (2016), on point of care testing for STIs evaluated test performance, cost effectiveness, acceptability and feasibility and concept articles introducing new tests. Most of these studies were set in developed countries. The review established that sensitive and specific POC tests are available for curable STIs but with room for further improvement. These tests were acceptable to patients and providers, and were also cost-effective (Herbst de Cortina et al., 2016). However, great emphasis should be laid on the fact that making judgements on relative prioritization of different health interventions is highly reliant on information provided by cost-effectiveness studies. For instance, a health intervention may have high costs but is more effective when compared to an alternative health intervention which may be less costly but less effective. The decision on the health intervention chosen will not only be based on the costs, but also on the societal benefits (i.e. improved health outcomes and quality of life) attained from that intervention (Musgrove and Fox-Rushby, 2006).

On the contrary, some cases of POC testing have poor the specificity and sensitivity, as low as 12%. This could be explained by specimen contamination with menstrual blood or other associated factors (Eden and Johnson, 2016). Additionally, a few of the POC test kits are complex to use. Some of the tests in current use include the Chlamydia Rapid Test (CRT) which has been found have 41% sensitivity in a recent study. Moreover, its utilization is a complex process that is time consuming (van der Helm et al., 2012). *Neisseria gonorrhoea* diagnosis with immunochromatographic and leukocyte esterase tests have shown sensitivities and specificities widely ranging between 54% to 70% and, 89% to 97% respectively for the former. Similarly, sensitivities and specificities for the leukocyte esterase test range between 23% to 86% and 30% to 99% respectively (Smith et al., 2012). Rapid antigen test for *Trichomonas vaginalis* has been found to be highly sensitive and specific at 90% to 95%, and 100% respectively, but involves numerous steps to complete (Campbell et al., 2008). These findings demonstrate that there is still room to develop new POC tests for STIs and BV with improved accuracy and that can be comparable to laboratory testing. Moreover, with the aim of being able to expedite clinical decisions and improve patient outcomes, POC tests with lower accuracy compared to laboratory tests still have clinical and public health benefits (Drain et al., 2014).

Overall, accurate and simple diagnostic POC tests that facilitate treatment within a single clinic visit are vital in reducing the STIs and BV disease burden, especially among target group populations (Herbst de Cortina et al., 2016). Some recently developed POC tests have shown high specificity and sensitivity, which is beneficial to both urban and rural health facilities (Eden and Johnson, 2016). One such test is the newly developed rapid cytokine biomarker POC test. This screening test detects cytokines IL-1B and IP-10 which have proven to predict an active STI, with 77% sensitivity, 72% specificity, 82% positive predictive value (PPV), and 65% negative predictive value (NPV). Compared to the sensitivity of clinical signs (19%), the

two cytokine biomarkers considerably improved sensitivity, detecting 58% additional women with laboratory diagnosed STIs/BV (Masson et al., 2015a). This test could positively impact the diagnosis and treatment of STIs and BV in women. Therefore, an economic assessment of genital inflammation screening in women using the cytokine biomarker POC test would be beneficial.

2.4 Economic evaluations of point of care testing for STIs and BV

The published data on costing of point of care testing for curable STIs and BV is limited, with most of the literature focusing the cost-effectiveness or clinical performance of these tests. Following a thorough search, only six studies were found (West et al. 2003; Levin et al. 2007; Benzaken et al. 2008; Huang et al. 2013; Terris-Prestholt et al. 2015; Rivard et al. 2017). Evidently there is need for more costing studies in this field. Table 1 below illustrates descriptions of these studies in further detail. Two of the studies were cost analysis; (Levin et al. 2007) and (Benzaken et al. 2008). The other studies varied namely: cost-effectiveness studies were (Huang et. al 2013) and (Terris-Prestholt et al. 2015); quasi-experimental trial (Rivard et al. 2017); and an evaluation study (West et al. 2003). As mentioned above, two out of the six economic evaluations that were reviewed were cost analysis studies, therefore, outcome measures were not included in the studies, (Levin et. al 2007) and (Benzaken et al. 2008). For the cost-effectiveness studies, Terris-Prestholt et al. (2015) used DALYs averted and Huang et al. (2013) used additional cases of disease prevented. The other two studies, West et al. (2003) and Rivard et al. (2017) presented cost calculations only and had no outcome measures.

In both the cost-effectiveness studies, rapid POC testing was found to be cost-effective (Terris-Prestholt et al. 2015; Huang et al. 2013) based on incremental cost-effective ratios (ICERs) and the additional cases of disease averted respectively. Rivard et al. (2017) showed that rapid POC testing for syphilis was more cost-saving compared to traditional testing, and improved the

treatment and outcome of patients. On the contrary, West et al. (2003) found FemExam rapid test to be costly than the gold standard test (Gram stain), and presumptive treatment of women being the most affordable strategy. However, FemExam greatly reduced the cost of overtreatment making it comparable to the other strategies. The cost analysis study in Brazil indicates that the cost per person screened ranged between \$3.41 and \$5.79, whereas in Mozambique, it ranged between \$0.83 to \$0.85 and \$1.14 to 1.43 in Bolivia (Benzaken et al. 2008, Levin et al. 2007).

Table 1: Summaries of economic evaluations for rapid point of care testing for STIs and BV

Study	Objective	Study participants & setting	Intervention	Outcome measure (s)	Perspective	Costs	Summary of results	Conclusion
(Huang et. al 2013)	To investigate the differences in costs and outcomes between a new chlamydia point-of-care (POC) test and traditional nucleic acid amplification test (NAAT).	Women ≥ 18 years of age, no antibiotic treatment within the past 21 days, ≥ 1 h since last urine void, and requiring a pelvic examination on the day of their visit. Setting was United States of America (USA).	Different specimens were collected for chlamydia screening with NAAT assay, and included: urine, cervical and self-collected vaginal samples. Also, for testing with the new POC chlamydia test, self-collected vaginal swab was obtained.	Cost to screening For the cost-effectiveness outcome was cases of disease prevented	Public healthcare perspective	Clinician labour costs, supply costs for visit, NAAT laboratory processing costs. Costs were adjusted to 2011 US dollars.	POC would be less expensive and more effective than NAAT.	Newer POC tests with additional improvements will increase the public health benefits of the cost-effective POC strategy.

Study	Objective	Study participants & setting	Intervention	Outcome measure (s)	Perspective	Costs	Summary of results	Conclusion
(Benzaken et. al 2008)	To evaluate the performance, usefulness and cost of a rapid treponemal antibody assay (VisiTect) to detect syphilis in high risk populations.	Patients attending an STI clinic including female and male sex workers and sex worker clients. Setting was Brazil	Informed consent obtained from participant. Finger prick blood sample was collected and tested with VisiTect Syphilis test.	Cost of syphilis detection	Provider's perspective	Incremental recurrent costs. Direct costs comprised of labour, diagnostic supplies and drugs. Costs were converted to 2006 US dollars at an exchange rate of 2.14 Reais per \$1.	The cost per case of syphilis was \$16.8 for VDRL, \$33.2 for low cost and \$56.3 for high cost VisiTect Syphilis.	To assess the usefulness and impact of these tests in high risk groups, more operational research is required.

Study	Objective	Study participants & setting	Intervention	Outcome measure (s)	Perspective	Costs	Summary of results	Conclusion
(Terris-Prestholt et. al 2015)	To assess the cost-effectiveness of algorithms using rapid syphilis immunochromatographic strip tests (RSTs) to screen pregnant women.	Pregnant women Setting was Zambia, Tanzania and Peru.	Women screened for syphilis, treated and followed up.	Disability-adjusted life years (DALYs) averted from syphilis treatment	Perspective not specified	Costs were modelled. Costs were presented in 2012 US dollars.	The single RST was the most cost-effective diagnostic approach across all countries, while mass treatment was the most cost-effective treatment approach in the higher prevalence settings (Tanzania and Zambia).	The single RST should be considered the best screening option unless the dual RST price is significantly reduced.

Study	Objective	Study participants & setting	Intervention	Outcome measure (s)	Perspective	Costs	Summary of results	Conclusion
(Levin et. al 2007)	To evaluate the difference in costs of antenatal syphilis screening with the rapid plasma reagin (RPR) test and the immunochromatographic strip (ICS) test in low-resource settings.	Pregnant women. Setting was Bolivia and Mozambique.	Nurses performed the ICS test as part of women's antenatal care visit. For RPR, laboratory staff took an intravenous sample from women and tested it using RPR.	The number of "true" active cases screened and treated using ICS and RPR. For the economic evaluation, the measure was the average cost per woman tested, and the average cost per woman treated.	Government perspective	The start-up costs, including social mobilization, information, education, and communication (IEC) and training, clinical screening, laboratory analysis, and treatment), salaries, and the resources used to test and treat women. Costs converted to 2004 US dollars at an exchange rate of 8 Bolivians per \$1 and 23,500 Metical per \$1.	The average costs for the ICS tests were found to be slightly higher than the RPR.	No sensitivity analysis mentioned.

Study	Objective	Study participants & setting	Intervention	Outcome measure (s)	Perspective	Costs	Summary of results	Conclusion
(Rivard et. al 2017)	To assess the impact of NG/CT rapid diagnostic testing (RDT) in an urban emergency department (ED) on treatment appropriateness, time to notification, and cost.	Women in the ED excluding those who were tested at a satellite facility or admitted to the hospital, left the ED prior to examination, or diagnosed with pelvic inflammatory disease (PID) Setting was United States of America (USA)	Samples utilized by the ED were received by the microbiology laboratory, samples were tested immediately using the RDT. The expected time from collection of specimen to results was approximately 120–180 minutes.	The percentage of patients who received appropriate treatment during their index ED visit using the traditional test versus the RDT for NG/CT. For the cost analysis, the outcome was cost per patient and cost savings.	Perspective not specified	Direct cost to the institution of the test, cost of the ED visit and revisit based on diagnosis code, and cost of antimicrobials. Costs were presented in 2014 US dollars.	Testing via RDT was associated with greater cost savings compared with traditional testing over the course of the study	No sensitivity analyses were mentioned.
(West et. al 2003)	To evaluate the performance of a new diagnostic test kit Fem Exam in developing countries.	Women older than 18 years, not pregnant and without advanced HIV disease. Setting was Gambia	Informed written consent was obtained, five vaginal swab specimens were collected, and two of them applied onto FemExam test.	Total cost, cost per patient, cost per true case, and cost of overtreatment per patient.	Perspective not specified	FemExam costs, laboratory consumable costs, clinician and technician time costs. Costs were presented in 1999 US dollars.	The Nugent Gram stain method was the cheapest. The one-card and two-card FemExam cost \$4.52 and \$8.72 respectively.	Reducing the cost of FemExam would increase its accessibility in developing countries.

Two of the studies employed the government's perspective (Levin et al. 2007; Huang et al. 2013), and one employed a provider's perspective (Benzaken et al. 2008). Relative to the study objective, the provider's perspective is used in most studies as this focuses on the costs incurred by institutions undertaking the study (Drummond et al. 2008). The six studies explore the different costs that are included as presented in Table 1 above. However, the two cost analysis studies broadly discuss the different provider costs (Levin et al. 2007, Benzaken et al. 2008).

In economic evaluations, uncertainties may arise due to the choice of analytical tools, the extrapolation of data over time, generalization of the results, and the data requirements of the study. Hence, to test the robustness of the findings sensitivity analyses are crucial (Briggs 1995). Only the cost-effectiveness studies in this review conducted sensitivity analysis (Huang et al. 2013; Terris-Prestholt et al. 2015).

Discounting of costs in economic evaluations is important in relation to 'positive time preference', as it takes into account the time the costs were incurred, the opportunity costs of the item, and calculates the present value of the good (Drummond et al. 2015). As there is no standard discount rate that is used, the chosen rate should be consistent to economic theory and comparable to other published studies (Morris et al. 2007). In this review, two of the studies used a discount rate of 3% for costs (Huang et al. 2013, Terris-Prestholt et al. 2015). The costing studies did not discount the costs given that the timeframe of the analysis was one year, and this was appropriate (Levin et al. 2007, Benzaken et al. 2008). However, the other two studies did not specifically mention discounting (West et al. 2003, Rivard et al. 2017).

The two cost-effectiveness studies used incremental cost-effective ratios (ICERs) and the additional cases of disease averted to judge cost-effectiveness (Terris-Prestholt et al. 2015; Huang et al. 2013). However, there was no explicit mention of a threshold in both studies.

2.5 Economic analysis of healthcare programs

Health economics is a scientific discipline that uses theories and methods from economics for analysis of the healthcare industry (Haycox and Noble, 2009). This involves the assessment of health programs, interventions and/or technology. Such assessments may consist of an economic evaluation, a cost study, and/or a budget impact analysis. Costing studies provide an insight on the costs of healthcare programs or services, and are essential for healthcare financing and resource allocation. Additionally, costing studies are a key component of economic evaluations whose result depends on the estimation of costs (Simoens, 2009, Hendriks et al., 2014). Costing studies have important benefits towards health system management such as negotiation of reimbursement contracts, forecasting costs for program expansion, decision-making in budgeting, and assessing performance and efficiency of programs (Walker, 2001) .

2.6 Methodology of costing health care services

Costs can be defined as the value of resources used in the provision of a health service or intervention. Costing entails the estimation of the resources used, and for healthcare interventions involves the following sequential steps; identifying the study perspective, identification of resources, measurement of resources, valuation of resources, and sensitivity analyses (Hendriks et al., 2014, Drummons and Jefferson, 1996) .

2.6.1 The perspective

In any economic evaluation, the perspective is the viewpoint from which the costs and/or benefits are measured. It defines the basis of analysis and the relevant costs that should be accounted for. In a costing study, the perspective is determined by the decision problem. The main perspectives often used in economic evaluations are societal, provider and patient perspectives (Drummons and Jefferson, 1996, Drummond et al., 2015).

Societal perspective is the broadest and most comprehensive in welfare economics, as it encompasses costs and outcomes from various parties. These are costs incurred by society, and are inclusive of provider and patient costs. Therefore, the data can be used for analysis from other viewpoints. The selected perspective determines the costs to be included in the evaluations and the outcomes to be measured (Drummond et al., 2015, Simoens, 2009). Moreover, Drummons & Jefferson (1996) argue that it might be cheaper to gather all costs from the outset than collecting supplemental costs later on, at an additional cost. Therefore, researchers opt to identify the potential key decision makers from the outset and ensure that the research question is relevant to the needs of the identified stakeholders (Drummons and Jefferson, 1996).

Patient perspective entails the patient related costs of seeking a health care service, and can either be direct or indirect costs, as illustrated in table 2.1. The direct costs include all out-of-pocket expenses accrued by the patient in the process of seeking a health service such as consultation fees, costs of medicines and diagnostic tests, transport costs, amongst others. The indirect costs would include the equivalent value of time and productivity losses for both the patient and family/guardian during the process of seeking healthcare (Drummond et al., 2015). The provider perspective includes all costs incurred by the health care provider in the provision of the health care service or intervention. This perspective consists of different health providers or institutions and within different sectors namely: public or private health care providers; public sector/government; health services sectors; and non-governmental organizations. The government or public health sector perspectives entails all the costs incurred in the provision of public goods in all sectors including the health sector. The public health provider perspective is a part of the government sector that includes costs of service provision within the health services sector only, which includes recurrent costs of service provision for example maintenance costs and staff salaries, capital costs such as infrastructure, vehicle and equipment

costs. In genital inflammation screening services for women, the public health perspective would include all relevant costs incurred by the public health clinic in this service provision. The health sector perspective involves all the provider and patient costs incurred within this sector (Gray et al., 2010).

Table 2.1: Perspectives in economic evaluation, Adapted from the guidelines for the Economic Evaluation of Health Technologies, (Canadian Agency for Drugs and Technologies in Health 2006)

Perspective		Type of Costs	Examples	
Societal	Public Sector/Government	Direct costs to all publicly funded services (other than health care)	Social services e.g. counseling by social workers Education e.g. training of interpreters, school based interventions	
		Direct costs to publicly funded health care provider may include contributions from international donors and similar agencies	Capital costs Buildings Medical Equipment Vehicles Recurrent costs Medical supplies Laboratory supplies Medicines Training materials Labor costs Overheads Utilities (water, electricity, telephone) Administration, Buildings and vehicle maintenance Other central services (e.g. catering or laundry)	
	Health services Sector	Public health Provider: Ministry of	Direct costs to patients and their families	Out-of-pocket expenditure (including co-payments) for Consultation, drugs, treatment etc. Cost of travel for treatment Paid caregivers
			Indirect costs to patients and families	Patient's time spent for travel and receiving treatment Loss of income due to illness Lost time at paid and unpaid work (e.g. housework) by patient and family Lost productivity: time costs to patients and their families caring for the patient

2.6.2 Identification of resource use

With selection of the appropriate study perspective, the subsequent steps in a costing study are to identify, measure and value the resources used. Identification of used resources is based on the description of the health intervention and its production function (Brouwer W, 2001). This


takes into account all resources that are relevant to the study perspective. In the societal perspective, both provider and patient costs are considered, whereas with the provider perspective only costs relevant to the provider are considered (Drummond et al., 2015).

Drain et al (2014) explain that in costing a POC test, different types of costs which can be near-universal or location specific are considered. They identified resources used in POC testing as materials, health worker time, equipment and logistical expenses. The costs to be considered are: manufacturer's price per test, time needed to operate the test, staff salary, transportation of specimen, time needed for counselling after the test, quality assurance programmes, local taxes costs of the supply chain management, wastage rates and maintenance costs. Additionally, the cost per test should include materials used to obtain the specimen, test consumables and materials for reporting and printing the test result. Depending on the technology, the test's estimated failure rate should be considered because this will result in repeating or confirming the test (Drain et al., 2014).

2.6.3 Measurement of resource use

The measurement of resource use is based on two costing approaches: macro-costing (gross costing) and micro-costing (ingredients approach). The precision of measurement varies along a continuum of these approaches as illustrated in table 2.2 (Simoens, 2009, Drummond et al., 2015). Micro-costing that involves detailed identification and measurement of services and determines the required resources, gives the most precise estimates. For new studies without previous cost estimates available, this is the most appropriate approach. However, it is often context specific and not generalizable. Additionally, this approach is time consuming and expensive. On the contrary, macro-costing that identifies and measures resources at an aggregate level, yields results with less precision but are comparable and generalizable to the broader context (Drummond et al., 2015, Simoens, 2009).

Table 2.2: Levels of precision in economic evaluation studies, Adapted from Drummond et al 2005

Precision	Method	Description
 <p>Most Precise</p> <p>Least precise</p>	Micro-costing	Each component of resource use e.g. laboratory tests, days of stay by ward, drugs, physicians' consultation, is estimated and a unit cost calculated for each component. This utilizes patient specific data for each episode.
	Case-mix group	Gives the cost for each category of case or hospital patient admitted. It takes into account the length of stay for each case. Its precision depends on the level of detail in specifying the type of cases.
	Disease-specific daily cost	Uses costs associated with specific ICD-10 codes and gives the average daily cost of treatment in each disease category e.g. Diabetes nephropathy.
	Average daily cost	This gives the average daily cost for all patients seen in the institution with no regard to the type of patients or case. e.g. the cost per patient day equivalent

2.6.4 Valuation of resource use

The valuation of resources in economic evaluations is often based upon economic costs instead of financial costs. Financial costs are the actual expenditures on the resources used in a program/intervention. Economic costs include the opportunity cost which represents the cost of using resources for a purpose, measured as the value of their next best alternative use (Simoens, 2009, Walker, 2001). For most program analyses in the developing world, the main non-market inputs are donations and volunteer time, and so all the resources should be valued where or not financial outlays were made (Drummond et al., 2015). One approach is to use market wages, for example, volunteer times valued through unskilled wage rates. The valuation of donated goods should include the international market value, the cost of insurance and freight of imported goods, and the domestic distribution costs. However, the valuation should exclude the excess profits of distributors and transfer payments (import subsidies) because they are not representative of a change in the resources available to society (Hutton and Baltussen, 2005).

2.6.5 Valuation of non-market inputs

According to Hutton & Baltussen (2005), goods can be distinguished as traded and non-traded in health economic evaluations. Non-traded goods are those produced on the domestic market such as buildings, domestic transport, labor, whereas traded goods are those purchased from the international market for example, vehicles, relevant equipment, amongst others (Hutton and Baltussen, 2005).

Hutton & Baltussen (2005) state that the valuation of non-traded and traded goods should be similar at international prices, and inclusive of any distortions existing within the local market. This allows for costing done to be uniform across studies in various regions. For instance, in the valuation of transport costs, all inputs can be classified as either non-traded or traded and calculated accordingly. However, in cases where the separation of these costs is difficult, the dominant market price for the good can be used (Hutton and Baltussen, 2005).

2.6.6 Cost categorization

In general, costs are classified according to the period of resource use, as either capital or recurrent costs, as shown in table 2.3. Capital costs represent the expenditure on goods that last for more than one year for example vehicles, buildings, equipment; while recurrent costs represent expenditure on resources used within one year such as rent, electricity expenses, staff salaries etc. (Drummond et al., 2015).

Table 2.3: Categories of costs in cost analysis of Programs (Source: (Johns et al. 2003))

Recurrent cost	
A.1 Personnel	Personnel time allocated to each intervention is netted out from time spent by those personnel in other interventions. The cost of labor is the value of the cost to company paid to the employee including all fringe benefits and tax. This includes per diems and travel allowances. The cost of voluntary labor should be valued at the wage rate of the health personnel who would be employed to perform the task under normal circumstances. Where non-skilled labor is used, the value used depends on location. In rural areas where the people would normally be in agricultural or fishing, the value of labor would take into account lost production adjusting for seasonality. In urban centers, one can use the annual incomes of the urban informal sector. In cases where minimum wage rates are legislated then one can use those.
A.2 Materials & Supplies	Quantities of all materials and supplies used multiplied by their unit costs are used to calculate the cost of materials and supplies used for the program. Examples are stationery, refreshments.
A.3 Media operating costs	All media costs are incorporated using their unit costs e.g. minutes for radio adverts or number of adverts per size per publication type.
A.4 Transport operating costs	Transport is measured in terms of total kilometers travelled per means of transport or bus fare where appropriate.
A.5 Equipment operating cost	In cases where equipment is rented, the number of equipment and the duration of rental (in months) are reported multiplied by the rental amount.
A.6 Maintenance	Maintenance costs of all capital items such as equipment, vehicles and buildings are included.
A.7 Utilities	Examples of utility items include electricity, gas, and water. The allocation of the quantities used by the programme is based on an allocation factor e.g. the surface area in square metres used by the programme, after applying any further allocation needed if the space is shared with other programs.
A.8 Building Rental costs	Where buildings are rented, both the total square meter surface area of the buildings and the duration of rental (in months) are used.
B. Capital Costs	
B.1 Building	The cost of space used by the programmer is reported in terms of the share of the total building surface area allocated to that program.
B.2 Transport	Includes all means of transport used by the program. Costs are allocated according to the percentage share of usage by the program.
B.3 Equipment and implements	The number of office equipment, storage and distribution, maintenance, cleaning and other capital equipment are reported here. If they are only partly used, appropriate allocation is made, which may be similar to the same allocation factors used for building space or allocated according to the amount of time used relative to other programs.
B.4 Furniture	The cost of furniture is calculated using the same allocation factor used for equipment or building space

2.6.7 Discounting and annuitization

The valuation of capital goods such as buildings, equipment etc., takes into account the time preference in valuing the resource and the annual replacement cost of the good. Therefore, the two methods applied to valuation of such goods are: discounting and annuitization. (Walker and Kumaranayake, 2002).

Discounting takes into account the time the costs were incurred, the opportunity costs of the item, and calculates the present value of the good. Capital costs are discounted because individuals are said to have a positive rate of time preference, based on the fact that individuals prefer to enjoy the benefit in the present and pay later (Drummond et al., 2015). The discount rate (r), presents the real rate of return in the private sector or social rate of time preference. The most commonly used is 3%, however, the appropriate discount rate is arbitrary. (Walker and Kumaranayake, 2002, Drummond et al., 2015). Drummond et al. (2005) state that given the subjectivity of the discount rate, sensitivity analysis should be done on the discount rate to determine how it influences the results obtained (Drummond et al., 2015). Walker & Kumaranayake (2002) state that the discount rate should be context specific and similar to the rate used by the finance ministry within that setting, and alternatively, the World Bank's discount rate (Walker and Kumaranayake, 2002).

Annuity computes the equivalent annual cost of a good using the capital and recurrent inputs. There are two approaches which are based on whether they are financial or economic costs. The first is depreciation which is the replacement cost of the capital item divided by its expected useful life. This assumes the services from a capital good are divided equally over the useful life of the item, but does not consider opportunity costs. The second approach for economic costs values the capital item by estimating an average combination of depreciation and interest on the undepreciated portion over the useful life of the capital good to produce the equivalent annual cost (Walker and Kumaranayake, 2002).

For capital goods such as buildings, Hutton & Baltussen (2005) state another approach for economic costs that uses the rental value of a similar space in a building that could provide the same function e.g. a private clinic in the same area, and the rental value includes depreciation and the opportunity costs of the asset. However, the authors recommend the second approach for economic costs because the rental method depends on a competitive market which varies

(Hutton and Baltussen, 2005). Therefore, for this study, the annuitization method for economic costs was used.

Calculation of the equivalent annual cost

The equation used to derive E, the equivalent annual cost is as follows;

$$E = \frac{K - (S/(1 + r)^n)}{A(n, r)}$$

Where,

E = equivalent annual cost

K = purchase price / initial outlay

S = resale value

n = the useful life of the asset

r = discount (interest) rate

A (n, r) is the annuity factor which is given by

$$\frac{1 - (1 + r)^{-n}}{r}$$

This formula can be used for new equipment, while the replacement cost should be used for old equipment (Walker and Kumaranayake, 2002).

2.6.8 Overhead costs

Overhead costs are costs that are shared by more than one department for example administration, cleaning, security, laundry services etc. There are different methods of handling overhead costs as outlined below (Drummond et al., 2015).

a) Direct allocation

This involves the direct allocation of each overhead cost such as cleaning or laundry to the final cost centres based on an allocation factor e.g. a surgical ward or theatre's department share of

cleaning services would be the area in square meters of the ward (the allocation factor) divided by the total square meters multiplied by the cost of cleaning services (Drummond et al., 2015). For this study, the direct allocation of costs method was used based on the allocation factor calculated from the proportion of the total space occupied by the family planning clinic. The choice of allocation based on surface area seemed appropriate because there was only one cost centre.

Alternative methods of handling overheads are step down, step down allocation with iteration and simultaneous allocation as outlined below (Drummond et al., 2015).

b) Step-down allocation

The step-down method allocates each overhead department in a stepwise manner to all the remaining overhead departments and the final cost centres. This enables a partial adjustment for the interaction of overhead departments (Drummond et al., 2015).

c) Step-down allocation with iteration

The overheads departments are repeatedly allocated in a stepwise manner to all the other departments and final cost centres until all amounts are allocated. This enables the full adjustment for the interaction of overhead departments (Drummond et al., 2015).

d) Simultaneous allocation

Similar to c), there is full adjustment for the interaction of overhead departments, however, it uses a set of simultaneous equations to allocate the costs (Drummond et al., 2015).

2.7 Budget Impact Analysis

Budget impact analysis (BIA) is vital component of an economic assessment of health technology and interventions. This analysis determines the affordability of a health intervention by examining the financial impact of implementation and expansion of a new healthcare intervention particularly within resource constraint health care settings. BIA looks at the impact

on the spending of a disease from the introduction of a new health intervention to the current mix of treatment strategies (Simoens, 2009, Mauskopf et al., 2007).

In combination with cost studies and economic evaluations, BIA plays a vital role in the comprehensive assessment of a health intervention and may inform reimbursement decisions. A health intervention with a high budgetary impact may result in withheld reimbursements. Alternatively, a cost-effective intervention with low budgetary impact may be reimbursed. The opportunity cost of adopting a low budget intervention is low, and its adoption may fulfil other important objectives of the decision-maker (Simoens, 2009). Additionally, this analysis is beneficial for forecasting and budget planning. It predicts how a change in the intervention will influence the trajectory of expenditure on that condition (Mauskopf et al., 2007).

Budget impact analysis is complementary to economic evaluations and should not be considered as a replacement. It is mainly used by individuals managing and planning health-care budgets in national health care programs, health-care delivery organizations and private insurance plans. BIA addresses the financial outcomes relating to the adoption of new health care intervention to evaluate their affordability. Both economic evaluations and BIA use similar data and methodological requirements but vary in how they are integrated into models as their intended use differs (Mauskopf et al., 2007). The methodology of BIA is still developing, however, the principles of good practice have recently been established (Sullivan et al., 2014). The first step is to provide all relevant epidemiological, clinical and economic information of the disease. Thereafter is the description of the current mix of treatment strategies. This may include non-active therapy, and also therapies that may or may not be replaced by the new health intervention. The introduction of the intervention may result in substitution and market expansion. Hence, BIA takes into account all the patients who might receive treatment from the new intervention, including previously untreated patients who are now seeking treatment. Lastly, this analysis considers the budgetary impact of various scenarios of how the current

mix of treatment strategies changes with the introduction of the new intervention (Simoens, 2009).

BIA synthesizes knowledge available at a specific time to approximate the likely financial consequences of a decision for a health care system. It provides a computing framework that allows application of input values and viewing of financial estimates specific to the setting. The outcomes represent scenarios consisting of data inputs and specific assumptions of interest to the decision maker instead of the generally applicable normative case. The analytic framework design is important and should consider relevant features of the health care system, the anticipated uptake of the new intervention, possible access restrictions, and the use and effects of the current and new interventions (Sullivan et al., 2014).

A limited number of BIA studies have been published more so those estimating the financial and health-care service impact of a new intervention for a defined national health plan. The results generated from these studies have demonstrated significant financial implications of certain health interventions on government budgets. Martin et al (2010) conducted a study on the expansion of the Human Immunodeficiency Virus (HIV) screening program in the United States of America (USA) forecasting on the impact of testing programs, discretionary treatment programs and entitlement programs on government budgets, establishing that although the financial burden of expanded screening would disproportionately fall on discretionary programs that funded care of newly identified patients, this represented a small proportion of the total budget. Hence, decision-makers were informed about which government programs required sufficient budgets to achieve early treatment goals (Martin et al., 2010).

Gidwani et al (2012) assessed the budget impact of implementing a new HIV testing program which was found to be cost-effective but not cost-saving, in comparison to the financial impact of following standard care in a veteran health administration emergency department. The

results demonstrated the relationship between both alternatives and provided evidence that the screening program did not pose a significant cost burden and provided a new component of support for HIV screening. Such findings may benefit decision-makers in integrated systems and exhibit the practical actual effect of implementing evidence-based policies (Gidwani et al., 2012).

Conclusion

Sexually transmitted infections remain a global public health concern even though various control strategies have been implemented over the years. Together with bacterial vaginosis, the association to HIV acquisition gives rise to challenges in the fight against HIV/AIDS. There is substantial literature linking the presence of STIs and BV to the rising prevalence of HIV in individuals. Subsequently, numerous studies have explored the different diagnostic and treatment strategies for STIs and BV, which have in turn influenced the standard treatment and management guidelines in current use.

Currently, there are two main approaches used for diagnosis and treatment of STIs and BV namely; aetiological approach (laboratory testing) and syndromic approach (clinical-based diagnosis). The aetiological approach is the most accurate and preferred for STIs and BV diagnosis and treatment. However, due to the expense and time-consuming nature, they are widely unavailable in resource constraint areas. Consequently, syndromic management was introduced by the WHO in order to improve the clinical management of these infections. Nonetheless, this approach fails to identify asymptomatic patients who account for a large proportion of the infections. Therefore, despite using both approaches for several years, the disease burden of STIs and BV still remains significant. Point of care testing was then introduced to complement syndromic diagnosis. Over the years, various POC tests have been developed and used. Although POC testing has been widely implemented, some of the major setbacks with diagnosis such as accuracy of the tests, ease of use and expense, have not made

a great impact on the disease burden of these infections. As such, this has left room to develop new improved POC tests, such as the rapid cytokine biomarker POC test. Therefore, in order to provide this service within health clinics, it is crucial to economically assess for efficiency, financial, and budget purposes.

The literature review revealed a fair amount of information on the diagnostic methods of STIs and BV, including POC testing. However, limited research has been done on costing of POC tests, with most focusing on the clinical performance and cost-effectiveness of POC tests. The few costing studies done were based in the developed world and therefore, may not be generalizable to resource limited areas. This study will contribute towards literature on the costs of POC tests for STIs and BV, which could be used to estimate cost-effectiveness of these tests within resource limited settings.

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PART C: JOURNAL ARTICLE

Proposed Journal BMC Public Health

ABSTRACT

Background: Sexually transmitted infections and bacterial vaginosis have been associated with HIV acquisition through genital inflammation in women, especially in asymptomatic cases. Diagnosis of asymptomatic women through genital inflammation screening reduces the cases of untreated women. The objectives of this study were to estimate the total and unit costs of screening using a cytokine biomarker rapid test device and, to determine the budget impact of providing the screening service in primary health facilities in South Africa.

Methods: Costs of screening were estimated for women of reproductive age (15 to 49 years) attending two family planning clinics in 2016. The micro-costing approach was used to calculate the unit cost per patient screened from a provider's perspective. The average utilization rate for patients was calculated, and combined with the average unit costs to obtain provider costs. The unit cost estimates were used to analyze the budget impact of scaling-up and providing this service in primary health facilities countrywide. Univariate sensitivity analyses tested the robustness of the study findings

Results: Over one year, the cost per woman screened for genital inflammation was \$24.26 at the Desmond Tutu HIV Foundation youth clinic, and \$14.32 at University of Cape Town student clinic. With personnel costs as the cost driver, recurrent costs accounted for the greater proportion of the total costs for both health facilities. The scaled-up costs ranged from \$107,183,655 to \$183,062,066 in South Africa. The screening intervention accounted for a significant amount of the available funds. The cost estimates were sensitive to the changes in personnel costs, utilization rate and population coverage rates.

Conclusion: The cost estimates of screening are high, and demonstrate that its implementation may not be affordable. However, this screening tool will increase the cases detected, contributing towards better STIs management and control, and reduce the risk of HIV

acquisition among women. The potential of reducing a double burden of curable STIs and HIV/AIDS in South Africa could be achieved through the genital inflammation screening program

Keywords:

Rapid point of care testing; genital inflammation screening; cost analysis; budget impact analysis

BACKGROUND

Globally, sexually transmitted infections (STIs) remain a major public health concern. Annually 499 million new cases of curable STIs (chlamydia, gonorrhoea, trichomoniasis and syphilis) occur in individuals aged 15 to 49 years. Developing countries account for 86% of the disease burden. Over the years, studies have established the association between STIs and their role in the transmission of Human Immunodeficiency Virus (HIV) infection, as a result increasing HIV prevalence. STIs and bacterial vaginosis (BV) have been associated with increased risk of HIV acquisition in women (1-5). Recent studies have associated female genital tract inflammation from STIs and BV infections with increased susceptibility to HIV infections. (4, 6) . In most cases women are asymptomatic, with studies in South Africa showing that 48% of STIs cases and 90% of BV cases are asymptomatic (7, 8). The levels of genital inflammation are similar in both symptomatic and asymptomatic women. Hence, asymptomatic women who go untreated are at even higher risk of acquiring a HIV infection and reproductive complications. (4, 7, 8).

Subsequently, substantial effort has been put into developing and implementing strategies for diagnosis and management of STIs and BV. In South Africa, STIs and BV infections are diagnosed using the syndromic approach, which is based on presumptive clinical diagnosis by a healthcare practitioner. This was introduced into primary healthcare in the 1990s (9). Although it is the most appropriate, both inadequate laboratory facilities and laboratory personnel limit this approach especially in detection of asymptomatic women who are the majority (10). Consequently, rapid point of care (POC) tests have gained great focus in complementing the syndromic approach (7, 10, 11). POC tests provide prompt precise results, and facilitate treatment within the same clinic visit as the testing (12). Various rapid POC tests for STIs diagnosis have been researched over time, yielding different tests in current use (13-15). In resource limited settings, POC testing has been found to be time efficient and beneficial

to patient retention for treatment. Additionally, this is a cost-saving strategy which contributes to improved STIs management (16-18). On the contrary, some of the POC tests in use are limited by poor sensitivity and specificity, and complexity in their utilization (15, 19, 20). These findings have demonstrated that there is need to develop new POC tests with improved accuracy and, that can be comparable to laboratory testing.

The rapid cytokine biomarker POC test is a newly developed screening test that detects cytokines IL-1B and IP-10. Compared to the sensitivity of clinical signs (19%), the two cytokine biomarkers have considerably improved sensitivity and can detect 58% additional women with laboratory diagnosed STIs and BV (6). In order to assess the financial resources required to provide this screening test in primary health facilities, policy makers need cost estimates, and therefore the present study. Currently, there are limited costing studies on STIs and BV POC tests both in developed and developing countries (21-26). Moreover, being a prospective study, there are no available costs estimates for genital inflammation screening within the South African context. Therefore, in order to advocate for funding, financial planners require the costs involved in providing this service efficiently and optimally. Additionally, the cost and budget impact analyses of this screening test have public health relevance in contributing towards STI and BV management through improved diagnostic testing, especially in the fight against Human Immunodeficiency Virus/ Acquired Immunodeficiency Syndrome (HIV/AIDS) in South Africa. This study is based on an on-going project, (GIFT- Genital Inflammation Test for HIV Prevention project), at the Division of Medical Virology in University of Cape Town (UCT). Based on this background, the study seeks to estimate the costs of genital inflammation screening using a cytokine biomarker rapid POC test in Cape Town South Africa, and the budget impact of this health service, with the aim of implementation in primary health facilities, and up-scaling countrywide.

METHODS

Study design

The study was a prospective cost analysis and budget impact analysis. The economic and financial costs of the health facilities were utilized to estimate the unit cost and were analyzed from a provider's perspective. Data was collected from facility records, financial reports and records and short staff interviews. The calculated unit costs were then used to analyze the budget impact of scaling up this intervention countrywide.

Study setting and population

South Africa is situated in the southernmost region of Africa with a population of around 55 million. The prevalence of STIs is high, with the public health facilities seeing 1.14 million incidents in 2015/16. Cape Town, located in the Western Cape Province, is the second most populous urban area in South Africa. (27) To a significant extent, the country's economic and political history have contributed to the high disease prevalence. Additionally, the low socio-economic status of women has played a significant role in the spread of STIs (28). The study was conducted in Cape Town, in two health facilities where the screening test will be piloted once its development has been finalized. The Desmond Tutu HIV Foundation (DTHF) Youth Centre located in Masiphumelele, is a non-governmental organization (NGO). The youth center was opened in 2011 to provide service to youth aged between 12 to 22 years. The center offers reproductive and sexual health services, and, programs for education and computer skills, and sports and recreation. Within the center, the health zone offers youth-friendly reproductive and sexual health services provided by two nurses, a general practitioner doctor and a youth health educator (29). The UCT Student Wellness Service (SWS) is a division of the Department of Student Affairs at UCT, which is a public research entity funded by private sources and the government. UCT SWS is located in Mowbray, and provides comprehensive outpatient health services to all UCT students. In addition to health services for various general

ailments, reproductive sexual health services are offered. These services are provided by four nurses and three medical practitioners (30). A convenience sampling method was used to select the two hypothetical costing sites. The Desmond Tutu Youth Clinic was one of the sites where the cytokine biomarkers for the screening test were validated. Additionally, being a resource limited area with an exceptionally high prevalence of STIs and BV within the community, the screening tool would be of great benefit to the girls and women. The UCT Student Wellness Service was selected to include a broader population of women with different ethnicities, originating from various Sub-Saharan regions, and those older than 22 years of age. The study population included women aged between 15 to 49 years attending the family planning (FP) clinic within primary health care facilities. However, this screening would be inclusive of women seeking other health services. Data for all patients attending both clinics was collected from electronic clinic records for the period of March 2016 to February 2017 for DTHF, and January 2016 to December 2016 for UCT SWS. This data was presented as a summary of the number of patients seen from both facilities, and did not contain personal information of any individuals. Based on the age limits of the target population, only data for females aged 15 to 22 years who attended the FP clinic in DTHF was included. Similarly, for the UCT SWS, data for all females who received FP services was utilized. This data was used to calculate the utilization rate for the cost analysis.

Description of the Screening

Genital inflammation screening would be offered to any woman of reproductive age coming into the clinic for any purpose. This screening aims to assess whether her genital tract is healthy, in which the genital sample would be applied to the lateral flow cytokine test device (GIFT). Being a prospective study, the process and timing of the screening procedure was described by health experts and collaborating researchers of the GIFT project. In addition, a hypothetical patient screening process for an ongoing contraceptive project (uCHOOSE) at DTHF was

observed and described by the nurse. This was based on the similarity of the screening process for genital inflammation.

During the clinic visit, the nurse or doctor would explain the screening process to the patient and obtain informed consent. Once the patient gave an informed consent, the nurse would collect a lateral vaginal wall swab, which would be placed in a tube containing buffer. The end of the swab would be snapped off, the lid closed, and the tube would be shaken vigorously. The swab would then be removed, and the end of the GIFT test strip dipped into the tube and taken out to read the result. The test strip would incubate for 5 minutes after which the results would be readable. The nurse would then read and interpret the results and if the test were positive, broad spectrum antibiotics would be administered or another sample would be collected for STIs/BV laboratory testing. For the latter, the patient would be contacted to return to the clinic for the results and appropriate treatment. This screening process would take an average of 20 minutes per patient.

Costing methods

Costs were estimated using an ingredient approach for each health facility (31, 32). As illustrated on table 1, we included capital costs (building, furniture and equipment, and procedure training) and recurrent costs (personnel, medical supplies, diagnostic GIFT test device, overheads and maintenance).

Table 1: Methods and data used in estimating costs: identifying and measuring CAPITAL costs

TYPE OF COST	IDENTIFICATION		MEASUREMENT		VALUATION	
Capital costs	Categories	Costing method	Related information for allocation purposes	Source of data	Valuation method	Source of data
Building	Consulting room, waiting room, toilet	Current replacement cost (CSIR building costs per m ² x square meter of facility). 20 year life span. 3% discount or annuitization	Space (square metres). Number of consultations and type of service	Observation and record reviews	Replacement and contract prices	Department of Public Works, building contractors
Medical equipment	Weighing scale, blood pressure machine, stethoscope, examination couch, bed screen, trolley.	Actual current replacement cost. 5 year life span. 3% discount rate for annuitization	Resources used by family planning clinic. Number of consultation and type of service	Observation and record reviews	Replacement and contract prices for equipment	Clinic expenditure records, commercial price lists
Furniture and other equipment	Tables, chairs, cabinets, office stationery, computer, printer, telephone.	Actual current replacement cost. 15 year life span for furniture and 5 year life span for equipment. 3% discount rate for annuitization	Resources used by the family planning clinic. Number of consultation and type of service	Observation and record reviews	Replacement and contract prices	Clinic records and contracts, commercial price lists.
In service-training	Personnel; doctors and nurses	Actual current cost of training. 5 year life span. 3% discount rate for annuitization	Number of staff trained. Time spent on different services by these staff	Management, training records	Course fees; for in-house training – staff remuneration	Remuneration packages of trainers (nurses)

Table 2: Methods and data used in estimating costs: identifying and measuring RECURRENT costs

TYPE OF COST	IDENTIFICATION		MEASUREMENT		VALUATION	
Recurrent cost	Categories	Costing method	Related information for allocation purposes	Source of data	Valuation methods	Source of data
Overheads:	Electricity, water and other utilities Rent (where applicable) Telephones, faxes & postage Stationery, computer consumables & photocopies	Actual costs from facility records	Number of consultations per type of service Space (square meters) used by each cost centre for utilities and rent	Procurement records, observation	Expenditure records	Expenditure records
Personnel:	Direct staff (doctors, nurses) Support staff (counsellor, administration, receptionist, manager, cleaning staff, data capturer)	Total remuneration costs (salary and all benefits) Calculate separately for each category of personnel listed	Number of consultations per type of service Time spent on different types of services	Observation and financial record reviews	Gross salary per annum, including benefits (Cost to clinic)	Clinic facility salary packages
Medical and surgical supplies:	Relevant medical supplies	Actual costs from facility/ service records (where 'internal') Unit costs to be obtained from supplier (e.g. provincial depot) where 'external'	Detailed list of types, quantities and unit costs of all medical supplies required	Observation and financial records reviews	Tender contract prices and expenditure records	Supply Chain Management: records, contracts; Medical supplies services: contracts, records
Diagnostic test (cytokine biomarker test)	Cytokine biomarker test device	Cost estimation from manufacturing company	Number of consultations per type of service	Observation	Manufacturing company price list	Manufacturing company price list
Maintenance		Actual costs of supplies related to maintenance activities	Number of consultations per type of service	Observation, record reviews	Clinic expenditure records	Clinic expenditure records

Data used for cost estimation was collected for the period March 2016 to February 2017 from DTHF facility and financial records, and, January 2016 to December 2016 from UCT SWS facility and financial records. We observed consultations, interviewed staff and reviewed facility and financial reports to estimate the resources used for all inputs of the screening process. For resources which were shared between FP and other services, the following allocation methods were used: the building costs were estimated by multiplying the total building space by the current replacement cost per square meter, sourced from an assessment

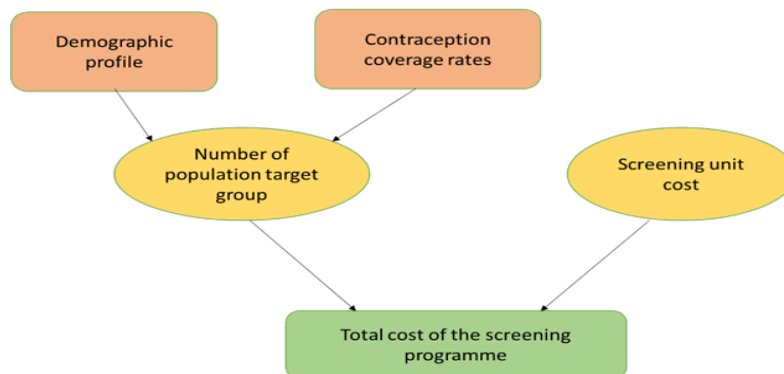
tool developed by Council for Scientific and Industrial Research (CSIR). Building space was allocated according to the utilization rate, and the service distribution within the clinic rooms. Furniture and equipment costs were sourced from company catalogues and sales quotations and, allocated to FP proportionally to the number of patients (from observations and staff interviews). Training on the screening process would be conducted by a nurse. The training cost was based on the time spent on training by the nurse and valued using local paid income. Capital costs were annuitized at a 3% discount rate using a useful life of 20 years for buildings, 15 years for furniture and 5 years for equipment and training. However, the costs were not discounted as the timeframe of the data was restricted to one year (33, 34). The use of relevant medical supplies and the test device was measured by short interviews and observations of the staff conducting the uCHOOSE study. Test costs were calculated by multiplying the quantity of inputs used by their price. Prices of inputs slightly vary, and there are no standard international prices available for medical supplies. Therefore, the prices were sourced from different catalogues and quotations from medical supplies companies. These costs did not include the wastage of supplies, and unused equipment capacity. The overheads and maintenance costs were calculated based on the utilization rate of the FP clinic. The staff costs were measured based on the time spent on the screening process and valued using wages specific to the facility. Administrative and support staff time were also included. We adopted top-down and bottom-up approaches to calculate the unit cost. In a top-down approach we divided the total expenditure for a given cost category by the FP utilization rate; for the bottom-up approach we identified the resources used within a cost category, allocated a value to them and added them to calculate the unit cost (34). We calculated the cost per patient screened by facility. The costs were collected in South African Rand (ZAR) based on 2016/2017 salaries and financial year prices. All costs were converted and reported in 2016 United States Dollars

using an average exchange rate of 1US\$ = 14.72 South African Rand (ZAR) (www.resbank.co.za).

Budget impact analysis

An expenditure-based model was developed in Microsoft Excel to estimate the budget impact of the unit costs. The modelling was done using a two-step approach. First, the size of potential target population was determined using available demographic and contraception coverage rates data (35, 36). The screening intervention targets women aged 15 to 49 years in South Africa. The limit of the potential target group reflects women of reproductive age who are mostly susceptible to asymptomatic STIs and BV, resulting in genital inflammation. Secondly, the screening unit cost estimate from the study was used to scale-up and provide national estimates under various coverage rates. Based on the estimated number of women in 2016, the model would provide an annual cost of implementing this health service. The model approach is summarized in figure 1 below.

Figure 1: Budget Impact Model Outline



The model aimed to estimate costs associated with screening based on the different contraception coverage rates within South Africa. This would reflect the number of women attending FP clinics, and, as the potential population to be screened. The different levels of coverage would provide insight on the most feasible level of implementation given the current

levels of infrastructure and capacity development. The levels of coverage were presented as percentages of the potential target group. The estimates were inclusive of a limited degree of capacity development necessary to implement scaled-up activities within existing levels of infrastructure. The cost of the levels of implementation that require wholesale changes in infrastructure were not included. Additionally, possible economies of scope that might arise by providing related health services was not considered due to lack of data.

Assumptions

Based on the prospective nature of the study, for the baseline costs we assumed that: 1) the contraception coverage rates were representative of the number of women aged 15 to 49 years attending FP clinics, with an average of 49% in South Africa (36); 2) this would be a once-off screening for every woman per year in addition to currently used primary prevention interventions for HIV prevention (37) ; 3) all women would attend either a semi-private or NGO funded primary health facility; 4) the overall service framework within which the scaling up of the screening program is modelled to occur at primary care level; and 5) the screening intervention would be made available as part of the routine service provision, therefore no additional program scaling-up costs would be included.

Data Analysis

The costing data was analysed using a costing-based model in Microsoft Excel 2013. The total costs at the facility level were added up and divided by the total number of female patients attending the FP clinic in 2016/17.

For the budget impact, the analysis was based on the South African national health budget estimates for 2016. Evidently, there was no specific budget for STIs programmes. However, within the health budget, programme 3 for HIV and AIDS, Tuberculosis (TB), and Maternal Child Health related to this screening service. Specifically, within the program, is the

expenditure estimate for the HIV and AIDS subprogram which financed policy formulation, coordination and monitoring and evaluation of HIV and sexually transmitted diseases services (National Treasury, 2017). Therefore, this estimate was used as the funds available to analyse the budget impact of this screening service.

Sensitivity analyses

The robustness of the cost estimates was explored by performing univariate sensitivity analyses using alternative assumptions on parameters that had uncertainty. The personnel costs varied based on the salary scales of different types of health facilities, and, the staff conducting the screening. In comparison to both doctors and nurses conducting the screening, we assumed the total personnel costs would differ in a clinic with only nurses screening the women. The test device is yet to be piloted and the price was an estimation from the manufacturing company. The utilization rate used for allocation of costs of resources was dependent on the main health service provided by facilities. For reproductive health clinics like DTHF, we assumed the utilization rate would be higher than that of general clinics like UCT SWS. The values of these parameters were each increased and decreased by 50%.

For the budget impact analysis, the coverage rate was varied to determine the total annual cost of screening. The base case assumed that 49% of the total number of women aged 15 to 49 years in South Africa attended FP clinics in 2016 (36). This value was increased and decreased by 10% to assess the difference in the total annual cost of screening.

RESULTS

Overall cost estimates

During the study period, a total of 4474 patients attended the DTHF clinic. Of these, 2137 (48%) patients were females 15 to 22 years of age, who received FP services. At UCT SWS, a total of 55,000 patients attended the clinic in 2016. Of these, 1687 (3%) female patients

received FP services. Table 3 summarizes the total unit cost per patient screened from both facilities. In general, the unit costs of genital inflammation screening at DTHF were higher than those of UCT SWS. The total cost per patient screened at DTHF would be \$24.26, compared to \$14.32 at UCT SWS. The total capital costs for DTHF were significantly higher at \$2.23 in comparison to the UCT SWS at \$0.37. Similarly, DTHF would incur an additional \$8.28 total recurrent costs compared to UCT SWS.

Table 3: Unit costs of genital inflammation screening in USD \$ (2016)

	DTHF	UCT SWS
	n = 2137	n= 1687
Cost category		
Capital costs		
Buildings	1.91	0.17
Equipment & furniture	0.28	0.13
Procedure training	0.05	0.06
Total capital costs	2.23	0.37
Recurrent costs		
Personnel	18.69	10.23
Medical supplies	0.97	1.23
Diagnostic GIFT test	0.30	0.30
Overheads	0.96	2.17
Maintenance	1.31	0.02
Total recurrent costs	22.23	13.95
Total unit cost	24.46	14.32

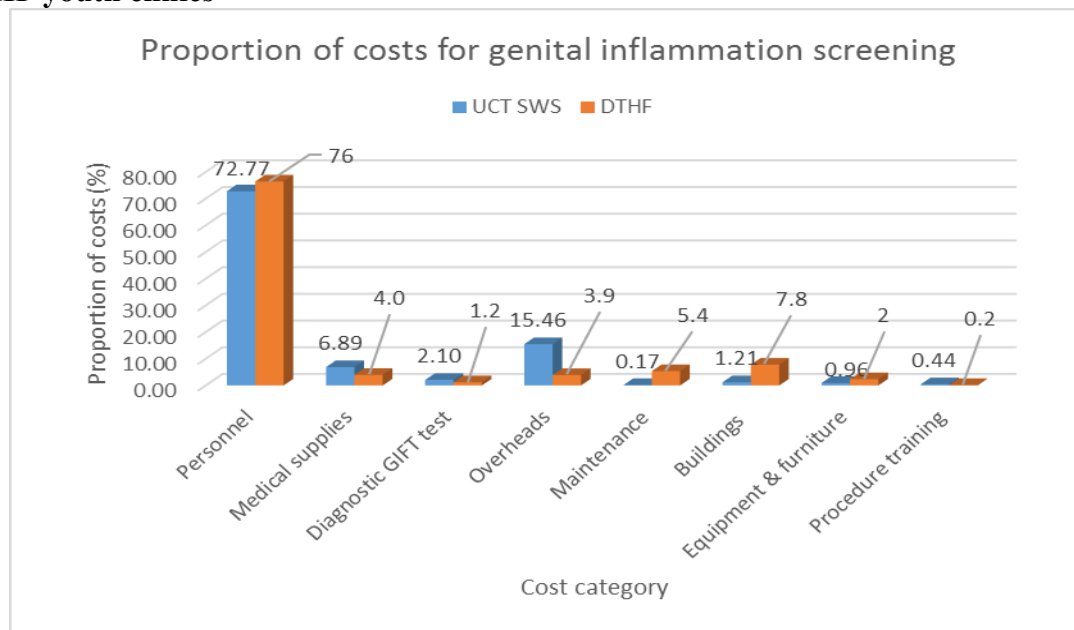
At the facility level, the total annual costs of genital inflammation screening were based on the utilization rate of 48% for DTHF, and 3% for UCT SWS. This represented the number of patients treated at the FP clinic. As presented in Table 4, the total annual cost of genital inflammation screening at DTHF was \$52,265.23, approximately double that of UCT SWS at \$23, 721.84.

Table 4: Total cost of genital inflammation screening at the facility level in USD \$ (2016)

	DTHF	UCT SWS
Cost category		
Capital costs		
Buildings	4 074.09	287.30
Equipment & furniture	1 233.46	227.00
Procedure training	104.04	104.04
Total capital costs	5 411.59	618.35
Recurrent costs		
Personnel	39 948.39	17 261.43
Medical supplies	2 070.22	1 634.28
Diagnostic GIFT test	631.52	498.54
Overheads	2 045.60	3 668.48
Maintenance	2 799.70	40.76
Total recurrent costs	47 495.43	23 103.49
Total cost	52 265.63	23 721.84

For each of the facilities, the proportion of cost categories to the total screening cost was similar at both the patient and facility level as illustrated in Figure 2. However, in comparison, these proportions slightly differed between the two facilities.

Figure 2: Proportion of costs for genital inflammation screening at the UCT SWS and DTHF youth clinics



The personnel costs were the main cost driver accounting for the largest proportion of the total screening cost, at 72.7% for UCT SWS, and, 76% for DTHF. Second to this was the proportion of overheads cost at 15.46% for UCT SWS, and for DTHF was the building cost at 7.8%. The least proportion of costs for the UCT SWS was maintenance costs at 0.17% whereas that of DTHF was training costs at 0.2%.

Budget impact analysis

Table 5 presents the target population in 2016 and the screening expenditure for the different provinces within South Africa. According to the data, the total number of women of reproductive age in South Africa are 15,262,143. Based on the various contraception coverage rates in each province, the women who would be potentially screened were 7,484,912. Gauteng was the most populous province with 1,803,410 whereas the Northern Cape was the least populous with 132,849 women. The estimated expenditure for screening differs based the type of health facility that the women would attend for screening. For a semi-private health facility similar to UCT SWS, the total screening expenditure would be \$107,183,655, whereas for an NGO funded health facility the estimated screening expenditure would be \$183,062,066.

Amongst the provinces, the expenditure varied greatly ranging from \$25,824,768 in Gauteng and \$1,902,392 in the Northern Cape.

Table 5: Estimated expenditure of screening in USD \$ (2016)

Province	Total women (15- 49 years) (n)	Contraception coverage rates (%)	Target population to be screened (n)	Total cost of screening (USD\$)	
				DTHF	UCT SWS
Eastern Cape	1 853 320	50.7	939 633	22 981 058	13 455 512
Free State	794 980	52.6	418 159	10 227 126	5 988 028
Gauteng	3 749 294	48.1	1 803 410	44 106 869	25 824 768
KwaZulu-Natal	2 971 480	50.1	1 488 711	36 410 127	21 318 291
Limpopo	1 627 561	46.3	753 561	18 430 195	10 790 961
Mpumalanga	1 215 162	45	546 823	13 373 909	7 830 483
Northern Cape	314 808	42.2	132 849	3 249 151	1 902 392
North West	979 554	46.3	453 534	11 092 285	6 494 582
Western Cape	1 755 984	54	948 231	23 191 347	13 578 637
South Africa	15 262 143	49	7 484 912	183 062 066	107 183 655

To scale up the program, the screening would be offered at a primary health care level, within FP clinics nationwide. The screening intervention would be made available as part of the routine service provision, therefore, would not incur additional scaling-up program costs. Currently, approximately 49% of the potential target population have access to family planning and STI services (36). As illustrated on table 6, the total cost of scaled-up screening of the eligible women in a semi-private health facility would be \$107,183,655 and \$183,062,066 in a NGO funded primary health facility.

Table 6: Total cost of screening program in USD \$ (2016)

Number of eligible women for screening at 49% coverage	7 484 912
UCT SWS unit cost of screening	14.32
Total cost of screening at 49% (USD\$)	107,183,655
DTHF unit cost of screening	24.46
Total cost of screening at 49% (USD\$)	183,062,066

The total annual resources required for genital inflammation screening in women countrywide are presented in table 7. On an annual basis, the costs estimates show that genital inflammation screening in a semi-private health facility would be less costly than when performed in an NGO funded health facility.

In comparison to the annual 2016 health budget for the HIV and AIDS subprogram, the screening service required less financial resources. However, the proportion of the screening costs to the available funds was quite significant at 17% for an NGO funded facility and 10% for a semi-private health facility.

Table 7: Total financial resources required for genital inflammation screening for women of reproductive age in South Africa

Facility	2016 annual budget ¹ (USD\$)	Unit cost per person screened (USD\$)	Total target population to be screened (n)	Total resources required annually (USD\$)	Proportion of 2016 annual budget (%)
DTHF	1 069 694 293	24.46	7 484 912	183 062 066	17
UCT SWS	1 069 694 293	14.32	7 484 912	107 183 655	10

1. National Treasury of South Africa, Estimates of National Expenditure 2017

Sensitivity analyses

The univariate sensitivity analyses results are presented in Table 8. The unit costs for both facilities were not sensitive to variation in the test device price. However, both unit costs were highly sensitive to differences in the total personnel costs, which was the main cost driver in the study. The variation of total personnel costs increased and decreased the DTHF unit costs by 38% and 36% for the UCT SWS unit cost. Likewise, the unit cost was sensitive to the utilization rates as the DTHF unit cost increased and decreased by 28% and that of UCT SWS by 13%. Moreover, for the budget impact, the variation of the target population coverage was equivalent to the percentage change of the total cost of screening.

Table 8: Univariate sensitivity analyses for the unit cost estimates in 2016 USD (\$)

Parameter	Unit costs (USD \$)			
	DTHF	% change	UCT SWS	% change
Base case	24.46		14.32	
Test device price				
-50%	24.31	-0.6%	14.17	-1%
+50%	24.61	+0.6%	14.47	+1%
Utilization rate				
-50%	17.59	-28%	12.46	-13%
+50%	31.33	+28%	16.18	+13%
Total personnel costs				
-50%	15.11	-38%	9.20	-36%
+50%	33.88	+38%	19.44	+36%
Coverage rate	Total cost (USD \$)			
Base case 7,484,912 women	183 062 066		107 183 655	
-10%	164 755 857	-10%	96 465 288	-10%
+10%	201 368 270	+10%	117 902 019	+10%

DISCUSSION

To our knowledge, this is the first study that comprehensively assesses the costs associated with genital inflammation screening for STI/BV in women aged 15- 49 years in South Africa. The cost estimates are compared between two types of primary health facilities: DTHF, an NGO funded primary health facility and, UCT SWS a semi-private primary health facility. The findings showed that the unit cost of screening a woman for genital inflammation at DTHF would be \$24.46 and at UCT SWS would be \$14.32. The unit cost at DTHF was almost double that of UCT SWS. This can be attributed to three factors. First, UCT SWS is a public facility (with additional private fund sources) which receives government subsidies on facility costs for resources used for this screening process. This may reflect in the unit cost, unlike DTHF youth clinic which incurs all facility costs at no subsidized rates. Second, UCT SWS as public entity that offers comprehensive health services would benefit from economies of scale in terms of facility operating costs, and also purchasing health service inputs at the government level.

This would contribute to a lower unit cost for genital inflammation screening in comparison to DTHF which as single entity NGO operates at a lower scale. Third, the personnel costs were the main cost driver. The study assumed that screening would be conducted by both doctors and nurses, and included salaries for both professional cadres. However, in FP clinics where only nurses attend to patients, the total personnel costs would be less. Additionally, it was assumed that both health facilities have salary scales slightly above that of government paid health professionals. Therefore, this would lead to an overestimate of the unit cost. This is further evidenced by the significant change of the unit cost amount when the utilization rates and total personnel costs are varied. As an economic cost analysis that includes opportunity costs (34), the unit cost per patient screened is high in comparison to other costing studies for STIs/BV POC test.

There is a paucity of recent literature estimating the costs associated with STI/BV screening using rapid tests, more so in developing countries. In the United States of America, a comparative study of a new point of care test for chlamydia, estimated the testing cost per patient to be \$33.48, adjusted to 2011 US dollars. Another study estimated the cost per patient of rapid testing for chlamydia and gonorrhoea to be \$24.46, in 2014 US dollars (24, 26). Although these costs are closely similar to our findings, both were conducted in developed countries and therefore may not be generalizable to this study. In comparable settings, a cost-effectiveness study of rapid tests for antenatal syphilis screening showed the cost per patient screened to range between \$1.9 to \$6.5 in Tanzania, \$2.2 to \$5.6 in Zambia, and \$2.63 to \$4.95 in Peru, in 2012 US dollars (25). Similarly, studies analysing costs for rapid tests used for detection of maternal syphilis found costs to range between \$ 1.26 and \$5.79 in Brazil (2006 US dollars, \$1 = 2.14 Reais), \$0.83 to \$0.85 in Mozambique (2004 US dollars \$1= 23,500 Metical), and \$1.14 to 1.43 in Bolivia (2004 US dollars, \$1= 8 Bolivians (22, 23). For BV, rapid POC testing ranged between \$4.24 and \$8.32 in Gambia, in 1999 US dollars (21).

However, it is important to note that most of these studies excluded various cost categories in the analysis, and excluded the economic costs of screening, resulting in much lower estimates than our findings. This accentuates the need for more economic costing studies especially with the increasing development of rapid diagnostics for STIs/BV. Rapid diagnostics for STIs/BV have proven to improve case detection and reduce overtreatment and its associated costs (11, 38, 39). Therefore, it would be paramount to establish the cost-effectiveness of this screening intervention in order to compare the costs and health outcomes of other STDs diagnostic interventions in current use. For instance, the syndromic approach may cost less but would miss infections especially for asymptomatic cases; whereas laboratory based tests are more accurate but are limited by non-availability of resources, are expensive, and have a prolonged process time, all of which affect the health outcomes (13, 40). This is further emphasized by Herbst de Cortina et al (2016), Huang et al (2013), and West et al (2003), who similarly established that rapid POC tests for STIs and BV are both cost saving and have improved health outcomes by minimizing loss to follow up, reducing false diagnosis and averting additional cases of disease complications (18, 21, 24). As such, scaling up the service of genital inflammation screening for women within family planning clinics would increase identification of asymptomatic women and improve STIs/BV treatment, and access of STIs health services to women.

With certainty, the affordability of any health intervention is central to decision makers in prioritizing and choosing between interventions (41, 42). The findings from the budget impact analysis question the affordability of the screening program in relation to the national health budget. Based on the aforementioned assumptions in the analysis, the costs for providing the screening service in primary health facilities countrywide would amount to 17% of the available funds if provided at an NGO funded health facility, and 10% if provided at a semi-private health facility. Amidst other interventions within HIV/AIDS, TB (Tuberculosis) and

STIs programs, this amount is significantly high. Moreover, the proportion of the total national budget that is allocated to the health sector has slightly declined over the recent years from 14.5% in 2011 to 14.2% in 2014 (43). This may challenge its prioritization over new or already implemented interventions that are less costly. Although the screening service may not be affordable within the current budget, improved case detection of asymptomatic women will reduce their susceptibility to HIV infection. Consequently, this would have a substantial impact on the reduction of overtreatment, its associated costs and, the reduction of new HIV infections. Furthermore, this aligns with the South Africa's HIV/STI prevention targets by 2022, which aim to increase identification of asymptomatic STI infections and, reduction of new HIV and STI cases (27).

Our study presents some limitations. First, as the cytokine biomarker POC test is yet to be piloted, we collected data from two potential pilot sites, in only one city, and, within an urban setting. Therefore, the findings can only be generalized to similar settings within South Africa. Additionally, the study sites were semi-private and NGO-funded health facilities which might not be representative of the majority of primary health facilities in South Africa. In our budget impact analysis, we assumed that all the women would be screened at these facilities, and this might not account for the limited access of such facilities to most women. Moreover, the costs from these two facilities may not be equivalent to that of a government primary health facilities. Specifically, personnel costs which were the main cost driver may differ, and also the equipment and overhead costs. Second, the observation and description of a hypothetical patient screening process presents information bias on the time taken for the screening process. Although a similar screening process for an ongoing project was used as reference, the time estimation may differ from the actual observation of the genital inflammation screening process. Third, the DTHF attends to youth aged 12 to 22 years which is not representative of the women of reproductive age. Additionally, this is a sexual and reproductive health clinic,

and so the utilization rate used for cost allocation of resources may have resulted in an over-estimation of the unit costs. Fourth, we assumed that women would be screened once per year not accounting for costs of a repeat screening within the same year. This assumption may lead to underestimation of the budget in forecasting future costs. Contrarily, the study presents some strengths. Comprehensive cost data was collected from a provider's perspective, from health facilities offering different primary health services. Finally, with uncertainty in assumptions such as the value of utilization rate, personnel costs and coverage rates, we present adequate estimation methods to test the robustness of our findings to these assumptions.

The policy recommendations on the costs of provision of genital inflammation screening within primary health facilities in South Africa are outlined below. However, it is important to acknowledge that the main caveat of using the study results in making these recommendations is that, the rapid POC test is yet to be piloted in health facilities. Therefore, these cost estimates should be interpreted as preliminary results. First, although the target population is well-defined, implementation of the screening program to achieve 49% coverage may not be feasible within the current budget. Therefore, it would be paramount to establish the cost-effectiveness of this screening intervention in order to compare the costs and health outcomes of other STDs diagnostic interventions in current use. Subsequently, shifting of financial resources within HIV, AIDS and TB programme would avail more funds. Additionally, an increase in the national health budget would be an added contribution. Second, the estimated costs could inform immediate decisions about investments for STIs control programs in South Africa. Establishment of funds specific to STI programs would ensure efficient financial planning and budget allocation for STI interventions and programs. Third, the implementation of the screening program could be integrated into FP services as a means to improve STI asymptomatic case detection, and achieve the prevention targets for HIV and STI infections, as per the South African national strategic plan on HIV, TB and STIs 2017-2022 (27).

CONCLUSION

This analysis estimates the costs and affordability of a new developed rapid POC test for STIs and BV, to be used complimentary to the standard of care. The results estimate the costs of screening as high, and demonstrate that its implementation may not be affordable. However, it would be paramount to establish the cost-effectiveness of this screening intervention in order to compare the costs and health outcomes of other STDs diagnostic interventions in current use. On the contrary, this screening tool will increase the cases detected, contributing to better STIs management and control, and reduce the risk of HIV acquisition among women. Numerous studies have proven rapid POCs tests for STIs/BV to be cost-effective. However, there is scarcity of literature on costing for these tests. Further research should investigate the impact of genital inflammation screening on STIs/BV health outcomes, and determine the benefits and cost-effectiveness of the intervention. The potential of reducing a double burden of curable STIs and HIV/AIDS in South Africa could be achieved through the genital inflammation screening program.

List of abbreviations used

BV- Bacterial vaginosis

CSIR- Council for Scientific and Industrial Research

DTHF- Desmond Tutu HIV Foundation

FP- Family planning

GIFT- Genital Inflammation Test

HIV/AIDS- Human Immunodeficiency Virus/ Acquired Immune Deficiency Syndrome

NGO- Non-Governmental Organization

POC- Point of care

STIs- Sexually Transmitted Infections

TB- Tuberculosis

UCT SWS- University of Cape Town Student Wellness Service

USD- United States Dollar

ZAR- South African Rand

Declarations

Ethical approval

The study was approved by University of Cape Town Human Research Ethics Committee (HREC 787/2016).

Consent application

Not applicable.

Availability of data and materials

All data generated or analysed during this study are included in this published article [and its supplementary information files].

Competing interests

The authors declare that they have no competing interests.

Funding

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Author's contributions

AK analysed and interpreted the cost data for the screening intervention and was major contributor in writing the manuscript. ES contributed in data analysis, interpretation of the findings. All authors read and approved the final manuscript.

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PART D: POLICY BRIEF

RAPID POINT OF CARE TESTING FOR SEXUALLY TRANSMITTED DISEASES AND BACTERIAL VAGINOSIS IN SOUTH AFRICA

What is the cost and budget impact of genital inflammation screening in women?



Curable sexually transmitted infections (STIs) and bacterial vaginosis (BV) have been strongly linked to an increased risk of HIV acquisition through genital inflammation in women, especially in asymptomatic cases (1).

Rapid point of care testing is an essential strategy for effective STIs and BV management. Existing rapid testing tools are costly, time-consuming, and unable to detect asymptomatic women who are the majority (2, 3). The cytokine biomarker rapid test with improved accuracy and detection of asymptomatic cases, is a newly developed genital inflammation screening tool.

This study estimated the costs of genital inflammation screening in women. Additionally, the study assessed the budget impact of providing this screening intervention in primary health facilities in South Africa. The findings suggest that the costs of screening in a semi-private health facility were 41% less costly than in an NGO funded health facility. Although the total costs on scaling up screening nationwide accounted for a significant amount of the national health budget, this screening tool would improve detection of asymptomatic cases, and potentially reduce the disease burden of STIs and HIV.

was representative of women with access to family planning clinics.

KEY FINDINGS

- Genital inflammation screening of women in a semi-private health facility (UCT SWS) was 41% less costly than in an NGO funded facility. The cost difference between the two facilities was influenced by staff costs and clinic utilization rates.
- The unit cost per woman screened was \$24.26 (R360.01) in an NGO funded primary health facility, and, \$14.32 (R210.79) in a semi-private primary health facility.
- In South Africa, the average contraception coverage rate is 49%, which was approximately 7,484,912 women aged 15-49 years. The total screening cost for these women at an NGO funded health facility would be \$183,062,066 (R 2,694,673,611), and, \$107,183,655 (R 1,577,743,402) at a semi-private health facility.
- Based on South Africa's national health budget (2016), the proportion of the total screening costs to the budget were 17% and 10% for an NGO funded and semi-private health facility respectively.
- The findings suggest that the costs of screening account for a significant amount of the health budget.

POLICY RECOMMENDATIONS

- 1) The financial resources for STIs programs could be increased through financial resource shifting from well-established health programs. Additionally, an increase in the annual national health budget would be beneficial. These

approaches aid in availing more funds for STIs programs.

- 2) Funds specific to STI programs within the health budget should be established in order to ensure efficient financial planning and budget allocation for future STIs projects.
- 3) Integration of this screening program within family planning services will greatly improve asymptomatic STIs/BV case detection, ensure better STI control and management, and eventually reduce the prevalence of STIs and HIV.
- 4) Further research on costing and effectiveness of rapid tests for STIs/BV, and the impact of genital inflammation screening on health outcomes is highly recommended to advocate for funding on new STIs/BV diagnostic interventions.

CONCLUSION

Although the costs of genital inflammation screening in women render the intervention unaffordable within the current health budget, this screening tool will increase detection of asymptomatic cases. Subsequently, this will positively impact on STIs/BV management and control, and reduce the risk of HIV acquisition among women. The potential of reducing a double burden of curable STIs and HIV/AIDS in South Africa could be achieved through this genital inflammation screening program.



NOTE: All the images used in this policy brief were sourced from Google images.

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PART E: APPENDICES

APPENDIX 1: GUIDE FOR AUTHORS: BMC PUBLIC HEALTH JOURNAL

BMC Public Health journal

Research article

Criteria

Research articles should report on original primary research, but may report on systematic reviews of published research provided they adhere to the appropriate reporting guidelines which are detailed in our [editorial policies](#). Please note that non-commissioned pooled analyses of selected published research will not be considered.

BMC Public Health strongly encourages that all datasets on which the conclusions of the paper rely should be available to readers. We encourage authors to ensure that their datasets are either deposited or in publicly available repositories (where available and appropriate) or presented in the main manuscript or additional supporting files whenever possible. Please see Springer Nature's [information on recommended repositories](#).

Preparing your manuscript

The information below details the section headings that you should include in your manuscript and what information should be within each section.

Please note that your manuscript must include a 'Declarations' section including all of the subheadings (please see below for more information).

Title page

The title page should:

- present a title that includes, if appropriate, the study design e.g.:
 - "A versus B in the treatment of C: a randomized controlled trial", "X is a risk factor for Y: a case control study", "What is the impact of factor X on subject Y: A systematic review"
 - or for non-clinical or non-research studies a description of what the article reports
- list the full names, institutional addresses and email addresses for all authors
 - If a collaboration group should be listed as an author, please list the Group name as an author. If you would like the names of the individual members of the Group to be searchable through their individual PubMed records, please include this information in the "Acknowledgements" section in accordance with the instructions below
- indicate the corresponding author

Abstract

The Abstract should not exceed 350 words. Please minimize the use of abbreviations and do not cite references in the abstract. Reports of randomized controlled trials should follow the [CONSORT](#) extension for abstracts. The abstract must include the following separate sections:

- **Background:** the context and purpose of the study
- **Methods:** how the study was performed and statistical tests used
- **Results:** the main findings
- **Conclusions:** brief summary and potential implications
- **Trial registration:** If your article reports the results of a health care intervention on human participants, it must be registered in an appropriate registry and the registration number and date of registration should be stated in this section. If it was not registered prospectively (before enrolment of the first participant), you should include the words 'retrospectively registered'. See our [editorial policies](#) for more information on trial registration

Keywords

Three to ten keywords representing the main content of the article.

Background

The Background section should explain the background to the study, its aims, and a summary of the existing literature and why this study was necessary or its contribution to the field.

Methods

The methods section should include:

- the aim, design and setting of the study
- the characteristics of participants or description of materials
- A clear description of all processes, interventions and comparisons. Generic drug names should generally be used. When proprietary brands are used in research, include the brand names in parentheses
- the type of statistical analysis used, including a power calculation if appropriate

Results

This should include the findings of the study including, if appropriate, results of statistical analysis which must be included either in the text or as tables and figures.

Discussion

This section should discuss the implications of the findings in context of existing research and highlight limitations of the study.

Conclusions

This should state clearly the main conclusions and provide an explanation of the importance and relevance of the study reported.

List of abbreviations

If abbreviations are used in the text they should be defined in the text at first use, and a list of abbreviations should be provided.

Declarations

All manuscripts must contain the following sections under the heading 'Declarations':

- Ethics approval and consent to participate
- Consent for publication
- Availability of data and material
- Competing interests
- Funding
- Authors' contributions
- Acknowledgements
- Authors' information (optional)

Please see below for details on the information to be included in these sections.

If any of the sections are not relevant to your manuscript, please include the heading and write 'Not applicable' for that section.

Ethics approval and consent to participate

Manuscripts reporting studies involving human participants, human data or human tissue must:

- include a statement on ethics approval and consent (even where the need for approval was waived)
- include the name of the ethics committee that approved the study and the committee's reference number if appropriate

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If your manuscript does not report on or involve the use of any animal or human data or tissue, please state "Not applicable" in this section.

Consent for publication

If your manuscript contains any individual person's data in any form (including individual details, images or videos), consent for publication must be obtained from that person, or in the case of children, their parent or legal guardian. All presentations of case reports must have consent for publication.

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Availability of data and materials

All manuscripts must include an ‘Availability of data and materials’ statement. Data availability statements should include information on where data supporting the results reported in the article can be found including, where applicable, hyperlinks to publicly archived datasets analysed or generated during the study. By data we mean the minimal dataset that would be necessary to interpret, replicate and build upon the findings reported in the article. We recognise it is not always possible to share research data publicly, for instance when individual privacy could be compromised, and in such instances data availability should still be stated in the manuscript along with any conditions for access.

Data availability statements can take one of the following forms (or a combination of more than one if required for multiple datasets):

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- The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.
- All data generated or analysed during this study are included in this published article [and its supplementary information files].
- The datasets generated and/or analysed during the current study are not publicly available due [REASON WHY DATA ARE NOT PUBLIC] but are available from the corresponding author on reasonable request.
- Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.
- The data that support the findings of this study are available from [third party name] but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of [third party name].
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The datasets generated during and/or analysed during the current study are available in the [NAME] repository, [PERSISTENT WEB LINK TO DATASETS].^[Reference number]

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All financial and non-financial competing interests must be declared in this section.

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Please acknowledge anyone who contributed towards the article who does not meet the criteria for authorship including anyone who provided professional writing services or materials.

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Examples of the BioMed Central reference style are shown below. Please ensure that the reference style is followed precisely.

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Web links and URLs: All web links and URLs, including links to the authors' own websites, should be given a reference number and included in the reference list rather than within the text of the manuscript. They should be provided in full, including both the title of the site and the URL, as well as the date the site was accessed, in the following format: The Mouse Tumor Biology Database. <http://tumor.informatics.jax.org/mtbwi/index.do>. Accessed 20 May 2013. If an author or group of authors can clearly be associated with a web link (e.g. for blogs) they should be included in the reference.

Example reference style:

Article within a journal

Smith JJ. The world of science. *Am J Sci.* 1999;36:234-5.

Article within a journal (no page numbers)

Rohrman S, Overvad K, Bueno-de-Mesquita HB, Jakobsen MU, Egeberg R, Tjønneland A, et al. Meat consumption and mortality - results from the European Prospective Investigation into Cancer and Nutrition. *BMC Med.* 2013;11:63.

Article within a journal by DOI

Slifka MK, Whitton JL. Clinical implications of dysregulated cytokine production. *Dig J Mol Med.* 2000; doi:10.1007/s801090000086.

Article within a journal supplement

Frumin AM, Nussbaum J, Esposito M. Functional asplenia: demonstration of splenic activity by bone marrow scan. *Blood* 1979;59 Suppl 1:26-32.

Book chapter, or an article within a book

Wyllie AH, Kerr JFR, Currie AR. Cell death: the significance of apoptosis. In: Bourne GH, Danielli JF, Jeon KW, editors. *International review of cytology*. London: Academic; 1980. p. 251-306.

OnlineFirst chapter in a series (without a volume designation but with a DOI)

Saito Y, Hyuga H. Rate equation approaches to amplification of enantiomeric excess and chiral symmetry breaking. *Top Curr Chem*. 2007. doi:10.1007/128_2006_108.

Complete book, authored

Blenkinsopp A, Paxton P. *Symptoms in the pharmacy: a guide to the management of common illness*. 3rd ed. Oxford: Blackwell Science; 1998.

Online document

Doe J. Title of subordinate document. In: *The dictionary of substances and their effects*. Royal Society of Chemistry. 1999. [http://www.rsc.org/dose/title of subordinate document](http://www.rsc.org/dose/title%20of%20subordinate%20document). Accessed 15 Jan 1999.

Online database

Healthwise Knowledgebase. *US Pharmacopeia*, Rockville. 1998. <http://www.healthwise.org>. Accessed 21 Sept 1998.

Supplementary material/private homepage

Doe J. Title of supplementary material. 2000. <http://www.privatehomepage.com>. Accessed 22 Feb 2000.

University site

Doe, J: Title of preprint. <http://www.uni-heidelberg.de/mydata.html> (1999). Accessed 25 Dec 1999.

FTP site

Doe, J: Trivial HTTP, RFC2169. <ftp://ftp.isi.edu/in-notes/rfc2169.txt> (1999). Accessed 12 Nov 1999.

Organization site

ISSN International Centre: The ISSN register. <http://www.issn.org> (2006). Accessed 20 Feb 2007.

Dataset with persistent identifier

Zheng L-Y, Guo X-S, He B, Sun L-J, Peng Y, Dong S-S, et al. Genome data from sweet and grain sorghum (*Sorghum bicolor*). *GigaScience Database*. 2011.

<http://dx.doi.org/10.5524/100012>.

APPENDIX 2: Human Research Ethics Committee



UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee



Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492

Email: sumayah.arietdien@uct.ac.za

Website: www.health.uct.ac.za/fhs/research/humanethics/forms

30 November 2016

HREC REF: 787/2016

A/Prof E Sinanovic
Health Economic Unit
Public Health & Family Medicine
Falmouth Building

Dear A/Prof Sinanovic

PROJECT TITLE: RAPID POINT OF CARE TESTING FOR SEXUALLY TRANSMITTED DISEASES AND BACTERIAL VAGINOSIS: COST ESTIMATION AND BUDGET IMPACT ANALYSIS. SUB-STUDY LINKED TO 267/2013 (Masters candidate- Ms AW KAIRU)

Thank you for your response letter dated 25 November 2016, addressing the issues raised by Human Research Ethics Committee (HREC).

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 NOVEMBER 2017.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

We acknowledge that the student; A Kairu will also be involved in this study.

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval before the research may occur.

Yours sincerely

PROFESSOR M. BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

HREC 787/2016