

Feasibility, validity and utility of HIV testing data as key components of HIV case-based surveillance

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Abstract

Background

HIV case-based surveillance (CBS) is recommended by the World Health Organization and other global agencies, for tracking progress towards achieving the 95-95-95 targets to end the HIV epidemic. CBS involves gathering individual-level data for each person diagnosed and linking these data from multiple data sources to other key data points along the HIV care cascade. Despite the high burden of HIV in sub-Saharan Africa and existing routine HIV program monitoring, opportunities to implement CBS have not been optimally used. The maturation of the health information system in the Western Cape province presents a unique opportunity to implement a version of case-based HIV surveillance that is integrated into a routine operation system within the antenatal services setting. This thesis seeks to explore the validity of HIV case ascertainment within a routine health information exchange, the feasibility of embedding HIV testing data into routine information systems and the utility of these routine data for enhanced HIV CBS.

Methods

Routine pregnancy and HIV data consolidated within the Provincial Health Data Centre (PHDC) from January 2010 to December 2020 were analysed using retrospective cohort and cross-sectional methods. Routine data were linked using a unique patient identifier to ascertain sentinel events within the HIV and vertical transmission prevention cascades. Temporal trends in HIV prevalence, HIV testing, linkage to care, ART coverage and vertical transmission estimates were evaluated and where relevant, triangulated with other key data sources historically used as sources for these estimates. These included routine aggregate data from the District Health Information System, national and provincial sentinel antenatal seroprevalence surveys and mathematical model estimates. Risk factors for vertical transmission were further evaluated using multivariable analyses. A specific intervention

implemented at a selected facility to enhance CBS through digitisation of routine point-of-care HIV tests was further evaluated for operational feasibility using both quantitative and qualitative research methods.

Findings

PHDC antenatal HIV prevalence estimates from 2011-2013 were widely disparate from aggregate and survey data (due to incomplete electronic data), whereas from 2014 onwards, estimates were within the 95% confidence interval of survey estimates, and closely correlated to aggregate data estimates ($r=0.8$; $p=0.01$). PHDC data show a slow but steady increase in provincial antenatal HIV prevalence from 16.7% in 2015 to 18.6% in 2020. ART coverage by the time of delivery in mothers of live births increased from 67.4% in 2011 to 94.7% by 2019. This pattern of increasing antenatal ART coverage was also seen in the DHIS data, and estimated by mathematical models, but was less consistent in the antenatal survey data. Ascertainment of HIV status among children exposed to HIV increased over time to 87.2% (16 908/19 382) in 2020. In recent years (2017 – 2020), 2.0% of children exposed to HIV (1 461/73 590) were diagnosed with HIV. Children born after implementation of lifelong ART in pregnant women, were less likely to have HIV than children born in the prior policy period (aOR 0.7; 95% CI 0.6 – 0.7), mediated through expanded ART access. Young maternal age, no antenatal ART, previous TB diagnosis and no records of antenatal visits were associated with vertical transmission. The intervention to enhance CBS through digitisation of HIV testing data, demonstrated that 51.3% (95% CI 48.4–54.1%) of patients testing HIV-positive at a selected health facility were retesting, supporting the utility of these data to enhance CBS. While the intervention is operationally feasible, various logistical, health system and cost-related challenges require careful consideration before scale-up.

Conclusions

This study demonstrates that CBS embedded within a routine health information exchange may be reliably used for HIV prevalence, ART coverage and vertical transmission surveillance,

providing more granular estimates, more efficiently than sentinel surveillance and aggregate programmatic data. This would enable more timely action in response to surveillance such as interventions targeting gaps in care or tailored for high-risk groups. However, these strategic gains may be strengthened by digitisation of HIV point-of-care data, implementation of which is operationally feasible but complex.

Dedication

“Commit to the Lord whatever you do, and he will establish your plans” Proverbs 16:3

I dedicate this work to my loving family for their unwavering support, love and encouragement. I thank the Lord, my God, for all that I am.

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Declaration

I, **Nisha Anne Sunny Jacob**, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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Date: 18 May 2024

This thesis includes 5 manuscripts (3 published, 1 under review and 1 prepared for submission). My contribution to each manuscript is outlined in the beginning of each chapter. In summary, I was the lead and corresponding author on all included papers and drafted all versions of the manuscripts. I confirm that I have been granted permission by the University of Cape Town's Doctoral Degrees Board to include the following publications in my PhD thesis, and where co-authorships are involved, my co-authors have agreed that I may include the publications.

Title	Journal	Authors
Utility of digitising point of care HIV test results to accurately measure, and improve performance towards, the UNAIDS 90-90-90 targets	PLOS ONE, 2020	Nisha Jacob , Brian Rice, Emma Kalk, Alexa Heekes, Jennie Morgan, James Hargreaves, Andrew Boulle
Consolidating strategic information to monitor progress against the UNAIDS 90-90-90 targets: evaluating the operational feasibility of an electronic HIV testing register in Cape Town, South Africa	BMC Health Services Research, 2020	Nisha Jacob , Brian Rice, Emma Kalk, Alexa Heekes, Jennie Morgan, Samantha Brinkmann, James Hargreaves, Marsha Orgill, Andrew Boulle
Can routine antenatal data be used to assess HIV antiretroviral therapy coverage among pregnant women? Evaluating the validity of different data sources in the Western Cape, South Africa	PLOS ONE, 2024	Nisha Jacob , Brian Rice, Alexa Heekes, Leigh F Johnson, Samantha Brinkmann, Tendesayi Kufa, Andrew Boulle
Exploring the validity of routine individuated service data for antenatal HIV surveillance in the Western Cape	BMC Infectious Diseases, 2024 (under review)	Nisha Jacob , Brian Rice, Alexa Heekes, Leigh F Johnson, Samantha Brinkmann, Tendesayi Kufa, Adrian Puren, Andrew Boulle

Signature:



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List of abbreviations

AIDS	Acquired immunodeficiency syndrome
ANC	Antenatal care
aOR	Adjusted odds ratio
ART	Antiretroviral therapy
CBS	Case-based surveillance
CHC	Community Health Centre
CI	Confidence interval
COVID	Coronavirus disease
DAG	Directed acyclic graph
DHIS	District Health Information System
ELISA	Enzyme-linked immunosorbent assay
EMTCT	Elimination of mother-to-child transmission
HIV	Human immunodeficiency virus
HTS	HIV testing services
ICD	International Statistical Classification of Diseases and Related Health Problems
IQR	Interquartile range
MTCT	Mother-to-child transmission
NHLS	National Health Laboratory Services
NICD	National Institute of Communicable Diseases
OR	Odds ratio
PCR	Polymerase chain reaction
PEPFAR	The President's Emergency Plan for AIDS Relief
PHDC	Provincial Health Data Centre
PHIAS	Population-based HIV Impact Assessment Survey
PMTCT	Prevention of mother-to-child transmission
PoCT	Point of care test
RPR	Rapid plasma reagin
TB	Tuberculosis
UNAIDS	United Nation's programme on HIV/AIDS
VCT	Voluntary counselling and testing
VL	Viral load
VT	Vertical transmission
VTP	Vertical transmission prevention
WCDHW	Western Cape Department of Health and Wellness
WCDOH*	Western Cape Department of Health
WHO	World Health Organization
WLWH	Women living with HIV

**Previous name, prior to WCDHW*

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Chapter 1: Introduction and Literature Review

Thesis Overview

This thesis consists of seven chapters, including an introductory chapter, five results chapters and a discussion chapter. Results chapters that have been published (chapters 3,4,5) are presented verbatim according to the relevant journal requirements. Formatting has been adapted to harmonise with the general thesis formatting.

The first chapter presents an overview of literature pertaining to HIV case-based surveillance, highlighting gaps in literature which this thesis aims to address. The chapter details the study setting, methods, data sources and data analysis plan for the thesis as a whole.

The second chapter is the first of the results chapters. This chapter focusses on validating HIV ascertainment within a routine individuated data system by comparing to sentinel HIV surveillance, aggregate data systems and mathematical model estimates.

Chapter 3 covers validation of antiretroviral coverage data by comparing different methods for measuring antenatal antiretroviral therapy coverage among women living with HIV. This chapter highlights the use of routine individuated data for coverage estimation in a high-burden setting.

In chapter 4, the operational feasibility of an intervention to improve routine HIV ascertainment from the point of diagnosis is evaluated. This intervention incorporates the digitisation of routine point-of-care HIV tests using two different processes. Data digitised through the intervention were compared with aggregate data to measure completeness. Lessons learnt from the implementation processes were explored to understand the key points of consideration when considering scale up.

Chapter 5 builds on the previous chapter by evaluating the utility of digitised point-of-care HIV testing data for enhanced HIV case ascertainment. This allows earlier ascertainment and better understanding of retesting and linkage to care.

In Chapter 6, utility of HIV case ascertainment through central laboratory HIV testing results of infants is demonstrated by exploring epidemiological trends in vertical transmission prevention over a 10-year period, spanning three distinct maternal ART policy periods.

Although each results chapter contains a discussion on key findings, the final chapter (Chapter 7) of this thesis weaves together cross-cutting themes across each results chapter to demonstrate the potential of case-based HIV surveillance embedded within routine individuated health information systems.

Background

In 2015, the United Nations Programme on HIV/AIDS (UNAIDS) established the 95-95-95 fast-track targets, following on from the 90-90-90 targets, which aim to achieve the following goals by 2030: diagnosing 95% of individuals infected with HIV, treating 95% of those diagnosed as HIV positive, and achieving viral suppression in 95% of individuals receiving antiretroviral treatment(1,2). These targets align with the World Health Organization's (WHO) universal test and treat principle, which was also introduced in 2015, aiming to ensure that all people living with HIV know their HIV status and are offered antiretroviral treatment (ART)(3).

HIV diagnosis is the first step of several along the HIV care cascade towards viral suppression(1). That many people do not immediately proceed beyond this first step reflects a system failure; high rates of pre-treatment loss-to-care among persons diagnosed HIV-positive have been reported in sub-Saharan Africa(4–6). If we are to meet the 95-95-95 targets it is essential that we accurately measure and improve optimal and timely linkage to, and retention in, HIV care for those newly diagnosed with HIV.

Robust health surveillance data are required to monitor progress towards these targets. HIV case-based surveillance (CBS) is recommended by WHO and other global agencies, to measure progress towards achieving the 95-95-95 targets(7). Features of CBS are obtaining *individual-level data* for each person diagnosed and *linking these data from multiple data sources* to other key data points along the HIV care cascade(7). These features apply to all levels of the health system(7). CBS shares objectives and approaches with similar initiatives that prioritise linked individuated data such as health information exchanges and data warehouses for consolidated person-level data which may be from routine information systems(8,9). Routine data, a component of surveillance, may be defined as “data that are routinely generated through service delivery, and routinely recorded in standard site data tools”(10). CBS systems (with or without routine data) have been implemented in many low, middle and high-income countries(7,11). Despite the high burden of HIV in sub-Saharan Africa and the existence of routine HIV program monitoring, opportunities to implement CBS have not been optimally used(7). Additionally, in some settings, the implementation of case-based HIV surveillance has focussed on post treatment initiation data. This is due to electronic systems being more widely used to monitor treatment programmes and the promotion and uptake of the treatment cascade as the primary HIV response monitoring framework(7). This focus results in a biased denominator as HIV diagnosis and linkage before treatment is inadequately quantified.

In high-burden countries, the initial steps in the HIV care cascade of testing and diagnosis are achieved through point-of-care initiatives in order to improve patient access to testing(7,12). These routine point-of-care initiatives predate electronic monitoring systems and are therefore not digitised and often overlooked in HIV care cascade data(7). Furthermore digitisation of these test results are much more difficult as they are not done in centralised laboratories which often have more resources and high levels of automation(12,13). Strategic information on HIV is frequently attained using parallel, costly donor-driven data collection processes due to weak health information systems(7,14). Recently, considerable media attention was given to a

proposed President's Emergency Plan for AIDS Relief (PEPFAR) funding cut for South Africa due to apparent poor performance of South African HIV programmes(14). Although this proposed funding cut was later reversed, it was widely appreciated that improved performance was needed and that this could be supported through digital solutions which include routine electronic monitoring of all persons newly diagnosed with HIV and their subsequent care.

Health information systems can significantly support the health system at large, however health information systems in different settings are notably context specific. In many low-and-middle income settings paper-based record keeping is the mainstay, with only aggregate data available digitally. In the Western Cape province of South Africa aggregate data systems are more recently complemented by an individuated data system that links and consolidates available routine electronic data using unique patient identifiers(9). The maturation of the health information system in the Western Cape province presents a unique opportunity to implement a version of case-based HIV surveillance that is integrated into a routine operational system that directly supports patient care, and evaluate its validity, feasibility and utility. The Prevention of Mother to Child Transmission (PMTCT) cascade or, preferably termed, vertical transmission prevention (VTP) cascade is closely interlinked with the HIV care cascade and existing HIV surveillance initiatives. The VTP cascade therefore provides a useful lens to evaluate CBS from the point of HIV testing of pregnant women, across the antenatal journey until HIV testing and further management of HIV exposed children.

Strengthening local information systems through various interventions may contribute to improved CBS using routine data with less reliance on costly external or disruptive parallel processes. Against the backdrop of digitisation of HIV service data in high burden settings being biased towards treatment data, this thesis seeks to explore the validity of HIV case ascertainment within a routine health information exchange, the feasibility of embedding HIV testing data into routine information systems and the utility of these routine data for enhanced HIV CBS.

Literature Review

Objectives

A literature review was conducted to better understand the role of surveillance within the health information system, current HIV surveillance within the South African context, with a focus on testing, and the principles of, and interventions to evaluate and strengthen HIV CBS. This section does not intend to provide a systematic review of all available studies, but to synthesise key findings from literature and identify gaps in literature. The literature review is restricted to studies which were available at the commencement of this research during the development of the protocol. The review represents what was known at that point (2019 - early 2020), with a focus on low-and-middle-income settings, which formed the basis of the thesis.

Search strategy

A comprehensive literature search was conducted using search engines Google Scholar and Pub Med. All literature, including published and grey literature in English from 1990 – 2020 was included in the search. Keywords included “case-based + surveillance” “case + surveillance” “health + surveillance” “epidemiology + surveillance” “health + information + system” “health + information + strengthening” “HIV + surveillance” “mother-to-child + transmission + HIV” “routine + data + health” “vertical + transmission + HIV” “HIV + testing”. In recent years, the terms “vertical transmission” is preferred over “mother-to-child transmission” to decrease stigma and labelling of women and children living with HIV. In this thesis, the terms were searched and used interchangeably since literature from earlier years made use of the then commonly used term of “mother-to-child transmission”. Literature from low-and-middle-income countries was prioritised for this review as the burden of HIV, resource availability and other contextual factors are vastly different to high-income settings. All study designs were included in the review.

Case-based surveillance

Surveillance is broadly defined as “the process of systematic collection, orderly consolidation and evaluation of pertinent data with prompt dissemination of the results to those who need to know, particularly those who are in a position to take action”(15). The key purpose of health

surveillance is therefore to inform action within the health system(15). Traditionally, health surveillance is broadly categorised as active and passive(16). Active surveillance entails activities such as field workers collecting and processing information or regular proactive follow-up of health reporting, for example outbreak response surveillance and verbal autopsies, while passive surveillance relies on the passive reporting of information by health care providers(16).

Disease notification systems are typical examples of passive surveillance(16). Notifiable diseases are those that are required to be reported to relevant governments by law(17), for the main purpose of providing early warning of potential outbreaks. The process of notification is separate to routine clinical record keeping. The revised WHO International Health Regulations of 2005 provides guidelines on criteria for notifiable diseases(17). Historically, passive systems are incomplete in the South African setting; this is for various reasons including reliance on additional reporting by busy clinicians who receive limited feedback from these reporting processes(7,16).

The WHO defines CBS, also a passive surveillance approach, as “surveillance of a disease by collecting specific data on each case”(15). The term case-based surveillance is used interchangeably with case surveillance. The WHO specifies that case surveillance “starts with diagnosis of a case followed by standardized sentinel events for public health action”(18). In 2017, the WHO published the “Consolidated guidelines on person-centred HIV patient monitoring and case surveillance”(18). These guidelines support the use of individual-level data for each person with HIV, linkage of individual-level data facilitated by personal identifiable information or a unique identifier and consolidation of individual data from multiple data sources(7,18). Currently discussions are underway to update these guidelines using pragmatic, context-specific examples. Much of the current literature focusses on CBS for HIV, however the principles of CBS may apply to all diseases(15). It is important to note that CBS is distinct from disease notification, although both may co-exist. CBS seeks to link and consolidate individual data from multiple routine data sources rather than notification of case

status for a regulated set of notifiable conditions. CBS is intertwined with the shift towards person-centred monitoring, placing emphasis on people primarily, along with measurement of service performance(18).

CBS was first advocated in high-income settings to compensate for the fact that data points were not already linked in a single system, enabling surveillance agencies to assemble full disease management pictures from multiple sources, by requiring the sharing of data from multiple custodians(19). Early examples of CBS were single disease focussed, particularly HIV, tuberculosis (TB) and vaccine-preventable diseases, and done as additional surveillance activities outside routine information systems(19,20). In high-burden settings such as Haiti, CBS successfully evolved from vertical disease programme surveillance to a broader multi-disease surveillance system through an interoperable, interconnected electronic reporting system(20). In the Western Cape, South Africa, another successful example of multi-disease CBS, person-level data were linked and consolidated by public health authorities within the Provincial Health Data Centre (PHDC)(9).

The WHO advocates for a multi-disease approach to surveillance as a more cohesive and efficient way of conducting surveillance(15). The 2019 coronavirus disease (COVID-19) pandemic has resulted in an urgent need for integrated public health surveillance data to understand the epidemiology of this previously unknown disease(21). This has further highlighted the importance of CBS within the broader health information system for any disease in order to efficiently inform and guide prevention and control without creating additional reporting pathways.

Sentinel events within the HIV care pathway are identified to enable HIV CBS(22,23). In the HIV setting, sentinel events are defined as “various events throughout medical care for a client with diagnosed HIV infection, such as HIV recency status (whether a person newly diagnosed with HIV has a recently acquired or long-standing infection), clinical laboratory values such as CD4 count and viral load (VL), change in antiretroviral treatment (ART) regimen and

death”(22). Vertical transmission of HIV is another example of a sentinel event that continues to occur despite VTP programmes(24,25). CBS using routine data may facilitate prompt identification of sentinel events and associated factors in order to address risk factors timeously and prevent adverse outcomes for the individual as well the health system.

Health information systems

Health information is one of the six WHO health system building blocks(26). By providing timely and actionable health data through different forms of surveillance, health information systems can support health systems and guide governance, planning, advocacy and resource allocation. Health information systems are, however, not universal across country contexts(7,27,28). They are complex, comprise of multiple diverse data sources and are often developed in response to different needs spatially and temporally, with limited interoperability between platforms(28). Although development and implementation of health information systems may appear to be purely technical in nature, social and contextual factors have notable impacts(29). In South Africa, health information systems were heavily influenced by the historical context of apartheid during which health services were fragmented and grossly inequitable(30). Different provinces in apartheid South Africa had completely different data sets and standards(30). Post apartheid, health information systems were shaped by efforts to develop a district health information system, as well various government collaborations between international donors and non-governmental organisations(29–31). Health services, particularly for priority diseases such as HIV and tuberculosis, were established with the support of international donors. Information systems supporting these services were frequently driven by international donors often resulting in multiple parallel databases focussed on aggregate vertical programme data(29,30).

Routine service data may be paper-based, electronic, or both, and available in aggregate or individuated form(32). In South Africa and many other countries, the District Health Information System (DHIS) was developed to support the district-based primary health care approach by collecting essential data to calculate indicators for use by health care workers and policy

makers, while also integrating and supporting other information systems(33,34). Over time, the DHIS evolved, resulting in the creation of an essential aggregate data set to streamline data processes(33). The requirement to regularly update the essential data set was highlighted in the HIV/AIDS experience as disease management guidelines changed rapidly over time in response to emerging evidence(33). In South Africa, DHIS data are predominantly captured from paper-based registers into aggregate reports in order to generate four types of indicators – count, proportion, rate and ratio(33). These indicators may be used at facility, district, provincial and national level to monitor and evaluate programmes. DHIS continues to be used widely in many countries in Africa, however the validity of manual paper-based recorded, patient level data which is later aggregated for reporting is difficult to assess, coupled with the administrative burden on clinical staff(34). Such data are known to be prone to error and double counting(32) and often lack the necessary detail required for active surveillance and important subgroup analyses(35). Register reports are also often delayed, and are rarely available to, or used by, the clinical staff who collect the data(36).

Many studies have highlighted the challenges and resultant underutilisation of routine aggregate data systems and this is explored further in this literature review using the HIV prevalence example(37,38). Historically, with many parallel databases available in health services, routine databases were considered inadequate for the monitoring and evaluation of disease-specific programmes(29). While many health systems across the world have transitioned to electronic information systems for routine data, the extent to which electronic platforms are used varies and is strongly dependent on resource availability(28). Whilst many countries, particularly in high income settings, have well established electronic health record keeping in the clinical environment(39), this is not a viable option in various low-and-middle income contexts for several reasons, including complex infrastructure, network requirements and user resistance(40–42). Paper-based records form the mainstay of health-care records in these settings. Even where digitisation of routine data has been implemented, the pervasive focus has been digitisation of aggregate-level data, rather than individual-level data(29).

Widespread use of aggregate data systems is therefore a notable barrier to harmonisation of individual-level routine data to facilitate CBS and so strengthen health information systems.

Recognising these limitations and the resource constraints preventing full transition to electronic medical records, some governments implemented registers within priority cohort-based treatment programmes, some of which are digitised, such as TIER.Net for HIV in South Africa and SmartCare for HIV/TB, maternal and child health and malaria in Zambia(38,40). While these systems contribute to improved continuity of care and monitoring, implementation challenges include disparities in use of these systems from facility to facility and resultant misclassification of people who self-transfer to other facilities(43).

In the South African setting, the gradual societal transition to electronic systems resulted in digitisation of component services within the health system such as laboratory test results, hospital discharges and pharmacy dispensing. Completeness and accuracy of different electronic systems varies, for example the poor completeness and quality of International Statistical Classification of Diseases and Related Health Problems (ICD-10) in the public sector is known(44–46), however the central laboratory electronic data systems are well-established and of better data quality(47). Electronic linkage and consolidation of available individual-level electronic patient data is possible using a unique patient identifier such as a patient folder number. However, these identifiers have not been fully implemented in many settings(9). The PHDC of the Western Cape Provincial Government (one of South Africa's nine provinces) consolidates all individual-level routine data captured on electronic platforms in the province on a single platform, leveraging the patient folder number as the unique patient identifier(9,48). The folder number is assigned at first presentation to a health service in the Western Cape public sector (at birth in the case of a newborn delivered in the public sector). A deterministic linkage algorithm is used to identify duplicates(9). This allows linkage of various information systems, including laboratory, pharmacy, and patient administration, providing a detailed source of individuated health information, in the absence of routine electronic patient health records. Within this environment, disease-specific patient cascades

(virtual cohorts) may be developed using specific markers of care at different points in the treatment cascade(9). Estimates from consolidated data within the PHDC have not been validated against other data sources as yet. Appropriate validation of these information systems may facilitate decision-making on appropriate methods of surveillance that are both efficient and cost-effective.

HIV surveillance

Within health information systems, vertical surveillance systems were often developed out of a need for data on key indicators in the absence of a comprehensive integrated surveillance system(20). HIV surveillance is a well-known example of vertical programme surveillance. Global HIV surveillance has evolved since the beginning of the epidemic in the 1980's, with first generation HIV surveillance being implemented in the early HIV epidemic, prior to widespread availability of optimal treatment(49–51). Surveillance focussed on quantifying the spread and burden of HIV through AIDS case reports, death reports, sentinel surveillance surveys and population-based surveys. While these remain important components of any surveillance system, they were ineffective as early warning systems to prevent onward transmission and HIV-related morbidity and mortality(50,51).

Recognition of weaknesses in these initial systems led to the development and expansion of second-generation HIV surveillance approaches in 2000's with systems which were more tailored to the needs of specific populations(51). This approach included information on behaviours driving transmission, and made better use of other sources of information to enhance understanding of epidemic dynamics(49,51). CBS is an integral component of second generation HIV surveillance that relies on linkage of data through different electronic platforms(7,26). Key types of data required for this enhanced surveillance and decision-making include sociodemographic, geographical, behavioural and biological data(50).

With the establishment of HIV treatment services in the 2000's, HIV surveillance systems further expanded to incorporate monitoring of uptake and outcomes of HIV treatment. The shift to HIV treatment information systems coincided with the global transition to electronic

information systems. Routine HIV treatment data were thus more likely to be digitised and available on electronic platforms than testing data which predate electronic information systems. Furthermore, testing information was likely less consequential than treatment information in terms of resources and structured outcome monitoring further enhancing efforts to electronically monitor treatment.

Since 2014, the Population-based HIV Impact Assessment Surveys (PHIAS), supported by PEPFAR, commenced in several countries, including countries in sub-Saharan Africa(52). This is one example of population-based surveys that complement HIV surveillance. The aim of PHIAS was to estimate HIV incidence and prevalence and measure progression towards the UNAIDS 95-95-95 targets through nationally-representative, HIV-focussed, cross-sectional, household-based population surveys of adults and adolescents aged 15 years and older(52). While these surveys may provide population prevalence and incidence estimates of varying accuracy and transparency, they miss the longitudinal dimension and do not satisfy CBS definitions. Furthermore, these data cannot be used to inform specific clinical decisions. Despite advances in HIV surveillance over the course of the HIV epidemic, CBS strategies are still not well-established in high burden settings in sub-Saharan Africa(7).

HIV surveillance in South Africa

HIV surveillance in South Africa is based on two broad approaches viz. survey-based approaches and clinical case reporting approaches.

Sentinel antenatal surveys

Sentinel antenatal surveys, using an unlinked anonymous testing strategy, are commonly used in many countries to monitor HIV trends(50,53–55). Since 1990, the National Antenatal Sentinel HIV Survey has been held in all nine provinces of South Africa annually or biennially during the months of October and November(56–58). Pregnant women at selected public health antenatal clinics are consented for inclusion in the survey during their first antenatal visit (booking visit). Key variables collected in the sentinel antenatal survey include demographic variables and laboratory testing for HIV and syphilis (Table 1.1) (57,58). The

survey blood specimens are collected simultaneously with routine blood specimens indicated at the first antenatal visit. In 2001, syphilis testing was discontinued in the national antenatal survey as no interpretable trends were observed(58).

Table 1.1: Variables collected in the Antenatal Sentinel HIV Prevalence Surveys

Age
Population group*
Level of education
Marital Status
Gravidity
Parity
Previous participation in survey
Age of partner
Awareness of HIV status
Laboratory confirmed HIV test result
Laboratory confirmed Rapid Plasma Reagin (RPR) test result

**Population group refers to historical racial categories used in South Africa viz. Black African, Coloured, White, Asian, Other. These terms are applied by the national survey for purposes of service delivery redress.*

Data collected are unlinked and anonymous(53,56). Although the use of antenatal HIV prevalence surveys is common, there are methodological concerns(53,59). Firstly, pregnancy confirms recent unprotected sexual activity, which is a known risk factor for HIV. Sampling of pregnant women may therefore overestimate HIV prevalence in the population(54,59).

Approximately 30% of women initiating antenatal care present for their first pregnancy (56,58). Women with higher parity will likely have had more opportunities to test for HIV in previous pregnancies compared to the general population. Additionally, sampling from selected public health facilities may further bias the sample(53). The national antenatal survey is also underpowered to provide accurate estimates at district and sub-district level. To generate more accurate local estimates, the Western Cape Provincial Department of Health expanded the national survey to additional sites from 2001 to 2016(57). Despite the known limitations, trends in antenatal prevalence may reflect trends in the broader population after appropriate adjustment. Additionally, certain variables collected during antenatal surveys are not routinely available e.g., education level and marital status.

In 2013, WHO and UNAIDS published “Guiding principles on Ethical issues in HIV surveillance” indicating that unlinked anonymous testing should only be used for surveillance where there is demonstrable inadequacy of program data for surveillance purposes(60). Thereafter, the WHO 2015 “Consolidated guidelines on HIV testing services” recommends that countries move towards the use of routine programmatic data for antenatal HIV surveillance(55,61). Subsequently, guidelines for conducting HIV surveillance among pregnant women attending antenatal clinics based on routine programme data were also published by WHO and UNAIDS in 2015(10,55). Evaluation of the adequacy of routine data is however required before this transition in surveillance strategy can take place.

Several studies in low- and middle-income countries have compared antenatal survey prevalence estimates with routine PMTCT data, as shown in Table 1.2 (54,55,57,62–71). Although studies in Uganda, Botswana, Kenya, Mozambique, Zimbabwe, Brazil, India and South Africa show similarities in HIV prevalence between sentinel surveillance and programme data, concerns around the validity of routine tests, data accuracy and completeness remain in most settings(62–64,67–71). Furthermore, granular estimates at district and sub-district level are disparate(57,66).

Given these concerns, individual data from surveys are preferred to aggregate programmatic data in low-and-middle income settings like South Africa. Poor validity of routine HIV testing data is of further concern given that patient management plans are determined by these routine test results. There are, however, no studies to date in the African context comparing antenatal survey estimates with estimates derived from linked routine individuated service data (with or without HIV testing data).

Table 1.2: Selected studies in low-and-middle-income countries evaluating routine programmatic data for HIV surveillance

Author, year (ref)	Sites	Study period	Datasets compared	Key findings
Hladik, 2005 (67)	Uganda, Botswana, Kenya, Thailand	Uganda 1992 - 2000; Botswana 2002; Kenya 2003	PMTCT and voluntary counselling and testing (VCT) programme data and sentinel surveillance	Prevalences similar in Uganda, Botswana and Kenya. Quality and availability of data varied in Botswana and Kenya. Thailand replaced sentinel surveillance in favour of PMTCT data in 2003.
Fabiani, 2005 (65)	North Uganda	2001 - 2003	PMTCT/VCT data and anonymous surveillance of antenatal clinic attendees	Prevalence similar (10.9 vs 11.1%)
Seguy, 2006 (68)	Kenya	2003	PMTCT/VCT programme data and sentinel surveillance	Prevalence in routine data was higher than sentinel surveillance (14.4 vs 12.8%). Data quality and HIV testing acceptance is variable and therefore cannot replace sentinel surveillance.
Gouws, 2008 (54)	26 African countries excluding South Africa, Botswana and eSwatini	Site specific, 2001 - 2006	Adult HIV prevalence from national population-based surveys and antenatal clinic surveillance	Prevalence from clinic surveillance data overestimated survey data by about 20%.
Kumar, 2010 (66)	India	2005 - 2007	Prevention of parent-to-child transmission programme data and sentinel surveillance data	Prevalence was similar (0.68 vs 0.61%). High correlation at state level ($r=0.9$), but low at district or site level ($r=0.6$)
Young, 2013 (62)	36 sentinel sites in Mozambique	2007; 2009	Matched routine PMTCT and sentinel surveillance tests	Prevalence was similar (14.4 vs 15.2%, relative difference -5.1%; absolute difference -0.78%). Positive percent agreement was 88.5% (95% CI 85.7 - 91.3) and negative percent agreement 98.9% (95% CI 98.5 - 99.2). Improvement noted from 2007 to 2009.
Essel, 2014 (57)	Western Cape, South Africa	2009 - 2012	Provincial antenatal survey data and aggregated PMTCT data	Prevalence similar at district level, but disparate at sub-district level
Sirengo, 2016 (69)	Kenya	2010	Routine HIV testing data and sentinel surveillance	Prevalence was similar (6.5 vs 6.2%), agreement 98%. Data accuracy and completeness concerns remain.
Pereira, 2017 (64)	219 maternity service clinics in Brazil	2010 - 2012	Routine HIV testing data and sentinel surveillance	Prevalence was similar (0.36 vs 0.38%; relative difference -0.05; absolute difference -0.02%). Positive percent agreement 84.1% (95% CI 74.8 - 91.0%) and negative percent agreement was 99.9% (95% CI 99.9 - 100.0). Consistent HIV prevalence estimates but positive percent agreement falls below WHO benchmark of 94.7%.
Diouf, 2018 (63)	Senegal	2011 -2012	Routine HIV testing data and sentinel surveillance	Prevalence was similar (1.1 vs 1.0%). Positive percent agreement 85.1% (95% CI 77.2 - 90.7) and negative percent agreement was 99.9% (95% CI 99.8 - 99.9). Data validity and completeness rates in registers were below WHO benchmark of 90%.
Gonese, 2016 (70)	53 sites in Zimbabwe	2012	PMTCT data from antenatal care registers and sentinel surveillance data linked by bar-code labels	Prevalence was similar (15.8 vs 16.3%), but percent positive agreement was 91.2% and negative percent agreement was 98.7%, falling below WHO benchmarks.
Billong, 2017 (71)	10 regions of Cameroon	2012	Routine HIV testing data and sentinel surveillance	Sensitivity 81.2% and specificity 99.3% with sentinel surveillance as gold standard. Need to improve quality of routine testing

Population surveys

Compared to antenatal surveys, population-based surveys are more geographically representative. The South African national HIV prevalence, incidence, behaviour and communication survey is a population-based survey, similar in concept to PHIAS, which also contributes to HIV surveillance(72). These types of surveys are however logistically challenging and may be underpowered for local estimates(21,54). As both antenatal and population-based surveys have utility they both are currently key components of national HIV surveillance and contribute to statistical and mathematical modelling of HIV prevalence estimates.

Mathematical models

The Thembisa model is a combined demographic and HIV mathematical model developed specifically for South Africa which uses survey, routine data and other data to determine the dynamics of the epidemic in the population and progress towards the 95-95-95 targets(73,74). Despite the usefulness of survey data for modelling estimates, they are heavily resource-intensive and costly to conduct(53,54). While newer models incorporating more routine data have been developed, providing an opportunity for more precise modelling, concerns around data quality of routine data persist(75,76).

Case reporting

The case-reporting approach for HIV surveillance relies on individual-level routine data on key events such as new HIV diagnoses or recorded HIV-related deaths. Individual clinical case reports may provide meaningful information, particularly new information on acute infection, modes of transmission, opportunistic infections or adverse treatment events. Case reports and case series of related reports may help to initiate broader monitoring and surveillance, though have limited utility in isolation.

Routine data

The majority of studies assessing routine data for HIV surveillance in South Africa focus on aggregate data from service delivery registers(77–79). Cohort studies using either research-driven information systems or routine data systems may also contribute to HIV surveillance.

There are several studies using routine individual data for defined geographic areas or sentinel sites, including longstanding seminal cohorts with a predominant focus on HIV treatment. For example, the Khayelitsha HIV Treatment Program Cohort was embedded within the first government service to provide antiretroviral therapy in antenatal services(78,80). The Themba Lethu Clinical Cohort is another HIV treatment cohort, located in Johannesburg to monitor and evaluate the HIV treatment roll-out and other aspects of HIV care and treatment(81,82). Covering multiple provinces of South Africa, the Kheth'Impilo HIV Cohort follows people living with HIV at different points along the HIV care continuum, using enhanced routine data to identify gaps in care and evaluate effectiveness of interventions(83,84). The International epidemiology databases to evaluate AIDS (IeDEA) is a global research consortium with a focus on the evaluation of HIV programmes in 46 countries, using routine observational data from designated sites(85). Sites in South Africa (including the aforementioned cohorts) form a key part of the Sub-Saharan Africa arm of the consortium(86,87). Findings from observational research through established cohorts such as these have contributed to policy development through collaboration with WHO and local health institutions(85). While these and other HIV cohorts provide important contributions in understanding different aspects of HIV at both individual and population level, studies evaluating routine individuated data at a scale appropriate for province-wide or national surveillance are rare. This is likely as linked electronic information systems are not available at scale in most South African settings(24,88). The South African national laboratory information system, governed by the National Health Laboratory Services (NHLS), is another key contributor of individuated HIV surveillance data(89), as specific laboratory tests are indicative of key points within the HIV care continuum. These laboratory tests are conducted centrally under rigorous quality control processes. Several HIV cohorts have also been assembled using NHLS data to evaluate HIV linkage to care and retention(90,91). A limitation of these data is that key events such as point-of-care testing and data points that do not involve laboratory testing (e.g., retention in care between viral load testing) are not identified.

HIV testing monitoring in South Africa

While NHLS individuated routine data contribute notably to HIV surveillance, the first step of HIV diagnosis is not reliably included in laboratory surveillance. This is because, an HIV diagnosis in South Africa is most often based on a point-of-care testing (PoCT) algorithm (Appendix A) using rapid HIV tests(7). HIV testing is conducted primarily by HIV counsellors and nursing staff and information is entered into paper-based registers. Testing data are subsequently manually tallied, with aggregates reported to the Provincial Departments of Health on a monthly basis(7). TIER.net does offer a platform for electronic capturing of individuated HIV testing information, but this is not fully implemented in many facilities, particularly information on those testing negative(40). It has been reported that PoCT are less accurate than central laboratory tests as the tests are conducted by busy clinical staff members who are not trained rigorously on laboratory quality control and quality assurance(12,13). However, PoCT are favoured in high-burden, resource limited settings as access to care is improved by more immediate availability of test results and linkage to further to care(13).

Without robust testing data, linkage to care cannot be effectively evaluated due to pre-treatment loss to care(4–6). It is important for the gap between HIV testing and treatment to be addressed if we are to achieve the 95-95-95 targets (92). In 2018, a sizable proportion of people diagnosed with HIV (up to 20%) had not yet initiated treatment worldwide(92). Prevention strategies may also be better targeted towards those testing negative if timeous negative testing data were available. Additionally, retesting amongst those previously diagnosed with HIV cannot be quantified without adequate estimation of testing. Without discernment of retesting among previously diagnosed, many patients testing positive and linked to care may be misclassified in aggregate data as newly diagnosed. No studies have quantified this phenomenon in the South African setting. Without valid estimates from diagnosis itself, HIV prevention and planning may be severely misdirected with underestimation of true linkage to care. Additionally, the lack of integration of PoCT results within the NHLS and linked systems may further limit information available to clinicians when

evaluating historical laboratory investigations as part of clinical decision-making. In high-burden clinical environments, this results in longer, less efficient clinical consultations and unnecessary and costly repetition of PoCT(12). An HIV CBS system therefore requires individual level data on diagnosis of HIV(7).

Vertical transmission surveillance

Vertical transmission of HIV is an example of a sentinel event within the HIV care cascade that should be thoroughly interrogated as a preventable adverse outcome with considerable morbidity and mortality in children(24,93). Vertical transmission may occur during pregnancy, during delivery and during the post-partum period if breastfeeding(94). Any such event should be considered a massive failure of the health system and measures put in place to identify systemic issues leading to this adverse outcome in order to ensure that future events are prevented(24).

Vertical Transmission Prevention Cascade

Similar to the HIV care cascade, the PMTCT or VTP care cascade or continuum is an evolving set of sequential steps in the health services pathway to prevention of perinatal HIV transmission(95). VTP relies on HIV testing both for identification of pregnancies at risk, and for determining the transmission outcome. The sentinel event of vertical transmission is dependent on an HIV testing event for the child, which then initiates a new HIV care cascade for the child. Key steps within the VTP cascade and their relationship to the HIV care cascade are illustrated in Figure 1.1(95,96).

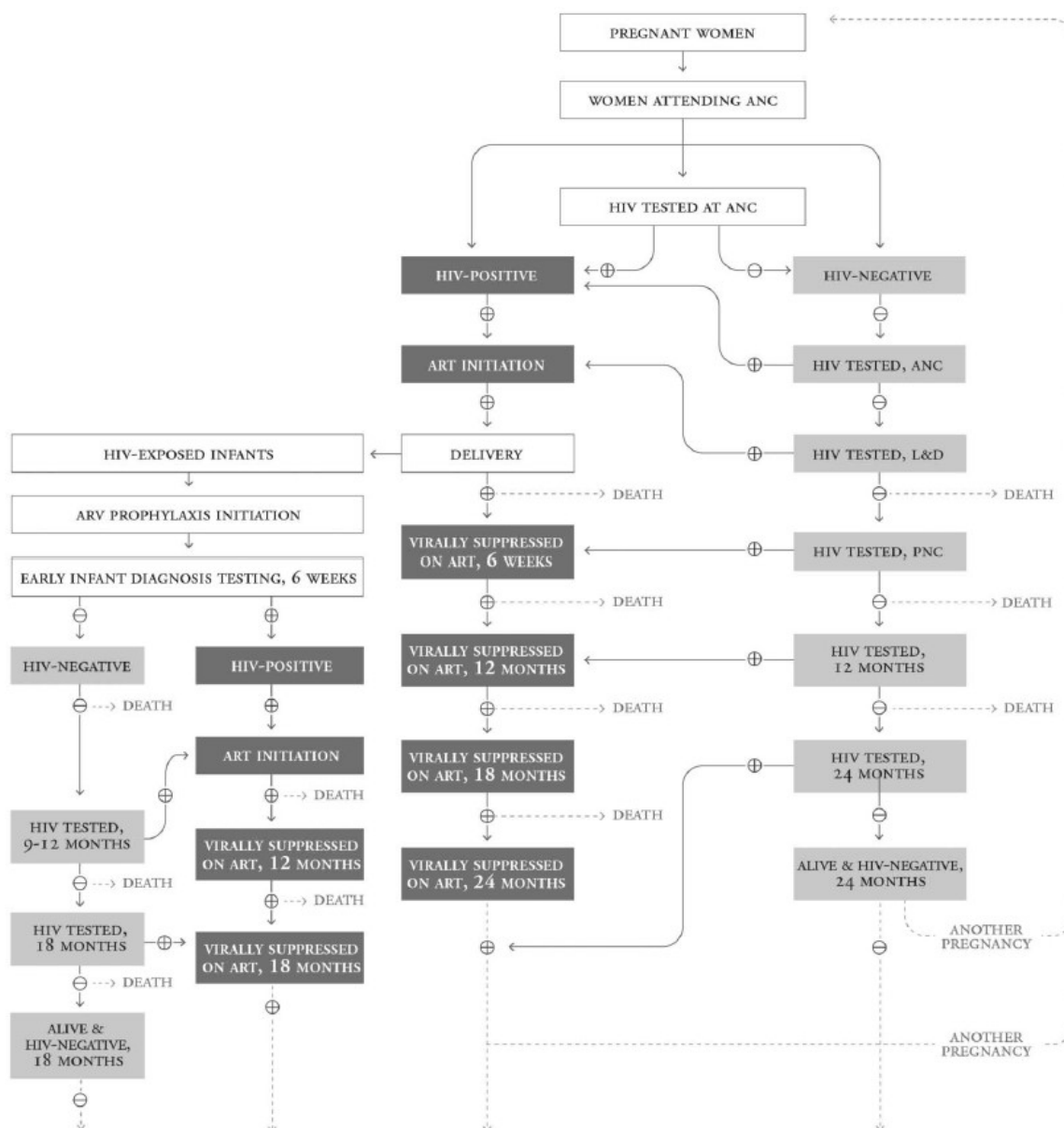


Figure 1.1: Expanded PMTCT (VTP) cascade(95)

Routine data for vertical transmission surveillance

Although HIV PoCT data are not currently digitised, HIV testing in infants is based on central laboratory polymerase chain reaction (PCR) tests with results electronically registered in NHLS and thereby available for electronic linkage. With existing HIV surveillance embedded in antenatal services through the antenatal HIV prevalence surveys, the advent of lifelong ART for all HIV positive pregnant women since 2015 (option B+, 2013 in the Western Cape province) and the availability of routine central laboratory testing for HIV exposed infants, the

antenatal journey presents a unique opportunity to better understand the role of routine data in surveillance, patient care and prevention of transmission. Several studies have been conducted in South Africa to evaluate early infant diagnosis of HIV and strategies to improve infant diagnosis, including changes to timing of routine testing from 6 weeks to birth testing (implemented in 2015) (94,97–100). Routine data, including laboratory data and facility administrative data have enabled many of these studies(94,98,100,101). Furthermore, routine data facilitate timeous monitoring of changes to guidelines and unintended consequences such as testing negative at birth resulting in less likely presentation for subsequent testing(102). Although PoCT for early infant diagnosis has been recommended to improve access to testing and turn-around-times, such a transition would require urgent implementation of a corresponding electronic data capturing system to ensure that this sentinel data point is available for linkage, monitoring and evaluation(102).

Measurement of VTP-related testing and treatment

The WHO Initiative on elimination of mother-to-child transmission (EMTCT) of HIV highlights the importance of early antenatal care for all women living with HIV (WLWH), early diagnosis of HIV and antiretroviral treatment (ART) initiation(103). Rigorous screening protocols are in place to ensure timely testing and management of HIV during pregnancy and the postnatal period. Over time, various protocol changes have been implemented regarding ART initiation of WLWH and HIV testing of pregnant women and HIV exposed children. The changes over time are illustrated in Figure 1.2(104–107).

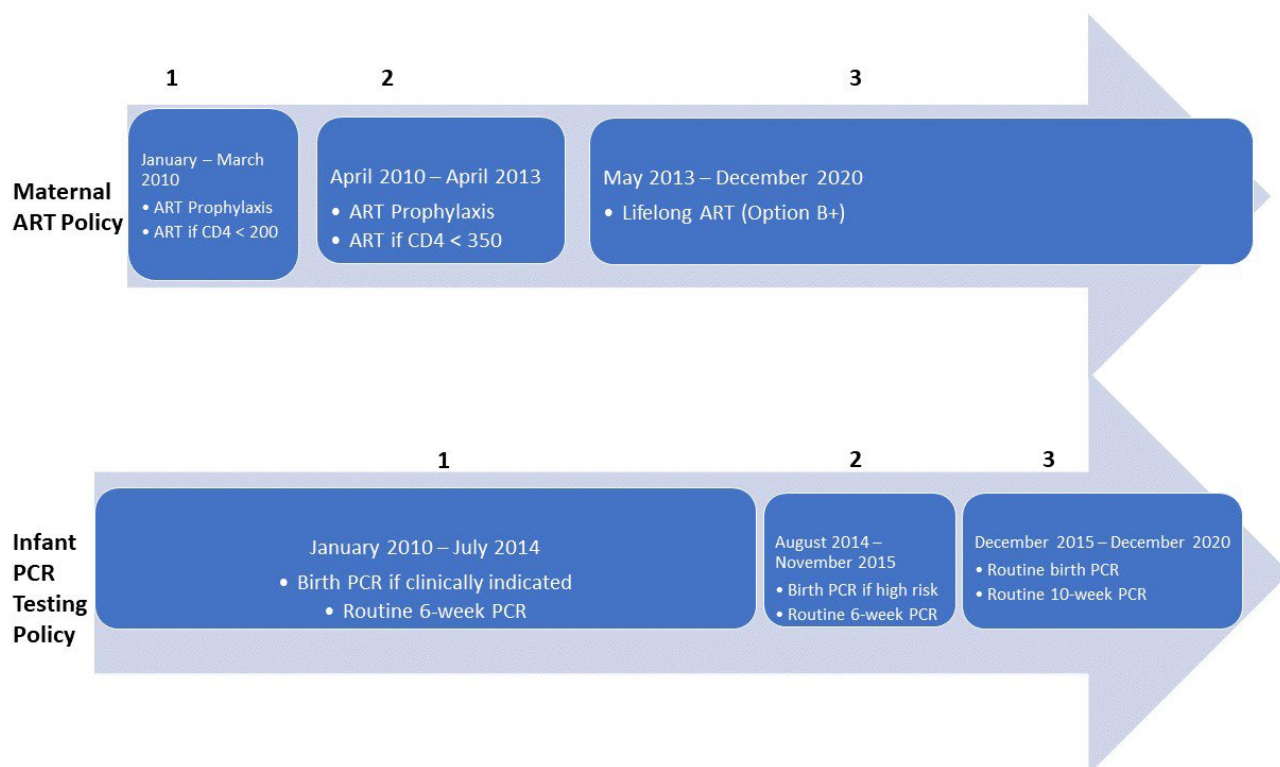


Figure 1.2: Changes in Maternal ART and Infant HIV PCR testing policies, Western Cape, South Africa 2010 – 2020

Currently, all newly pregnant women receive rapid HIV testing on the day of presentation to a health facility(106). Repeat testing during the perinatal period takes place at the following time periods:

- 20 weeks gestation (second trimester)
- 32 weeks gestation (third trimester)
- In labour or immediately after delivery
- At 6 weeks after delivery
- Every 3 months while breastfeeding (106,108)

With the introduction of option B+, followed by universal test and treat, many pregnant women had already initiated lifelong ART in an earlier pregnancy or prior to pregnancy and therefore were known to the HIV care cascade in subsequent pregnancies. However, the extent of ART use and treatment interruption in pregnant women is poorly understood.

In 2014, the Western Cape Government included an additional question to the provincial antenatal survey to determine ART use amongst survey participants(58). This question was subsequently added to the national antenatal survey in 2017. The validity of this additional question has not been formally evaluated. Recent studies in South Africa and Uganda support the use of self-reported ART to estimate ART coverage, however both studies highlighted underreporting of ART use amongst younger people, 15 – 19 years and under 30 years respectively(109,110). As antenatal populations are typically younger on average than general populations, the validity of the additional question on ART in antenatal surveys warrants further evaluation. Studies of ART coverage in low-and-middle income countries using routine programmatic data were mainly conducted prior to the era of Universal Test and Treat and made use of aggregated data(77,78). No recent studies have evaluated ART coverage in pregnant women using routine *individuated* programmatic data.

In addition to adequate ART coverage in pregnant WLWH, retention of HIV negative women until the end of breastfeeding is paramount to prevention of vertical transmission(95). HIV-exposed infants are tested for HIV using a PCR test at the following ages:

- Within 48 hours of birth (since 2015)
- 10 weeks
- 18 weeks (if breastfeeding and received Nevirapine for 12 weeks)
- 6 months (replaced 18 week testing from 2020) (106,108)

These laboratory-based test results are available digitally on the laboratory information system. Early PCR testing is followed by rapid testing at 18 months and 6 weeks after final breastfeed and/or if clinically indicated(106). All positive rapid tests under 18 months are verified with a confirmatory HIV PCR test(106). Despite successes in PMTCT programmes and access to ART in the perinatal period and beyond, approximately 2.7% of HIV-exposed infants in South Africa test positive for HIV(25). While transmission may occur in the antenatal,

peripartum and postpartum period, there is growing concern of increased transmission in the postpartum period(95). The availability of sequential testing data for both mother and child is paramount to determine timing of transmission and address drivers of transmission at appropriate points in the VTP cascade.

Measurement of factors associated with VTP

There is a large body of literature, including systematic reviews, evaluating PMTCT programmes and interventions in low-and-middle income countries(96,111–121). These studies evaluated progress in maternal and infant HIV testing and management and factors impacting poor uptake of PMTCT interventions in order to inform changes to HIV prevention, treatment and monitoring. Antenatal and postnatal barriers to VTP are highlighted such as poor retention in care, delayed or limited antenatal care, poor infant testing and prophylaxis coverage, poor postnatal follow-up and mixed feeding(96,112,121,113–120). Idele *et al* reviewed the evolution of monitoring of PMTCT programmes with changing policies and guidelines over time, highlighting the need for more robust routine information systems with disaggregated data for adequate monitoring and evaluation of programme effectiveness(122).

Several studies have been conducted in South Africa to evaluate risk factors for VT using routine data or cohort data(24,88,123). In keeping with other studies in sub-Saharan Africa, these studies have highlighted risk factors including late presentation for antenatal care, young age, lack of viral load monitoring, limited repeat antenatal testing and inadequate prophylaxis(24,123–125). Missing incident infections in previously HIV-negative pregnant women is another cause for concern(95). A recent mixed-methods study included a qualitative synthesis of systemic factors hindering VTP. The findings echoed health information systems challenges well-known to CBS, such as network infrastructure, poor alignment between routine indicators and programmatic interventions, and lack of longitudinal monitoring of patients(100). Compared to high-income settings, routine data studies on systemic risk factors for VTP in the South African setting are either based on aggregate data, or notably limited in sample size(24,77,84,88,125–130). Studies using routine individual data from health services

are frequently based on case histories from single or a few selected facilities and therefore have limited external validity(24,84,88,128,131). Additionally, data collection from the postpartum period e.g. breastfeeding is limited(95). The South Africa PMTCT Evaluation study was a facility-based survey providing the first population-level VTP analysis for South Africa(93,123). Table 1.3 summarises selected South African studies evaluating VT and the data sources used. Few studies using broader linked individuated routine surveillance data have been conducted in the South African setting. Province-wide CBS using routine data may provide a rich dataset enabling a much larger sample size to more thoroughly evaluate a wider range of risk factors and reliably inform public health decision-making.

Table 1.3: Selected studies evaluating vertical transmission of HIV in the South African context

Author, year (ref)	Site	Study period	Data source	Proportion children infected	Factors associated with vertical transmission
Sherman, 2004 (131)	Coronation Women and Children's Hospital, Johannesburg	2001 -2002	Routine individual clinical records enhanced by research data	8.7%	Risk factors not analysed
Coetzee, 2005 (79)	Khayelitsha, Western Cape	2003	Routine data - clinic registers	8.8% (95% CI 6.2 - 10.9)	Maternal age>25 years
Draper 2008 (77)	Western Cape, South Africa	2003 - 2004	Routine aggregated data	<10%	Risk factors not analysed
Fitzgerald, 2010 (125)	Gugulethu CHC, Western Cape	2002 - 2008	Cohort study	5.1% (95% CI 2.8 - 9.0)	Advanced WHO disease stage, follow-up VL above 50 copies/ml, late presentation for antenatal care
Hoffman, 2010 (128)	Selected antenatal care (ANC)-ARV clinics in Johannesburg, Gauteng	2004 - 2008	Routine data - individual medical records	4.9%	Late initiation of highly active antiretroviral therapy (HAART)
Horwood, 2012 (129)	All primary-health-care facilities in 6 districts of Kwazulu-Natal	2008 - 2009	Cross-sectional study	2.8%	Incomplete ARV prophylaxis

Stringer, 2013 (130)	South Africa, Cameroon, Cote D'Ivoire, Zambia	2007 - 2009	Household survey	9.1% (South Africa)	No statistically significant risk factors identified
Ibeto, 2013 (24)	Khayelitsha Site B CHC, Western Cape	2012 - 2013	Routine data - individual medical records	1.6% (15/926)	Late presentation for antenatal care, inadequate antenatal prophylaxis, lack of viral load monitoring
Fatti, 2014 (84)	3 sentinel surveillance sites, Nelson Mandela Bay Metropolitan	2009 -2012	Enhanced routine individual clinical data	3.4%	Younger women (adolescents and women aged 20 -24 years), women who presented for the first during labour
Goga, 2015 (123)	South Africa (nationally representative sample from 500+ clinics)	2010	Facility-based survey	3.5% (95% CI 2.9 - 4.1)	Incomplete ARV prophylaxis or not receiving ARV drugs with exclusive or mixed breast feeding
Woldesenbet, 2015 (124)					Adolescent (<20 years) mothers, low socioeconomic score, low education level, primiparous mothers, delayed first antenatal visit, homebirth, and non-disclosure of HIV status
Kendall, 2015 (88)	Bethesda Hospital, Kwazulu-Natal	2013	Routine data - individual medical records	Evaluation of 19 infants with HIV	Maternal seroconversion during pregnancy and breastfeeding; false-negative HIV tests
Goga, 2018 (100)	South Africa	2016 -2017	Routine birth testing data - NHLS; qualitative data from EMTCT stock-taking workshops	0.9% (national in utero transmission rate) Provincial range 0.6 - 1.3% District-level range 0.4 - 1.9%	Varying MTCT risk and case rates by province and district. System-related factors affecting vertical transmission include poor internet connectivity, poor alignment between routine indicators and programmatic interventions, lack of longitudinal monitoring, poor maternal viral load monitoring and inconsistent feeding advice.

Challenges in HIV CBS Implementation

Whilst consolidated HIV data has the potential to contribute to health system strengthening, implementation of HIV CBS is complex, challenging and dependent on adequate resources, expertise and stakeholder commitment at all levels of the health system(7). Furthermore, data are only meaningful if utilised, however utility often cannot be adequately demonstrated without first implementing CBS strategies. The value of these strategies is therefore difficult to demonstrate before implementation. For example, even in the absence of adult PoCT data, consolidated electronically captured data from existing information systems may still provide reliable case identification and subsequent sentinel event data in CBS. In developing and strengthening information systems, we need to evaluate the utility of these data to inform decision-making. There is, however, limited evidence demonstrating the utility of routine data CBS in low- and middle-income health systems, particularly for direct service improvement. In high resource settings where CBS is implemented, such as the United Kingdom, the value of these data are clearly demonstrated by directly informing provision and improvement of HIV prevention and care services(11).

Studies in India, Nigeria and Ethiopia have shown limited availability and use of routine local data for health-system planning and decision-making(36,132). A seminal situational assessment of data collection systems in Tanzania, Kenya and South Africa revealed several barriers to implementation of CBS, including multiple data collection systems, poor interoperability and inadequate capacity(7). Many of these data collection systems are paper-based(7). Additionally, health information system strengthening interventions face many implementation challenges at facility level due to conflicting approaches to implementation, differing needs and priorities, poor feedback to front line staff and limited understanding of front line challenges(133–135). Another challenge in establishing HIV CBS is privacy and security issues given that individuated data are used, coupled with the stigma associated with HIV in many high-burden settings. Furthermore, privately owned data may be difficult to access and link with public sector information systems. Patient confidentiality legislation may further complicate establishment of CBS systems(136). However, with appropriate

implementations strategies and regulatory frameworks in place, CBS may present a cost-effective method to monitor and evaluate HIV programmes and improve patient and programme management(7).

Conclusion

HIV CBS can contribute to health information system strengthening by enabling earlier and more accurate ascertainment of HIV diagnosis, improved monitoring and evaluation of progress in HIV prevention and treatment, and informing service provision. There is currently a gap in the literature documenting comprehensive CBS systems in high-burden HIV settings(7,32), with most experience being based on monitoring HIV treatment programs through cohort studies or national registers. Whilst the Western Cape province has made significant progress in the establishment of HIV CBS through the PHDC, challenges and areas for further improvement remain in this and aligned settings. These include:

1. the absence of critical HIV testing information within CBS with limited efforts to systematically digitise point-of-care testing data
2. validation of key HIV surveillance metrics such as HIV prevalence, ART coverage and VTP estimates from routine individuated data
3. limited evidence on the utility of CBS using routine data for direct service improvement and for informing policy

Purpose, Aims and Objectives

Purpose

The purpose of this study is to enhance opportunities for using person-level HIV data to improve operational efficiency and clinical governance, better evaluate HIV services, and support the transition to person-centred monitoring recommended by the WHO. The cascade of care for VTP provides an ideal context for exploring opportunities for using routine data for HIV surveillance. Sentinel antenatal surveillance has long been used as a key tool for monitoring the HIV epidemic, and HIV testing, data for which are identified above as an

important gap in current CBS initiatives, is central to identifying both mothers and infants for intervention, and evaluating VTP effectiveness and missed opportunities.

Aim

To determine the feasibility, validity and utility of digitised data on HIV ascertainment as key components of HIV CBS through the lens of vertical transmission of HIV.

Objectives

1. To determine the validity of routine HIV prevalence estimates in pregnant women as compared to sentinel surveillance
2. To validate estimates of current ART use in pregnancy derived from both routine data and antenatal survey data.
3. To evaluate the operational feasibility of an intervention to digitise HIV testing data
4. To evaluate the utility of digitised HIV testing data within CBS systems
5. To explore vertical transmission of HIV as both a sentinel event and testing event, and systemic risk factors for these events using routine CBS data

Figure 1.3 shows where each research objective is situated along the VTP cascade with objectives 1 and 2 focussing on validation of HIV surveillance indicators from the first step of utilisation of antenatal care, objectives 3 and 4 centring on HIV testing, and objective 5 looking across the cascade from maternal antenatal care and HIV testing to postnatal follow-up and testing of children exposed to HIV.

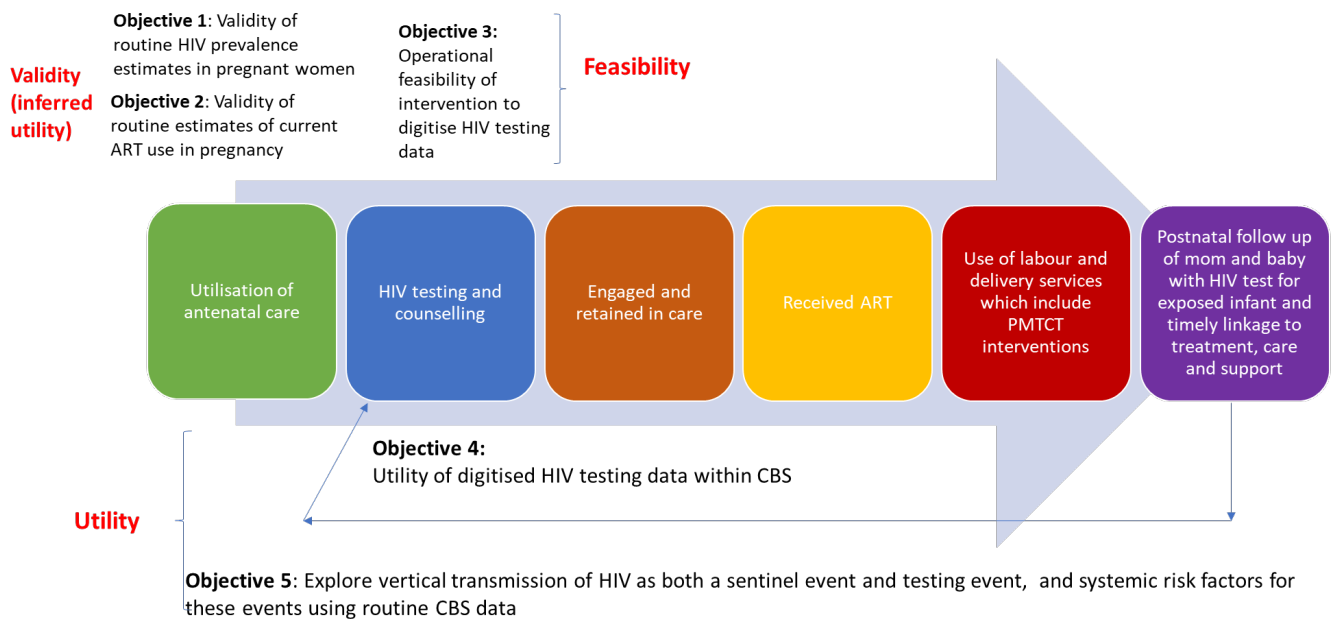


Figure 1.3: Research objectives situated within the VTP cascade

Methods

In this section, I discuss the methods as pertaining to the thesis as a whole. Although each individual results chapter has a detailed methods section, this chapter covers the overall methods and common data sources.

Definition of terms

Feasibility

Feasibility may be simply defined as “the state or degree of being easily or conveniently done”(137). For the purposes of this study, feasibility is further defined according to the TELOS framework, which stands for 5 dimensions viz. **t**echnology and systems, **e**conomic, **l**egal and political and **o**perational and **s**cheduling feasibility(132).

Operational feasibility

Operational feasibility focusses on whether an intervention works in practice, for example, whether existing procedures and protocols support the intervention(132). Different measures may be used to evaluate operational feasibility depending on the context of an intervention.

Validity

A simple definition of validity is “the quality of being logically or factually sound”(137). In epidemiology, validity refers to the extent to which a tool explores what it is purported to measure (i.e. provides the ‘true’ answer and minimises bias)”(138). Different types of validity include face validity, construct validity and criterion validity(16). Face validity is the extent to which a tool is subjectively viewed as covering the concept it seeks to measure(16). Construct validity is the extent to which a measurement agrees with other operational measurements of the same concept, none of which is the gold standard by itself(16). Criterion validity is the extent to which a measurement agrees with an objective test or gold standard(16).

Utility

Utility is a transdisciplinary term which may be simply defined as the “state of being useful, profitable, or beneficial”(137). For the purposes of this study, utility refers to the usefulness of an intervention to strengthen HIV surveillance. Different measures may be used to evaluate utility depending on the context of an intervention.

Study setting

The study will be set in the Western Cape province of South Africa, which is comprised of one metropolitan district, Cape Metro and five less urbanised districts viz. Overberg, Garden Route, Central Karoo, West Coast and Cape Winelands. Districts are further divided into sub-districts, as well as sub-structures in the more populous Cape Metro district. The province includes both public and private sector health services, with the majority of the population utilising public health care and the minority, high-income population predominantly utilising private health care(139). The Western Cape Department of Health and Wellness (WCDHW), formerly the Western Cape Department of Health, oversees the public healthcare sector, which is rooted in the Primary Health Care philosophy of providing comprehensive health services, including preventive, promotive, curative and rehabilitative care(139,140). The District Health System policy was implemented throughout South Africa post-apartheid, in 1995, and is the main service delivery vehicle in all provinces of South Africa. Community

health centres (CHC) and district hospitals provide the main primary level health care services to the district population(139,141). Regional and tertiary hospitals provide more specialised care, serving as referral centres from primary levels of care. The DHIS emerged in the late 1990's to support the decentralised District Health System by providing standardised information for monitoring and surveillance of health programmes and services(30). Over time, the DHIS was complemented by individual routine data systems, culminating in the development of the Provincial Health Data Centre (PHDC) in the 2010's, which consolidates routine patient-level data from multiple electronic data systems(9).

The Western Cape province, like other provinces in South Africa, is impacted by the quadruple burden of disease. HIV and TB are the leading causes of premature mortality in the province, with non-communicable diseases and intentional injuries showing a notable increase over time(142). Maternal health has shown positive trends over time with a decrease in maternal mortality ratio to less than 70 per 100 000 live births(142). There are approximately 100 000 deliveries in the Western Cape annually(142). Access to maternal health is high with an estimated 94% of women in the province accessing antenatal care at least once during pregnancy(143).

Study population

The study population includes the public sector population of the Western Cape, with this study focussing on pregnant women nested within the provincial population from 2010 – 2020 or attendees of a specific facility, depending on the study objective. Additionally, objectives 1 and 2 triangulates data from antenatal sentinel survey participants. These include all pregnant women attending their first antenatal visit in a public health facility during a 6-week period of a survey year. Objectives 3 and 4 focusses on all attendees of Gugulethu CHC HIV testing services between May 2017 and June 2018, where an intervention was piloted by the Western Cape Department of Health. No sampling was undertaken as all patients within the specified time periods for the different objectives were included in the study. No formal recruitment took place for the study as existing records within the PHDC and DHIS, housed by the WCDHW

were used. Although sampling and recruitment strategies were employed for the sentinel antenatal surveys, data from these surveys were only used in this thesis for comparison purposes.

Data sources

Provincial Health Data Centre (PHDC)

The main data source for this study, cross cutting all 5 objectives, is the PHDC. The PHDC is contained entirely within the WCDHW. It consolidates routine data from various provincial data platforms on a daily basis, using a unique patient identifier(9). Consolidation of data on a single central platform supports integrated clinical care, whilst also facilitating more timely and comprehensive surveillance and further epidemiological and operational analyses. This is enabled through the immediate availability of management reports and dashboards, patient-level disease-specific line lists, e-mail alerts, a web-based patient-level clinical viewing platform (Single Patient Viewer) and the provision of data for operational and research requests in keeping with the WCDHW Data Access Policy Guidelines. Since its inception in 2015, the PHDC has recorded more than 8 million unique people who have accessed healthcare services in the provincial public sector(9). Disease-specific cascades, based on systematic identification and consolidation of high confidence electronic data points, includes the enumeration of over 430 000 people with HIV and, annually, over 110 000 pregnancies(9). Figure 1.4 illustrates the architecture of the PHDC(9).

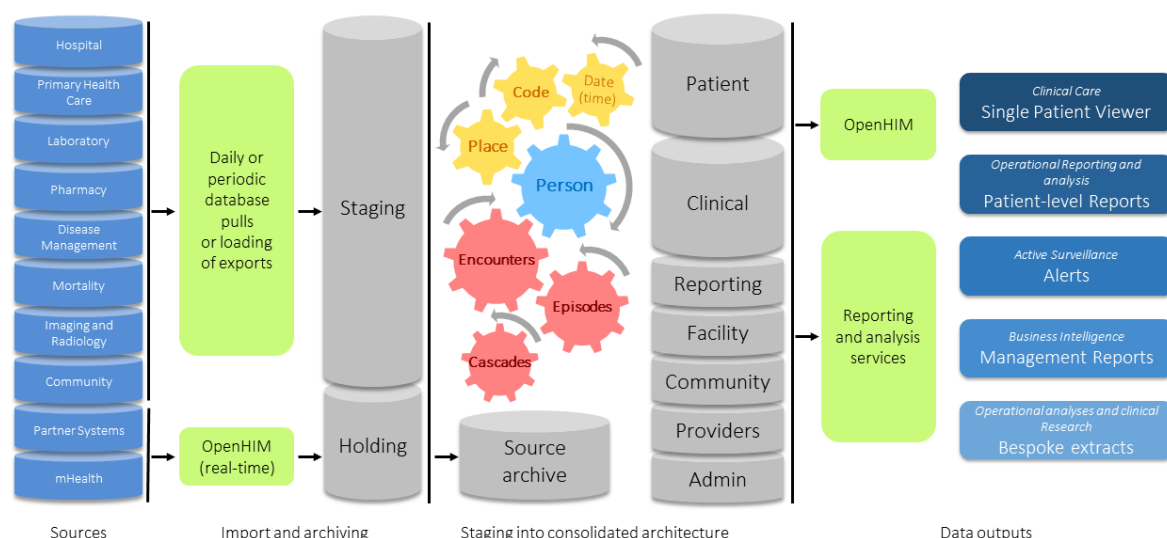


Figure 1.4: PHDC High-level architecture (9)

In the HIV care cascade, electronic evidence of HIV diagnosis is based on laboratory markers (where PoCT is discordant, or from other laboratory tests often conducted shortly after diagnosis, such as CD4 tests and viral load), ICD-10 coding, register entries and ART drugs. The HIV care cascade includes treatment information, such as initiation dates, regimen details, last dispensing dates, as well as information on viral suppression.

Although the PHDC provides a platform for CBS, monitoring and surveillance systems that are not part of an electronic information system cannot be linked to the PHDC. This is true for all PoCT information in the province, which is not collected digitally. Although aggregate HIV testing data are reported electronically, individual testing data remain in paper-based registers and paper-based facility patient records. Currently, the only electronically captured adult HIV test results within the NHLS are from enzyme-linked immunosorbent assay (ELISA) tests which are conducted at the central laboratory if rapid PoCT results are discordant. Negative HIV PoCT results are not captured electronically in any routine information system.

Given these circumstances, the intervention of digitising paper-based HIV testing records and linking to the PHDC may contribute towards strengthening of CBS. Such an intervention was piloted by the WCDHW, led by the PhD candidate, in Gugulethu CHC from April 2017 but not taken to scale. Data from this pilot were consolidated within the PHDC.

Other data sources

Objectives 1 and 2 also includes aggregated DHIS data, mathematical model estimates from the Thembisa HIV Model and unlinked, anonymous national and provincial antenatal sentinel survey data.

Summary of data sources

Table 1.4 summarises the key data sources for each objective.

Table 1.4: Data sources

Objective	Data Source
1. To determine the validity of routine HIV prevalence estimates in pregnant women as compared to sentinel surveillance	Provincial Antenatal Survey data 2011 – 2016 National Antenatal Survey data 2017-2019 PHDC maternity and HIV cascade data 2011 – 2020 DHIS Primary Health Care and HIV Testing Services data 2011 – 2020 Thembisa HIV model estimates
2. To validate estimates of current ART use in pregnancy derived from both routine data and antenatal survey data.	2014 Provincial Antenatal Survey ART data Provincial Antenatal Survey data 2014 – 2016 National Antenatal Survey data 2017-2019 PHDC maternity and HIV cascade data 2011 – 2020 DHIS Primary Health Care and HIV Testing Services data 2011 – 2020 Thembisa model estimates
3. To evaluate the operational feasibility of an intervention to digitise HIV testing data	DHIS HIV provincial indicator dataset 2017 – 2019 PHDC HIV POCT Digitisation Pilot data
4. To evaluate the utility of digitised HIV testing data within CBS systems	PHDC HIV cascade data 2017 – 2019 PHDC HIV POCT Digitisation Pilot data
5. To explore vertical transmission of HIV as both a sentinel event and testing event, and systemic risk factors for these events using routine CBS data	PHDC HIV cascade data 2010 – 2020

Provincial and national antenatal survey data are anonymous, unlinked data. Survey data from 2011 – 2016 were obtained from the Western Cape provincial antenatal survey database. Survey data from 2017 - 2019 were obtained from the NICD. These survey data were used for objectives 1- 2.

Data sources incorporated within the PHDC HIV Cascade which were used for this study (objectives 1 – 5) include:

- National Health Laboratory Service (NHLS) data – includes laboratory HIV testing data, CD 4 count and viral load data
- Point-of-care testing data from the intervention site
- Primary Health Care Information System (PHCIS) data on HIV-associated visits
- Clinicom hospital data on admissions and out-patient visits
- Pharmacy data from JAC (facility-based dispensing) and the Chronic Dispensing Unit (pre-packaged drugs)
- TIER.Net
- ICD-10

For objective 3, provincial aggregate data were obtained from a web-based aggregate data portal within the Western Cape DHIS, known locally as SINJANI. The 2018 HIV Testing Services register comprised 49 reporting elements that can be broadly grouped as elements pertaining to:

- Antenatal care
- Children under 15 years of age
- All patients including antenatal care
- All patients excluding antenatal care

For the purposes of this research objective, 13 key reporting elements, representative of these categories and the patient population, were analysed (Table 1.5).

Table 1.5: Selected provincial indicator dataset reporting elements

Total HIV test client accept test (incl. ANC)
Clients PRE-TEST counselled for HCT (incl. ANC)
Antenatal client counselled for HIV testing - 15 to 24 years
Antenatal client counselled for HIV testing - 25 years and older
Accept testing - PMTCT initial test
Accept testing - PMTCT repeat test at 20 weeks
Accept testing - PMTCT repeat test at 32 weeks
HIV positive client category - PMTCT initial test
Antenatal client eligible for ART
Known HIV positive antenatal client
HIV test 15 years and older (excl. ANC)
HIV test client 15-24 years (excl. ANC) accept test
HIV PRE-TEST counselled client (excl. ANC)

Study design

Routine pregnancy and HIV data consolidated within the PHDC from January 2010 to December 2020 were analysed using retrospective cohort and cross-sectional methods. Routine data were linked using a unique patient identifier to ascertain sentinel events within

the HIV and VTP cascades. A specific intervention implemented at a selected facility to enhance CBS through digitisation of routine point-of-care HIV tests was further evaluated for operational feasibility using both quantitative and qualitative research methods. Further details of methods for each objective are elaborated below.

Data Management and Analysis

Data were analysed using Microsoft Excel and Stata 17 (StataCorp, College Station, Texas).

Personal data were de-identified prior to release for study analyses. Temporal trends in HIV prevalence, HIV testing, linkage to care, ART coverage and vertical transmission estimates were evaluated and where relevant, triangulated with other key data sources historically used as sources for these estimates, including DHIS, national and provincial sentinel antenatal seroprevalence surveys and mathematical model estimates. Risk factors for retesting and vertical transmission were further evaluated using multivariable analyses. A specific intervention implemented at Gugulethu CHC to enhance CBS through digitisation of routine point-of-care HIV tests was further evaluated for operational feasibility using measures of correlation. This analysis was supported by a more in-depth thematic analysis of stakeholder personal reflections regarding the implementation process. Further details of data analysis plan for each objective are elaborated below.

Methods and analysis for individual objectives

This section provides a high-level overview of specific study designs, data sources and link to the overall thesis objectives, for each analysis. More detailed descriptions of methods are included in each results chapter.

Objective 1

Objective 1 focuses on the validity of routine case-based HIV prevalence estimates. This objective was met using a comparative study comparing over time cross-sectional survey estimates to a retrospective cohort derived from the PHDC, aggregated programme data from the DHIS and Thembisa model estimates. The retrospective cohort included all women

attending their first antenatal visit at public health facilities in the Western Cape between 2011 – 2020.

Data were analysed at both provincial and district level. The proportion of women with evidence of HIV within the PHDC, was used to calculate HIV prevalence estimates. Prevalence estimates from datasets for each survey year were compared with PHDC HIV cascade data using correlation coefficients as well as absolute and relative differences. Prevalence within different demographic groups were compared. In the absence of a gold standard, routine data were compared to survey data, a current key contributor to HIV modelling. **High correlation and consistent trends served as a measure of the validity of PHDC HIV cascade data for CBS.**

Objective 2

In 2014, the Western Cape Government included an additional question in the provincial antenatal survey to determine ART use amongst survey participants. The validity of this additional question was not formally evaluated. As part of another study (HREC 528/2010) on antiretroviral coverage, supported by the WCDHW, a sample of antenatal survey blood specimens were tested for common ART drugs i.e., lopinavir, efavirenz and nevirapine. In this PhD research, these data were used to validate the additional survey question on ART use and compared with PHDC HIV cascade estimates for ART use. Sensitivity and specificity of the question was assessed, with the blood test as the gold standard. Positive and negative predictive values were calculated. Descriptive characteristics of the sub-sample including demographic characteristics and commonly used ART were reported.

The survey question was subsequently added to the national antenatal survey. A second retrospective descriptive review was conducted to analyse and compare routine antenatal ART use data (both individuated and aggregated) to cross-sectional antenatal survey data from 2014, 2017 and 2019 as well as Thembisa model estimates. Datasets were compared using correlation coefficients and absolute and relative differences. **Consistent trends**

between the datasets served as a measure of validity of PHDC HIV cascade ART data for CBS.

Objective 3

As defined above, the TELOS framework categorises feasibility into five distinct dimensions i.e., 1. technology and systems, 2. economic, 3. legal and political and 4. operational and 5. scheduling feasibility(132). Objective 3, to evaluate the operational feasibility of an intervention to digitise HIV testing data, focussed on whether the intervention worked in practice. This objective used a cross-sectional design to compare aggregate routine data with digitised data generated from the intervention, as a measure of operational feasibility. Data from all attendees of HIV testing services (HTS) at Gugulethu CHC (a health facility in the peri-urban township of Gugulethu in the Cape Metro district) during the intervention period (April 2017 – July 2018) were validated through double-capturing and exported and linked to existing patient records in the PHDC, using unique folder number or combinations of other identifiers. Linked data were then anonymised, filtered by month, aggregated and compared with monthly aggregate data of key reporting elements from the paper-based register submitted to DHIS. Correlation coefficients were calculated to quantify the correlation between datasets. **Correlation functioned as a measure of operational feasibility of establishing an electronic HIV testing register. Other measures of operational feasibility included completeness of digitised testing data and the proportion of digitised testing records which could be linked to existing PHDC records.**

In addition to quantitative measures of operational feasibility, detailed descriptions of the development and implementation process as well as reflections by the candidate and intervention team on implementation issues in a real-life setting provided greater insight to the quantitative data. Personal reflections captured in weekly logs, personal notes, stakeholder meetings and correspondence with project staff were used to generate implementation lessons. The candidate consolidated these lessons thematically for review by members of the implementation team, before presentation of the results.

Objective 4

Objective 4, to evaluate the utility of digitised HIV testing data within CBS systems, used cross-sectional analyses to determine HIV prevalence and descriptive characteristics of patients testing and retesting (following a previous HIV diagnosis) at the Gugulethu CHC. Individuated data from all attendees of HTS services at Gugulethu CHC during the intervention period (April 2017 – July 2018) were analysed. Elements documented on the routine paper forms (Appendix B) and digitised included patient identifiers, demographic data, testing consent, self-reported previous HIV test results, reasons for accessing HTS and results of the rapid HIV PoCT. Retrospective cohort analyses were used to determine linkage to care and ART after testing. The contribution of testing data to earlier ascertainment of HIV status and earlier intervention to ensure linkage to care, was quantified. The proportion of patients retesting was also calculated using existing evidence of HIV within the PHDC. Multivariable logistic regression was used to determine factors associated with retesting among patients previously diagnosed with HIV. Cohort analyses using laboratory and pharmacy indicators were used to assess linkage to care. **Retesting data and linkage to care functioned as measures of utility of HIV testing data within routine CBS systems.**

Objective 5

Objective 5 (to explore vertical HIV transmission as both a sentinel event and testing event and systemic risk factors for these events using routine CBS data) made use of electronic records of HIV (primarily HIV PCR test) in children under 24 months of age from 2010 – 2020. Child HIV diagnosis was used as a sentinel event indicator of vertical transmission of HIV. Retrospective cohort analyses were used for this objective, with HIV as the outcome. Routine data from mother-child pairs with electronic records of HIV were analysed. Maternal ART and infant HIV status over 3 distinct maternal ART policy periods from 2010 to 2020 were evaluated. Objective 5 explored risk factors for vertical transmission of HIV, including ART policy period, using multivariable logistic regression. **Trend and risk factor analyses served as a measure of the utility of sentinel event monitoring within CBS.** As this sentinel event

is based on a testing event, **trend and risk factor analyses also serve as a measure of the utility of HIV testing information within HIV CBS systems.**

Ethical considerations

The study was approved by the University of Cape Town Human Research Ethics Committee (HREC 083/2021) (Appendix C) and the Western Cape Provincial Health Research Committee. All antenatal HIV survey data, DHIS and Thembisa data were provided in aggregated form. Data from the PHDC were de-identified before study release according to the Western Cape Department of Health Data Access Policy Guidelines. The research followed the ethical standards outlined in the Helsinki Declaration(144) and the National Health Act(145). The risks to study participants were minimal. It is anticipated that the study may be beneficial to the community and health system, through improved surveillance and monitoring of HIV services at both individual and population level. All research findings will be presented to relevant stakeholders, including the provincial and national departments of health and specific study facility for objectives 3 and 4, in formats that are easily understandable by and useful to the various audiences. At the time of examination of this thesis, key findings from published chapters had been discussed with various stakeholders and discussions on implementation of recommendations are underway.

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Chapter 2: Exploring the validity of routine individuated service data for antenatal HIV surveillance in the Western Cape

Relevance to this thesis:

This chapter focusses on validating HIV ascertainment within a routine individuated data system by comparing to sources historically used for surveillance, including sentinel HIV surveillance, aggregate data systems and mathematical model estimates. Validation of HIV ascertainment over the full 10-year study period also serves as a measure of inferred utility of routine individuated data for case-based surveillance.

Contribution of candidate and co-authors:

The candidate, NJ, conceptualised the study under the guidance of AB and BR. NJ conducted the study, analysed the data, interpreted the results and wrote the manuscript. AH, SB, TK and LJ contributed to data curation and provided data support. All co-authors commented on drafts and approved the final version for publication submission.

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Abstract

Background

In the Western Cape province of South Africa, public-sector individual-level routine data from various sources are linked on a unified platform through the Provincial Health Data Centre (PHDC). This allows monitoring of provincial antenatal HIV seroprevalence over time. We assessed the validity of these data compared to aggregated program data and population-wide sentinel antenatal HIV seroprevalence surveys for the Western Cape.

Methods

We conducted a retrospective cohort analysis of pregnancies identified in the PHDC from January 2011 to December 2020. Unique identifiers were used to link antenatal and HIV care records from routine electronic systems. HIV prevalence estimates were compared with available antenatal seroprevalence survey estimates and register-based aggregate program data from the District Health Information System. Provincial, district-level and age-group HIV prevalence estimates were compared between data systems using correlation coefficients, absolute differences and trend analysis.

Results

Of the 977 800 pregnancies ascertained, PHDC HIV prevalence estimates from 2011-2013 were widely disparate from aggregate and survey data (due to incomplete electronic data), whereas from 2014 onwards, estimates were within the 95% confidence interval of survey estimates, and closely correlated to aggregate data estimates ($r=0.8$; $p=0.01$), with an average prevalence difference of 0.4%. PHDC data show a slow but steady increase in provincial HIV prevalence from 16.7% in 2015 to 18.6% in 2020. The highest HIV prevalence was in the Cape Metro district (20.3%) Prevalence estimates by age group were comparable between

sentinel surveys and PHDC from 2015 onwards, with prevalence estimates stable over time among younger age-groups (15-24 years) but increased among older age-groups (>34 years).

Conclusions

This study compares sentinel seroprevalence surveys with both register-based aggregate data and routine individuated data. We show that in this setting linked individuated data may be reliably used for HIV surveillance and provide more granular estimates with improved efficiency compared to seroprevalence surveys and register-based aggregate data.

Keywords: HIV surveillance, sentinel surveys, routine data, HIV prevalence

Introduction

Monitoring the progress of HIV programmes is reliant, in part, on robust surveillance. Whilst global HIV surveillance has evolved since the beginning of the epidemic(1,2), survey-based approaches remain the mainstay in many settings. Since 1990, the National Antenatal Sentinel HIV Survey has been conducted among pregnant women at selected public health antenatal clinics in all nine provinces of South Africa annually or biennially(3–5). Until 2015, the surveys were limited to women presenting for their first antenatal visit, but since then follow-up antenatal visits have also been included(3,6,7). Due to the national antenatal survey being underpowered to provide accurate estimates at district and sub-district level, the Western Cape Provincial Department of Health expanded the national survey to additional sites from 2001 to 2015 to generate more accurate sub-provincial estimates(4).

In 2013, WHO and UNAIDS published *Guiding principles on ethical issues in HIV surveillance* indicating that unlinked anonymous testing should only be used where there is demonstrable inadequacy of program data for surveillance purposes(8). The WHO 2015 *Consolidated guidelines on HIV testing services*, and the WHO 2022 *Consolidated guidelines on person-centred HIV strategic information*, recommend moving towards using routine programmatic data for antenatal HIV surveillance(8–10). To facilitate this transition in surveillance strategy,

evaluations of routine data are required. A 2020 assessment of the national prevention-of-mother-to child programme concluded that South Africa was close to achieving the transition to routine data surveillance in relation to HIV testing, but that further evaluation of data completeness and accuracy was required(11,12). While these studies look specifically at the validity of routine HIV testing data in comparison to laboratory-based HIV testing data from surveys, it should be emphasised that HIV patient management in South Africa is based on routine HIV point-of-care testing results. Reassuringly, available literature shows high antenatal HIV testing coverage in South Africa of up to 98% by 2011(13). Use of routine data for surveillance purposes requires further validation with other surveillance data sources.

In the Western Cape province of South Africa there are two routine programmatic health information systems related to maternal and HIV care. Aggregated provincial data captured from service-based registers are housed in the District Health Information System (DHIS)(14). The HIV testing services register comprises 46 reporting elements (manual and calculated) for key HIV indicators. The Western Cape Provincial Government has established a Provincial Health Data Centre (PHDC) to consolidate all electronically captured individual-level routine data within the province onto a unified platform. This initiative utilises the patient folder number as the unique patient identifier(14,15), facilitating the integration of various information systems, including laboratory, pharmacy, and patient administration data. Consequently, this setup offers a comprehensive individuated health information exchange. Within this framework, disease-specific patient cascades (referred to as virtual cohorts), such as the HIV care cascade and maternity cascade, can be constructed by tracking specific markers of care(14).

Several studies in low- and middle-income countries have compared antenatal survey estimates with routine HIV data(8,16–21). A 2013 study in the Western Cape showed comparable estimates between antenatal survey data and aggregated antenatal HIV data, but also reported disparities at the sub-district level(4). To date there have been no studies in the South African context comparing antenatal survey HIV estimates with *individuated* routine

data estimates. We sought to evaluate the validity of routine HIV prevalence estimates in pregnant women in the Western Cape Province of South Africa as compared to sentinel surveillance.

Methods

The study was set in the Western Cape province of South Africa, which is comprised of one metropolitan district, Cape Metro and five less urbanised districts (Overberg, Garden Route, Central Karoo, West Coast and Cape Winelands). We compared cross-sectional HIV antenatal survey estimates to those derived from aggregated program data and individuated program data from 2011 to 2020. To evaluate the validity of routine HIV prevalence estimates in pregnant women we analysed four datasets; these are described below.

National antenatal survey data

National sentinel antenatal survey HIV prevalence estimates for the Western Cape province were obtained from the South African National Department of Health. District-level and age-disaggregated estimates were provided on all pregnant women attending their first antenatal visit in a public health facility in the Western Cape during a 6-week survey period in the years 2011-2015. Post 2015, the national antenatal survey was conducted biennially. In years 2015, 2017 and 2019, the national survey data included pregnant women attending first antenatal visits or follow-up antenatal visits in a public health facility during a 6-week period. However, to promote consistency with earlier surveys, we limit our estimates to first antenatal visit. Blood specimens of survey participants were tested for HIV at a central laboratory using HIV ELISA tests.

Expanded provincial antenatal survey data

Provincial sentinel antenatal survey data 2011-2015 (subsequently discontinued), incorporating larger, proportionally weighted sample sizes, were obtained from the Western Cape Department of Health. To attain provincial estimates, sub-district data were weighted using the proportional distribution of antenatal first visits in the prior year.

DHIS (Routine aggregated HIV program data)

Aggregated program data included all women attending their first antenatal visit at primary health care facilities in the Western Cape 2011–2020. All women, regardless of HIV status, are offered a point-of-care HIV test at first antenatal visit. Results of these tests are captured in facility-based registers, initially prevention-of-mother-to-child transmission (PMTCT) register and later primary health care services register. As PMTCT register data were limited from 2011-2013, provincial estimates from 2011 and 2012 were obtained from a study comparing routine aggregated data to sentinel surveys(4). From 2014 to 2020, the proportion of pregnant women at first visit with evidence of prior HIV diagnosis or new diagnosis, derived from the primary health care services register, was used to calculate prevalence estimates. “HIV positive PMTCT initial test” and “Known HIV positive client” elements were combined as the numerator, with total “Antenatal first visit” as the denominator. Routine HIV testing is based on a point-of-care HIV testing algorithm (Appendix A) conducted by an HIV counsellor or nurse, where only discordant test results are confirmed by central laboratory-based ELISA testing. Known HIV positive status is captured by an HIV counsellor or nurse based on self-reported HIV and medical records confirming HIV diagnosis.

PHDC (Routine individuated HIV program data)

A retrospective cohort was derived from the PHDC which included de-identified linked data of all pregnant women attending public health facilities across the province 2011-2020. The cohort was enumerated using the PHDC maternity cascade which links electronic records of all patients with administrative or laboratory evidence indicative of pregnancy. Pregnancies inferred with high confidence were included, as they have at least one high confidence evidence such as a rhesus antibody test (conducted routinely at first antenatal visit), pregnancy test, International Classification of Diseases (ICD) Tenth Revision code indicating pregnancy or pregnancy outcome, maternal discharge summary or repeat moderate confidence evidences such as antenatal visits. Since information specific to the first visit is not routinely captured in all public health facilities, it was not possible to distinguish between first

and follow-up antenatal visits, however all pregnancies were only captured once. District and sub-district for pregnancy was determined by the geographic location of the facility of first pregnancy evidence. The pregnancy period was estimated using the pregnancy outcome date and/or any available evidence on gestational age, with year allocated according to the date of first record of pregnancy. Since HIV diagnosis is based on point-of-care testing, these results are not digitised and therefore not available to the PHDC. In the absence of these testing data, administrative, laboratory and pharmacy evidence of HIV diagnosis before or during the estimated pregnancy period was used to determine antenatal HIV status of women in the maternity cohort. The proportion of pregnancies with electronic evidence of HIV diagnosis prior to pregnancy or during pregnancy amongst all pregnant women was used to calculate antenatal HIV prevalence estimates.

Analysis

Data were analysed using Microsoft Excel and Stata 17 (Stata Corporation, College Station, Texas, USA). Measures of central tendency and dispersion were used to describe continuous variables, depending on distribution. Categorical variables were described using proportions and 95% confidence intervals, using the normal approximation to the binomial distribution. Descriptive characteristics of the PHDC cohort (2014–2020) were validated with 2014 provincial antenatal survey data. Prevalence estimates from provincial surveys, and aggregated and individuated program data, were calculated for comparison with national survey estimates, serving as the gold standard in this comparative analysis. Data were analysed by year at provincial and district level for comparison.

Provincial estimates from all datasets were further compared with provincial antenatal HIV prevalence estimates from the Thembisa mathematical model(22). This is an integrated demographic and HIV model for South Africa, calibrated to a number of HIV data sources including antenatal HIV prevalence surveys(22). Quantitative comparisons were analysed using correlation coefficients and average percentage differences. Individuated data from 2015 onwards were further disaggregated by district and age for prevalence estimates.

Provincial age-group estimates were compared between PHDC and the national antenatal survey from 2015. There were no comparators available for district-level age group estimates as the national antenatal survey is underpowered for this purpose. Data were categorised using age categories routinely used in antenatal survey reporting.

The DHIS estimates (2011 – 2020) and survey estimates (2011 – 2015) are limited to pregnancies registered for antenatal care, whereas PHDC estimates (2011 – 2020) include all pregnancies in the public sector such as those presenting only at delivery as well as non-viable pregnancies and terminations of pregnancy.

Ethical considerations

This study was approved by the University of Cape Town Human Research Ethics Committee (HREC 083/2021) and the Western Cape Provincial Health Research Committee. All antenatal HIV survey data, DHIS and Thembisa data were provided in aggregated form. Verbal informed consent was obtained from the antenatal HIV survey participants as per survey protocol, however only aggregated survey data were provided for this study. The PHDC and DHIS data used in the study include unconsented, de-identified routine service data housed by the Western Cape Department of Health and Wellness. Data from the PHDC were de-identified before study release according to the Western Cape Department of Health and Wellness Data Access Policy Guidelines. Use of these routine, unconsented, de-identified service data was approved by both the University of Cape Town Human Research Ethics Committee and the Western Cape Provincial Health Research Committee.

Results

From 1 January 2011 to 31 December 2020, 977 800 and 989 568 pregnancies were enumerated by the PHDC and DHIS, respectively. Table 2.1 presents study population size per year compared with sample sizes of both provincial and national antenatal surveys. As compared to the DHIS, fewer pregnancies were enumerated by PHDC prior to 2015.

Amongst women presenting for their first antenatal visit as recorded in the DHIS aggregated data, the percentage known to be living with HIV increased from 9.5% (95% CI 9.4-9.7%) in

2014 to 15.0% (95% CI 14.8-15.2%) in 2020. Over the same period, the percentage of women accepting an HIV test at first antenatal visit declined from 90.4% (95% CI 90.2-90.6%) to 81.0% (95% CI 80.8 – 81.2) (Table 2.1). The characteristics of the women participating in the PHDC cohort (2014–2020) and the 2014 antenatal survey (unweighted) are shown in Table 2.2. As seen in Table 2.1 and Figure 2.1, PHDC HIV prevalence estimates from 2014 onwards are closely aligned to national, provincial and DHIS data.

Table 2.1: Antenatal HIV prevalence estimates by dataset

	Pregnancies (N)					HIV testing (DHIS)		HIV prevalence§					
	National Survey	Provincial Survey	DHIS	PHDC	DHIS/PHDC difference	Known HIV positive among all first antenatal visits (%)	Accepted testing among all first antenatal visits (%)	National Survey (% , 95% CI)		Provincial Survey (% , 95% CI)		DHIS (%)	PHDC (%)
2011	4044	9812	97588	46703	-50885			18.2	14.3 - 22.8	18.4	17.7 - 19.2	18.4†	11.1
2012	4010	8711	97144	59826	-37318			16.9	13.8 - 20.5	17.8	16.7 - 18.3	18.7†	12.3
2013	3793	8125	96993	81761	-15232			18.7	15.1 - 23.0	17.1	16.4 - 18.0		14.0
2014	4036	7480	99454	94200	-5254	9.5	89.7	18.7	15.7 - 22.3	18.6	17.7 - 19.4	15.0	15.9
2015	7517†	7560	92168	101730	9562	9.8	90.1	18.9	16.4 - 21.7	17.6	16.8 - 18.4	15.6	16.7
2016			90034	106256	16222	11.8	90.4					17.0	17.0
2017	3571		95334	115704	20370	15.1	89.2	18.0*	16.5 - 19.7			19.3	18.2
2018			101044	120547	19503	14.6	84.7					18.2	18.1
2019	3943		110145	123907	13762	14.3	82.6	18.8**	17.1 - 20.5			17.4	18.5
2020			109664	127166	17502	15.0	81.0					17.6	18.6

†2015 national survey included additional Western Cape data and was limited to women presenting for first antenatal visit.

‡2011 and 2012 DHIS estimates denominator was total number of women refusing or accepting PMTCT initial tests whereas later estimates used the denominator of total antenatal visits

**Prevalence estimate is among first antenatal visit only. 2017 reported prevalence including both first and follow-up attendees is 15.9% (95% CI 14.2 -17.8).*

***Prevalence estimate is among first antenatal visits only. 2019 reported prevalence including both first and follow-up attendees is 17.9% (95% CI 16.2 – 19.7).*

§95% Confidence intervals are not reported for routine data estimates as the whole population is included precluding the need for sampling

Table 2.2: Descriptive characteristics of PHDC Cohort (2014 – 2020) compared to 2014 Provincial Antenatal Survey

	PHDC Cohort 2014 – 2020 (n=789510) Percentage	95% CI	Antenatal survey 2014 (n=7526) Percentage	95% CI
Electronic evidence of current and prior pregnancy*			Gravidity	
1	57.9	57.8 – 58.0	30.4	29.4 – 31.5
2	28.0	27.9 – 28.1	32.0	30.9 – 33.0
3	10.2	10.2 – 10.3	21.7	20.8 – 22.7
4	2.9	2.9 – 3.0	10.1	9.5 – 10.8
5 or more	0.9	0.9 – 1.0	5.8	5.3 – 6.3
Age (median; IQR)	27.0 (22.6 – 32.0)		26.4 (22.0 – 31.0)	
Age Category				
<15	0.5	0.4 – 0.5	0.4	0.3 – 0.6
15 -19	11.8	11.7 – 11.9	13.5	12.7 – 14.2
20 - 24	26.4	26.3 – 26.5	28.5	27.5 – 29.5
25 - 29	27.3	27.2 – 27.4	26.9	25.9 – 27.9
30 - 34	20.5	20.4 – 20.6	19.8	18.9 – 20.8
35 - 39	10.6	10.5 – 10.6	8.6	8.0 – 9.3
>39	3.0	3.0 – 3.1	2.2	1.8 – 2.5
District**				
Cape Winelands	13.7	13.7 – 13.8	15.8	15.0 – 16.7

Central Karoo	0.97	0.95 – 1.0	1.9	1.3 – 1.9
Cape Metro	67.4	67.3 – 67.5	52.9	51.8 – 54.1
Garden Route	9.0	8.9 – 9.0	15.0	14.2 – 15.8
Overberg	3.6	3.5 – 3.6	5.5	5.0 – 6.0
West Coast	4.6	4.5 – 4.6	9.1	8.5 – 9.8
No district recorded	0.7	0.7 – 0.8		

**Gravidity estimates (number of times a woman has been pregnant, including current pregnancy) in the PHDC are not reliable since historic data are incomplete. Electronic evidence of current and prior pregnancy is used as a proxy to provide a full description of the cohort.*

***Unweighted*

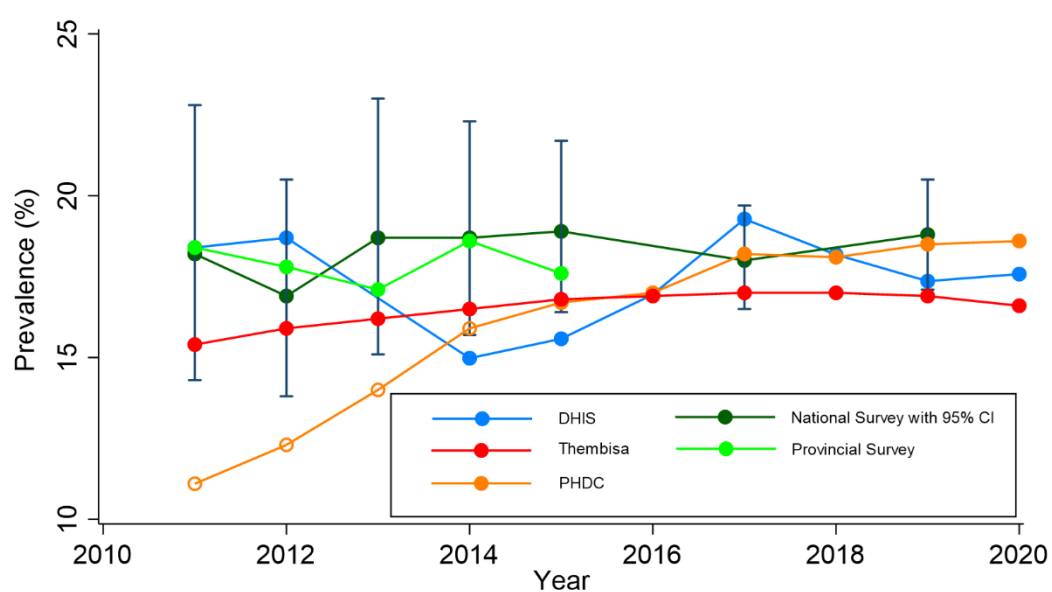


Figure 2.1: Western Cape Antenatal HIV Prevalence 2011 – 2020 by dataset

The average difference in antenatal HIV prevalence between the PHDC and other datasets are shown in Table 2.3. A positive correlation was observed between PHDC and DHIS ($r=0.8$).

Table 2.3: Comparison of antenatal HIV prevalence between PHDC and other datasets (2014 – 2020)

Datasets compared	Mean absolute difference*	Mean difference	Pearson's correlation coefficient
PHDC vs DHIS	0.8	0.4	$r = 0.8$ ($p=0.01$)
PHDC vs National Survey	1.4	-1.3	$r = -0.4$ ($p = 0.480$)

**Absolute difference is the difference between two integers regardless of whether the numbers are positive or negative*

District level prevalence estimates are shown in Supplementary Figure 2.3. Prevalence estimates between DHIS and PHDC were closely aligned from 2015 to 2020. PHDC and national antenatal survey district estimates were also closely aligned in 2017 and 2019 in all districts except Overberg, with an average percentage point difference of -4.4 from 2015 to 2020.

HIV prevalence estimates remained stable over time among younger age-groups (aged 15–29 years) but increased among older age-groups (>34 years). Prevalence estimates between PHDC and national antenatal survey data were closely aligned by age group (Figure 2.2).

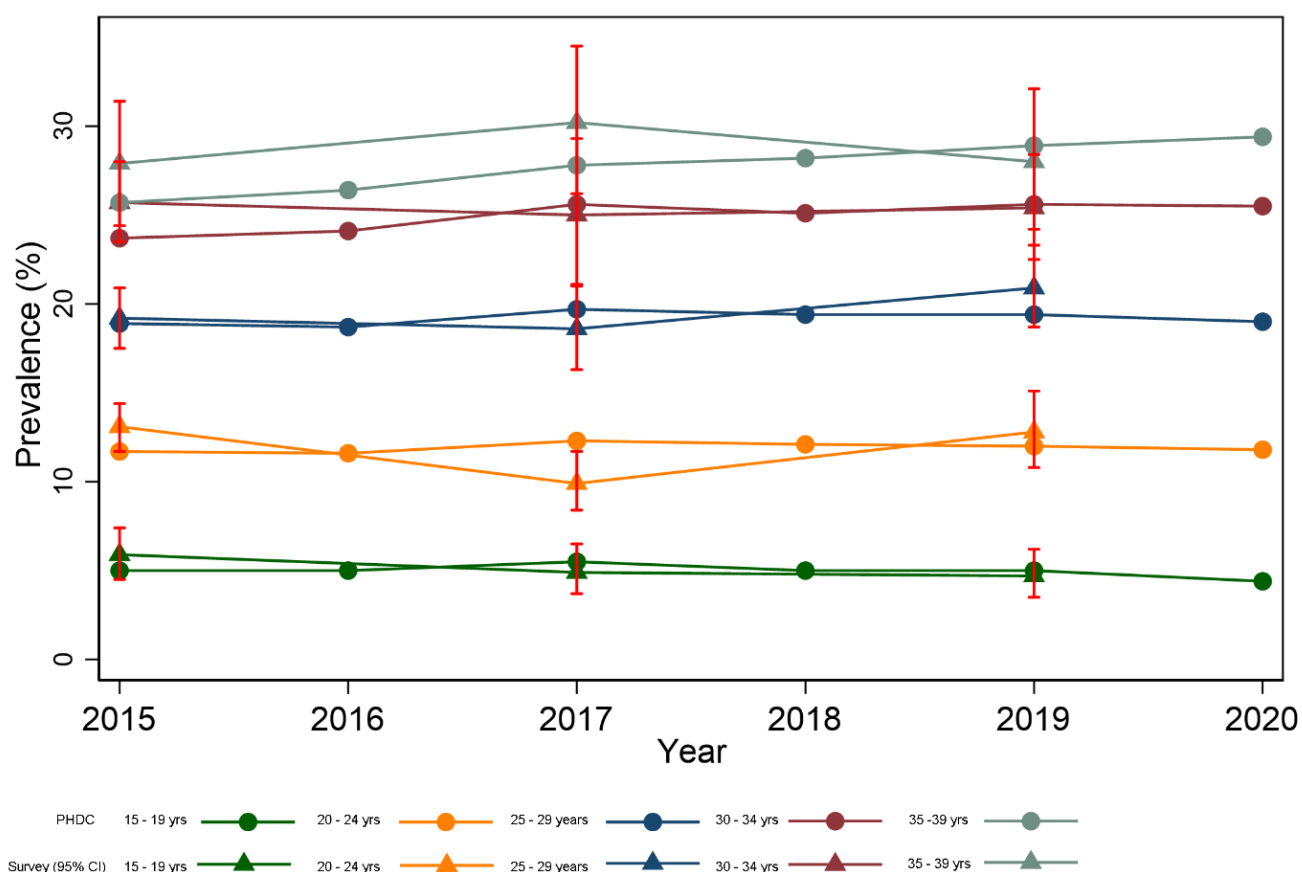


Figure 2.2: Western Cape Antenatal HIV Prevalence by Age Group: 2015 – 2020 (PHDC and National Antenatal Survey)

Discussion

This is the first study to compare sentinel HIV seroprevalence surveys with both routine aggregated and individuated data. Our results show that from 2015 onwards, the PHDC provides a reliable source of individuated data for accurate and timely antenatal HIV surveillance at provincial, district and age-group levels. These are essential for a responsive health system to plan and evaluate programmes.

From 2015 onwards, the PHDC dataset enumerated more pregnancies than reflected in routine aggregate antenatal first visit registers (DHIS), supporting the completeness of these individuated data. The lower enumeration of pregnancies prior to 2015 is most likely due to limited availability of electronic data for linkage in earlier years, when electronic data systems

were less widely established. As more public health facilities began using routine electronic data systems, patients with any contact with public health facilities would have some electronic record enabling inclusion in the PHDC. Given that the routine individuated data represent the entire population utilising public health services, these data are more representative of the population than survey data. It is also likely that linked individuated data are less prone to the biases of routine aggregated data such as duplication and lack of completeness, both numerically and within available records. A single unique identifier across the province prevents duplication of records where patients attend different facilities. Linkage of different electronic systems using a unique identifier also allows more opportunities for ascertainment of pregnancy and HIV status than fixed variables used in aggregate data.

Comparison of descriptive characteristics between PHDC cohort and survey cohort enabled validation of the PHDC cohort prior to estimating HIV prevalence. The median age of women in the PHDC cohort (26.9 years) was similar to that in the antenatal survey population(3,6), supporting the close alignment in demographic profile of the two cohorts. PHDC, however, had a higher proportion of women with no prior evidence of pregnancy (60%) when compared to recorded gravidity in the survey (approximately 30%)(3,6). This is likely due to less well-established electronic systems in earlier years for prior pregnancy ascertainment. Furthermore, the PHDC cohort had a higher proportion of patients from the Cape Metro district and lower proportion from the rural districts. This is also likely due to increased PHDC coverage in the Cape Metro, particularly in earlier years as electronic systems were better established in urban areas. The national surveys may further include oversampling of rural districts to generate accurate district-level estimates. We would suggest whole population surveillance negates a need for oversampling.

HIV prevalence estimates in both national and provincial antenatal surveys remained consistent between 2011 and 2015, with provincial surveys providing more precise estimates due to the larger sample size. From 2014 onwards, PHDC estimates are closely aligned to the survey. Given the wide confidence intervals for survey estimates, trends are difficult to infer.

DHIS HIV prevalence estimates for 2011 and 2012 were consistent with survey estimates, as shown in a comparative study(4). This study, however, used HIV-service specific denominators from DHIS viz. PMTCT initial HIV test acceptance or refusal. From 2014 onwards, refusal of PMTCT initial test was no longer recorded hence first antenatal visit was used as the denominator, resulting in lower estimates than in earlier years. DHIS data, however, showed an increasing proportion of women over time to be presenting for their first antenatal visit and known to be living with HIV. This increase corresponded with a decreasing proportion of women accepting HIV testing at first antenatal visit. The lower proportion of test acceptance is most likely due to increasing awareness of HIV positive status, in keeping with a recently published modelling study(23). Additionally, some women with known HIV positive status may still retest in antenatal settings, as seen in a recent study in the Western Cape(24). The change in DHIS elements likely represents the changing HIV context with greater awareness of HIV status and wider roll-out of antiretroviral therapy (ART) over time(23). Variability presented in DHIS estimates is likely, in part, due to challenges in maintaining routine aggregate data systems where contextual factors, such as staff turnover, high workload, and social unrest impact data collection and consolidation from registers.

PHDC HIV prevalence estimates from 2011 to 2013 were lower than survey estimates, most likely due to incomplete electronic data. From 2014 onwards, estimates were better aligned and more consistent over time. As PHDC estimates do not distinguish between pregnancies with or without antenatal care, prevalence was expected to be slightly higher than that estimated using DHIS and survey data, as these data are limited to pregnancies with antenatal care. Antenatal first visit coverage is however high in the Western Cape at 94% and therefore the contribution of pregnancies without prior antenatal care to HIV prevalence is small in the PHDC estimates(13,25,26). Reassuringly, PHDC estimates remained within the 95% confidence intervals of the national survey, and PHDC and DHIS estimates showed a positive correlation and low average difference. It should be noted, however, that average difference may mask the volatility of prevalence trends over time. Low average difference between

survey and PHDC estimates suggest the PHDC may be reliably used to estimate antenatal HIV prevalence at provincial level. PHDC estimates over time were also similar to the Thembisa model estimates. Since the Thembisa model includes both private and public sector data, lower estimates than the PHDC were expected (reflecting lower HIV prevalence among private patients)(27).

At a more granular level, from 2015 onwards, estimates from PHDC were closely aligned to both DHIS and survey at district level, with disparities noted more in sparsely populated rural districts like Overberg. These disparities may reflect survey under-sampling in smaller rural districts as well as differences brought about by migrant populations such as workers(28). Age-group HIV prevalence estimates from the PHDC were closely aligned to the national survey from 2015 onwards, showing consistent HIV prevalence in all age groups over a 5-year period, with higher estimates in older age groups. Higher prevalence in older age groups is expected due to a combination of factors, including increased cumulative incidence with age, and use of ART extending life expectancy. Since DHIS cannot provide age-disaggregated estimates, comparisons with PHDC and survey could not be made. Furthermore, in recent years, estimates at sub-district level are only possible with the PHDC data as the national survey is underpowered at sub-district level. This again highlights the advantages of linked individuated data over both survey data and aggregate routine data in providing granular estimates, not limited to predetermined indicators.

Limitations

A comparative study of this nature is subject to several limitations. Firstly, routine data were validated against sentinel surveillance data, with national surveys serving as the most accurate HIV prevalence estimates or “gold standard”. These survey estimates are however based on smaller sample sizes, over a limited time period, and underpowered for granular estimates which may impact accuracy. PHDC data were less reliable before 2014 due to incomplete electronic data in earlier years. Estimates from each dataset are derived using differing numerators and denominators with differing levels of quality and completeness.

Furthermore, both individuated and aggregated routine data are subject to various pitfalls such as capturing errors, administrative errors and consolidation errors which may impact quality and completeness of these data. Pregnancy ascertainment may differ between districts and sub-districts due to differing use of electronic information systems. Since detailed patient characteristics such as socio-economic status and education level are not captured routinely, in-depth comparisons with survey data were not possible. Contextual factors impacting on observed trends in routine data are diverse and require further investigation – these include clerical changes in capturing approaches, widespread impact of the COVID-19 pandemic on service utilisation and staffing, migration patterns etc. Survey and routine data sources evaluated in this study include only patients utilising public health care services, excluding those in the private sector and those without access to public health care. Lastly, while the Western Cape province has established individuated data systems, most other provinces in South Africa are still reliant on aggregated register-based data. The results of this study are therefore not representative of the whole country and highlight the need and potential to strengthen *individuated* routine information systems for improved surveillance.

Conclusion

Our study demonstrates the validity of routine individuated data for timely and efficient HIV antenatal surveillance, without the additional cost and logistical complexity brought about by regular surveys and with fewer biases compared to routine aggregated data. We highlight the added utility of routine individuated data in providing more granular estimates than sentinel surveillance at district and sub-district level, thereby facilitating more detailed and timely population-level epidemiological trend analysis. While provincial antenatal HIV prevalence trends have increased slowly over time, notable differences in district level trends require further investigation. Strengthening of routine individuated data systems will create an actionable platform to support service delivery and allow richer, more efficient, less costly and more timeous HIV surveillance.

List of abbreviations

ART – Antiretroviral therapy

DHIS – District Health Information System

PHDC – Provincial Health Data Centre

PMTCT – Prevention-of-mother-to-child transmission

Declarations

Ethics approval and consent to participate

This study was approved by the University of Cape Town Human Research Ethics Committee (HREC 083/2021) and the Western Cape Provincial Health Research Committee. All antenatal HIV survey data, DHIS and Thembisa data were provided in aggregated form. Verbal informed consent was obtained from the antenatal HIV survey participants as per survey protocol, however only aggregated survey data were provided for this study. The PHDC and DHIS data used in the study include unconsented, de-identified routine service data housed by the Western Cape Department of Health. Data from the PHDC were de-identified before study release according to the Western Cape Department of Health Data Access Policy Guidelines. Use of these routine, unconsented, de-identified service data was approved by both the University of Cape Town Human Research Ethics Committee and the Western Cape Provincial Health Research Committee.

Consent for publication

Not applicable

Availability of data and materials

All antenatal HIV survey data, DHIS and Thembisa data were provided in aggregated form. The PHDC and DHIS data used in the study include unconsented, de-identified routine service data housed by the Western Cape Department of Health. Release of these data to a public domain would violate the Data Access Policy of the Western Cape Department of Health. Ethically approved data requests which may be targeting the same or similar data sources

may be sent to or discussed with the Western Cape Provincial Department of Health and Wellness: Health.Research@westerncape.gov.za. The survey data are available from the National Department of Health, South Africa. Restrictions apply to the availability of these data; however these data may be requested from the National Department of Health, South Africa at adrianp@nicd.ac.za. Thembisa model data can be accessed from <https://www.thembisa.org/>.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

NJ, BR and AB conceptualised the study. NJ conducted the study, analysed the data and wrote the manuscript. AH, SB, TK and LJ contributed to data curation and provided data and analysis support. LJ, BR, AB, TK, AH, SB and AP made intellectual contributions to the manuscript. All authors read and approved the final manuscript.

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Supplementary figures

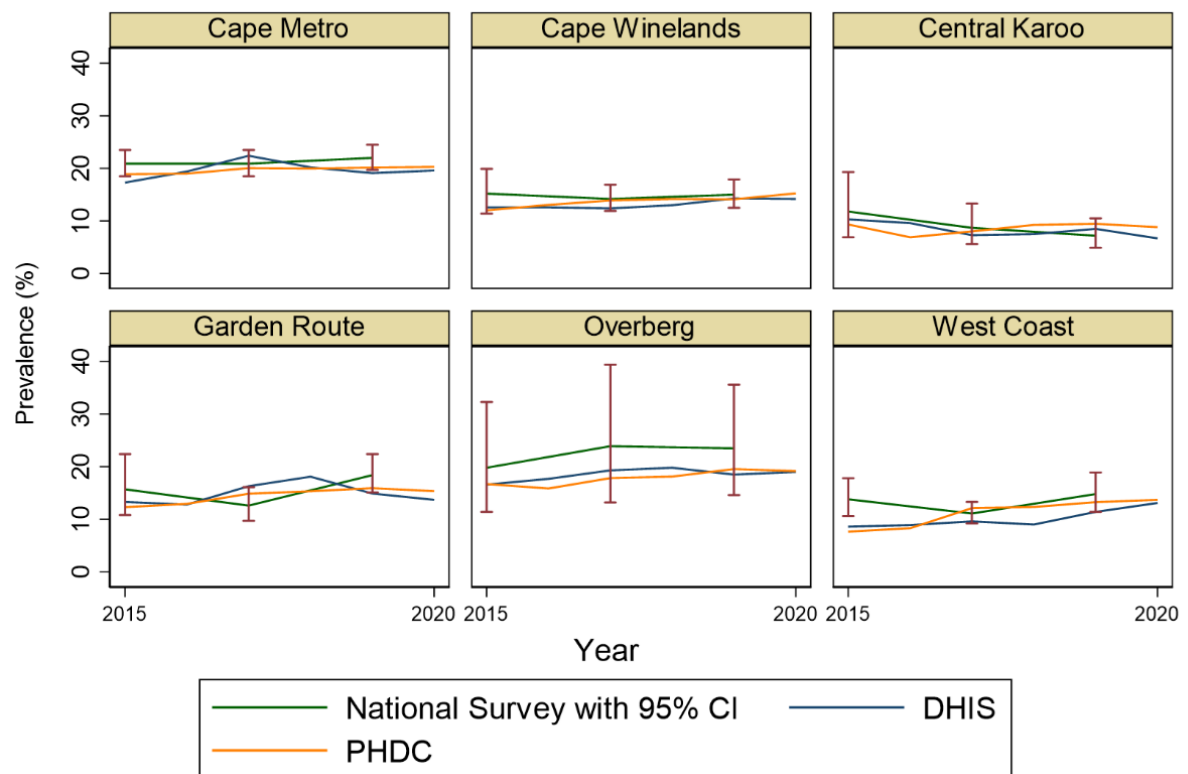


Figure 2.3: District HIV prevalence estimates by dataset

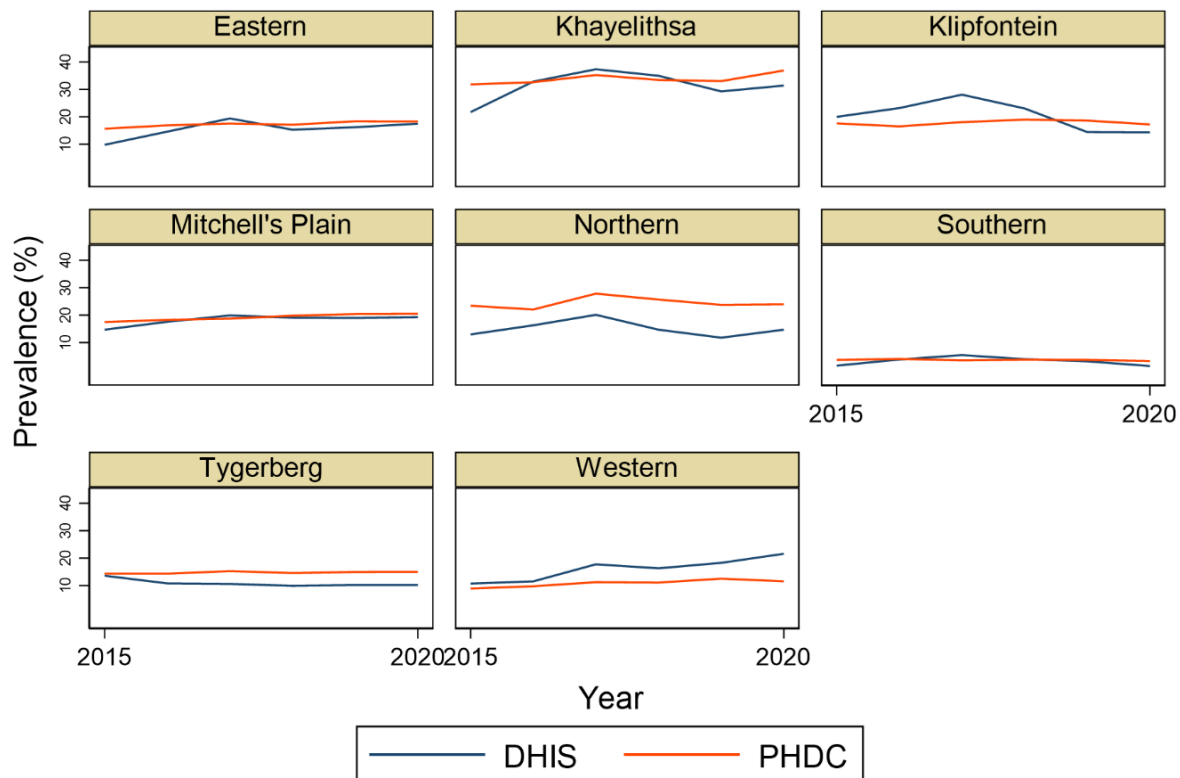


Figure 2.4: Sub-district antenatal HIV prevalence in the Cape Metro: 2015 – 2020 (DHIS & PHDC)†

†2017 and 2019 Western Cape antenatal survey is underpowered for sub-district estimates therefore not included

Chapter 3: Can routine antenatal data be used to assess HIV antiretroviral therapy coverage among pregnant women? Evaluating the validity of different data sources in the Western Cape, South Africa

Relevance to this thesis:

Chapter 3 expands on Chapter 2, focussing now on validation of antiretroviral coverage data by comparing different methods for measuring antenatal antiretroviral therapy coverage among women living with HIV over the 10-year study period. This chapter highlights the use of routine individuated data for coverage estimation in a high-burden setting. Validation of ART coverage estimates from routine individuated data further demonstrates the utility of routine individuated data for case-based surveillance of different sentinel events such as HIV treatment.

Contribution of candidate and co-authors:

The candidate, NJ, conceptualised the study under the guidance of AB and BR. NJ conducted the study, analysed the data, interpreted the results and wrote the manuscript. AH, SB, TK and LJ contributed to data curation and provided data support. All co-authors commented on drafts and approved the final version for submission.

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This published chapter is presented verbatim in this thesis with only changes to table and figure numbering as well as formatting for consistency with the overall thesis.

Abstract

Background

Accurate measurement of antenatal antiretroviral treatment (ART) coverage in pregnancy is imperative in tracking progress towards elimination of vertical HIV transmission. In the Western Cape, South Africa, public-sector individual-level routine data are consolidated from multiple sources, enabling the description of temporal changes in population-wide antenatal antiretroviral coverage. We evaluated the validity of different methods for measuring ART coverage among pregnant women.

Methods

We compared self-reported ART data from a 2014 antenatal survey with laboratory assay data from a sub-sample within the survey population. Thereafter, we conducted a retrospective cohort analysis of all pregnancies consolidated in the Provincial Health Data Centre (PHDC) from January 2011 to December 2020. Evidence of antenatal and HIV care from electronic platforms were linked using a unique patient identifier. ART coverage estimates were triangulated with available antenatal survey estimates, aggregated programmatic data from registers recorded in the District Health Information System (DHIS) and Thembisa modelling estimates.

Results

Self-reported ART in the 2014 sentinel antenatal survey (n=1434) had high sensitivity (83.5%), specificity (94.5%) and agreement ($k=0.8$) with the gold standard of laboratory analysis of ART. Based on linked routine data, ART coverage by the time of delivery in mothers of live births increased from 67.4% in 2011 to 94.7% by 2019. This pattern of increasing antenatal ART coverage was also seen in the DHIS data, and estimated by the Thembisa model, but was less consistent in the antenatal survey data.

Conclusion

This study is the first in a high-burden HIV setting to compare sentinel ART surveillance data with consolidated individuated administrative data. Although self-report in survey conditions showed high validity, more recent data sources based on self-report and medical records may be uncertain with increasing ART coverage over time. Linked individuated data may offer a promising option for ART coverage estimation with greater granularity and efficiency.

Introduction

Accurate measurement of antenatal antiretroviral treatment (ART) coverage in pregnancy is imperative in tracking progress towards the elimination of vertical transmission[1–3]. To monitor progress towards elimination of vertical transmission, the World Health Organization (WHO) Elimination of Mother-to-Child Transmission Initiative requires countries to report on three process measures with the targets that 95% of pregnant women attend antenatal care, 95% are tested for HIV and 95% of pregnant women living with HIV (WLWH) initiate ART prior to or during pregnancy[1].

Antenatal HIV sentinel surveillance is one approach to measuring these process indicators, and is a long-standing tool used in South Africa[4–7]. Since 1990, antenatal HIV sentinel surveys have taken place annually or biennially in all provinces of South Africa. Until 2015, the Western Cape province of South Africa extended the national survey to a larger proportionally weighted sample to generate sub-district level estimates. WHO has recommended sentinel surveillance be replaced by routine programmatic data, a shift that is reliant on accurate and complete routine data[7,8]. While the focus of sentinel antenatal surveys is HIV seroprevalence, the widespread roll-out of ART and drive toward elimination of vertical transmission necessitates the monitoring of ART coverage in conjunction with prevalence[9].

South Africa has a high antenatal coverage, with an estimated 94% of women in the Western Cape province attending a health facility at least once for an antenatal visit[10]. While coverage is high, coverage below 100% remains a risk in the context of vertical transmission

prevention (VTP). All women, regardless of HIV status, are offered an HIV test at first pregnancy visit. Those with unknown HIV status are encouraged to test at first visit and at various other antenatal time points, using an “opt-out” system[11]. Although test refusal amongst antenatal clients was captured routinely in the past, these data are no longer captured. Available literature shows high antenatal HIV testing coverage in South Africa since 2009 (above 90%), increasing to 98% by 2011[12].

In 2013, the Western Cape province of South Africa adopted a policy of lifelong ART for all pregnant WLWH (Option B+)[11,13,14]. Subsequently, the Western Cape Provincial Department of Health (WCDOH) added an additional question on ART use to the 2014 provincial antenatal survey, which was also incorporated in national surveys[15–17]. This question measured current ART use in the 3 days prior to survey participation[15]. The validity of self-reported ART use as a method to evaluate ART coverage using existing sentinel surveillance methods requires formal evaluation. An alternative method for measuring ART use is using routine data. The WCDOH makes use of two routine health information platforms. Firstly, aggregated data from facility-based registers are captured in the District Health Information System (DHIS). Secondly, individuated electronic patient data are consolidated by the Provincial Health Data Centre (PHDC). These include administrative, pharmacy and laboratory data linked via a unique patient folder number, in the absence of electronic medical records. ART coverage can therefore be estimated using pharmacy dispensing data of triple-regimen ART or entries in HIV treatment registers.

We evaluated the validity of different methods for measurement of ART coverage by assessing self-reported ART use in sentinel antenatal surveys and comparing sentinel survey estimates with routine programmatic data estimates over a 10-year period.

Methods

This study was conducted in the Western Cape province of South Africa. The province is comprised of six districts: Cape Metro, Overberg, Garden Route, Central Karoo, West Coast and Cape Winelands. The study was comprised of two parts: validation of 2014 self-reported

ART data with laboratory data, and the comparison of cross-sectional sentinel survey ART coverage estimates as well as modelling estimates with routine data from 2011 to 2020. The datasets used are described below.

Antenatal survey data

Antenatal ART coverage estimates for the Western Cape Province for 2014 and 2015 were obtained from the Western Cape provincial sentinel antenatal survey. In 2016, the provincial survey was discontinued and annual national surveys were replaced by biennial surveys. Antenatal ART coverage estimates for the Western Cape province for 2017 and 2019 were obtained from the South African National Department of Health as reported in the national sentinel antenatal survey reports.

Estimates were derived from data that included all pregnant women attending their first antenatal visit in a public health facility during a 6-week period of a survey in years 2014 and 2015. In years 2017 and 2019, the national survey data included pregnant women attending first antenatal visits or follow-up antenatal visits in a public health facility during a 6-week period (in this current analysis, only data collected at first antenatal visit are included). The survey question for current ART use in 2014, 2015 and 2017 surveys was: “Have you taken ARVs in the last 3 days?”. This question measured ART use at enrolment as a proxy for ART use prior to the pregnancy or by the time of conception, excluding any prior treatment interruption. This question was discontinued in 2019. In 2017 and 2019, participants were asked if they had ever taken ARVs and if so when, therefore measuring any ART use (prior or current). From 2019, the health care worker asking the question was further expected to verify the response with information in the participant’s medical records if available.

Laboratory validation sub-sample

As part of a WCDOH analysis, a third of the HIV positive specimens from the 2014 provincial antenatal survey were sampled, stratified by district, obtaining a sub-sample of 450

specimens. These were tested by the University of Cape Town (UCT) Department of Pharmacology for lopinavir, efavirenz and nevirapine, using a cut-off of 50ng/ml. At least one of these drugs were included in all ART regimens in use in South Africa in 2014. These data were used to validate the additional survey question on current ART use introduced in the 2014 provincial antenatal survey.

Provincial Health Data Centre (Routine individual-level HIV program data)

A retrospective cohort of pregnancies was enumerated from the PHDC on 26 May 2022, which included anonymised linked data of all pregnant women attending public health facilities in the Western Cape between 2011 to 2020. All available pregnancies were linked to a patient master index and allocated a quantitative confidence score to measure the degree of confidence in the recorded information/data points, indicating a true pregnancy. Pregnancies scoring 0.7 or higher out of a maximum of 1 were included as they have at least 1 high confidence data point such as a rhesus antibody test (conducted routinely at first antenatal visit), pregnancy test, International Classification of Diseases (ICD) Tenth Revision code indicating pregnancy, antenatal visit or maternal discharge summary. The geographic location of the facility of first pregnancy-related attendance was used to determine district of pregnancy. Pregnancy outcome date and available information on gestational age were used to estimate pregnancy period, with the date of the first evidence of pregnancy used to stratify pregnancies by year. Within this cohort, administrative, laboratory and pharmacy evidence of HIV diagnosis before or during the estimated pregnancy period was used to determine antenatal HIV status. Antenatal ART coverage was based on the proportion of women known to be living with HIV during the antenatal period with evidence of ART initiation before or during pregnancy. Women who interrupted treatment would be included as having started ART by enrolment.

District Health Information System (Routine aggregated HIV program data)

Aggregated program data of women recorded as attending public antenatal facilities in the Western Cape for the first time during their current pregnancy in 2011 to 2020 were included in the DHIS dataset. For this analysis, the element “Known HIV positive client on ART at first visit” was used to determine ART coverage at first antenatal visit among all those known with HIV before pregnancy and diagnosed with HIV at first antenatal visit. This data element is intended to measure ART use at conception and excludes women who had interrupted treatment at the time of the first antenatal visit. The denominator combined the two elements “Known HIV positive antenatal client” and “HIV positive PMTCT initial test”. Known HIV positive antenatal client is captured by an HIV counsellor and includes a combination of self-reported HIV and medical records confirming HIV diagnosis. HIV positive PMTCT initial test includes those who tested HIV positive at first antenatal visit.

Thembisa Model

Thembisa is an integrated demographic and HIV model, developed for South Africa. The model is applied at both national and provincial levels; the estimates used in this study are from version 4.6 of the Western Cape model[18]. The provincial model is calibrated to a number of HIV data sources: age-specific HIV prevalence data from antenatal clinic surveys and household surveys, recorded numbers of deaths by age and sex, total numbers of ART patients and age/sex distributions of ART patients, and antiretroviral metabolite data. Assumptions about fertility rates in HIV-positive women and the effect of ART on fertility are informed by Western Cape PHDC data[18,19]. The model makes assumptions about rates of ART interruption and re-initiation, which make it possible to estimate both current ART coverage and proportions of WLWH ever initiated on ART at the time of conception.

Analysis

Data were analysed using Stata 17 (Stata Corporation, College Station, Texas, USA). Descriptive characteristics of the laboratory validation sub-sample were tabulated. Given the higher validity of laboratory-based ART testing[20], this dataset functioned as the gold

standard for comparison with the newly introduced survey question in 2014[9]. Discordance between self-report and laboratory ART was calculated. Demographic risk factors for discordance were analysed using logistic regression. Sensitivity, specificity, positive predictive value and negative predictive value were calculated to validate the survey question on ART use. Agreement between self-report and lab ART detection was quantified using the kappa statistic.

Given the 10-year duration of the PHDC cohort (2011 – 2020) and the notable changes in ART guidelines and data availability over this time period, descriptive characteristics of the cohort were tabulated across all years and for the 2019 cohort specifically, as the most recent year pre-COVID19, to reflect the most recent characteristics.

ART-specific survey data and time trends from 2014 to 2019 were compared with PHDC, DHIS and Thembisa 4.6 estimates. The 2014 and 2015 provincial antenatal survey measured current ART use (excluding treatment interruption). The 2017 and 2019 national antenatal surveys measured any ART use before pregnancy (which may include treatment interruption). ART coverage estimates from the surveys were compared with PHDC estimates for women initiating ART before pregnancy among those with prenatal or antenatal evidence of HIV diagnosis (includes treatment interruption). The survey data were similarly compared with DHIS data which were limited to first visit ART coverage (excluding treatment interruption). The survey estimates, PHDC ART coverage estimates before pregnancy and DHIS estimates were further compared with ART at conception estimates from the Thembisa mathematical model estimates for the Western Cape, with and without treatment interruption[18].

PHDC estimates for women initiating ART before or during pregnancy among those with prenatal or antenatal evidence of HIV diagnosis (both with live births or any pregnancy outcome) were further compared with Thembisa estimates of ART at delivery among those with live births. A sensitivity analysis including moderate-low confidence pregnancies was conducted to determine the contribution of these pregnancies to ART coverage. The PHDC data were analysed further for estimates of ART coverage by district and age-group. These

analyses were limited to a 5-year period (2015 – 2020) when the test and treat ART policy was fully implemented and individuated electronic data systems were better established.

Ethical considerations

The study was approved by the University of Cape Town Human Research Ethics Committee (HREC 083/2021) and the Western Cape Provincial Health Research Committee. All antenatal HIV survey data, DHIS and Thembisa data were provided in aggregated form. Verbal consent was obtained from survey participants as per survey protocol, however only aggregated survey data were provided for this study. The PHDC and DHIS data used in the study include unconsented, de-identified routine service data housed by the Western Cape Department of Health. Data from the PHDC were de-identified before study release according to the Western Cape Department of Health Data Access Policy Guidelines. Use of these routine, unconsented, de-identified service data was approved by both the University of Cape Town Human Research Ethics Committee and the Western Cape Provincial Health Research Committee.

Results

From 1 January 2011 to 31 December 2020, 977 800 and 989 568 pregnancies were recorded by the PHDC and DHIS, respectively, with the PHDC enumerating more pregnancies than DHIS from 2015 onwards. Sample sizes for the provincial surveys in 2014 and 2015 were 7470 and 7517, respectively. Following the discontinuation of provincial surveys, the Western Cape sample size of the national surveys in 2017 and 2019 were 3571 and 3943, respectively.

The descriptive characteristics of the laboratory sub-sample were comparable to the 2014 survey population with HIV (Table 3.1). Within the sub-sample, 13 participants (2.9%) did not disclose ART status.

Table 3.1: Characteristics of women living with HIV in the laboratory validation sub-sample compared to antenatal survey, 2014

		Lab sub-sample (N=450)		2014 Antenatal Survey (N=1434)	
Variable		Median, Percentage	95% Confidence interval†	Median, Percentage	95% Confidence interval
District	Cape Winelands	12.0 %	9.3- 15.4	11.9 %	10.3 -13.6
	Central Karoo	0.5 %	0.1 – 1.8	0.5 %	0.2 – 1.0
	Cape Metro	61.9 %	57.3 – 66.3	62.1 %	59.5 – 64.5
	Garden Route	14.0 %	11.1 – 17.6	14.0 %	12.3 – 15.9
	Overberg	4.5 %	2.9 – 6.8	4.4 %	3.5 – 5.6
	West Coast	7.1 %	5.1 -9.9	7.2 %	6.0 – 8.6
Age in years (median; IQR)		28	IQR 24 - 33	29	IQR 24 -33
Age category	10-14	0.2 %	0.03 – 1.6	0.1 %	0.01 – 0.5
	15-19	5.5 %	3.7 – 8.0	4.3 %	3.3 – 5.5
	20-24	20.7 %	17.2 -24.8	22.8 %	20.7 – 25.1
	25-29	29.8 %	25.7 – 34.3	30.1 %	27.7 – 32.5
	30-34	27.6 %	23.6 – 31.9	27.7 %	25.4 – 30.0
	35-39	13.7 %	10.8 – 17.2	12.7 %	11.1 – 14.6
	40-44	2.3 %	1.2 – 4.2	2.2 %	1.6 – 3.1
	45-49	0.2 %	0.03 – 1.6	0.1 %	0.04 – 0.6
Age of partner in years (median; IQR)		32	IQR 28 -32	32	IQR 28 - 37
Gravidity	1	22.4 %	18.8 – 26.5	19.2 %	17.6 – 21.7
	2	37.4 %	33.1 – 42.0	35.5 %	33.0 – 37.9
	3	25.1 %	21.3 – 29.4	28.7 %	26.4 – 31.0
	4	10.3 %	7.8 – 13.5	12.0 %	10.3 – 13.7
	5	3.6 %	2.2 – 5.8	3.2 %	2.3 – 4.1
	6	0.9 %	0.3 -2.3	1.0 %	0.6 -1.7
	>6	0.2 %	0.03 – 1.6	0.4 %	0.1 – 0.8
Population group	Black African	85.7 %	82.1 – 88.6	85.8 %	83.9 – 87.5
	Coloured*	14.3 %	11.4 – 17.9	13.9 %	12.2 – 15.8
Level of education	None	3.0 %	1.7 – 5.1	2.2 %	1.6 – 3.2
	Finished primary	52.5 %	47.8 – 57.2	52.1 %	49.5 – 54.8
	Finished secondary	42.0 %	37.5 – 46.7	43.2 %	40.6 – 45.8
	Finished tertiary	2.5 %	1.4 – 5.1	2.5 %	1.8 – 3.4
Marital status	Single	75.8 %	71.6 – 79.6	76.1 %	73.8 – 78.3
	Married	21.9 %	18.3 – 26.0	22.3 %	20.2 – 24.6
	Widow	1.4 %	0.6 – 3.0	0.7 %	0.3 – 1.2
	Divorced	0.9 %	0.3 -2.4	0.9 %	0.5 – 1.5
Awareness of HIV status	Yes	91.0 %	88.0 – 93.4	90.3 %	88.6 – 91.7
	No	9.0 %	6.6 – 12.0	9.7 %	8.3 – 11.4

Self-reported ART use**		35.0 %	30.7 – 39.6	35.5 %	33.0 – 38.1
ART detected on lab analysis		37.2 %	32.8 – 41.8		
	Lopinavir (LPV)	3.3 %	2.0 – 5.5		
	Efavirenz (EFV)	31.2 %	27.1 – 35.6		
	Nevirapine (NVP)	2.7 %	1.5 -4.7		
Overall discordance		9.6 %	7.2 -12.8		
	Discordance – ART self-reported but not detected	3.4 %	2.1 – 5.6		
	Discordance – ART detected but not self-reported	6.2 %	4.3 – 8.9		

†95% confidence intervals were calculated using the normal approximation to the binomial distribution

*This term is applied by the national survey for purposes of service delivery redress

**Sensitivity 83.5% (95% CI 77.0 – 88.9), specificity 94.5% (95% CI 91.1 – 96.9), kappa 0.8 (p<0.001), NPV 90.5% (95% CI 86.5 – 93.6), PPV 90.1% (95% CI 84.2 – 94.4)

No risk factors for discordance between the laboratory sub-sample and 2014 survey population were noted on bivariable and multivariable analyses. Self-reported ART use (35%) was similar to ART detected on lab analysis (37.2%), with 2.2% absolute difference. Self-reported ART was further compared to laboratory markers showing a sensitivity of 83.5% (95% CI 77.0 – 88.9) and a specificity of 94.5% (95% CI 91.1 – 96.9), positive predictive value of 90.1% (95% CI 84.2 – 94.4) and negative predictive value of 90.5% (95% CI 86.5 – 93.6). Agreement between self-report and laboratory markers was also high at 90.4% (kappa statistic 0.8, p<0.001).

Descriptive characteristics of the PHDC cohort are summarised in Table 3.2. The majority of women (69.8%) having no electronic record of HIV status, suggests either HIV negative (most commonly given high antenatal HIV testing coverage) or unknown status. Of those with electronic records of positive HIV status, 7.7% had no record of ART (Table 3.2). Of all pregnant women with HIV in the 10-year cohort, 72.6% had records of ART initiation before or during pregnancy and 87.2% in 2019.

Table 3.2: Descriptive and HIV-specific characteristics of PHDC Cohort (2011 – 2020) compared to PHDC Cohort 2019

	PHDC Cohort 2011 – 2020 (n=977800) Percentage	PHDC Cohort 2019[§] (n= 123907) Percentage
Prior electronic evidence of pregnancy*		
1	60.3%	52.4%
2	27.2%	29.7%
3	9.2%	12.4%
4	2.5%	4.0%
5 or more	0.8%	1.5%
Age (median; IQR)	27.4	27.2
Age Category		
<15	0.5%	0.5%
15 -19	12.0%	11.1%
20 - 24	26.6%	25.7%
25 - 29	27.4%	27.3%
30 - 34	20.1%	20.8%
35 - 39	10.4%	11.5%
>39	3.0%	3.1%
District**		
Cape Winelands	13.4%	13.1%
Central Karoo	0.8%	1.2%
Cape Metro	70.2%	65.7%
Garden Route	8.3%	9.2%
Overberg	3.0%	4.3%
West Coast	3.7%	5.5%
No district recorded	0.6%	1.1%
Pregnancy Outcomes		
Delivered	83.4%	81.1%

Ectopic pregnancy	1.4%	1.7%
Termination	5.4%	7.2%
Stillbirth	1.5%	1.3%
Miscarriage	3.4%	4.9%
Mother died prior to delivery	0.02%	0.02%
Outcome unknown	4.9%	3.8%
Evidence of HIV status		
HIV status unknown†	69.8%	71.6%
HIV status known	30.2%	27.9%
HIV evidence timing		
HIV positive before or during pregnancy	16.7%	18.5%
HIV positive postnatally	4.0%	1.4%
HIV negative	9.5%	8.3%
HIV unknown	69.8%	71.8%
ART (n=202575)		(n=24644)
HIV Positive but no evidence of ART	7.7%	5.9%
Antenatal ART (before or during pregnancy)	72.6%	87.2%
Postnatal ART	19.7%	6.9%
Antenatal ART (n=163649)‡		(n=22910)
ART started before pregnancy	54.7%	69.5%
ART started during pregnancy	35.2%	24.3%
No antenatal ART	10.1%	6.2%

§2019 reflects the most recent characteristics pre COVID-19

*Gravidity estimates (number of times a woman has been pregnant, including current pregnancy) in the PHDC are not reliable since historic data are incomplete. Prior electronic evidence is used as a proxy to provide a full description of the cohort.

**Unweighted

†HIV diagnosis is based on point-of-care tests that are not recorded electronically. Unknown HIV status therefore includes those who tested negative on point-of-care tests and therefore have no subsequent electronic evidence of HIV

‡Excludes women who only tested HIV positive postnatally

Among those living with HIV, survey, DHIS, PHDC and Thembisa estimates show that ART coverage before pregnancy increased over time, however a slight decrease is noted in the

survey estimate in 2019 (Table 3.3 and Figure 3.1). The 2014 laboratory and PHDC estimates of ART coverage were similar (37.2% v 37.4%, respectively). The 2015 survey estimate of 44.2% was similar to the PHDC estimate of 42.8%. The 2017 survey estimate of 62.3% was higher than PHDC data (58.4%), but lower in 2019 (61.2%) compared to PHDC (69.5%), when comparing ART coverage before pregnancy. DHIS estimates were notably higher than Thembisa estimates, excluding treatment interruption, and more aligned to PHDC estimates which included treatment interruption. Thembisa estimates of those ever on ART prior to conception (including treatment interruption), were higher than PHDC until 2016 and thereafter reasonably close to PHDC estimates. From 2015 to 2020, Thembisa estimates of ART at delivery were higher than PHDC estimates of ART at delivery, however the difference between estimates is lower when restricting PHDC estimates to live births only. A sensitivity analysis to assess the contribution of moderate-low confidence pregnancies to ART coverage did not materially impact the PHDC estimates and associated comparisons.

Table 3.3: Western Cape Antenatal ART Coverage (%) amongst women living with HIV by dataset (2011 – 2020)

	Before pregnancy						At delivery		
	Antenatal Survey		DHIS	Thembisa 4.6	PHDC	Thembisa 4.6	PHDC	PHDC	Thembisa 4.6
Year	Antenatal Survey (on ART among WLWH)	Lab validation	Proportion on ART among those with HIV at antenatal first visit (excluding treatment interruption)	Antenatal ART coverage prior to conception (excluding treatment interruption)	Proportion on ART before pregnancy among those known with HIV (including treatment interruption)	Antenatal ART coverage prior to conception (including treatment interruption)	Antenatal ART coverage at delivery (all pregnancy outcomes)	Antenatal ART coverage at delivery (live births only)	Antenatal ART coverage at delivery (live births only)
2011				32.4	27.0	34.8	67.1	67.4	51.7
2012				36.0	33.7	39.2	72.8	73.9	62.3
2013				39.7	35.4	43.5	83.7	85.3	77.0
2014	35.5 (33.0 - 38.0)*	37.2 (32.7 -41.7)*		43.4	37.4	47.6	88.9	90.6	88.6
2015	44.2 (41.6 - 46.8)*		43.9	47.3	42.8	52.0	90.6	92.4	93.8
2016			51.4	51.0	51.6	56.5	91.4	92.9	95.3
2017	61.5 (57.7 - 65.1)* 62.3 (58.5 -66.0)**		62.0	54.1	58.4	60.5	92.4	93.9	96.1
2018			62.9	57.1	63.6	64.1	92.6	94.0	96.4
2019	61.2 (57.2 -65.1)**		68.3	59.7	69.5	67.3	93.8	94.7	96.6
2020			70.1	61.3	72.6	69.5	93.5	94.1	96.7

*Current ART use (excludes treatment interruption)

** Includes treatment interruption. Stratified to first visit only. ART before pregnancy amongst first and follow-up attendees is 58.4 for 2017 and 58.2 for 2019.

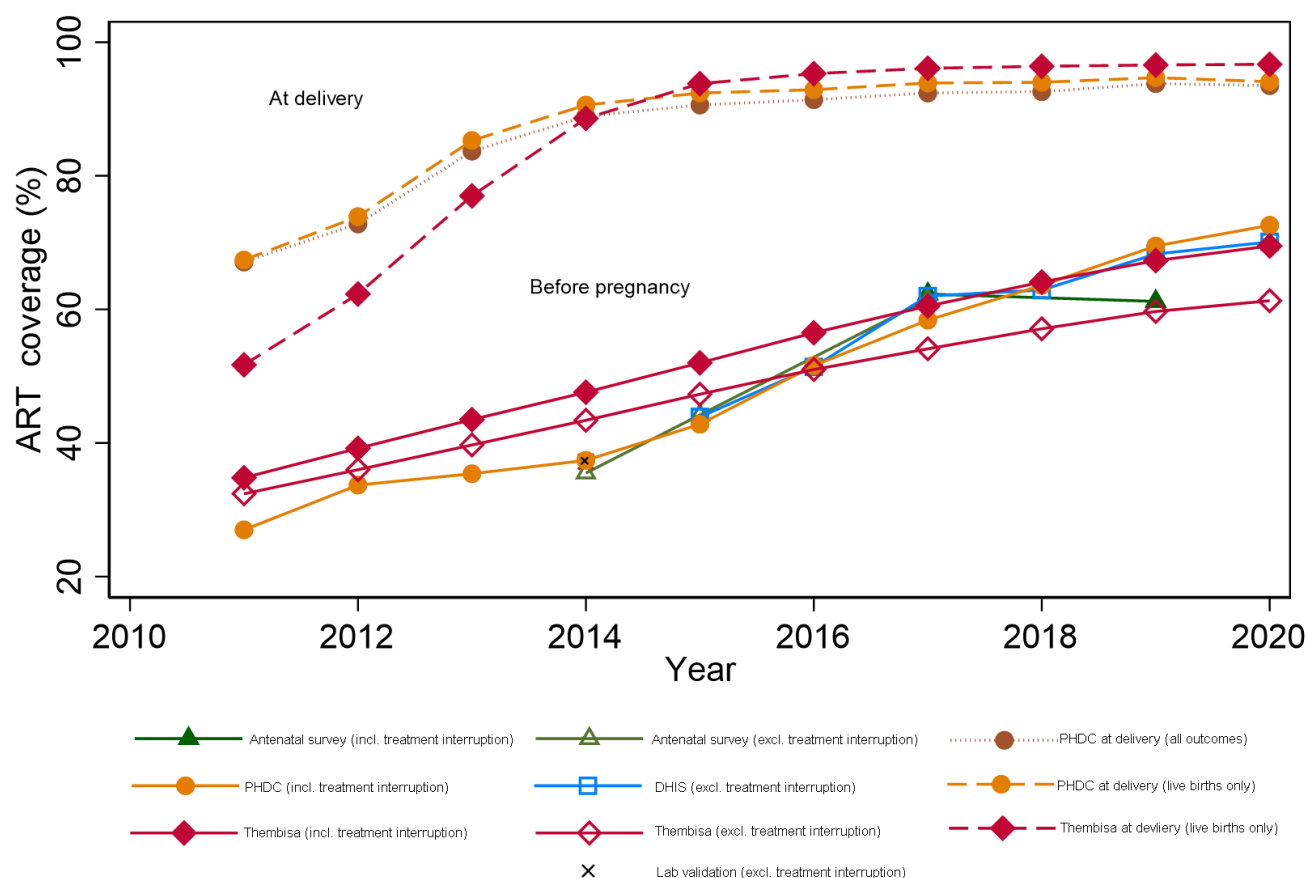


Figure 3.1: ART coverage before pregnancy and at delivery by dataset (2011 – 2020)

Figure 3.2 presents Western Cape antenatal ART coverage among those with HIV over a 10-year period according to PHDC data. ART coverage prior to pregnancy amongst WLWH increased over time from 42.8% in 2015 to 72.6% in 2020. Higher coverage was observed in older age groups, with coverage as high as 81.1% in the 35-39 age group in 2020 (Figure 3.1). An increasing proportion of women are shown to be on ART before pregnancy and from 2015 onwards ART coverage exceeds 90% before or during pregnancy. ART coverage during the antenatal period (ART commenced before or during pregnancy) was high amongst pregnant WLWH in all districts, except Central Karoo, and across all years. Over time, there was variability of coverage estimates in Central Karoo, Overberg and West Coast, with Cape Metro having the most consistent increase in coverage.

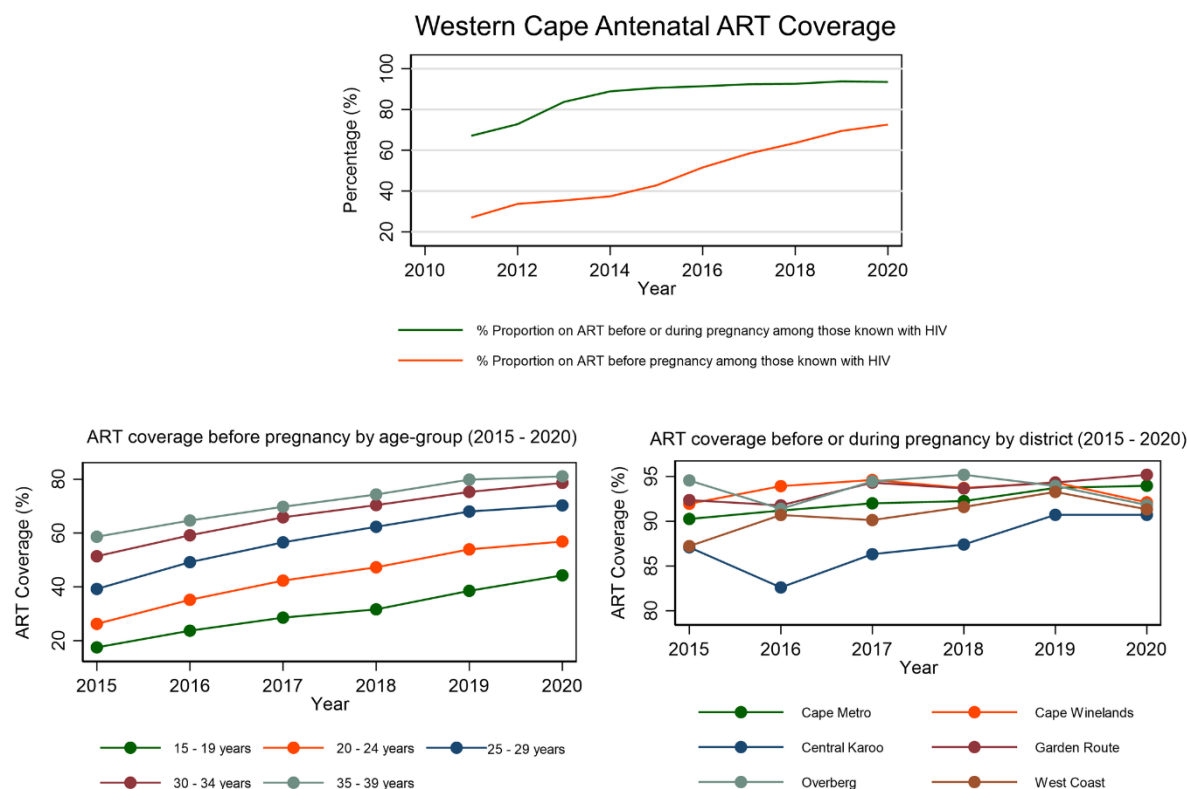


Figure 3.2: Temporal trends in antenatal ART coverage in the Western Cape by timing, district and age (PHDC)

Discussion

Our study is the first to assess and compare different methods of antenatal ART coverage ascertainment in the Western Cape province. All datasets documented the increasing ART coverage in pregnant women over time. The challenges in dataset comparisons where numerators and denominators are disparate were highlighted.

The self-reported survey-based antenatal ART question was confirmed as a valid measure of ART use by comparison to the gold standard of laboratory detection, with good overall concordance. Discordance was higher amongst those self-reporting no ART use but having positive laboratory detection of ART than vice versa. This may represent misunderstanding of the question, false positive laboratory results or reluctance in disclosing ART use due to stigma or other reasons. Interestingly, 15 participants who self-reported ART use had no laboratory

evidence of ART. In addition to question misinterpretation or false negative laboratory results, this may also suggest poor recent medication adherence. Discordance proportions and agreement between self-report and laboratory detection were in keeping with a similar study conducted in the Kwazulu-Natal province, however non-disclosure of ART status (2.9%) was notably lower in our cohort compared to this study (8.1%)[9]. Several other studies in sub-Saharan Africa comparing self-report and biomarkers of current or previous ART use showed higher proportions of ART non-disclosure, however these studies had smaller sample sizes and the study population was not restricted to pregnant women presenting for antenatal care[21-24]. While the study by Huerga et. al. in KwaZulu Natal found younger individuals were at higher risk of discordance, our study found no demographic risk factors for discordance[9]. The ART question had high agreement beyond chance, and high specificity, sensitivity and positive and negative predictive values, suggesting good performance of this question as a measure of ART use. Other studies have shown a similarly high specificity and positive predictive value, however sensitivity and negative predictive value are notably lower[25–27]. Reasons for better performance of self-reported ART in our study may include lower social desirability bias due to lower perceived stigma of ART use amongst those actively seeking antenatal care in a clinical setting. Furthermore, since the ART question was asked by clinicians during routine clinical care, more explanation of the question may have been given compared to other study settings. Our findings arguably support the continued use of the question in survey settings and the utility of survey ART estimates for further validation with routine data. However, we note that the question on current ART use was discontinued after 2017 and replaced with a question “has the participant ever taken ARV’s,” thereby including those not on ART at the time due to prior treatment interruption. Additionally, from 2019, survey questions were complemented with information from medical records if available. Further validation of survey data is therefore recommended.

Our study suggests lower completeness of PHDC data in earlier years when compared to DHIS data. This finding is further supported by a recent study which compared live births from

Thembisa with PHDC data[19]. From 2015 onwards, however, the PHDC enumerated more pregnancies than DHIS, suggesting good completeness of these data. Higher numbers in the PHDC may be due to inclusion of non-viable pregnancies and terminations of pregnancy, which may not be captured in DHIS amongst antenatal service attendees. Lower enumeration prior to 2015 is likely due to less well-established electronic systems in earlier years. Within the PHDC cohort, 69.8% had no information of HIV status. This is likely representative of the HIV negative antenatal population whose HIV status is determined solely by point-of-care rapid HIV testing, the results of which are not captured electronically on routine information systems[28]. Those with evidence of HIV negative status had laboratory confirmation via HIV ELISA test results which are captured electronically on routine systems. Those testing positive for HIV on point-of-care testing may have further validation of test results by laboratory HIV ELISA testing as well as other laboratory, pharmacy and administrative evidences of HIV, thus providing a complete dataset of antenatal patients with HIV in the public sector of the Western Cape province [28].

Estimates of ART coverage in the antenatal population living with HIV were similar across the survey and PHDC datasets for 2014 and 2015, although higher estimates were expected in 2015 due to inclusion of treatment interruption in the PHDC dataset. The 2017 and 2019 antenatal surveys report ART use prior to pregnancy among women presenting for their first antenatal visit, and therefore may include those who interrupted treatment[16,17]. When compared to PHDC estimates of ART before pregnancy, PHDC estimates were lower than survey estimates in 2017, but notably higher in 2019. The differences between survey estimates and PHDC may reflect sampling bias in the survey population as well as interviewer-related differences in asking the survey question on ART use prior to pregnancy, participant-related interpretation of the question as well as availability of relevant medical records in 2019 survey participants. Whether the estimates include or exclude treatment interruption may be dependent on how the survey question was interpreted by both interviewer and participant.

Thembisa estimates of ART at delivery were higher than PHDC estimates, however the difference was slightly less when restricting PHDC estimates to live births only. This may indicate that ART initiation is prioritised where transmission to an infant is possible, and less urgent in non-viable pregnancies such as ectopic pregnancies. Additionally, pregnancies where the outcome is unknown may represent those who are lost to the health care system for reasons such as migration to a different province and therefore not recorded on ART within the PHDC. The high ART coverage estimates reflected in the PHDC dataset is reassuring and in keeping with recent literature[29]. These findings support the importance of antenatal first visits for early engagement in HIV care and effective prevention of vertical transmission of HIV. ART initiation prior to pregnancy among WLWH would, however, be most ideal in prevention of vertical transmission as well as prevention of onward transmission to sexual partners[29]. Any engagement with health services for WLWH, regardless of pregnancy intention or outcome, should be considered an opportunity for ART initiation in keeping with test and treat guidelines. Systemic factors associated with delayed ART initiation requires urgent research in order to optimise prevention of vertical transmission of HIV.

DHIS estimates of ART coverage among WLWH at first antenatal visit are notably higher than survey estimates and Thembisa estimates and more aligned to PHDC estimates, despite differences in treatment interruption ascertainment. The reasons for these disparities may be multifactorial and difficult to identify. It should be noted that Thembisa estimates include both the private and public sector. When including treatment interruption, Thembisa estimates are notably higher than PHDC estimates until 2016. PHDC estimates may be higher in recent years and increasing over time due to greater ascertainment of patients using the public sector for HIV services. Overall, PHDC estimates appear to track Thembisa estimates closely in recent years. Since the Thembisa model uses many different sources for model calibration, the uncertainty from these estimates is likely less than the uncertainty of individual estimates used for calibration. The model estimates also show consistency and coherence over time which is comparable to PHDC estimates from 2015 onwards. DHIS estimates include those

currently on ART (excluding those interrupting ART) and trends may further represent changes in capturing of routine information on service-based registers or other contextual factors. While DHIS indicators are clearly defined, the exact question asked to ascertain current ART use at first antenatal visit may differ from clinician to clinician, resulting in variable patient interpretation and responses. Where data is not collected for research purposes it is difficult to determine how a question is asked. Data sources based on responses therefore may be uncertain, particularly with increasing ART coverage over time.

Population-wide datasets from the PHDC allow better discernment of current ART versus ever on ART and more detailed analysis such as district-level and age disaggregated temporal trends, which the antenatal survey is underpowered to generate, while the DHIS is limited to specific indicators. Age-group trends over time show an expected higher ART coverage prior to pregnancy in older age groups who have likely had more opportunities for HIV diagnosis and care than younger age groups (in whom HIV is likely to have been more recently acquired). District-level trends are in keeping with provincial trends, showing a high ART coverage during the antenatal period, with most districts above 90%. The lower coverage estimates in Central Karoo are reflective of the smaller population and lower HIV prevalence in this sparsely populated rural district. Other demographic characteristics associated with ART coverage could not be evaluated as these are not routinely captured in health information systems.

Limitations

Routine data are subject to various caveats impacting both quality and completeness. Firstly, routine public sector data exclude those who do not access public health services both due to access issues and use of the private healthcare sector. ART coverage may therefore be overestimated as pregnant WLWH who do not access services are excluded from the denominator. Given the wide range of information systems used and the diverse staff members involved in data capturing, these data are subject to varying administrative and capturing errors. Completeness of data cannot be accurately quantified. Pregnancies

enumerated in the PHDC prior to 2015 were notably less than pregnancies in the DHIS over this time period, suggesting incomplete data in the PHDC cohort in earlier years. Contextual factors at different facilities may further impact the quality of data - this includes changes in capturing approaches, staff training, staff turnover, and COVID-19 pandemic impacts. Ascertainment of both pregnancy and ART use is dependent on how electronic systems are used in different facilities. However, the PHDC approach to using multiple data sources to enumerate pregnancy and HIV ascertainment, may mitigate against gaps in single data sources such as DHIS. ART coverage ascertained from routine data is inferred through dispensing of ART from pharmacy. This does not necessarily translate to administration and adherence to ART.

This study highlights the challenges in comparing datasets with differing numerators and denominators, particularly with respect to treatment interruption. Routine data are limited to variables captured routinely. Since information specific to the first antenatal visit is not routinely captured in all public health facilities, it was not possible to distinguish between first and follow-up antenatal visits in the PHDC dataset. While first visit can be ascertained in DHIS, aggregated data are susceptible to double counting if the patient attends multiple antenatal clinics.

Detailed demographic and treatment characteristics are not captured, precluding a deeper understanding of epidemiological trends. DHIS consists of data elements for both national and provincial reporting purposes, some of which measure the same variable but are captured in different registers and by different staff members. As such, different data elements may be used for both numerator and denominator in order to calculate ART coverage. ART estimates may therefore vary depending on the data elements selected.

Since the national antenatal survey is underpowered for detailed estimates, routine data cannot be adequately validated at district, sub-district and age-group levels. Furthermore, the findings on self-reported ART use in surveys reflect findings in the last decade. We recommend repeating the validation to confirm if this concordance has persisted.

Lastly, it should be noted that while Thembisa estimates were used for comparison with antenatal survey and PHDC estimates, the Thembisa model is partially dependent on estimates from the antenatal survey for model calibration and assumptions on fertility are derived from the PHDC.

Conclusion

Our study demonstrates the validity and utility of antenatal ART coverage using routine individuated data. While laboratory detection is the most accurate measure of ART use, this is neither affordable nor practical at a population level. Routine individuated data provide an efficient and less costly method of estimation compared to surveys and more accuracy and granularity than aggregate data. Trends in the Western Cape province are reassuring in that the large majority of WLWH are initiated on ART before or during pregnancy. This is supportive of the province soon meeting the third target of the WHO Elimination of Mother-to-Child Transmission Initiative of 95% of pregnant WLWH initiating ART prior to or during pregnancy. Reasons for non-initiation during pregnancy require further investigation as this has serious implications for prevention of vertical transmission and child morbidity and mortality. Strengthening of routine information systems, including improved digitisation of point-of-care HIV testing and ascertainment of treatment interruption, in addition to being invaluable tools to directly support patient care, may allow more accurate epidemiological trend analysis for timely action and improved quality of HIV care.

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Chapter 4: Consolidating strategic information to monitor progress against the UNAIDS 90-90-90 targets: evaluating the operational feasibility of an electronic HIV testing register in Cape Town, South Africa

Relevance to thesis:

In chapter 4, the operational feasibility of an intervention to improve routine HIV ascertainment from the point of diagnosis is evaluated. This intervention incorporates the digitisation of routine point-of-care HIV tests using two different processes. Data digitised through the intervention were compared with aggregate data to measure completeness. Lessons learnt from the implementation processes were explored to understand the key points of consideration when considering scale up. The findings of this chapter demonstrate how to enhance HIV case-based surveillance from the point of HIV diagnosis.

Contribution of candidate and co-authors:

The candidate, NJ, conceptualised the study under the guidance of AB and BR. NJ led the implementation of the intervention in collaboration with the Western Cape Department of Health and Wellness, conducted the study, analysed the data, interpreted the results and wrote the manuscript. NJ managed all stakeholder engagements from which stakeholder reflections were generated. EK and JM provided operational support. AH and SB contributed to data curation. All co-authors commented on drafts and approved the final version for submission.

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This published chapter is presented verbatim in this thesis with only changes to table and figure numbering as well as formatting for consistency with the overall thesis.

Abstract

Background

HIV diagnosis in South Africa is based on a point-of-care testing (PoCT) algorithm with paper-based record-keeping. Aggregated testing data are reported routinely. To facilitate improved HIV case-based surveillance, the Western Cape Province implemented a unique pilot intervention to digitise PoCT results, at an individual level, and generate an electronic register using the newly developed Provincial Health Data Centre (PHDC). We describe the intervention (phased) and present an evaluation of the operational feasibility of the intervention. We also offer implementation insights into establishing electronic capture of individual level testing data.

Methods

Cross-sectional analyses were conducted on records of all patients attending a local Community Health Centre who had an HIV-PoCT during the study period. Data from the intervention were linked to the PHDC using a unique identifier and compared with aggregate data from the paper-based register. Correlation coefficients were calculated to quantify the correlation between the two monthly datasets. To support an understanding of the findings, the Department of Health project management team generated reflections on the implementation process, which were then grouped thematically into implementation lessons.

Results

In total, 11 337 PoCT records were digitised (70% (7954) during Phase I; and 30% (3383) during Phase II). Linkage of forms to the PHDC was 96% in Phase I and 98% in Phase II. Comparison with aggregate data showed high correlation during Phase I, but notable divergence during Phase II. Divergence in Phase II was due to stringent data quality requirements and high clinical staff turnover. Factors supporting implementation success in

Phase I included direct oversight of data capturing by a manager with clinical and operational insight. Implementation challenges included operational, health system, and high cost-related issues.

Conclusions

We demonstrate that rapid digitisation of HIV PoCT data, without compromising currently collected aggregate data, is operationally feasible, and can contribute to person-level longitudinal HIV case-based surveillance. To take to scale, we will need to improve PoCT platforms and clerical and administrative systems. Although we highlight challenges, we demonstrate that electronic HIV testing registers can successfully replace manual registers and improve efforts to monitor and evaluate HIV testing strategies.

Keywords

digitisation, HIV point-of-care testing, case-based surveillance, implementation, health information systems

Background

Monitoring progress towards the 90-90-90 targets

The United Nation's programme on HIV/AIDS (UNAIDS) set the 90-90-90 targets in 2015, aiming to diagnose 90% of those who are HIV infected, treat 90% of those who are diagnosed HIV positive and virally suppress 90% of those receiving antiretroviral treatment[1]. These targets are based on the World Health Organization (WHO) universal test and treat principle, also introduced in 2015[2]. HIV case-based surveillance is a cost-effective method, recommended by WHO, to measure progress towards achieving the 90-90-90 targets[3]. Distinctive features of case-based surveillance are obtaining individual-level data for each person diagnosed and linking these data to other key data points along the HIV care cascade[3]. Such systems have been implemented in many low, middle and high-income countries[3,4]. Many countries, particularly in high income settings, have also welcomed electronic health record keeping in the clinical environment[5], however this is not a viable

option in various low-and-middle income contexts for several reasons, including complex infrastructure, network requirements and user resistance[6–8]. Despite the high burden of HIV in sub-Saharan Africa and the existence of routine HIV program monitoring, case-based surveillance has not been implemented fully[3]. Strategic information on HIV is frequently attained using parallel, costly donor-driven data collection processes due to weak health information systems[3,9].

The first important steps to achieving the 90-90-90 targets is people living with undiagnosed HIV being diagnosed, and diagnoses both at the individual and population level being accurately monitored and measured[3]. Studies in India, Nigeria and Ethiopia have shown limited use of routine local data for health-system planning and decision-making[10,11]. A situational assessment of data collection systems in Tanzania, Kenya and South Africa revealed several barriers to implementation of case-based surveillance, including multiple data collection systems, poor interoperability and inadequate capacity[3]. Many of these data collection systems are paper-based[3]. The validity of manual paper-based recorded patient level data which is later aggregated for reporting is difficult to assess, coupled with the administrative burden on clinical staff. Such data are known to be prone to error and double counting[12] and often lack the necessary detail required for active surveillance[13].

Health information systems in South Africa

Health information systems can significantly support the health system at large, however health information systems are not universal across country contexts[3,14]. In South Africa, TIER.Net is an HIV health information system which electronically captures longitudinal individual-level information on patients on antiretroviral *treatment* (ART)[3,6]. However, HIV *testing* information is not captured on this system in many facilities, particularly information on those testing negative. Electronic linkage of individual-level patient data is possible in South Africa using a unique patient identifier e.g. patient folder number, but these identifiers have not been fully implemented in many provinces[15]. The Western Cape Provincial Government (one of South Africa's nine provinces) has developed a Provincial Health Data Centre (PHDC)

in which all individual-level routine data captured on electronic platforms in the province are consolidated on a single platform, leveraging the patient folder number as the unique patient identifier[15,16]. This allows linkage of various information systems, including laboratory, pharmacy, and patient administration, providing a rich source of individuated health information, in the absence of routine electronic patient health records. Within this environment, disease-specific patient cascades may be developed using specific markers of care at different points in the treatment cascade[15]. The laboratory information system, governed by the National Health Laboratory Services (NHLS), is a key contributor of HIV surveillance data[17], as specific laboratory tests are indicative of key points within the HIV care continuum. These laboratory tests are conducted centrally under rigorous quality control processes. These central laboratory data are consolidated in the PHDC daily along with datasets from various other provincial data platforms. Consolidation of data on a single central platform supports integrated clinical care, whilst also facilitating more timely and comprehensive surveillance and further epidemiological and operational analyses[15].

Point of care HIV testing in South Africa

While the PHDC platform supports health surveillance using routine data, an HIV case-based surveillance system requires individual level data on diagnosis of HIV[3]. An HIV diagnosis in South Africa is based on a point-of-care rapid-testing algorithm with paper-based record-keeping[3]. HIV testing is conducted primarily by HIV counsellors and nursing staff and information is entered into paper-based registers. Testing data are subsequently manually tallied, with aggregates reported to the Provincial Departments of Health on a monthly basis[3]. It is well-recognised that PoCT are less accurate than central laboratory tests as the tests are conducted by busy clinical staff members who are not trained rigorously on laboratory quality control and quality assurance[18,19]. However, PoCT are favoured in high-burden, resource-limited settings as access to care is improved by more immediate availability of test results and linkage to further to care[18].

Monitoring and surveillance systems that are not part of an electronic information system cannot be linked to the PHDC. This is true for all point of care testing (PoCT) information in the province, which is not collected digitally. Although aggregate HIV testing data are reported electronically, individual testing data remain in paper-based registers and paper-based facility patient records. The lack of integration of PoCT results within the NHLS, and the broader PHDC, may hamper laboratory-informed case-based disease surveillance, HIV prevention planning, as well as limit information available to clinicians when evaluating historical laboratory investigations as part of clinical decision-making. In high-burden clinical environments, this results in longer, less efficient clinical consultations and unnecessary and costly repetition of PoCT[19]. Currently, the only electronically captured HIV test results within the NHLS are from enzyme-linked immunosorbent assay (ELISA) tests which are conducted at the central laboratory if rapid PoCT results are discordant. Negative HIV PoCT results are not captured electronically in any routine information system. In addition, the maintenance of the existing paper-based registers is onerous for busy clinical staff. Register reports are often delayed, and are rarely available to, or used by, the clinical staff who collect the data.

Various advanced PoCT devices are available which have the functionality to capture test results and patient information directly into electronic information systems[19]. Such devices are not widely used in the South African public health sector and may require significant resource and training investment before wide-scale implementation. Manual PoCT systems are thus likely to remain in the clinical setting.

There is currently a gap in literature on establishment of case-based surveillance systems in high-burden settings, including the digitisation of HIV PoCT[3,12]. The maturation of the health information system in the Western Cape province presented a unique opportunity to implement case-based surveillance through inclusion of routine individual-level electronic HIV testing data.

Development of a pilot intervention to establish an electronic HIV testing register

Integration of PoCT results into an existing consolidated individual patient data environment was considered by provincial health managers, as it was likely to be more efficient and less onerous than developing a parallel system just for PoCT result digitisation. Given the close link between laboratory tests and PoCT and given that the NHLS is equipped with an efficient transport service that has daily contact with all provincial health facilities where PoCT is utilised, integration of PoCT into the NHLS was considered. Since NHLS is widely used by clinicians for retrieval of results, integration into the NHLS would further enhance accessibility of patient results. Furthermore, digitisation would enable the creation of actionable patient lists where linkage to care is delayed, thus further improving clinical care. Digitisation using the NHLS platform was an opportunity to use existing infrastructure which assumed a greater prospect of more immediate scale up of HIV PoCT digitisation as well as PoCT for other conditions.

The Department of Health in the Western Cape consequently implemented a pilot intervention to digitise HIV PoCT results with support from the NHLS transport mechanism and information system in order to establish HIV case-based surveillance. In this study, we evaluated the operational feasibility of this pilot intervention to generate an electronic HIV testing register at a local Community Health Centre (CHC) that would make available individual-level digitised testing data to inform prevention and treatment activities. In this study we adopted a definition of operational feasibility as the ease with which the intervention is supported by the procedures and protocols within the health facility[10]. This study focussed primarily on the recreation of the HIV testing register as a test of operational feasibility and completeness of the digitisation process. Designed to move away from often misleading aggregate data reports to more accurate digitised reporting, the intervention is a critical step in achieving more accurate surveillance of HIV testing and crucial strategic information for moving towards control of the HIV epidemic. In this study we wanted to understand what was operationally possible in a real-

world setting. The utility of the intervention, demonstrated by the analysis of individuated data, is reported on elsewhere[20].

In this paper we describe the pilot intervention, present the results of an evaluation, and discuss the operational feasibility of the intervention. We also offer practical implementation reflections into establishing and taking to scale the electronic capture of individual level testing data.

Setting and intervention

The PoCT intervention evaluated in this study was designed with emphasis on minimal interference to existing workflow, recognising the heavy staff workload and limitations to digitisation within the facility environment.

The intervention involved transporting carbonated copies of standard HIV testing services (HTS) forms, completed manually by facility staff, to a central point for digitisation and inclusion in the laboratory information system and PHDC (Figure 4.1). Routine HTS forms, familiar to staff, were pre-carbonated thereby not requiring the introduction of a new form for digitisation purposes. Pre-carbonation ensured that no additional workload was imposed on staff to duplicate the results for digitisation.

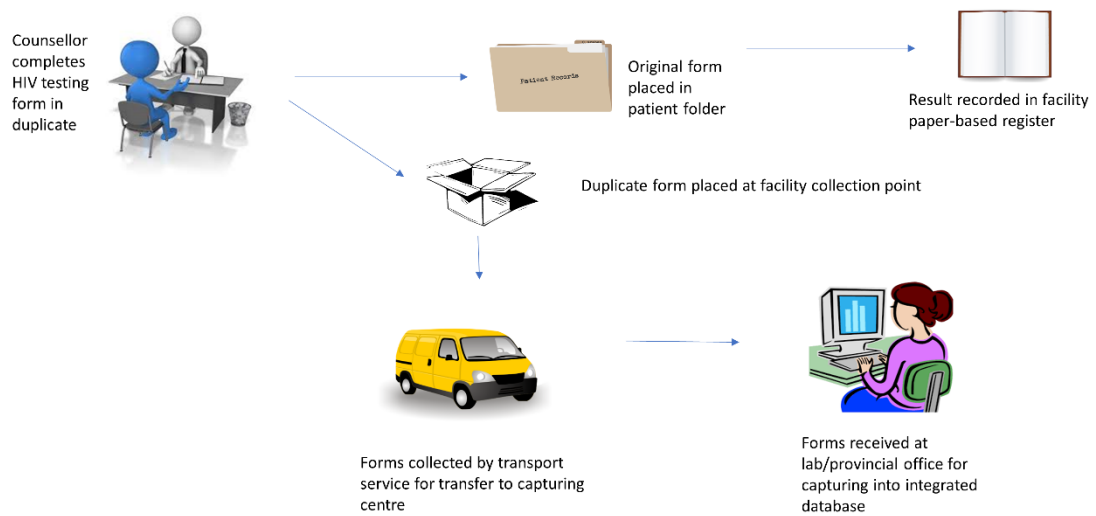


Figure 4.1: Intervention data flow pathway

During April 2017, counselling and nursing staff involved in HTS were trained on completion and routing of the carbonated form. Only identifiable patient data (hand-written or on patient labels stuck on the form) and fields relevant to PoCT were captured, including unique HTS form number, demographic data, consent to HIV test, self-reported previous HIV test result, reason for accessing HTS and results of the rapid HIV PoCT. ART data were indicated on forms as free written text and hence not captured due to concerns regarding interpretation errors.

Identifiable data on patient labels included patient name, surname, sex, South African identification number, barcoded folder number, address and telephone number where available. The patient folder number is a computer-generated, barcoded 9-digit number with a coded facility location prefix. This unique folder number is generated by the provincial patient administration system. Patient labels are placed in patient folders on arrival at the reception of most health facilities. These labels are placed on all clinical stationery pertaining to the patient. In order to increase access to HIV testing, patients presenting to health facilities solely

for HIV testing are permitted to consult an HIV counsellor directly, without obtaining a folder and patient label at the facility reception. Patient identifying information is then hand-written by HIV counsellors on the PoCT HIV stationery. This reduces waiting times at health facilities for those wanting to test for HIV, thus improving access to testing. Only patients who subsequently test HIV-positive are referred to reception to obtain a folder for further clinical consultation and management.

From May 2017 to June 2018, data were captured from the carbonated copies. It was intended for data to be captured throughout the study period by the NHLS. However, due to logistic delays with the NHLS beyond the study start date, data capturing was divided into two distinct phases which changed the original shape of the intervention.

In Phase I (May to December 2017), forms were transported during regular visits by a project team member and individuated data were captured by an independent trained data capturer on to a provincial database located within the Western Cape Government Health Complex, which was later integrated into the PHDC. Double capturing on to the same database was employed for cross-checking to minimise capturing errors; discrepancies were identified and corrected by the data capturer through validation with the carbonated form copy. Data capturing during Phase I was supervised by a project manager with a clinical background (first author). Issues that could not be resolved immediately by the project manager, such as poor identifiers or incomplete forms, were discussed directly with the HIV counsellors and facility management team by the project manager.

In Phase II (January to June 2018), following extensive discussions on pros and cons with NHLS stakeholders, data capturing responsibilities were transferred to laboratory clerks employed by the NHLS. These discussions provided valuable implementation lessons which are discussed as key results of this evaluation. The Phase II approach allowed the use of the routine NHLS transport systems that collect blood and other samples daily from the facility to transport the forms directly to the NHLS. The forms were then captured into the NHLS as per standard operating procedures. Data were checked by a supervisory laboratory technologist

who authorised entry into the NHLS information system, with a disclaimer indicating that the results were not verified by NHLS as the tests were conducted by facility staff. Test results were then made available for look-up by clinicians on the NHLS information platform, TrakCare Web Results Viewer. During Phase II, the laboratory project supervisor provided weekly e-mail feedback to the project manager and facility manager on capturing issues. These issues, primarily relating to data quality and completeness, were discussed periodically with the project team (co-authors) and a record of challenges discussed, and solutions developed were documented.

Independent to the intervention, the study facility employed an additional non-governmental organisation (NGO) during Phase II to increase HIV testing at the facility. This change resulted in an increased drive for opportunistic HIV screening in the facility and facility parking lot (community outreach).

Methods

Study population

The study population included patients using HTS at Gugulethu CHC, an urban primary care facility in Cape Town. HIV PoCT is offered routinely to pregnant women presenting to the Midwife Obstetric Unit of the CHC, as an outpatient service and during community outreach activities. All patients attending the CHC may voluntarily use HTS or be referred for HTS by health care providers in the CHC. No formal recruitment for the study was required as existing records in routine databases housed by the Department of Health were used for the evaluation.

Study design

Cross-sectional analyses were conducted on records of all patients at Gugulethu CHC who had an HIV PoCT during the study period. Feasibility research intends to generate evidence on the viability of health system interventions[10]. According to the TELOS framework, this may be categorised into five dimensions, including technology and systems, economic, legal and political and operational and scheduling feasibility[10]. In this study, we focussed on

evaluation of the operational feasibility of the pilot intervention, centring on whether the intervention works in practice[10,21]. Data arising from the intervention were linked to the PHDC using the unique patient identifier and compared with monthly aggregate data from the paper-based register to determine whether electronic registers could be reliably generated from pilot data. Correlation between electronically captured data and paper-based aggregate data was the main indicator of operational feasibility. Percentage linkage to PHDC and completeness of captured variables were secondary indicators of operational feasibility.

Data analysis

Data were analysed using Microsoft Excel and Stata 14 (Stata Corp, USA). Personal data obtained from the PHDC were de-identified before release for analyses.

HIV outcome was calculated electronically using the National Department of Health HIV testing algorithm, in which serial HIV rapid testing is required[22]. If the initial screening rapid test is positive, this is followed by a different confirmatory rapid test. If both rapid tests are positive, a diagnosis of HIV is made. The rapid test algorithm is repeated immediately if initial results are discordant. If discordance persists, an ELISA test for laboratory confirmation is required[22].

Once validated, captured data were exported and linked to existing patient records in the Patient Master Index through PHDC, using unique patient folder numbers. Where folder numbers were unavailable or illegible, linkage was attempted using combinations of other patient identifiers such as name, surname and date of birth. Unlinked forms were those with limited identifiers or that could not be definitively linked to a single patient with the available information[23].

Data arising from the intervention were compared with monthly aggregate data from the paper-based register submitted to the District Health Management Information System equivalent in the province, a web-based aggregate data portal named SINJANI. Electronically captured data were filtered according to month to generate monthly electronic HIV testing registers for

comparison with routine monthly aggregate data. Key reporting elements in the 2018 official HTS register as reported on SINJANI were used for more granular comparisons of aggregate data from July 2017 to December 2017. Correlation coefficients were calculated to quantify the correlation between the two monthly datasets. Pearson's correlation coefficient (r_p) was used for normally distributed variables and Spearman's coefficient (r_s) was used for non-parametric variables. Of the 49 reporting elements in the 2018 official HTS register, 13 were used for comparisons (Table 4.1). The register comprises of 4 broad categories viz. 18 elements specific to antenatal care (ANC), 11 elements specific to children under the age of 15 years, 13 elements pertaining to all patients, including ANC and 7 elements excluding ANC. Selected elements represented these categories, however those with respect to children 15 years and under were excluded, as Gugulethu CHC does not cater specifically for children. Ethical approval for the evaluation was obtained from the University of Cape Town Human Research Ethics Committee (HREC 198/2018).

Table 4.1: Selected official 2018 provincial indicator dataset reporting elements and definitions

Reporting element	Definition
Total HIV test client accept test (incl. ANC)	Any client who accepted an HIV test including antenatal clients
Clients PRE-TEST counselled for HCT (incl. ANC)	Any client counselled for HIV test including antenatal clients
Antenatal client counselled for HIV testing - 15 to 24 years	Antenatal client aged 15-24 years counselled for HIV testing
Antenatal client counselled for HIV	Antenatal client aged 25 years and older counselled for HIV testing

testing - 25 years and older	
Accept testing - PMTCT initial test	Antenatal client who was tested for the first time during her current pregnancy
Accept testing - PMTCT repeat test at 20 weeks	Antenatal clients who tested negative for HIV during an earlier antenatal visit and were re-tested for HIV at 20 weeks during the pregnancy
Accept testing - PMTCT repeat test at 32 weeks	Antenatal clients who tested negative for HIV during an earlier antenatal visit and were re-tested for HIV at 32 weeks during the pregnancy
HIV positive client category - PMTCT initial test	Antenatal clients who tested positive for the first HIV test done during the current pregnancy
Antenatal client eligible for ART	Antenatal client eligible for ART as per current guidelines
Known HIV positive antenatal client	Antenatal clients with known HIV positive status. In the absence of documented proof, verbal confirmation of HIV status is acceptable
HIV test 15 years and older (excl. ANC)	Any client aged 15 years and older tested for HIV excluding antenatal clients
HIV test client 15-24 years (excl. ANC) accept test	Any client aged 15 - 24 years tested for HIV excluding antenatal clients
HIV PRE-TEST counselled client (excl. ANC)	Any client counselled for HIV test excluding antenatal clients

Management team reflections and observations while managing implementation

To support the presentation of the evaluation results, the project management team (co-authors of the paper) in the Provincial Department of Health, who function as participant observers in managing the overall implementation of the intervention, have pooled together their personal reflections to generate implementation lessons. These personal reflections were captured in weekly logs including personal notes and reflections on stakeholder meetings, weekly face to face correspondence with project staff and e-mails. The first author consolidated these personal reflections and grouped them thematically into lessons. These were reviewed by the members of the project management team. We acknowledge the limitations of one perspective on implementation, as the project management team brings only one viewpoint on successes and challenges. Other local level actors, including the CHC facility manager and data capturers in both phases, for example, may have different or additional viewpoints on successes and challenges.

Results

Key evaluation results

From May 2017 to June 2018, 11 337 HTS forms were digitised. These were linked to the PHDC, with 70% (7954) being captured during Phase I and 30% (3383) during Phase II. In total, 137 forms were excluded from aggregate analyses due to incorrectly entered dates of test. Overall, 97% linkage to the PHDC was achieved. Linkage of forms to the PHDC was 96% (7667/7954) in Phase I and 98% (3315/3383) in Phase II. Completeness of variables exceeded 97% apart from HIV testing outcome (86%) and reason for accessing service (73.9%).

A comparison of aggregate data submitted to SINJANI, independent of the pilot, and monthly data collected during Phase I, showed a high correlation ($r=0.93$, $p<0.001$). In Phase II, correlation between the two datasets was lower ($r=-0.71$, $p=0.1812$). Figure 4.2 illustrates the differences between the two phases. The divergence between the two phases presents an

opportunity for us, the project management team, to reflect on the implementation opportunities and challenges that may have influenced these differences.

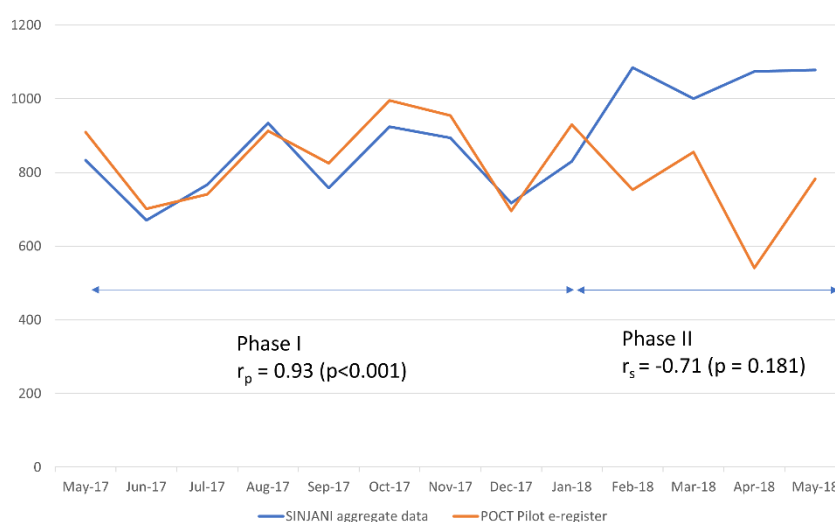


Figure 4.2: Comparison of total number of patients accepting an HIV test (including antenatal testing)

Key reporting elements from the routine HIV testing register extracted from SINJANI (Table 4.1) were further compared to pilot data for the period July to December 2017, when Phase I was well established. Figure 4.3 demonstrates closely correlated trends between the official aggregate totals reported from the paper-based HTS registers, and the aggregated digitised data from the PoCT-digitisation intervention.

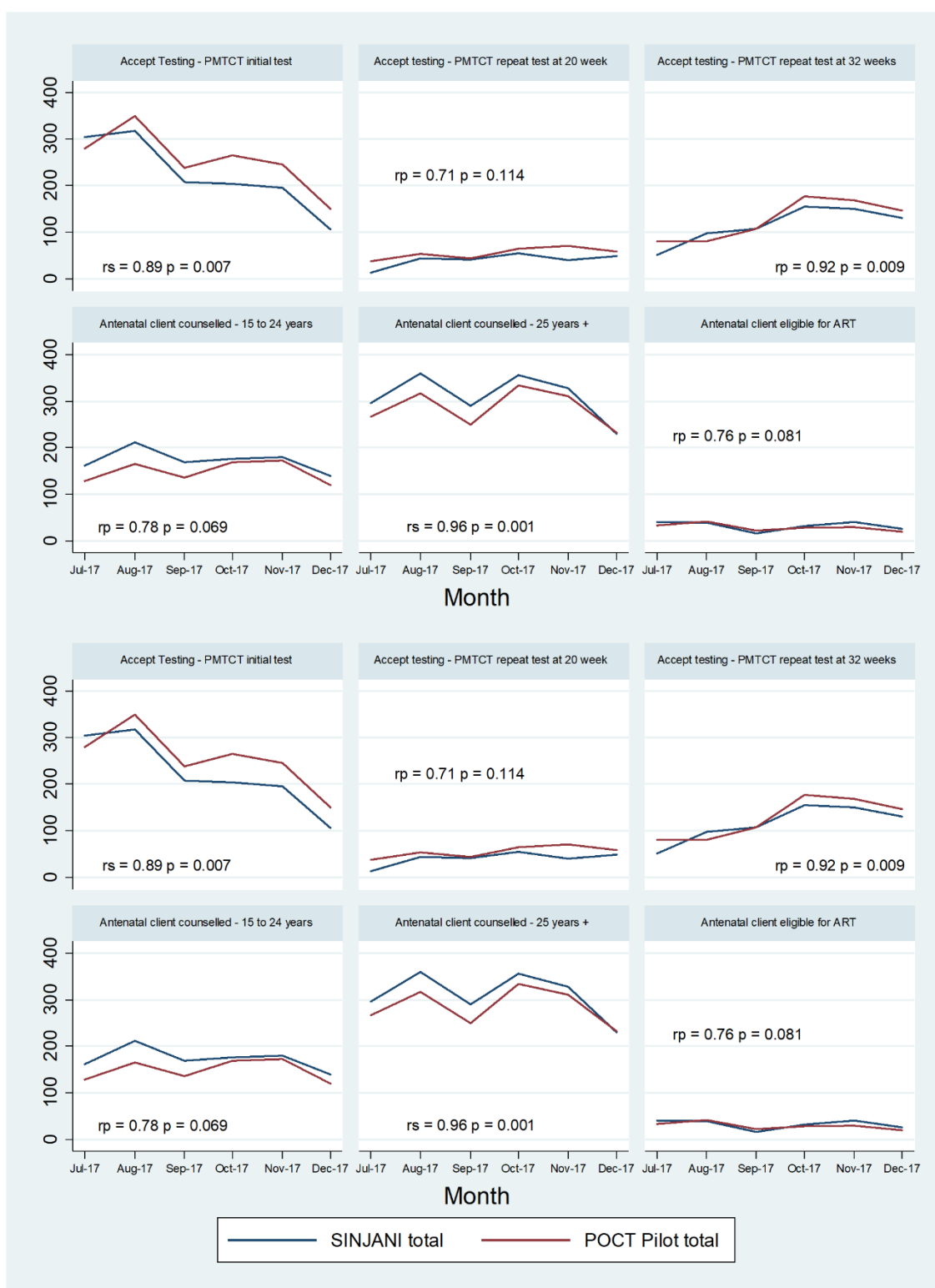


Figure 4.3: Comparison of HIV testing register reporting elements, July to December 2017

Key Implementation lessons

While implementing the pilot intervention, there were a number of challenges and opportunities during the digitisation process. Key challenges included stakeholder concerns around data quality issues and logistics. Some of these challenges were mitigated over time through a series of helpful solutions, while others remained unresolved.

Stakeholder concerns

Before commencing the intervention, several stakeholder engagements took place in the form of face-to-face meetings and via e-mail. A key concern expressed by the NHLS was the perceived lack of quality assurance for PoCT conducted by clinical staff who lacked laboratory training in quality control. The NHLS has strict quality control measures in place for testing which is different from the daily practices at facility level. Furthermore, the capturing of hand-written results from clinical stationery, did not always comply with the strict accreditation standards upheld by NHLS. The NHLS was cautious about issuing results for assays they had not performed, and which were not subject to standard laboratory quality controls. The complexity of the routine clinical form used in the clinical environment which had multiple fields with clinically-relevant information, was also identified by NHLS as a barrier to capturing in a laboratory setting, compared to the structured laboratory-request forms used for requesting tests conducted by them. Additionally, the NHLS was concerned that the presentation of HIV PoCT results on the web viewer may cause confusion in clinical settings where other tests may be discordant with the PoCT, particularly given the quality concerns. In order to address these concerns, a clear disclaimer was used on the web look-up to waive NHLS responsibility for the results and circumvent reputational risk. PoCT results for each rapid test (both screening and confirmatory test) performed on a patient were presented exactly as captured by the counsellor, without any interpretation of the final HIV outcome. This would allow clinicians to exercise clinical judgement when reviewing PoCT results in conjunction with other laboratory results.

Confidentiality of PoCT information on route to NHLS and during capturing by laboratory clerks was another concern raised by NHLS. Following extensive discussion, it was acknowledged

that whilst HTS forms do contain sensitive patient information, the information is similar in nature to clinical information written on standard laboratory request forms that are routinely transported from facilities to NHLS and captured by laboratory clerks. Many laboratory request forms contain HIV status information as required clinical background for laboratory tests. These are transported routinely in laboratory specimen bags. The pilot intervention therefore does not confer any additional risk when compared to standard laboratory transport practices. However, in order to ensure confidentiality of HTS forms during transport in both phases, forms were sealed in envelopes (instead of transparent specimen bags) in the counsellors' offices before transferring to capturing sites.

There were concerns that the proposed intervention would increase NHLS workload for data clerks and technologists and that any such increases would not be adequately compensated. After 10 months of discussions on the pros and cons of the intervention, at both the national and provincial level (February to December 2017), NHLS agreed to participate in Phase II of the pilot. Capturing processes were handed over to the NHLS at a higher cost than Phase I and were based on internal NHLS assessments of the fixed costs associated with specimen transport and registration.

Data quality

Having commenced the pilot, it became clear that poorly legible and incorrectly completed forms were an issue in both phases of the pilot. Incorrectly completed forms included those in which identifiers were poorly completed in the absence of patient labels, incomplete consent fields and testing results entered in incorrect fields. Inconsistent entries were also identified; for example, free text indicating that a patient testing HIV negative is on ART. Regular face-to-face feedback was provided to counsellors and facility management in order to address these data quality issues. While some issues were resolved during Phase I, many of these data quality issues persisted in both phases and worsened in Phase II when more counsellors provided HTS at the facility. Issues specific to the printing of forms included legibility of carbonated copies, uniformity of carbonation and erroneous printing of duplicate form numbers. These issues were discussed with the printers and form books modified accordingly.

Incorrect application of the testing algorithm was identified as a major testing and data quality issue which would impact both paper-based and electronic registers. In order to mitigate this data quality issue in study analyses, only electronically calculated HIV outcome was analysed, based on the screening and confirmatory test results.

During Phase II, resolution of the above-mentioned form-specific issues were not addressed efficiently, as in Phase I, due to limited direct communication between NHLS and facility management and staff. Furthermore, poorly legible forms and incomplete forms were immediately rejected for capturing due to the strict accreditation protocols followed by NHLS.

The introduction of the additional NGO at the facility during Phase II resulted in new HTS counsellors who required training, and among whom there was a high staff turnover. This in turn appears to have resulted in more data quality issues and form rejections by NHLS. Furthermore, the increase in outreach testing resulted in more patients without computer-generated patient labels and unique folder numbers. The hand-written patient identifiers used for these patients were unacceptable to the NHLS. Forms without patient labels frequently lacked a location code, another accreditation requirement. Other challenges included the use of computer-generated temporary numbers due to technical issues on the electronic administrative platform, which were not recognised by the NHLS and poor-quality printing of patient labels impacting legibility. These were also rejected by NHLS. Some counsellors erroneously used computer-generated patient labels from other sites that patients occasionally kept with the patient-held case record. These labels contained location codes of facilities external to the pilot site and hence were rejected by the NHLS.

As a response to these challenges, a direct weekly e-mail communication chain between NHLS and the facility manager was instituted during Phase II so that both parties could better understand and address form-related concerns and facility-related factors such as training of HIV counsellors, patient registration issues and others. Despite these efforts, both parties had limited direct communication, leaving many issues unresolved during Phase II. The digitisation process, however, was able to identify errors in HIV testing and form completion which has

the potential to meaningfully contribute towards clinical governance by identifying areas for further staff training and support.

Logistical issues

Several logistical issues relating to routing and transport of the forms were identified and addressed on an ongoing basis. These issues were the unavailability of envelopes for confidential transport, poor labelling of envelopes, delays in the daily routing of forms and incorrect routing of original forms, instead of the carbonated copy. Although the NHLS requested that forms were sent to them daily for a consistent workload, counsellors often batched forms over several days due to delays in entry into the paper-based register. This also limited the ability of the NHLS to accommodate the extra workload. The issues were addressed by providing pre-labelled envelopes to the facility, regular monitoring of form and envelope stock availability by the project manager and direct communication of issues with facility staff by the project manager. The use of pre-labelled envelopes for matters unrelated to the pilot was difficult to manage remotely as the project manager was not based in the facility. Adopting an implementation process of identifying and addressing challenges as they arose by the project management team in consultation with those working on the ground led to success during Phase I.

Feasibility of intervention

During the pilot (Phase I and II combined) we achieved almost universal (97%) linkage in the PHDC and variable completeness (most variables >97%). High levels of data completeness, data linkage and, most importantly, correlation between the aggregated data and Phase I data, indicates that it is operationally feasible to replace manual testing registers with electronic registers in the Western Cape. A comparison of specific reporting elements from routine reports during Phase I revealed marginal differences, confirming that electronic registers may efficiently replace paper-based registers at a more granular level. We have included implementation lessons in this paper that supported that success in Phase I, including a dedicated project manager, regular discussions with the project management team on challenges and the following up with solutions.

Although Phase I was able to closely replicate the paper-based register, notable divergence occurred in Phase II due to the high number of form rejections. Only forms with clear identifiers were captured during Phase II, resulting in the observed higher linkage to the PHDC. During Phase I, however, all available identifiers including hand-written identifiers, temporary numbers and identifiers on labels from other facilities were captured as best as possible for potential linkage to the PHDC. These different approaches may represent differing stakeholder priorities during the two phases. During Phase I, the Western Cape Department of Health captured and linked all validated forms through the PHDC, as any data indicative of an encounter with HTS services can considerably enrich monitoring and surveillance of the PHDC HIV treatment cascade, which is intended to directly impact individual patient care. The provincial platform had high interest in the success of the pilot and the outcome of the intervention was of primary focus. Phase II was more process-driven as adherence to accreditation criteria and quality control was paramount to the NHLS.

During Phase I, data quality issues were better addressed with clinical input and direct communication and feedback between facility staff, counsellors and data capturer. This communication was heavily driven by the project manager who visited the site weekly. Additionally, double capturing of data allowed identification and resolution of capturing errors. Without a regular feedback mechanism and the clinical and contextual understanding in Phase II, issues remained unresolved leading to greater numbers of form rejections and incomplete electronic registers. For the NHLS, central laboratory test results are requested by a named clinician, therefore there is an inherent feedback loop where incorrect testing procedures or specimen request entries will impact the availability of results needed by the clinician. In the Phase II setting, however, the counsellors were not involved in the feedback loop, as the captured data are not required by the counsellors and a form rejection does not affect the relevant counsellor directly. Direct involvement of facility management may thus increase accountability of individual counsellors who report to the facility manager.

Discussion

Operational feasibility

Phase I was successful in replicating the manual register. Phase II showed that the capturing mechanism worked but cannot replicate the paper-based register yet. Our study shows that the pilot intervention introduced by the Western Cape Department of Health to digitise PoCT HIV test results could successfully replace paper-based HIV registers. However, we note that there are a number of implementation factors that need to be proactively managed in context to achieve success. Key reflections from the project management team to inform a sustainable scale-up strategy for an electronic HIV testing register in a high diagnosing setting include the importance of regular communication between central data managers and facility staff, the value of clinical and operational insight when designing and implementing health information system interventions and the need for detailed stakeholder engagement prior to implementation. Also, in Phase I, a project manager being available at all times to address challenges and propose solutions in real time played an important role.

This intervention, if scaled up, can contribute to case-based surveillance and improved monitoring of performance towards the 90-90-90 targets. Importantly, this approach can also provide actionable individuated patient data which can directly improve the care of individual patients by identifying those who do not link to ongoing care. Furthermore, the study demonstrates the value of the intervention in strengthening clinical governance and its potential to improve operational efficiency at health facilities by decreasing workload required to maintain paper-based registers and enhancing clinical information available for consultations, should electronic registers be implemented.

Stakeholder engagement

A highly consultative, bottom-up approach was used in the design of the intervention, where the needs of frontline staff members were considered and incorporated in the development of the intervention. A key characteristic of the intervention was its minimal disruption to routine facility practices. Although this bottom-up approach was welcomed by facility staff, it conflicted

with central laboratory implementation methods where a predominantly top-down approach is employed. The latter approach assumes a well-resourced environment where implementation is a straightforward technical process guided by strict criteria and standards[24]. Although both have their advantages and disadvantages, a fine balance is required for successful implementation and scale-up[25–27]. Balthuis *et al* clearly describe the importance of considering all stakeholder perspectives when planning scale-up of an intervention[28]. In this study, the discord in stakeholder approaches resulted in the two distinct phases of data capturing and notably different findings during the phases.

The divergence between Phase I and Phase II may be closely linked to NHLS concerns relating to quality assurance, differentiating PoCT results from central laboratory tests and adherence to accreditation criteria. These are all well-documented concerns[18,19]. Studies have shown an increase in pre-analytical errors with PoCT compared to central laboratory testing, resulting in a greater potential for false negative and false positive results[18,19]. Recording of PoCT results in patient records were found to have far more errors than recording of central laboratory tests[19]. Given the data quality issues identified during the pilot, concerns regarding the quality of PoCT are well-founded and may be addressed through more rigorous training. Interventions such as these may have been better received when driven by stakeholders with expertise in central laboratory processes. This notion of professional exclusivity is well-described in literature as a health system-related barrier to adoption of PoCT strategies[18]. Differing workplace priorities and routine practices contribute significantly to these different stakeholder approaches[19]. Strict adherence to high standards is paramount to uphold the quality of services. This ardent and commendable commitment to quality service provision was evident in the NHLS approach to the intervention. In practice, different stakeholders may have different goals and standards which can cause friction during implementation. Issues related to PoCT, described above, exist regardless of whether paper-based or electronic information systems are used. However, digitisation and linkage into electronic information systems may more readily identify quality control and other systemic

PoCT issues for targeted remedial action, and therefore enable better collaboration and trust between facility and central laboratory stakeholders.

Champions in healthcare

A key success of Phase I was the direct communication and feedback mechanism that was introduced between data capturers, situated at the Provincial Department of Health complex, and facility staff. This was driven by the project manager, who adopted the role of an implementation “champion” and liaised between different actors. The champion construct is defined as an “implementation-related role occupied by people who are internal to an organisation, generally have an intrinsic interest and commitment to implementing a change; work diligently and relentlessly to drive implementation forward; are enthusiastic, dynamic, energetic, personable, and persistent; and have strength of conviction”[29].

The appointment of an intervention champion has previously been shown to positively impact on healthcare-related implementation in various clinical and organisation roles[29,30]. During Phase II, the role of champion at the Provincial Department of Health was diminished as capturing took place at NHLS. Regular supervision of data capturing was undertaken by NHLS rather than the project manager; a move that represents a more feasible strategy for future scale-up using the NHLS platform. Although efforts were made to set up a communication mechanism between NHLS and the facility, these were largely unsuccessful due to competing priorities and limited direct interest in the project. Communication mechanisms may have benefited from an active champion in Phase II.

Our findings concur with a number of other studies on the value of champions in healthcare[29]. However, champions alone are insufficient to ensure implementation success as other contextual factors also require consideration such as stakeholder buy-in, training needs and resource availability [29]. Inclusion of champions may strengthen sustainability of a new intervention; however, this approach may notably increase the costs of scale-up as further human resources may be required in an already over-burdened health care environment.

Implementation challenges

Data quality issues, including illegible, incomplete or incorrect data entry, were a concern during implementation and reflect poor clinical record keeping more generally. Completeness and accuracy of routine data entry is imperative for a functional health information system[14].

The intervention was designed to have minimal impact on routine facility workflow, as a commonly held perception among staff at facility level is that improved data collection requires increased administrative workload for staff. Despite these considerations, the poor quality of routine data is an ongoing challenge in many settings [13,31]. Reasons for poor quality of routine data include lack of accountability, limited understanding on the use of data, conflicting priorities in clinical work environments and involvement of multiple individuals in data entry [13].

Of interest, reason for accessing service, which was generally poorly captured, was better captured in antenatal services where reporting elements specific to this variable are required in the HTS register. This suggests that form completion may be driven by an awareness of what the data are used for, and that providing routine feedback to persons collecting the data (rarely experienced) that makes clear how these data are used for individual and population gain may result in improved data collection[13].

The value of an intervention such as ours cannot be demonstrated fully until the process is adequately implemented over time. This issue was exacerbated in Phase II due to the scale-up of testing services and high turnover in counselling staff. Minimal staff turnover is a recognised advantage in health system strengthening interventions due to limited training needs[32]. Without routine and on-going training of new facility staff, the benefits of increased testing are limited due to errors in testing, interpretation of results and data entry[18,19]. Line management hierarchies are also complex: the HIV counselling staff are not direct employees of the facility or the Department of Health, but members of NGOs contracted by the province to provide these services. In implementing our intervention, it would be preferable to standardise training and registration of HIV counsellors centrally. In the current setting, the

drive to meet 90-90-90 targets may result in unintended negative consequences such as retesting of known HIV-positive patients in an effort to achieve testing targets set by the Department of Health.

A formal analysis of costing was not conducted in this evaluation, however resourcing will have a notable impact on scale-up. The high cost incurred during Phase II is a notable challenge to province-wide scale up. Subramanian et. al. note the need for stakeholder engagement, strong leadership and realistic financing for scale-up[33]. Despite initial assumptions of the Phase II model being more pragmatic, scale-up using the Phase I model appears more operationally feasible and less costly, but will still require significant resource investments for stationery, transport and capturing on a wider scale as well as rigorous staff training and involvement of facility management. This may, however, result in higher costs due to inefficiencies in maintaining a parallel provincial system and the need for a champion to drive the process forward. From the central laboratory perspective, the intervention is onerous, poorly adherent to laboratory standards and of limited value. Higher level collaboration is required to streamline the intervention if it is to be supported by NHLS.

Advantages of digitisation

The eventual replacement of manual testing registers with electronic registers has several advantages. The digitisation of individuated data provides significant gains in population-level case-based surveillance[3], while also enriching available patient information at clinical consultations. Further surveillance analyses, beyond the standard reporting elements, is possible through digitisation and linkage to individuated data. The exclusive use of electronic registers has the potential to significantly reduce the workload of clinical staff tasked with maintaining large paper-based registers. A complete replacement of paper-based registers with electronic registers can create more incentive to implement the intervention successfully while also tangibly decreasing the workload of maintaining paper-based systems during the intervention and thus enhancing feasibility of the intervention.

The intervention also uncovered various training gaps in routine clinical record-keeping and the HIV testing protocol and algorithm. Improved training, support and management of frontline healthcare staff, including externally contracted staff, is essential to ensure quality of patient care and data integrity. Digitisation may also provide more accurate workload estimates for counselling staff, thus facilitating evidence-based resource allocation within facilities and improved operational efficiency[5,14].

The intervention may further demonstrate the contribution and inefficiencies of massive testing campaigns to achieve the first 90 of the 90-90-90 strategy. Although not detailed in this study, the added contribution of individuated data within the electronic register, may further contribute to improving linkage to care through active surveillance and improved monitoring of the second and third 90 within the 90-90-90 strategy.

Looking to the future in South Africa

Since the PHDC integrates various data sources, including laboratory data, there may be no added value in digitisation on the NHLS platform as long as the PoCT results are accessible to clinicians in a similar way to central laboratory results look-up. Despite the potential for false negative or positive results due to data quality issues, digitisation of PoCT will still confirm engagement at HTS services for PoCT, which is valuable clinical information for case-based surveillance and individual patient history-taking.

The presence of facility-based laboratories and laboratory staff within facilities may be an alternative implementation model, preferable from the laboratory perspective[18,19]. Similarly, the use of PoCT devices or mobile devices with direct electronic capturing are useful options, particularly with current approaches to expand testing to outreach sites, outside traditional facilities. Direct digital capture would also eliminate manual entry and subsequent challenges related to poor handwriting. These options are, however, notably resource intensive, with limited scope for scale up currently in both clinical and community settings[19]. Capturing of HTS forms at the facility, either by counselling staff or by dedicated data capturing staff may also be considered, thus eliminating the need to route forms offsite. These options again rely

on the availability of infrastructure and networking capabilities in all clinical environments as well as additional trained staff members, given the heavy workloads of facility-based staff members. Further analysis of the feasibility and cost implications of implementing such models is required.

This pilot clearly illustrates the importance of balancing the needs and values of different stakeholders when developing and implementing an intervention. Appropriate stakeholder (health care facility management and staff, NHLS, NGO and operational staff) ownership of the intervention is needed in order to facilitate better communication and feedback. A more detailed stakeholder analysis with consideration of preconceived stakeholder attitudes is thus imperative before considering scale-up[34,35]. Furthermore, the challenges identified are reflective of broader health-system, operational and economic challenges in resource-limited settings[3,14].

Limitations

We recognise that our study has several limitations. The findings of this study are context specific. Given that health information systems may vary significantly within districts, provinces and countries, implementation strategies may need to be adapted according to the context[33]. The focus of the study was operational feasibility, thus other dimensions of feasibility have not been explored and may impact scale-up. Similarly, economic viability of the intervention was not formally evaluated. The validity of the data captured in the routine aggregate SINJANI reports was not explored in this study and may be subject to the known biases of routine data[13]. A key limitation of the implementation lessons is that it only reflects the views of the provincial implementation management team. We did however send drafts of these lessons for member checking to the NHLS project manager, who was one of the key implementing partners. Drafts were approved by the NHLS project manager as adequately representative of their implementation experience. Evaluation of the roll out of a systems intervention of this nature would no doubt benefit from a formal implementation analysis including multiple stakeholder perspectives.

Conclusions

In Phase I, this study demonstrated the operational feasibility of rapidly digitising HIV PoCT data to contribute to consolidated actionable person-level longitudinal HIV case-based surveillance without compromising currently collected aggregate indicator data. The implementation model of minimally changing current practices through simple interventions such as pre-carbonated forms and utilising existing transport mechanisms for specimens to centralise forms to a high throughput capture environment, was demonstrated to be readily achievable. Routing the data through the NHLS had unanticipated challenges and costs and may require further improvements in both PoCT platforms as well as clerical and administrative systems before the approach reaches its full potential. There are a number of options for HIV (and other) PoCT digitisation ranging from the Phase I model in this study (centralisation of duplicate forms) to a variety of facility-based and tester-based solutions, the optimal choice of which is likely highly context-specific.

List of abbreviations

ANC	Antenatal care
ART	Antiretroviral treatment
CHC	Community Health Centre
ELISA	Enzyme-linked immunosorbent assay
HIV	Human immunodeficiency virus
HTS	HIV testing services
NHLS	National Health Laboratory Services
PHDC	Provincial Health Data Centre
PoCT	Point of care test
UNAIDS	United Nation's programme on HIV/AIDS
WHO	World Health Organization

Declarations

Ethical approval and consent to participate

The data used in the study are unconsented, de-identified routine service data housed by the Provincial Health Data Centre of the Western Cape Department of Health. Only aggregate data were analysed for this study. Ethical approval for the evaluation was obtained from the University of Cape Town Human Research Ethics Committee (HREC 198/2018). Subsequently, approval for release of data was obtained from the Provincial Health Data Centre as per the Data Access Policy of the Western Cape Department of Health.

Consent for publication

Not applicable.

Availability of data and materials

The dataset supporting the conclusions of this article is available in the Provincial Health Data Centre, Western Cape Provincial Department of Health. Release of these data to a public domain would violate the Data Access Policy of the Western Cape Department of Health. Data requests may be sent to the Western Cape Provincial Department of Health: Phdc.Pgwc@westerncape.gov.za

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

NJ, AB and BR conceptualised the study. NJ conducted and managed the study, analysed the data and wrote the manuscript. EK and JM provided operational support. AH conducted data linkage and provided data support. MO, AB, BR, JH, EK, AH, SB and JM made intellectual contributions to the manuscript. All authors edited and reviewed the final manuscript.

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Chapter 5: Utility of digitising point of care HIV test results to accurately measure, and improve performance towards, the UNAIDS 90-90-90 targets

Relevance to this thesis:

Chapter 5 builds on Chapter 4 by evaluating the utility of digitised point-of-care HIV testing data for enhanced HIV case ascertainment within a routine individuated data system. These data were made available through the intervention described in the previous chapter. Linked HIV testing data allows earlier ascertainment of HIV and better understanding of retesting and linkage to care, thereby strengthening HIV case-based surveillance and its utility to inform action.

Contribution of candidate and co-authors:

The candidate, NJ, conceptualised the study under the guidance of AB and BR. NJ led the implementation of the intervention in collaboration with the Western Cape Department of Health and Wellness, conducted the study, analysed the data, interpreted the results and wrote the manuscript. AH contributed to data curation. All co-authors commented on drafts and approved the final version for submission.

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This published chapter is presented verbatim in this thesis with only changes to table and figure numbering as well as formatting for consistency with the overall thesis.

Abstract

Introduction

High rates of pre-treatment loss to care among persons diagnosed with HIV persist. Linkage to care can be improved through active digitally-based surveillance. Currently, record-keeping for HIV diagnoses in South Africa is paper-based. Aggregated testing data are reported routinely, and only discordant findings result in a specimen being tested at a laboratory and digitised. The Western Cape Province in South Africa has a Provincial Health Data Centre (PHDC) where person-level routine electronic data are consolidated in a single database, leveraging the existence of a unique patient identifier. To facilitate improved HIV surveillance, a pre-carbonated point-of-care test (PoCT) form was piloted, where one copy was routed to a central point and digitised for PHDC inclusion.

Methods

We evaluated the utility of the intervention using cross-sectional and retrospective cohort analyses, as well as comparisons with aggregate data. Data were linked to the Patient Master Index of the PHDC using unique identifiers. Prior evidences of HIV within the PHDC were used to differentiate newly diagnosed patients and those retesting, as well as linkage to care and treatment.

Results

From May 2017 to June 2018, 11337 digitised point-of-care HIV testing records were linked to the PHDC. Overall, 96% of records in the aggregate dataset were digitised, with 97% linked to the PHDC. Of those tested, 79% were female (median age 27 years). Linkage demonstrated that 51.3% (95% CI 48.4 – 54.1%) of patients testing HIV-positive were retesting. Of those newly diagnosed, 81% (95% CI 77.9 – 84.3%) were linked to HIV care and 25% (95% CI 21.6 – 28.7%) were initiated on antiretroviral therapy immediately.

Conclusion

Digitisation of PoCT results provides individuated HIV testing data to assist in linkage to care and in differentiating newly diagnosed patients from positive patients retesting. Actionable and accurate data can improve the measurement of performance towards the UNAIDS 90-90-90 targets.

Introduction

The last decade has seen marked changes in the management of the global HIV epidemic. The United Nation's programme on HIV/AIDS (UNAIDS) set the 90-90-90 targets in 2015, aiming to diagnose 90% of those who are HIV infected, treat 90% of those diagnosed HIV-positive and virally suppress 90% of those receiving antiretroviral treatment[1]. These targets provide a framework for the universal test-and-treat principle introduced by the World Health Organization (WHO) in 2015[2].

HIV diagnosis is the first step of several along the HIV treatment cascade towards viral suppression[1]. That many people do not immediately proceed beyond this first step reflects a system failure; high rates of pre-treatment loss-to-care among persons diagnosed HIV-positive have been reported in sub-Saharan Africa[3–5]. If we are to meet the 90-90-90 targets it is essential that we improve, and accurately measure, linkage to HIV care for those newly diagnosed with HIV.

In South Africa, as with many countries in the region, HIV testing is based on a point-of-care test (PoCT) algorithm; only discordant findings result in a specimen being sent to a laboratory and digitised. This is against a backdrop of what is otherwise a comprehensive National Health Laboratory Services (NHLS) information system in which all laboratory test results performed anywhere in the country in the public sector are accessible on a central information system, and can contribute to surveillance activities[6]. The move towards universal access to treatment, and high targets for identifying those infected with HIV, requires that the treatment

cascade is monitored from the point of HIV testing. At testing facilities, PoCT HIV results are currently entered manually into a paper-based register, with aggregated data then submitted to the District Health Information System on a monthly basis.

The Western Cape Province has recently developed a Provincial Health Data Centre (PHDC) in which all person-level hospital and clinic administrative, laboratory, and pharmacy records, and data from disease information systems for HIV and TB, are consolidated in a single environment, leveraging the existence of a unique patient identifier which is used as the folder number in all health facilities in the public sector[7–9] . Within this environment, disease-specific patient cascades (virtual cohorts), such as the HIV treatment cascade, are in development using specific markers of care. In the HIV treatment cascade, electronic evidence of having HIV is based on laboratory markers (where PoCT is discordant, or from other laboratory tests often conducted shortly after diagnosis, such as CD4 tests and viral load) as well as ICD-10 (10th revision of the International Statistical Classification of Diseases and Related Health Problems) coding, for which the poor completeness and quality in the public sector is known[9–11]. The HIV cascade includes treatment information, such as initiation dates, regimen details, last dispensing dates, as well as information on viral suppression (Figure 5.1).

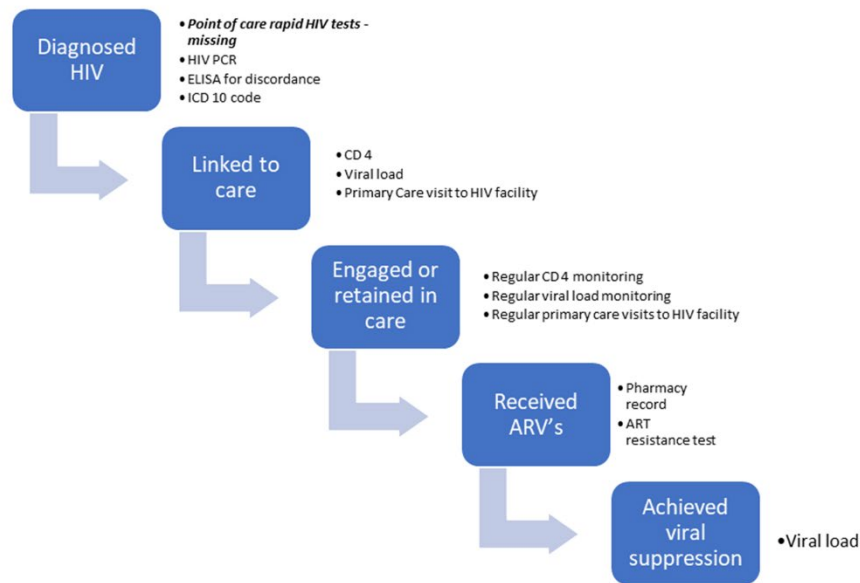


Figure 5.1: Individuated electronic evidences for steps of the HIV treatment cascade

Recently, considerable media attention was given to a proposed PEPFAR funding cut for South Africa due to apparent poor performance of South African HIV programmes[12]. Although this proposed funding cut was later reversed, it was widely appreciated that improved performance could be supported through digital solutions which include routine electronic monitoring of all persons newly diagnosed with HIV and their subsequent care.

To facilitate improved HIV surveillance, the Department of Health in the Western Cape implemented a pilot intervention at a local Community Health Centre (CHC) to digitise PoCT HIV test results. At the facility, HIV counsellors obtained informed consent and performed the rapid PoCT HIV assays routinely as per National protocol[13]. Carbonated copies of standard HTS forms completed at the facility were transported via routine systems to a central point for data capturing and inclusion in the PHDC. From May to December 2017 (Phase I) data were entered by a dedicated capturer located at the Provincial Department of Health. From January to June 2018 (Phase II), capturing was undertaken by data clerks at the NHLS following extensive stakeholder discussions on more pragmatic approaches to data capture. PoCT

results were thus available electronically at a population *and* an individual level. In this study, we evaluated the utility of this pilot intervention, in meeting reporting requirements, and more importantly providing a province-wide individuated actionable reporting mechanism for assessing and improving linkage to care of clients newly diagnosed with HIV.

Methods

The intervention was evaluated by applying cross-sectional and retrospective cohort analyses, as well as comparisons with reported aggregate data. The study took place at Gugulethu, a peri-urban township near Cape Town in the Western Cape province of South Africa. The study population included all patients accessing HIV Testing Services (HTS) at Gugulethu CHC between May 2017 to June 2018. This included patients attending HTS as part of routine antenatal care, patients referred for HTS and those self-presenting for HTS. No formal recruitment was required as existing records in routine databases housed by the Department of Health were used for the evaluation.

Elements documented on the routine paper forms and digitised included patient identifiers, demographic data, testing consent, self-reported previous HIV test result, reason for accessing HTS and results of the rapid HIV PoCT. HIV status was calculated using the National Department of Health HIV testing algorithm[13].

Data were linked to the Patient Master Index and existing HIV cascade of the PHDC using patient folder numbers. Where folder numbers were unavailable or illegible, linkage was attempted using combinations of other patient identifiers such as name, surname, civil identifier and date of birth.

Analysis

Data were analysed using Microsoft Excel and Stata 14 (Stata Corporation, College Station, Texas, USA). The PHDC provided de-identified linked data for the analyses on 1 July 2019, one year after study closure.

Patients attending HTS were described using appropriate descriptive statistics. All patients with evidence of HIV prior to PoCT were termed “cascade known HIV-positive”. Retesting was

determined using self-reported HIV status and cascade status. Patients who self-reported a previous positive HIV test result and tested positive again during the pilot PoCT were termed “self-reported retest HIV-positive”. Patients with prior evidence of HIV but self-reported a previous negative or unknown HIV status and had a calculated HIV-positive test outcome were termed “unreported retested HIV-positive”. Patients with no prior evidence of HIV, who had a calculated HIV-positive test outcome were termed “true newly diagnosed HIV-positive”.

To assess linkage to care, cohort analyses were conducted for all patients who tested HIV-positive using laboratory and pharmacy indicators of HIV care, including viral load and antiretroviral treatment (ART). ART uptake was calculated for patients who were not immediately initiated on treatment following a positive HIV PoCT result. Any patient who initiated ART after PoCT date and before time of analysis (1 July 2019) was classified as “Delayed ART initiation”. Any patient without records of ART initiation at the time of analysis (1 July 2019) was classified as “No ART”.

Multivariate logistic regression was used to explore associations with retesting in patients previously diagnosed with HIV. Variables were selected a priori and included in the model to address the effects of confounding.

Ethical considerations

Ethical approval for the study was obtained from the University of Cape Town Human Research Ethics Committee (HREC 198/2018). De-identified data were obtained from the Provincial Health Data Centre according to the Western Cape Department of Health Data Access Policy guidelines.

Results

From May 2017 to June 2018, 11 337 HIV counselling and testing forms were captured. Over this period, all digitised HIV PoCT records were linked to the PHDC to determine the contribution of the testing data to earlier ascertainment of HIV status and linkage to care. Table 5.1 shows the key descriptive characteristics of patients tested during the pilot intervention (missing data are presented as “no entry”). Most patients were female (79.3%). Overall, the

main reason for accessing HTS was antenatal care (39.8%). Only 13.4% of patients reported not having ever tested previously.

Table 5.1: Characteristics of patients attending HTS

	Median/IQR[†] /% (N=11 337)
Median age	28 years (IQR 23 – 34)
Median age for females	27 years (IQR 23 – 33)
Median age for males	31 years (IQR 24 – 42)
Sex	
Female	8987 (79.3%)
Male	2042 (18.0%)
Indeterminate/Unknown	23 (0.2%)
No entry	285 (2.5%)
Reason for accessing HIV service	
Antenatal care 1 st visit	2414 (21.3%)
20-week antenatal repeat visit	637 (5.6%)
32-week antenatal repeat visit	1465 (12.9%)
Provider-initiated counselling and testing (PICT) - other services	2849 (25.1%)
Self-referred	597 (5.2%)
HIV exposed infants	340 (3.0%)
Provider-initiated counselling and testing (PICT) - TB services	75 (0.7%)
Perinatal (delivery)/Baby other	3 (0.03%)
No entry	2957 (26.1%)
Previous HIV result	
Self-reported positive	1492 (13.2%)
Self-reported negative	8325 (73.4%)

No entry	1520 (13.4%)
HIV test result	
Tested negative	8700 (76.7%)
Tested reactive on 1 rapid test	218 (1.9%)
Tested positive on 2 rapid tests (National Protocol)	997 (8.8%)
Discordant result	13 (0.1%)
No entry [‡]	1359 (12.0%)
Inconclusive result	50 (0.4%)

[†] IQR: interquartile range; [‡] Includes those self-reported HIV-positive and not retested

Digitisation of records

During the study period, 11564 PoCT entries were tallied from paper registers as part of routine aggregate reporting over 13 completed months (May 2017 – May 2018). Therefore, 96.0% (11119/11564) of entries in the aggregate dataset were individually digitised as part of this project.

Overall, 97.0% of records could be linked to the Patient Master Index. Unlinked records could not be definitively linked to a single patient with the available identifiers.

HIV status: PoCT result, self-reporting and re-testing

Of the 11337 patients, 76.7% (8700) tested HIV negative, with 10.7% (1215) testing positive. The remaining 12.5% (1422) did not have a conclusive PoCT outcome recorded. The overall prevalence of HIV among those attending HTS, was 21.2% (2399), almost half of whom (1132) self-reported a positive HIV status and did not retest.

Linkage of the apparent 907 newly diagnosed HIV-positive patients to the HIV cascade indicated that over a third (34.7%; 95% CI 31.6 – 37.9%; 315) were already known to the cascade as HIV-positive, supporting an established diagnosis of HIV in the past. These 315 patients were therefore retesting following a previous positive test result, having not self-reported a positive HIV status. Of those who retested with reporting their HIV-positive status,

46.7% (95% CI 41.1 – 52.3%; 147/315) had commenced ART prior to their latest PoCT. Overall, 51.3% (95% CI 48.4 – 54.1%; 623/1215) of patients who tested HIV-positive on at least one rapid test had previously been diagnosed (Figure 5.2).

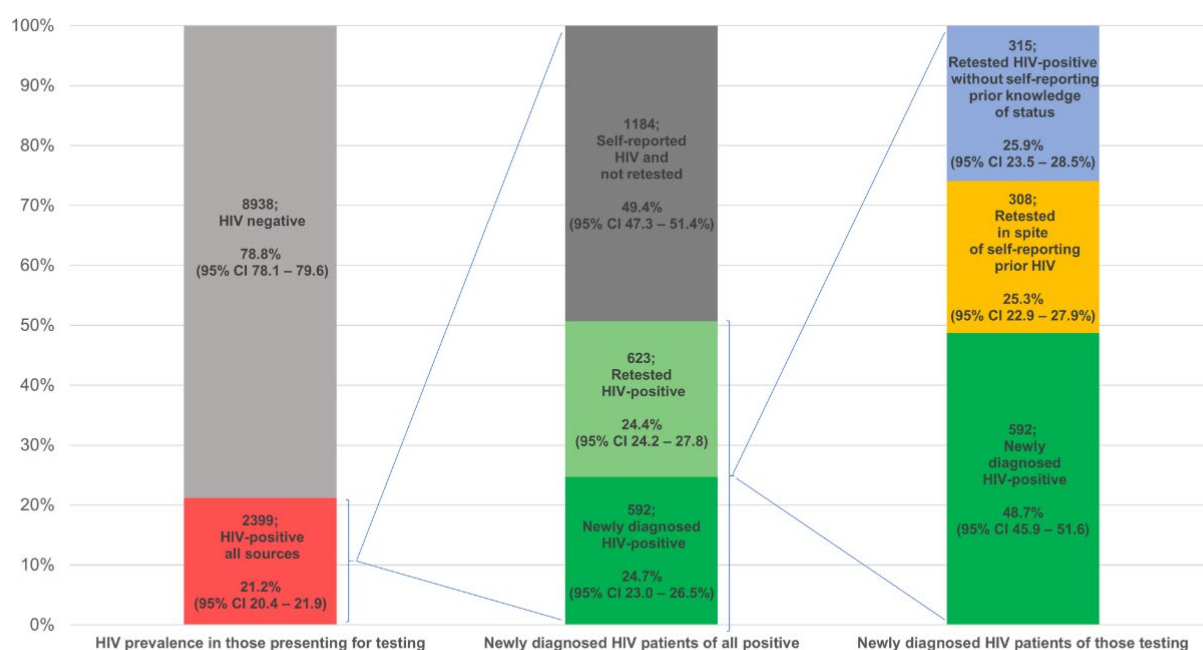


Figure 5.2: HIV positivity and yield by testing and prior testing status

Of patients who self-reported a positive HIV status, 88.2% (95% CI 86.5 – 89.8%; 1316/1492) were already known to the PHDC HIV cascade as HIV-positive. Based on available laboratory and pharmacy evidence, an additional 8.3% (125) entered the HIV cascade after their HIV PoCT during the pilot intervention. The remaining 3.4% (51) did not have any prior or subsequent evidence of HIV and were thus not known to the HIV cascade. Of persons self-reporting a positive HIV status, 24.1% (95% CI 22.0 – 26.4%; 360/1492) retested (self-reported retest). Figure 5.3 demonstrates the utility of digitisation and individual data linkage to the HIV cascade compared to information garnered from aggregate systems in isolation. Although 50 patients retested HIV negative, having self-reported HIV-positive status, linkage

to the HIV cascade shows that 38 of these patients had previous evidence of HIV diagnosis in the HIV cascade.

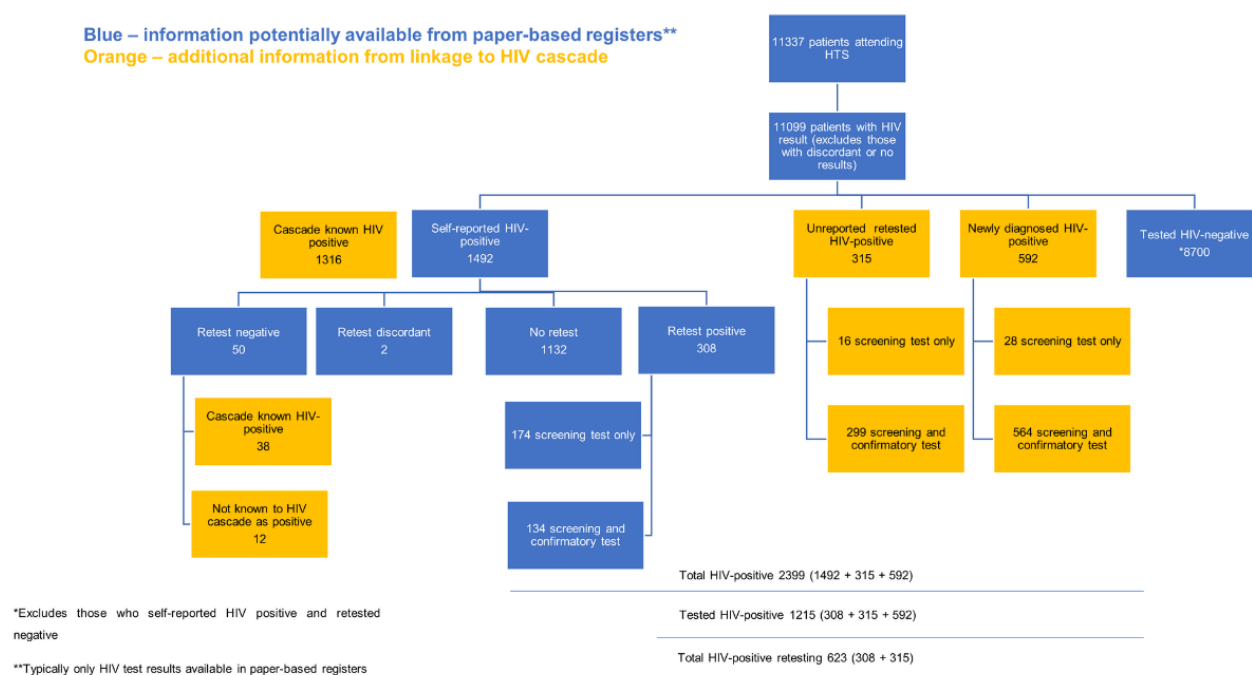


Figure 5.3: Contribution of HIV cascade data linkages to testing information

Factors associated with re-testing in patients with known HIV

Apparent bivariate associations of older age and women with retesting in spite of HIV-positive status having been ascertained previously were attenuated through adjusting for the reason for testing. In the adjusted model, reason for attending HTS services was highly associated with retesting (Table 5.2). For example, those attending for provider-initiated counselling and testing (PICT) from TB services were 10.6 (95% CI 2.8- 39.7) times more likely to retest compared to those attending initial antenatal visits. The association between younger age and retesting also persisted.

Table 5.2: Factors associated with retesting in patients already diagnosed with HIV

Variable	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Sex (reference male)	2.45 (1.91 – 3.15)	<0.001	1.50 (0.85 – 2.66)	0.163
Age category (reference 25-49 years)				
15 – 24 years	1.39 (1.03 - 1.88)	0.029	1.54 (1.10 – 2.16)	0.012
25-49 years	1.00 (ref)		1.00 (ref)	
>50 years	4.17 (1.63 – 10.68)	0.003	0.77 (0.29 – 2.08)	0.611
ART status (reference prior ART)				
Prior ART	1.00 (ref)		1.00 (ref)	
Current ART	0.59 (0.37 – 0.93)	0.022	1.64 (0.95 – 2.84)	0.075
No ART	1.27 (0.77 – 2.10)	0.041	1.47 (0.82 – 2.63)	0.199
Reason for accessing service (reference Antenatal 1st visit)				
Antenatal 1st visit	1.00 (ref)		1.00 (ref)	
20-week antenatal repeat visit	0.09 (0.03 – 0.25)	<0.001	0.09 (0.03 – 0.25)	<0.001
32-week antenatal repeat visit	0.72 (0.48 – 1.08)	0.111	0.70 (0.47 – 1.06)	0.092
PICT TB services	10.54 (2.87 – 38.74)	<0.001	10.67 (2.86 – 39.73)	<0.001
PICT other services	6.81 (5.03 – 9.24)	<0.001	7.07 (4.93 – 10.13)	<0.001
Self-referred	7.51 (3.23 – 17.47)	<0.001	7.71 (3.16 – 18.80)	<0.001
HIV exposed infants	0.62 (0.35 – 1.12)	0.111	0.60 (0.34 – 1.08)	0.090

Linkage to care and ART

Of patients confirmed as being newly diagnosed HIV-positive (as per linked HIV cascade data), 81.3% (95% CI 77.9 – 84.3%; 481/592) had evidence of further HIV care at the time of analysis, including 58.1% (95% CI 54.0 – 62.1%) who had started ART (Figure 5.4). Of those who were retesting HIV-positive, 71.4% (95% CI 69.2 – 73.4%) had already started ART previously, and a further 13.6% (95% CI 12.1 – 15.3%) subsequently started ART (Figure 5.4).

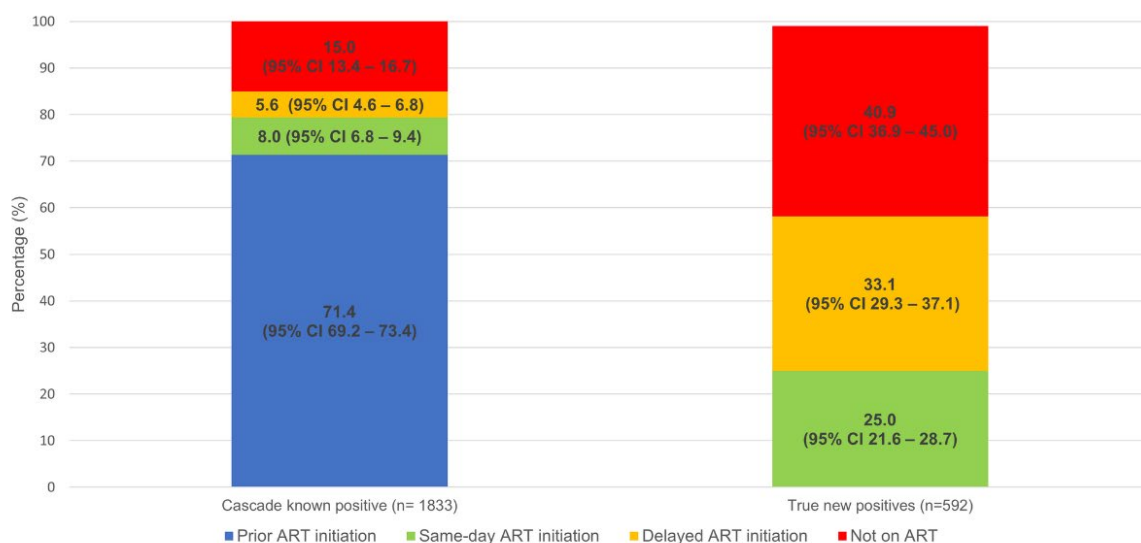


Figure 5.4: Antiretroviral (ART) status among cascade known positive and true new positive patients on 1 July 2019

Discussion

This is the first study to quantify the important contribution of routine HIV PoCT data to earlier digital ascertainment of HIV status and linkage to care. We show that digitisation of PoCT records is both useful and feasible, having captured electronically the majority (96.0%) of expected records. Linkage of HIV PoCT data using the unique identifier further allows discernment of newly diagnosed HIV-positive patients from those who are retesting. We found that half of patients testing HIV-positive on at least one rapid test were retesting following a previous HIV diagnosis, reducing to a third if excluding those who retested positive in spite of indicating that they already knew they had HIV.

Completeness of ascertainment and linkage of records

Linkage was close to 100% indicating that most patients who had attended HTS during the pilot were registered with public health care services. The majority of patients who self-reported a positive HIV status were known to the HIV cascade, validating the completeness

of the cascade within the PHDC. Since HIV PoCT are not routinely digitised, and hence not part of the electronic PHDC HIV cascade, the 176 patients who self-reported HIV-positive in the pilot but did not appear in the cascade, most likely did not engage in further HIV-specific care following an earlier positive PoCT. Overall, 8.4% of patients who self-reported a positive HIV status only entered the HIV cascade following PoCT during the pilot study, when further HIV-specific management was initiated. This pre-treatment loss to care is well-documented throughout sub-Saharan Africa but notably challenging to quantify in the absence of robust health information systems[3,4].

The most recent population-level HIV survey in South Africa showed an HIV prevalence of 12.6% (95% CI 9.7 – 16.1) in the Western Cape province[14]. The most recent antenatal HIV prevalence survey, another key source of HIV prevalence data, showed that the Western Cape province antenatal HIV prevalence was 20.8%[15]. The higher prevalence amongst antenatal patients is expected given that these patients are at higher risk of HIV through recent sexual transmission[14,15]. In this study, 10.7% of patients tested HIV-positive on at least one rapid test, although this includes retesting and excludes those who elected not to retest following a self-reported previous HIV-positive result. The overall prevalence of HIV among those presenting for HTS was 21.2%, including those who self-reported a previous positive result. This finding is similar to the overall provincial antenatal HIV prevalence and is expected as antenatal patients comprise a large proportion of the study population.

Retesting in patients already known to have HIV

Retesting among patients with a previous positive HIV diagnosis but who self-reported a negative or unknown status was an important finding that is not quantifiable in the absence of PoCT digitisation. Paper-based records are limited in revealing this phenomenon due to the movement of patients between different public health facilities. We identified known HIV-positive patients as being a substantial proportion of those testing, and additionally identified a further proportion who were retesting without revealing their HIV status. Half of the patients who knew they had HIV and who retested did not declare a previous HIV-positive result and

hence were misclassified as new HIV-positive diagnoses in aggregate data. In practice, all retesting is likely to be misclassified in aggregate data due to challenges in tallying data across multiple columns in paper-based registers. Such misclassification has significant implications for South Africa's approach to measuring progress towards the UNAIDS 90-90-90 goals[1]. Considerable resources have been committed to expanding HIV testing and counselling programmes to achieve the first 90. Our results suggest a third (34.8%) of HIV-infected patients identified by programmes may already be aware of their status. Furthermore, of these patients, almost a half (46.7%) had evidence of prior ART. Attention thus needs to be directed at retaining such individuals in care and on ART (the second and third 90 targets).

Understanding retesting

There is a paucity of literature exploring reasons for retesting after a positive HIV result, particularly among those who are already initiated on ART. Since all pregnant patients are referred to the HIV testing counsellors regardless of HIV or ART status, the opportunity for reaffirmation of diagnosis may have prompted retesting, however further research may be needed to better understand reasons for retesting more broadly.

Various factors may be associated with non-disclosure of HIV-positive status to healthcare professionals. Most studies have explored non-disclosure of HIV status to family and friends[16,17]. One study indicates that non-disclosure to health professionals is as high as 40% in certain settings[16]. Societal stigma, feelings of embarrassment, and denial may all contribute to non-disclosure and seeking repeat testing[3,16,18]. Another reason, less explored in the literature, is patient understanding of a diagnosis of HIV. A survey conducted in South Africa, showed that only 91% of patients with a previous HIV test were aware of their results[19]. Whether an awareness of a positive result translates to understanding the diagnosis is not well defined. While there are several studies that demonstrate the link between health literacy and health outcomes, most focus on print literacy[20,21]. In the South African setting, patients may be more reliant on oral literacy which may be limited by language barriers between patients and healthcare professionals, rushed consultations and long waiting

times. Prior to implementation of the universal test-and-treat strategy in 2015, patients were not eligible for ART until certain criteria were met. This may have led to false perceptions that patients who tested positive for HIV but were not treated, and remained asymptomatic, did not have the infection. These factors may have resulted in apparent non-disclosure of HIV status and subsequent retesting, although further research is imperative to better understand this phenomenon. Additionally, both quantitative and qualitative studies have shown the impact of patient-provider engagement on retention in HIV care[22,23]. Poor quality engagement between patient and provider may prompt a need for re-diagnosis and treatment elsewhere. Further research is needed to explore the impact of quality of care on retesting and retention in care.

Those who were referred for PoCT by healthcare workers in other CHC services were more likely to be retesting than those receiving PoCT as part of antenatal care. Younger patients were more likely to retest than older patients. Reasons for these associations require more detailed analyses with consideration for confounding factors such as educational status, socio-economic status, and family support. Linkage of PoCT results to a consolidated individuated data environment contributes to uncovering such phenomena and the ensuing bias introduced when interpreting HIV testing data.

Linkage to care and treatment in those testing positive

Longitudinal analyses of individual patient data can assess implementation of HIV care guidelines, in this case, universal test-and-treat. Of those newly diagnosed with HIV, more than half (58.1%) were initiated on ART at study closure, while only a quarter (25%) initiated ART on the day of testing. Our results indicate that the universal test-and-treat strategy has not been fully implemented. Further research is needed to better understand why 41% of newly diagnosed HIV-positive patients had not initiated ART. Although reasons for non-initiation may not be explicit in data available on the PHDC, alerting systems can be developed to flag patients who have not engaged in appropriate HIV care at future consultations or to find and encourage patients to return to HIV care for further management.

Limitations

There are various pitfalls of using routine data for monitoring and evaluation[24,25], particularly data accuracy and completeness. Since PoCT data are entered as routine clerical tasks in settings where staff have high patient loads, the risk of inaccuracies is high. The 50 patients who self-reported HIV-positive but retested negative likely represent capturing errors of the result on the HTS form, as three quarters of these patients had evidence of HIV in the cascade. However, further studies are warranted to explore whether these may represent patients who had a previous false positive HIV PoCT. Furthermore, high staff turnover among HIV counsellors and nursing staff may result in inadequately trained staff members conducting tests and completing forms, resulting in erroneous entries and incomplete data. The use of a single rapid test for many retesting HIV-positive patients was most likely for reaffirmation of diagnosis, hence the deviation from the National HIV testing protocol. However, there were patients without prior evidence of HIV who had a single positive test or results entered in incorrect fields, suggesting training gaps. By uncovering such training gaps, digitisation may prompt targeted training interventions, thereby strengthening clinical governance. Limited staff involvement and understanding of data use may also contribute to de-prioritisation of data capturing in the face of more pressing clinical concerns[25]. The quality of PoCT and the validity of the results may be called to question as facility staff are not laboratory-trained and may not be able to adhere to strict quality control criteria[26]. Additionally, during both phases of the intervention, we relied on internal data fidelity processes. A formal assessment of captured data quality was therefore not conducted and may have impacted the results. Since HIV PoCT is the standard of care for HIV diagnosis and referral, digitisation of available results will nonetheless add value to the HIV cascade through earlier ascertainment of HIV status and linkage to care. Predictors for retesting could not be fully evaluated in this study, as variables were limited to routinely captured HTS forms. Data on other confounding factors were thus not collected and adjusted for. Furthermore, groups included in the regression analysis for retesting may well be heterogenous. Further analyses are needed to explore these factors.

Conclusions

This study clearly demonstrates the important contribution of digitised PoCT data, within a robust PHDC system, to better evaluate the HIV treatment cascade at both a population and an individual level. Improved estimation of the magnitude of retesting may have substantial implications for assessing interventions to achieve 90-90-90 targets. Considerable resources are channelled into achieving the first 90 through wide-scale HIV testing. However, without quantifying the proportion of HIV-infected patients who are retesting, this target cannot be appropriately evaluated. Furthermore, the findings of this study demonstrate the contribution of PoCT in evaluating the second 90 using routine data within the PHDC, and differentiating those who need linkage to care following a new diagnosis, from those who need retention and re-engagement on ART.

While this study evaluated the population-level utility of PoCT, individual utility may also be demonstrated. Health care professional access to PoCT results along with other laboratory data, may enhance clinical consultations by improving efficiency during patient history-taking and avoiding duplication of tests, which are uncomfortable and invasive to patients as well as costly to the health system. Timely access to PoCT data and subsequent care access may provide actionable opportunities to follow-up individual patients who have not linked to care and may enhance operational management by facilitating improved monitoring of testing services. It is recommended that quantitative and qualitative studies are conducted to better evaluate these other perceived benefits of PoCT result digitisation.

Authorship

All authors have read and approved the final manuscript. NJ, AB, BR and JH designed the research study. NJ conducted the research. NJ and AB wrote the manuscript. BR and JH made significant intellectual contributions to the manuscript preparation. EK and JM provided practical support for the research and contributed to the manuscript preparation. AH provided technical support in data linkage and analyses.

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Chapter 6: The impact of evolving maternal antiretroviral therapy guidelines on vertical transmission of HIV in the Western Cape, South Africa

Relevance to this thesis:

Chapter 6 brings together the different cascade points evaluated in the previous chapters in order to demonstrate the utility of HIV case ascertainment from maternal utilisation of antenatal care all the way along the vertical transmission prevention cascade, to HIV ascertainment among infants (primarily through laboratory-based HIV testing). Epidemiological trends in vertical transmission prevention over the full 10-year study period are explored, highlighting the changes over three distinct maternal ART policy periods. This chapter emphasises the value of routine individuated data for case-based surveillance using a vertical transmission prevention lens.

Contribution of candidate and co-authors:

The candidate, NJ, conceptualised the study under the guidance of AB and BR. NJ conducted the study, analysed the data, interpreted the results and wrote the manuscript. AH and FP contributed to data curation and provided data support. All co-authors commented on drafts and approved the final version for publication submission.

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Abstract

Introduction

Despite the universal HIV test and treat policy in South Africa, vertical transmission continues to occur. We evaluated the temporal effectiveness of vertical transmission prevention (VTP) over three maternal antiretroviral treatment (ART) policy periods (three-drug ART accessible to those with CD4 counts <200 cells/ μ l [January 2010 – March 2010]; <350 cells/ μ l [April 2010 – April 2013]; and lifelong ART regardless of CD4 count [May 2013 – December 2020]) in Western Cape, South Africa using public sector routine individuated data.

Methods

We conducted a retrospective cohort study with child HIV infection as the primary outcome. The cohort of 842 641 pregnancies from 2010 – 2020, inclusive of child HIV exposure, maternal ART, and child outcomes, was enumerated using administrative, laboratory and pharmacy data. Multivariable logistic regression was used to explore associations with vertical transmission.

Results

The proportion of pregnant women living with HIV (WLWH) initiating ART prior to pregnancy increased from 20.9% in 2010 to 71.1% in 2020. Of all pregnancies 17.1% (143 987/842 641) were HIV exposed and 16.3% (137 572/842 641) were assigned a child HIV outcome, of whom 3966 (2.9%) were HIV positive by 24 months. Among children with known maternal HIV exposure (143 987), 32.0% had unknown HIV status and 2.1% were diagnosed with HIV by study closure. In 2020, HIV status was ascertained in 87.2% (16 908/19 382) of children exposed to HIV. Children born in policy period 3 were less likely to have HIV than children born in policy period 2 (aOR 0.66; 95% CI 0.60 – 0.72), mediated through expanded ART access. Between 2017 and 2020, 16.5% of child HIV diagnoses were from pregnancies without maternal HIV exposure records. Young maternal age, no antenatal ART, previous TB and no records of antenatal visits were associated with vertical transmission in all periods.

Conclusions

Using individuated routine data, we report an increase in WLWH initiating ART prior to pregnancy, and a decline in vertical transmission of HIV over three ART policy periods. Although HIV diagnosis amongst children exposed to HIV has reduced over time, the proportion of infections in children without established exposure emphasises the need to optimise VTP opportunities.

Introduction

Vertical transmission (VT) of HIV (known previously as mother-to-child transmission) from pregnant women living with HIV (WLWH) to their children is a preventable adverse outcome of HIV in pregnancy and carries considerable risk of paediatric morbidity and mortality(1,2). The WHO Initiative for elimination of vertical transmission of HIV highlights the importance of early antenatal care for all WLWH, early HIV diagnosis and antiretroviral treatment (ART) initiation(3,4). Despite the implementation of lifelong ART for all pregnant WLWH (option B+) and later Universal Test and Treat in South Africa, VT continues to occur during pregnancy, delivery and during the post-partum period, if breastfeeding(5,6).

As ART access in South Africa progressed from 1999, several large studies were conducted using routine data to highlight the impact of ART and vertical transmission prevention (VTP) programmes on maternal and child outcomes and the need for scale up and revision of guidelines, both internationally and locally(7–13). In the current universal ART era, few studies have used routine data to evaluate vertical transmission throughout pregnancy and post-partum. This may be due to challenges of accessing complete routine programmatic data. More recent studies in the Western Cape province, South Africa have been based on case histories from single facilities or limited to a few selected facilities(1,14–16). Although these studies provide valuable insights, results have limited external validity for population-wide inference and action.

The Western Cape Provincial Government in South Africa has developed a Provincial Health Data Centre (PHDC) in which all public-sector electronic individual-level routine data are consolidated on a single platform, enabling the description of temporal changes in population-wide outcomes and risk factors for VT along the VTP cascade (an evolving set of sequential steps in the health services pathway to prevent VT)(17). Using routine province-wide individuated data, we evaluated the temporal effectiveness of VTP over different maternal ART and infant polymerase chain reaction (PCR) testing policy periods since 2010, and associations with transmission.

Methods

Study Design and Population

The study was set in the Western Cape province, South Africa, which is comprised of one urban district, the Cape Metropolitan, and five less urbanised districts, Overberg, Garden Route, Central Karoo, West Coast and Cape Winelands. We conducted a retrospective cohort study including all pregnancies of women attending public health facilities within the Western Cape from January 2010 to December 2020 with child HIV infection as the primary outcome.

Data Sources and Processing

The study cohort was enumerated using the PHDC Maternity Cascade which links electronic records of all patients with electronic administrative or laboratory evidence indicative of pregnancy. Pregnancies were identified by a rhesus antibody test (conducted routinely at first antenatal visit), a pregnancy test, birth register record, antenatal visit or maternal discharge summary. Only pregnancies with live birth outcomes were included. Mother-child pairs were electronically linked by the PHDC.

The PHDC HIV care cascade was linked to the maternity care cascade to determine maternal and child HIV status and associated HIV interventions (Figure 6.1).

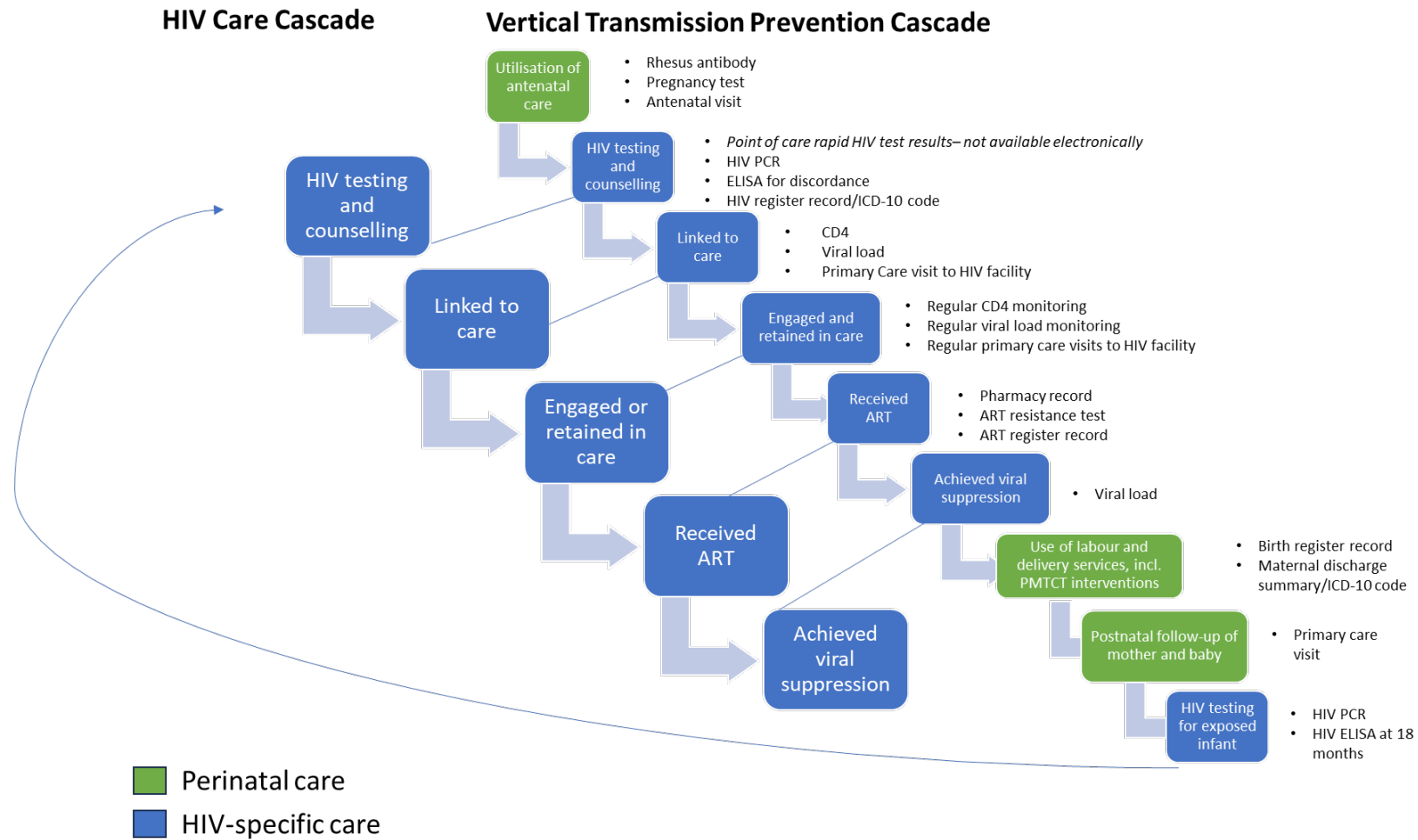


Figure 6.1: PHDC HIV and VTP Cascade data points

The first step of the HIV care cascade, diagnosis of HIV, is typically instigated following positive point-of-care tests for adults. By protocol, all pregnant women not known to have HIV, are offered rapid point-of-care HIV testing on their first antenatal presentation to a health facility(18). Since 2013, repeat HIV testing with point-of-care HIV rapid assays should be offered to women with negative/unknown HIV status, in the second and third trimesters, in labour or immediately after delivery, at 6 weeks after delivery and every 3 months while breastfeeding(18,19). These results are not routinely digitised and are therefore unavailable to the PHDC. Maternal HIV positive PHDC status is ascertained if laboratory testing shows a detectable viral load, positive HIV ELISA test, a test for ART resistance or evidence of initiating ART in either pharmacy or administrative information systems, HIV register record or HIV-related International Classification of Diseases (ICD) Tenth Revision code.

Over time, various policy changes have been implemented which impacted routine data available to the PHDC. For example, changes in CD4 and viral load (VL) monitoring in pregnant women took place in 2013 with VL testing becoming the preferred tool for treatment monitoring and follow-up CD4 testing being no longer conducted routinely(18–20). Notable policy changes to ART initiation for WLWH and HIV testing of children HIV exposed are shown in Figure 6.2 (21,22).

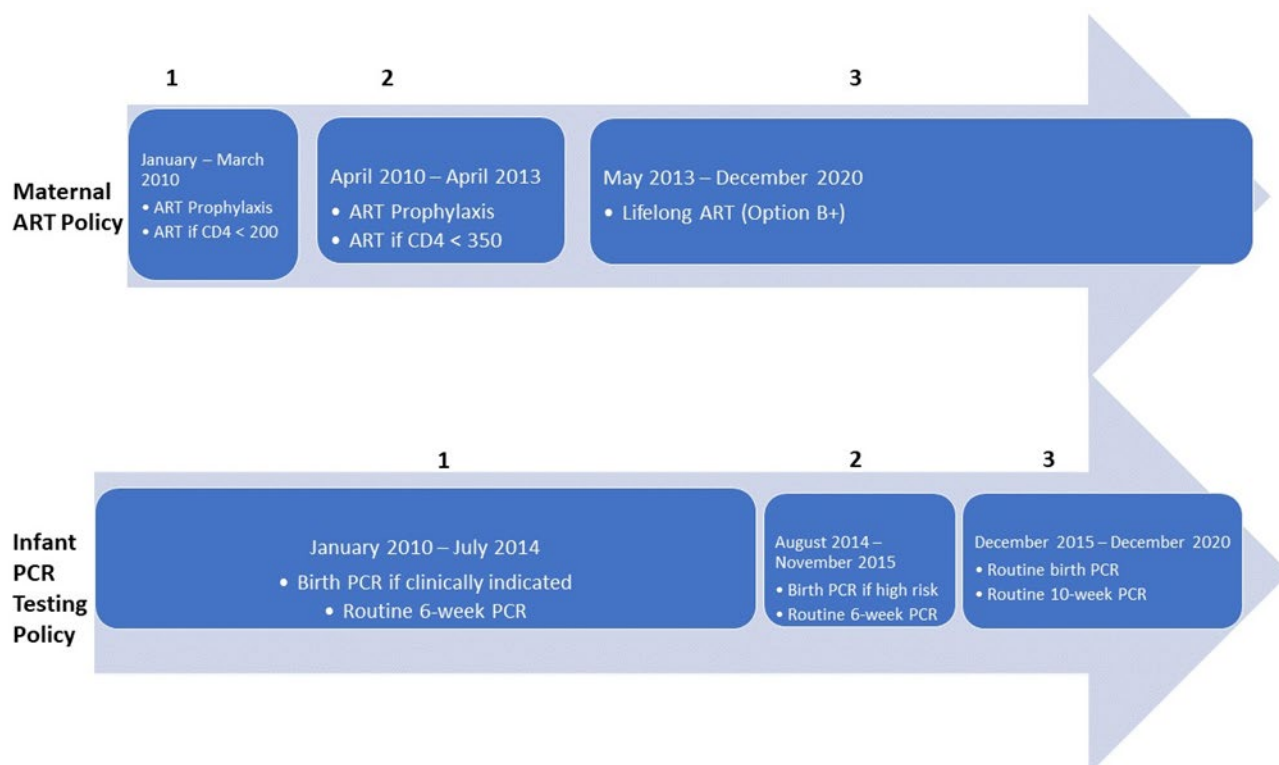


Figure 6.2: Changes in Maternal antiretroviral therapy (ART) and Infant HIV PCR testing policies, Western Cape, South Africa 2010 – 2020

Infants exposed to HIV are tested for HIV using an HIV PCR test (Figure 6.2). From 2015 onwards, routine infant PCR tests were conducted in all infants exposed to HIV within 48 hours of birth, at 10 weeks and 18 weeks (only if breastfeeding and received Nevirapine for 12 weeks), followed by a rapid HIV test at 9 months with confirmatory PCR test if positive. From 2020, routine tests at 18 weeks were replaced by a PCR test at 6 months(18,19). These results are digitised in the National Health Laboratory System (NHLS) and integrated by the PHDC, providing reliable routine evidence of HIV status of infants in addition to other HIV-specific routine data such as viral load testing and ART.

HIV exposure was defined as a child whose mother had evidence of HIV antenatally or up to two years from delivery, as breastfeeding is more likely to be discontinued by 24 months(23). Children whose mothers had no evidence of HIV up to two years from delivery were considered to have unknown exposure. For multiple pregnancies (e.g. twins and triplets), only the first child's HIV outcome was assigned to the pregnancy. Vertical transmission diagnosis

was defined as “early” if a child’s HIV diagnosis was recorded at or before seven weeks of age, and “late” if diagnosis was after seven weeks of age.

Analysis

Data were analysed using Stata 17 (Stata Corporation, College Station, Texas, USA). Measures of central tendency and dispersion were used to describe continuous variables, depending on distribution. Categorical variables were described using proportions and 95% confidence intervals. Viral load and CD4 test results within one year before and after the estimated pregnancy start date were categorised according to Western Cape protocol-related result thresholds(18,19). Viral load status was considered viraemic or suppressed if the last available VL, within 1 year of estimated pregnancy start date, was greater (inclusive) or less than 1000 copies/ml, respectively. Data were further analysed according to maternal ART policy period as described in Figure 6.1 (22,24), with 2019 descriptive characteristics also presented as the most recent pre-COVID-19 patient profile within the dataset. Vertical transmission characteristics were analysed for the full cohort period and a shorter three-year period (2017 – 2020) to reflect more recent characteristics under updated policy guidelines.

Routine data on antenatal care, maternal and child HIV care, ART and other descriptive characteristics were included for multivariable analyses of risk factors for vertical transmission. A directed acyclic graph was drawn using DAGitty v3.1 (Appendix D) to explore causal relationships and select variables available from routine data for model building, addressing collider, collinear and confounder effects. Electronic evidence of prior pregnancy was excluded from model building due to incomplete electronic systems in earlier years precluding ascertainment of pregnancy. Four logistic regression models were built to demonstrate the impact of selected variables. Model 1 included maternal ART policy period without adjustment for maternal ART status and associated laboratory outcomes. Model 2 included both maternal ART policy period and maternal ART status, to explore potential mediation by ART status. Models 3 and 4 were restricted to policy period 3 to demonstrate the effect of VL and CD4 independently due to collinearity with policy period. Model 3 included VL status combined with

ART status into a composite variable. Model 4 included combined VL and ART status as well as CD4 status. Unadjusted and adjusted odd ratios are reported. For variables with missing data, a missing data category was included. This was preferred to imputation methods as these are not data missing at random, and the fact of missingness is of interest.

Ethical considerations

The study was approved by the University of Cape Town Human Research Ethics Committee (HREC 083/2021) and the Western Cape Provincial Health Research Committee. Data from the PHDC are unconsented, de-identified data housed by the Western Cape Provincial Department of Health. Data were fully de-identified before release for the study according to the Western Cape Department of Health Data Access Policy Guidelines.

Results

Between 2010 and 2020, 842 641 pregnancies were included in the study (Table 6.1). Most pregnancies (70.5%) were recorded in the Cape Metro district, with the proportion differing by policy period (Table 6.1). The proportion of pregnancies among women diagnosed with HIV prior to or during pregnancy was higher in maternal ART period 3 (17.2%) than in periods 1 (9.2%) or 2 (10.9%).

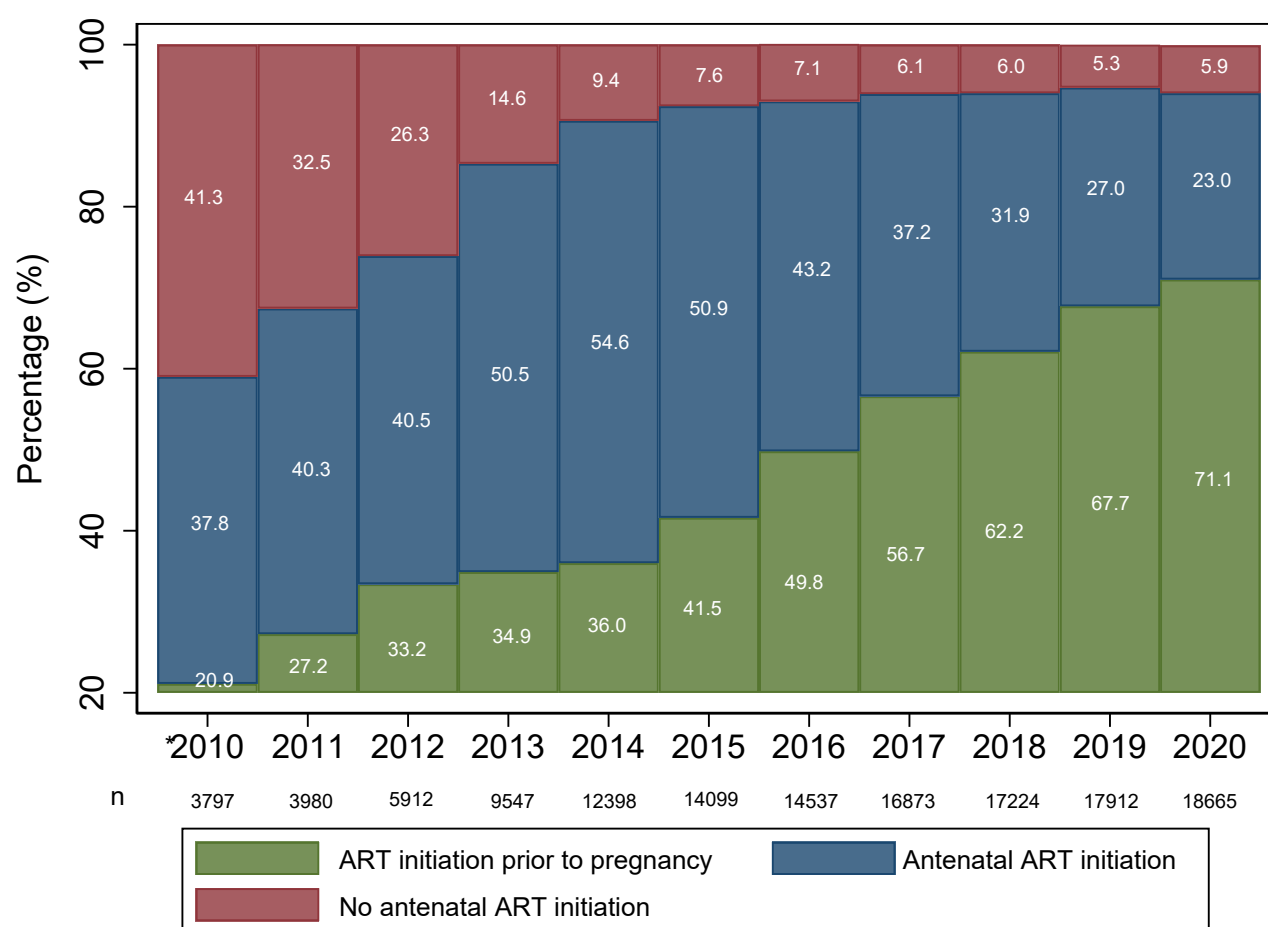
With respect to PCR testing policy periods, 29.1% of pregnancies were during policy period 1 (January 2010 – January 2014), 13.2% in period 2 (August 2014 to November 2015) and 57.7% in period 3 (December 2015 to December 2020).

Table 6.1: Descriptive characteristics of pregnancy cohort by Maternal ART Policy Period

Variables	Maternal ART Policy Period 1		Maternal ART Policy Period 2		Maternal ART Policy Period 3				Total	
	Jan – Mar 2010		Apr 2010 – Apr 2013		May 2013 - Dec 2020		2019		2010 - 2020	
	(n=9 946)		(n= 140 710)		(n=691 985)		(n = 99 055)		(N= 842 641)	
	1.2%		16.7%		82.1%					
	n	%	n	%	n	%	n	%	n	%
District										
Cape Winelands	999	10.0	16412	11.7	95132	13.8	12858	13.0	112543	13.4
Central Karoo	10	0.1	52	0.0	6246	0.9	1234	1.3	6308	0.8
City of Cape Town Metro	8626	86.7	114552	81.4	471183	68.1	64891	65.5	594361	70.5
Garden Route	284	2.9	9126	6.5	61511	8.9	9242	9.3	70921	8.4
Overberg	10	0.1	191	0.1	23127	3.3	4220	4.3	23328	2.8
West Coast	3	0.0	90	0.06	29770	4.3	5476	5.5	29863	3.5
Unknown	14	0.1	287	0.2	5016	0.7	1134	1.1	5317	0.6
Maternal age (median, IQR in years)	26.3 (22.1 – 31.4)		26.4 (22.1 – 31.2)		26.8 (22.4 – 31.7)		27.0 (22.7 – 32.1)		26.7 (22.4 – 31.6)	
Electronic evidence of prior pregnancy										
0	7929	79.7	103011	73.2	405737	58.6	51827	52.3	516677	61.3
1	1733	17.4	31043	22.1	192283	27.8	29440	29.7	225059	26.7
2	248	2.5	5761	4.1	68704	9.9	12268	12.4	74713	8.9
3	33	0.3	773	0.6	19244	2.8	4021	4.1	20050	2.4
≥4	3	0.03	120	0.1	6015	0.9	1499	1.5	6138	0.7
Maternal HIV status at close of study*										
Evidence of HIV - status	996	10.0	13777	9.8	58119	8.4	7183	7.3	72892	8.7
Evidence of HIV + status	2056	20.7	29957	21.3	137153	19.8	18968	19.2	169166	20.1
No HIV evidence	6894	69.3	96976	68.9	496713	71.8	72904	73.6	600583	71.2
Maternal HIV timing in pregnancy period										
HIV + before or during pregnancy	911	9.2	15370	10.9	118663	17.2	17912	18.1	134944	16.0
HIV + within 2 years of delivery	191	1.9	2582	1.8	6270	0.9	708	0.7	9043	1.1
HIV + 2 years after delivery	954	9.6	12005	8.5	12220	1.8	348	0.4	25179	3.0
HIV - or unknown	7890	79.3	110753	78.7	554832	80.2	80087	80.9	673475	79.9
Previous TB	1026	10.3	13317	9.5	54904	7.9	6943	7.0	69247	8.2
No recorded antenatal visits	3401	34.2	51952	36.9	183207	26.5	22347	22.6	238560	28.3
Maternal ART (n=169 166)	2056		29957		137153		18 968		169166	
ART started before pregnancy	171	8.3	4596	15.3	65613	47.8	12121	63.9	70380	41.6
ART started during pregnancy	281	13.7	6308	21.1	44786	32.7	4836	25.5	51375	30.4
ART started postnatally HIV + during pregnancy	202	9.8	1722	5.8	1842	1.3	174	0.9	3766	2.2
ART started postnatally	1049	51.0	13785	46.0	16004	11.7	824	4.3	30838	18.2
No ART	353	17.2	3546	11.8	8908	6.5	1013	5.3	12807	7.6
Antenatal VL (copies/ml) status among those with HIV before/during pregnancy (n=134 944)	911		15370		118663		17 912		134944	
VL suppressed (<1000)	190	20.9	6205	40.4	82637	69.6	12 975	72.4	89032	66.0
Viraemic (≥1000)	49	5.4	1092	7.1	18002	15.2	2 624	14.7	19143	14.2
VL not available	672	73.8	8073	52.5	18024	15.2	2 313	12.9	26769	19.8
Viral load status and Antenatal ART status amongst those with HIV before/during pregnancy (n=134 944)	911		15370		118663		17912		134944	
Suppressed, on ART before/during pregnancy	181	19.9	5930	38.6	79149	66.7	12497	69.8	85260	63.2
Viraemic, on ART before/during pregnancy	40	4.4	933	6.1	16700	14.1	2469	13.8	17673	13.1
VL unavailable, on ART before/during pregnancy	231	25.4	4041	26.3	14550	12.3	1991	11.1	18822	14.0
Suppressed, no antenatal ART record	9	1.0	275	1.8	3488	2.9	478	2.7	3772	2.8
Viraemic, no antenatal ART record	9	1.0	159	1.0	1302	1.1	155	0.9	1470	1.1
VL unavailable, no antenatal ART	441	48.1	4032	26.2	3474	2.9	322	1.8	7947	6.0
Last CD4 (cells/μl) within 1 year before estimated pregnancy start among those with antenatal initiation of ART (n= 51375)	281		6308		44786		4836		51375	
Median; IQR	301 (233.9 – 342.9)		336.9 (254 – 430.9)		505 (366.0 – 671)		455 (305.5 – 640.5)		470 (332.1 – 640.0)	
CD4 <200	6	2.1	145	2.3	381	0.9	36	0.7	532	1.0
CD4 200 – 350	25	8.9	468	7.4	1006	2.3	65	1.3	1499	2.9
CD4 >350	9	3.2	521	8.3	4785	10.7	211	4.4	5315	10.4
CD4 result not available	241	85.8	5174	82.0	38614	86.2	4524	93.6	44029	85.7
Last CD4 (cells/μl) among those with a CD4 test within 2 weeks of antenatal ART initiation (n=31 813)	24		1069		30720		3557		31813	
Median; IQR	179.2 (118.5 - 222.3)		249.6 (169.7 - 318)		376 (253 - 533)		362 (246 - 510)		369.2 (248 - 526.8)	
CD4 <200	17	70.8	363	34.0	4824	15.7	587	16.5	5204	16.4
CD4 200 – 350	5	20.8	553	51.7	8856	28.3	1113	31.3	9414	29.6
CD4 >350	2	8.3	153	14.3	17040	55.5	1857	52.1	17195	54.1

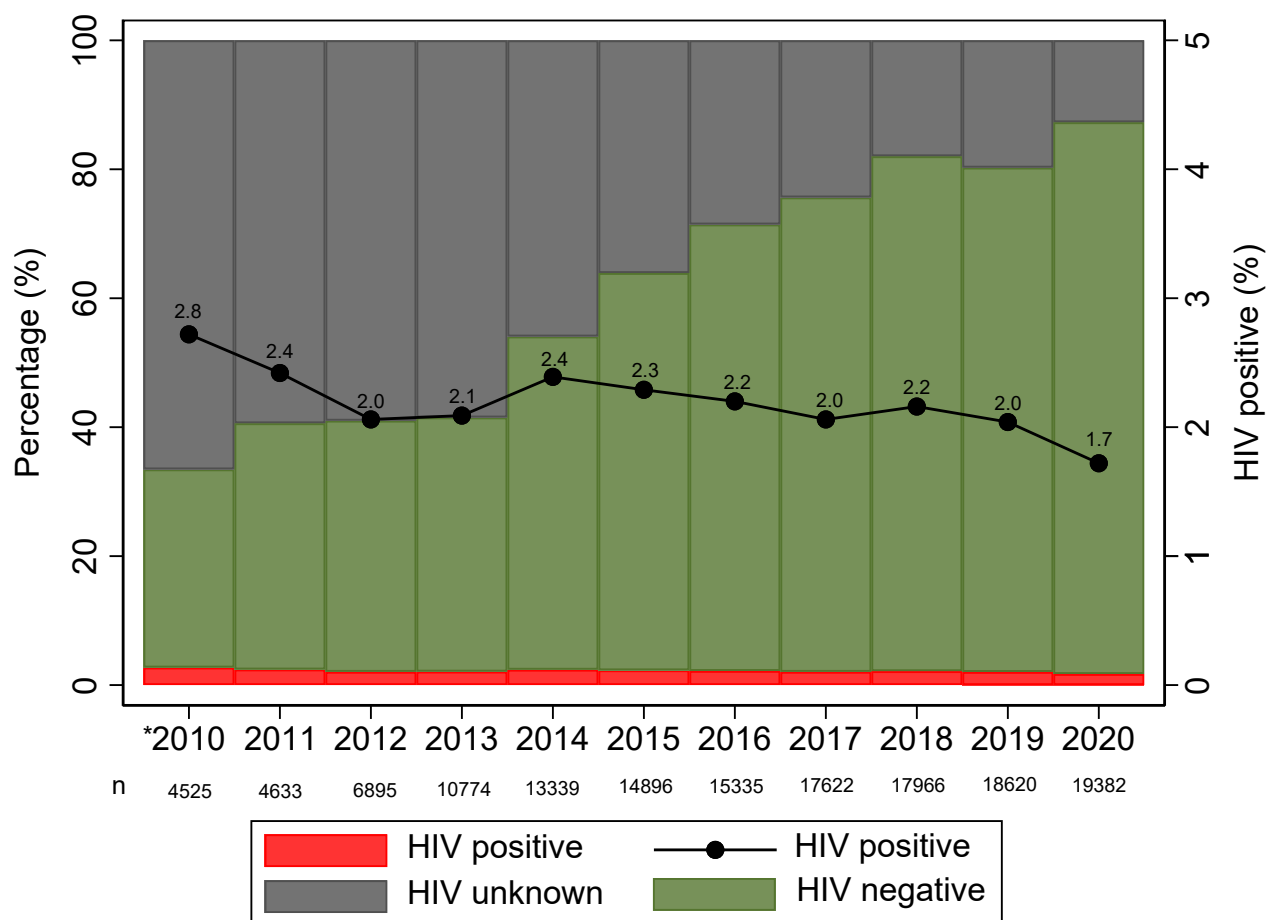
* HIV diagnosis is based on point-of-care tests that are not recorded electronically. No HIV evidence therefore includes those who tested negative on point-of-care tests and therefore have no subsequent electronic record of HIV.

The proportion of WLWH initiating ART prior to pregnancy increased over time. In 2020, 5.9% (1 103/18 665) of pregnant women with HIV had not initiated ART prior to or during the antenatal period compared to 41.3% (1 568/3 797) in 2010 (Figure 6.3).



*Policy period 1: Jan – Mar 2010; policy period 2: Apr 2010 – Apr 2013; policy period 3: May 2013 – Dec 2020

Figure 6.3: Proportion of maternal antenatal antiretroviral therapy (ART) initiation 2010 – 2020



***Policy period 1:** Jan – Mar 2010; **policy period 2:** Apr 2010 – Apr 2013; **policy period 3:** May 2013 – Dec 2020

Figure 6.4: HIV status at 24 months among children HIV exposed 2010 – 2020

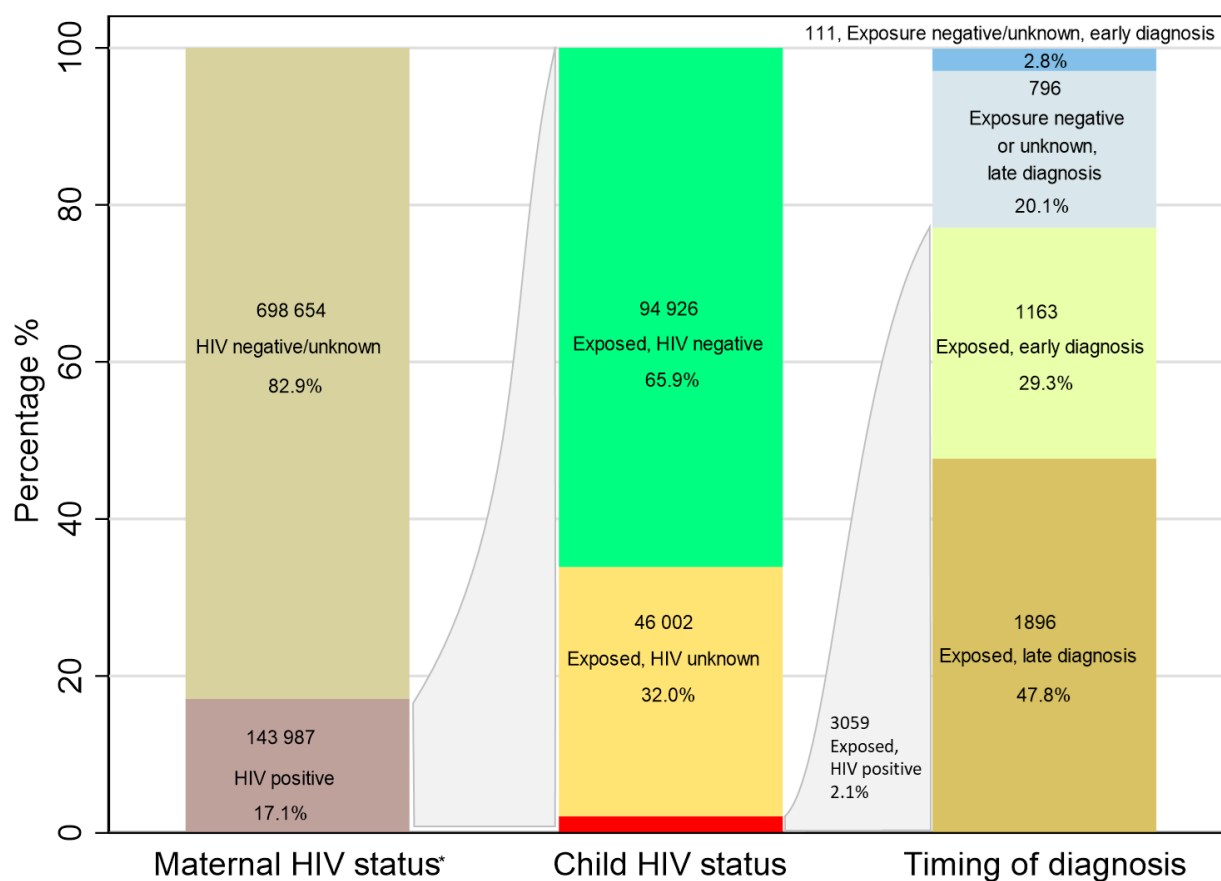
Vertical transmission of HIV

Of the 842 641 pregnancies, 137 572(16.3%) had a record of child HIV status. Of these, 133 606 (97.1%) children were HIV negative and 3 966 (2.9%) HIV positive by 24 months. Amongst the 3966 children with HIV, median time from birth to HIV diagnosis was 181 days (IQR 33 – 603), and 3 083 (77.7%) were diagnosed with at least one positive HIV PCR test. HIV status of the remaining 883 (22.3%) children with HIV was determined by HIV ELISA testing for children above 18 months of age, or other evidence of HIV where PCR data were not available (for example ART details). Of these 883 children, only 10.2% (90) were diagnosed early (before 7 weeks of age). Among all children with HIV, the percentage of early diagnosis was higher in maternal ART policy period 3 (33.9%) compared to policy periods 1

(29.8%) and 2 (23.7%). This is likely reflective of earlier routine infant PCR testing in maternal ART policy period 3.

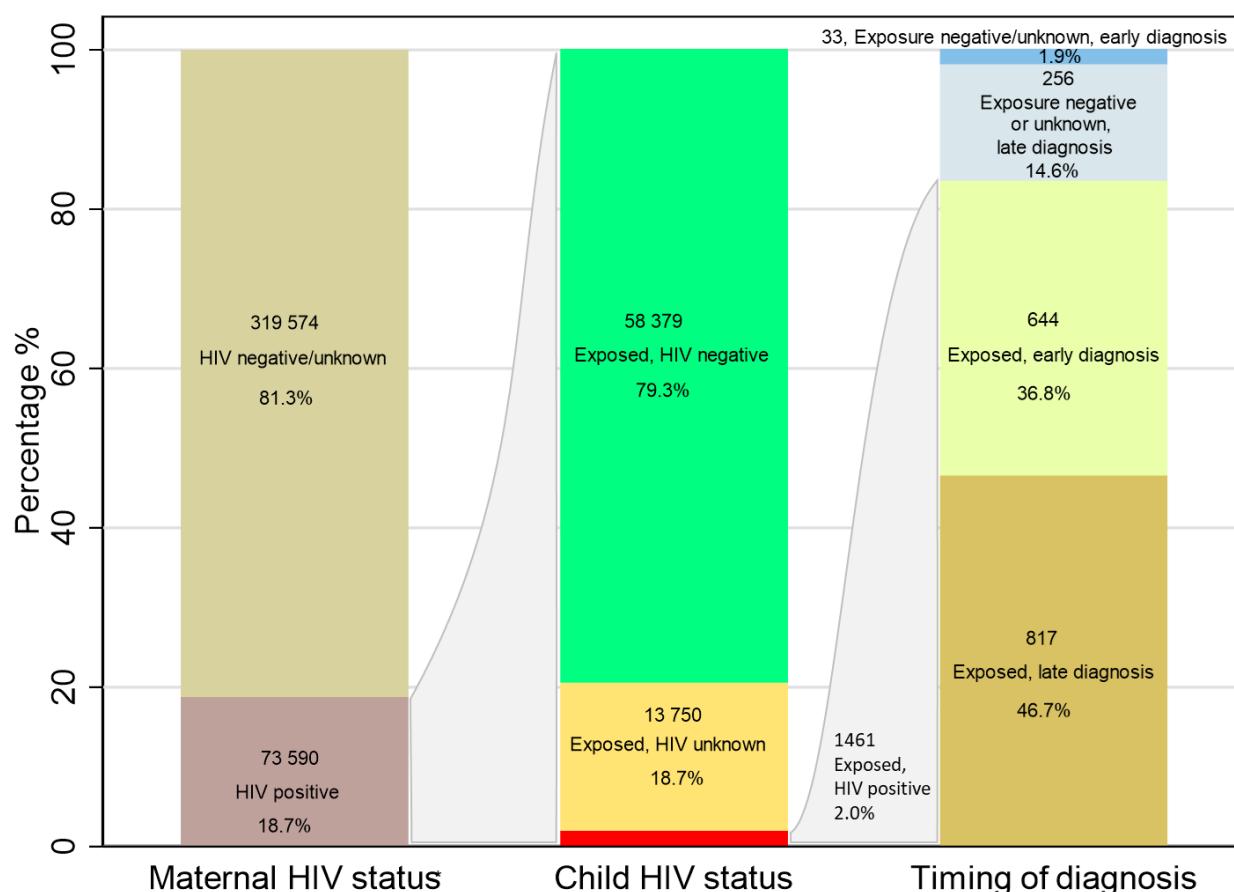
Figure 6.4 shows that while the proportion of children with HIV remained low, the proportion of children exposed with unknown HIV status decreased whilst those testing HIV negative increased. Of the 3 966 children with HIV, 73.2% had evidence of initiating ART.

Overall, 390 (9.8%) of the 3966 children with HIV had apparent negative maternal exposure (electronic record of negative HIV status during pregnancy up to 2 years after delivery) and 517 (13.0%) had unknown maternal exposure. Figures 6.5a and b summarise maternal and child HIV status over the full study period and more recently (2017 – 2020), respectively. Of all pregnancies, 17.1% (143 987) had known maternal HIV exposure. Of these, 2.1% (95% CI 2.1 – 2.2) had a child diagnosis of HIV, 65.9 % (95% CI 65.7 – 66.2) were HIV negative and 32.0% (31.7 – 32.2%) had no HIV diagnosis (Figure 6.5a).



*Maternal HIV status is mother's HIV status during the index pregnancy or within 2 years of delivery

Figure 6.5a: Vertical transmission characteristics (2010 – 2020)



**Maternal HIV status is mother's HIV status during the index pregnancy or within 2 years of delivery*

Figure 6.5b: Vertical transmission characteristics (2017 – 2020)

Factors associated with vertical transmission of HIV

Children born in maternal ART policy period 3 were less likely to be diagnosed with HIV than children born in policy period 2 (aOR 0.66; 95% CI 0.60 – 0.72) (Model 1, Table 6.2). Across all periods, younger maternal age, lack of maternal antenatal ART, a previous TB diagnosis and no record of antenatal visits prior to delivery were associated with vertical transmission of HIV (Table 6.2). Comparing models 1 and 2, Table 6.2 shows that the association with maternal ART policy period is mediated by maternal ART use. The impact of suppressive antenatal ART is clearly demonstrated in policy period 3 with those not on ART, 14.44 (95% CI 12.90 – 16.16) times more likely to have vertical transmission of HIV than those on suppressive ART (Model 3).

Table 6.2: Comparison of different models for factors associated with vertical transmission of HIV based on routine data

Variable*	Policy periods 1 - 3			Policy period 3	
	OR (95% CI)	Model 1 aOR (95% CI)	Model 2 aOR (95% CI)	Model 3 aOR (95% CI)	Model 4 aOR (95% CI)
Maternal ART Policy period					
Policy period 1	1.33 (0.98-1.81)	1.29 (0.95-1.76)	1.06 (0.75-1.50)		
Policy period 2	1.00	1.00	1.00		
Policy period 3	0.59 (0.54 -0.64)	0.66 (0.60-0.72)	1.12 (1.00-1.24)		
Maternal age category (years)					
15 - 19	1.42 (1.26-1.59)	1.46 (1.30-1.63)	1.67 (1.46-1.91)	1.35 (1.16-1.59)	1.37 (1.17-1.61)
20-24	1.24 (1.15-1.34)	1.29 (1.20-1.39)	1.31 (1.20-1.42)	1.17 (1.07-1.29)	1.18 (1.07-1.31)
25-39	1.00	1.00	1.00	1.00	1.00
>39	0.82 (0.67-1.00)	0.80 (0.66-0.98)	0.78 (0.62-0.98)	0.86 (0.67-1.10)	0.86 (0.67-1.10)
Electronic evidence of prior pregnancies					
0	1.00				
1	0.90 (0.83-0.97)				
2	0.83 (0.75-0.93)				
3	0.90 (0.74-1.08)				
≥4	0.96 (0.70-1.32)				
Maternal ART					
ART prior to pregnancy	1.00		1.00		
Antenatal ART	1.24 (1.14-1.36)		1.31 (1.20-1.43)		
No antenatal ART	6.43 (5.91-7.00)		4.82 (4.40-5.28)		
No recorded antenatal visits	1.72 (1.60-1.84)	1.57 (1.47-1.69)	1.36 (1.25-1.47)	1.13 (1.02-1.24)	1.13 (1.02-1.24)
Metropolitan district	0.75 (0.70-0.80)	0.85 (0.79-0.91)	0.94 (0.86-1.02)	0.99 (0.91-1.09)	0.99 (0.90-1.08)
History of TB	2.16 (2.01-2.32)	2.14 (1.99-2.29)	2.18 (2.02-2.35)	1.85 (1.69-2.02)	1.79 (1.64-1.96)
Viral Load and ART status **					
Suppressed, ART before/during pregnancy	1.00			1.00	1.00
Viraemic, ART before/during pregnancy	5.17 (4.66-5.74)			4.75 (4.27-5.28)	4.56 (4.10-5.08)
VL unavailable, ART before/during pregnancy	4.10 (3.63-4.64)			3.93 (3.47-4.45)	3.90 (3.44-4.42)
VL unavailable, no antenatal ART record	15.60 (14.01-17.38)			14.44 (12.90-16.16)	14.31 (12.75-16.07)
Last CD4 before booking value (cells/μl) **					
CD4 < 200	1.00				1.00
CD4 200 – 350	0.66 (0.52-0.84)				0.87 (0.68-1.11)
CD4 >350	0.32 (0.26-0.40)				0.52 (0.42-0.65)
CD4 result not available	0.54 (0.45-0.65)				0.65 (0.53-0.79)

OR - Odds Ratio, aOR - Adjusted Odds Ratio, CI - confidence interval

*Outcome variable is infant HIV status at 24 months. Model 1 includes maternal ART policy period without adjustment for maternal ART, VL and CD4 count which are all impacted by the policy period. Model 2 includes both maternal ART policy period and maternal ART status. Model 3 includes VL status combined with ART status into a composite variable. Model 4 includes combined VL and ART status as well as CD4 status. Patients with VL status but no corroborating ART records were included in Models 1 and 2 but dropped from the models 3 and 4 (effect sizes remain unchanged).

**Restricted to maternal ART policy period 3

A sensitivity analysis excluding infant deaths during the study period (8712) did not show major impacts on model effects or child HIV trends.

Discussion

Our findings illustrate temporal trends in vertical transmission of HIV over three maternal ART policy periods in the Western Cape province, with an increasingly greater proportion of WLWH initiating ART prior to pregnancy, and declining vertical transmission of HIV over a 10-year period.

As we used routine data to assemble the study cohort, changes to the cohort over time may be related to variations in availability of routine electronic data. For example, the proportion of pregnancies from non-metropolitan districts was likely lower in earlier years as electronic evidence of pregnancy was limited due to less robust electronic systems in earlier years. Evidence of maternal HIV positive status was stable over time with estimates in earlier years higher than expected and estimates in later years more aligned with antenatal HIV seroprevalence surveys(25,26). This likely reflects more complete electronic records for WLWH in earlier years compared to those with no evidence of HIV.

Evidence of negative HIV status is low as HIV diagnosis is primarily based on point-of-care HIV tests that are not electronically captured(27). Amongst those testing positive, electronic records of HIV diagnosis and management after point-of-care diagnosis enable enumeration within the HIV cascade. Since antenatal HIV testing coverage in the Western Cape is high and a recent study reporting digitised point-of-care HIV test results showed the majority of pregnant WLWH testing negative, those with no evidence of HIV likely include a large proportion of women who tested HIV negative in point-of-care tests(27–29). The increasing proportion of maternal HIV diagnosis before pregnancy supports improved HIV ascertainment. The proportion of women testing HIV positive after pregnancy was lower in later years. This may be due to improved antenatal and pre-pregnancy diagnosis as well as there being less time within the maternal cohort for later pregnancies (cohort bias).

Trends in viral load and CD4 results reflect changing policy, with more viral load testing and fewer CD4 results available in later years illustrating the evolving guidance for more regular viral load testing in pregnancy, and CD4 count testing no longer being indicated for patients stable on ART, as well as earlier initiation of ART following implementation of Option B+ in 2013(30,31). We found an expected increase in median CD4 count at pregnancy start over time as access to maternal ART increased.

Temporal trends in ART initiation are progressing steadily in that greater proportions of WLWH were initiated on ART prior to or during pregnancy in later years. However, our study showed lower percentages of ART initiation prior to pregnancy in recent years (63.9% in 2019) compared to a smaller study in the Khayelitsha subdistrict (77.9% in 2017)(16). This difference may be expected given that Khayelitsha has the longest-standing ART programme in the Western Cape, but highlights the need for improved efforts to ensure all service opportunities to test and treat WLWH are utilised appropriately(13). Of concern, however, is the proportion of women with no evidence of ART in the most recent years pre-COVID (e.g., 5.3% in 2019). This may be due to loss to follow-up for various reasons including migration to a different province as well as incomplete electronic data capturing. These reasons may also apply to children HIV exposed with unknown HIV status, which, although decreasing over time, remains high at 18.7% in recent years (2017 – 2020).

The median age at HIV diagnosis in children of 181 days suggests either late transmission through breastfeeding or delayed diagnosis in many children. Since birth PCR records were not available for all children, exact timing of transmission cannot be discerned, but the lower proportion of late diagnosis in later years suggests improved access to HIV testing in PCR testing policy period 3. A recent study, however, notes that receipt of birth PCR testing from 2015 onwards decreased the likelihood of returning for follow-up testing, which may result in delayed diagnosis(5). With improved VTP programmes over time, a need for improvement in postnatal VT has been highlighted in several studies(23,24,32). The overall incidence of VT amongst those with known HIV exposure was 2.1%, comparable to findings in recent South

African literature(16,33). However, a considerable proportion of children with HIV had apparent negative (9.8%) or unknown (13.0%) HIV exposure. These may represent false negative maternal HIV results, missed opportunities for repeat maternal HIV testing, linkage to care and management during pregnancy, or women who may have been diagnosed and managed in other provinces. The decrease in the proportion of children HIV exposed with unknown HIV status and the corresponding increase in children with evidence of negative HIV status suggests temporal trends are understated as undiagnosed child HIV is less likely over time. For example, if a greater proportion of undiagnosed children were HIV positive in earlier years, there may have been a steeper decline in HIV positivity over time than reflected in this analysis.

Of concern is that 26.8% of children with HIV had no evidence of ART initiation. While this may again reflect incomplete electronic records or migration to other provinces, it is important to explore whether there were missed service opportunities for linkage to care, and to explore mechanisms to strengthen follow-up and record these actions electronically.

While our findings clearly demonstrate the impact on VT of evolving guidelines with expanded ART access in pregnancy, the importance of early suppressive ART initiation or intensification was also evident. This supports the urgent need to strengthen access to HIV testing and early antenatal care amongst all women to ensure prompt initiation of ART. In keeping with similar studies, findings from multivariable modelling demonstrate the impact of viraemia ($VL \geq 1000$) on vertical transmission, highlighting the urgent need to initiate ART in all eligible women and monitor viral load appropriately(1,14,33). Although CD4 count, viral load and ART are correlated, the association between CD4 count and vertical transmission persisted after adjustment, with a decreased risk of vertical transmission at higher CD4 counts.

The risk of vertical transmission of HIV decreases with maternal age, with those aged 15 – 19 years most likely to have a child with HIV. This may be because younger age groups are more likely to be diagnosed with HIV during pregnancy, rather than before, following acquisition during recent unprotected sexual encounters(27,34,35). Furthermore, risk factors for

adolescent HIV acquisition and pregnancy may also be risk factors for poor access to health care, including access to HIV testing. Diagnosis and treatment are further delayed if access to antenatal care is delayed, hence exposing the unborn infant to higher viral loads and increasing the risk of vertical transmission(1). The association between no antenatal care before delivery and vertical transmission is highlighted, supporting findings from similar studies(1,14,33). The notably lower proportion of pregnancies without antenatal care in policy period 3, and specifically 2019, suggest improved access to antenatal care as well as improved electronic record-keeping during pregnancy in later years. However, targeted interventions for adolescents and young women on regular HIV testing, HIV prevention, including safe sexual practices, and early antenatal care may be of benefit to address the high levels of vertical transmission in younger age groups(2,33,36). Previous TB was found to be another notable factor associated with vertical transmission. Although timing of TB disease in relation to HIV diagnosis and pregnancy were not evaluated in our study, this association may represent the association of co-morbidities with maternal health through immunosuppression, increased viral load and drug interactions, and as proxies for unmeasured socio-economic associations(37).

Limitations

Pregnancies from 2018 were evaluated for less than 24 months thus allowing fewer opportunities for ascertainment of HIV diagnosis and management in both mother and child. Since child HIV status was not known for all children who died during the study period, HIV trends may be impacted in either direction. While routine linked individuated information systems provide large, representative datasets for temporal trend and risk factor analysis, these data are prone to administrative errors, incompleteness, varying levels of data quality and contextual factors such as staff training, performance and turnover, disease impacts such as the COVID-19 pandemic, social unrest and natural disasters. Data captured within paper-based systems, such as point-of-care HIV tests, are not integrated into routine electronic data systems. This prevents a clear picture of HIV status amongst those testing negative or testing positive but without records of linkage to HIV care. This study uses ART dispensing as a proxy

for ART administration and adherence, however dispensing of ART does not equate to patient adherence. Furthermore, treatment interruption during pregnancy was not evaluated. Even with adjustment for confounding, residual confounding may still impact factors associated with vertical transmission. It should also be noted that these risk factors, described using observational epidemiological methods, are not causal. Since this study was limited to routinely collected data, potential confounding by factors such as socio-economic status, infant feeding methods and co-morbidities (other than previous TB) were not evaluated.

Conclusions

Our study demonstrates the positive impact of maternal ART policy change and universal test and treat to reduce vertical transmission amongst WLWH. Despite the improvements in maternal ART initiation prior to pregnancy and progress towards prevention of vertical transmission, the higher risk of vertical transmission amongst adolescents and young women, those without antenatal care and those with previous TB highlights the potential value of targeted interventions. Our findings emphasise the need for improved methods of support and follow-up amongst pregnant and breastfeeding women with HIV to ensure that all service opportunities to prevent vertical transmission and appropriately manage HIV in both mother and child are utilised optimally.

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Chapter 7: Discussion and Conclusion

Introduction

In this thesis, I present the findings from five papers evaluating the feasibility, validity and utility of HIV testing data as key components of HIV CBS in the Western Cape. I demonstrate, for the first time in a high-burden setting, that linked *individuated* routine data may be reliably used for antenatal HIV prevalence and ART coverage surveillance, providing more granular estimates, more efficiently than sentinel surveillance and aggregate programmatic data. This would enable more timely action in response to surveillance such as interventions targeting gaps in care or tailored for high-risk groups. However, these strategic gains would have been strengthened by digitised HIV PoCT data. Current routine electronic data analyses for HIV are subject to limitations as surveillance is only possible if linkage to care takes place. I demonstrate that inclusion of PoCT data enriches HIV surveillance through earlier ascertainment of HIV status and linkage to care, as well as quantifying retesting and testing-related operational challenges. I further show that the inclusion of HIV PoCT data within the health information system is operationally feasible, evidenced by high correlation with aggregate data, adequate completeness and a high proportion of data linkage to individuated data systems. Although inclusion of these PoCT data may contribute to health system strengthening, implementation is fraught with complexity.

Lastly, I demonstrate the utility of existing province-wide digitised testing data for infants, through vertical HIV transmission trend and risk factor analysis. These analyses showed reassuring trends of improved maternal access to ART and earlier diagnosis of infants over time, while also identifying high-risk groups for targeted intervention. This further serves as an example of the potential contribution of complete adult HIV testing data to HIV CBS, that may inform timely public health action.

While each chapter includes a discussion specific to the relevant thesis objective at the time of publication, this discussion aims to cover cross-cutting themes from the thesis in its entirety.

The evolution of HIV surveillance in the last decade

The past four decades have seen a gradual evolution in HIV surveillance in keeping with the progression of HIV from a new, emerging infectious disease to a major cause of mortality and morbidity and later to a preventable and manageable condition(1). Robust surveillance mechanisms are required to monitor progress in meeting disease targets such as the 95-95-95 targets or WHO Elimination of Mother-to-Child Transmission initiative, identify gaps in service delivery and develop and improve appropriate interventions(1,2). This thesis highlights the evolution of HIV in the Western Cape province over the past decade through a surveillance lens, including changing HIV policy guidelines, the digital transition, societal changes in attitudes and behaviours, increasing access to HIV testing and even changing terminology in HIV literature.

In Chapter 2 and 3, notable changes in information system characteristics are documented over time. For example, completeness in DHIS vs PHDC appear to shift around 2014, with more individual records captured from 2014 onwards. This may represent the gradual transition from paper-based systems to electronic systems. In high-income settings, this transition usually took place earlier and was typically followed by another significant shift to electronic patient records(3–5). In the Western Cape and most other low-and middle-income settings, however, patient clinical records remain paper-based primarily due to limited resources to support a complete digital transition.

Despite the absence of electronic medical records and PoCT results, Chapters 2, 3 and 6 illustrate how available linked routine data still reflect temporal changes in HIV surveillance. A notable challenge in data analysis for chapters 2 and 3 was the difficulty in comparing datasets, particularly where indicators had changed, resulting in disparate numerators and denominators. These changes, however, may represent underlying shifts in attitudes towards

HIV over time. For example, in aggregate data sets, refusal of PMTCT initial tests were no longer recorded over time as these were negligible. This supports greater acceptance of HIV testing over time, possibly driven by less stigma towards HIV and greater awareness regarding HIV and the importance of knowing one's status. These findings are supported by a recent modelling study in sub-Saharan Africa based on 183 population-based surveys, highlighting the increase of knowledge of HIV status from 5.7% in 2000 to 84% in 2020(6).

The wider roll out of ART driven by changing maternal ART policy guidelines likely also impacted attitudes towards HIV. Changing guidelines further impacted surveillance through the development of new indicators within aggregate registers to accommodate new interventions and progress targets such as ART initiation at varying CD4 thresholds(1). CBS may be more adaptable to such changes as diverse variables are readily available for further analysis, unlike aggregate systems that are limited to predetermined reporting indicators. CBS may also uncover unintended consequences of changing guidelines. For example, in Chapter 5, retesting amongst people known to be living with HIV is highlighted through digitisation and linkage of HIV testing data. While some patients self-reported a known diagnosis of HIV and retested, a notable proportion of patients were classified as new diagnoses despite prior records of HIV positive diagnosis. Reasons for these discrepancies are not explored in this thesis, however poor understanding of HIV diagnosis may be contributory(7–9). Prior to Universal Test and Treat, patients with HIV were only initiated on ART if meeting specific disease and laboratory marker thresholds(10,11). This may have resulted in a false perception that those ineligible for ART and asymptomatic were not infected, resulting in non-disclosure of HIV status and retesting. This example demonstrates the complex relationships between policy guidelines, patient perceptions and surveillance, highlighting the utility of CBS in understanding the evolution of diseases by efficiently demonstrating changes over time using consistent indicators.

With changing ART guidelines and the transition to Universal Test and Treat, laboratory monitoring guidelines also changed, consequently impacting surveillance trends. As

demonstrated in Chapter 6, more viral load testing took place in later years and fewer CD4 results were available, in keeping with findings from other countries in sub-Saharan Africa(12). These monitoring changes reflect a shift in HIV programme objectives from treating severely ill patients with HIV/AIDS in earlier policy periods to treating all people living with HIV in policy period 3. Ford *et al* argue that such shifts may result in unintended consequences such as the neglect of advanced HIV disease and inadequate management(13). CBS systems may facilitate better monitoring of such unintended consequences as these systems are not limited to pre-specified monitoring objectives.

Lastly, the past decade culminated in the devastating COVID-19 pandemic which stressed the importance of resilient health information systems in the management of emerging diseases. The analysis period for this thesis ended in December 2020, 9 months into the COVID-19 pandemic. While no major anomalies in trends were noted during the pandemic year, it is likely that more prospective data is needed to adequately evaluate the impact of COVID-19 on HIV surveillance. Linkage and consolidation of province-wide data within CBS systems enables more granular analysis of trends, thereby better uncovering contextual differences over wide geographic areas.

The role of HIV ascertainment in CBS

All five results chapters of this thesis demonstrate different methods of HIV ascertainment. While HIV testing is the first step of the HIV care cascade, these data are not available digitally for adults in the Western Cape PHDC for CBS purposes(14,15). In Chapters 2 and 3, sentinel antenatal surveys are described in detail, which make use of laboratory-based HIV testing data(16–18). PoC HIV testing results are captured in paper-based registers for aggregation in the DHIS. In the absence of complete testing data, the PHDC makes use of other markers of HIV care such as HIV-related laboratory markers, administrative evidence of HIV service utilisation and HIV treatment records. Although these data points rely on successful linkage to care after testing, I show that estimates of HIV prevalence using these methods of HIV ascertainment are comparable to sources utilising HIV testing data. This highlights that the

absence of digitised testing data does not preclude CBS initiatives. Comparable estimates between different data sources demonstrate the strength of integrated systems in offering a range of proxies available routinely for missing variables such as testing.

While there are several studies comparing routine data estimates and sentinel surveillance in low-and-middle income countries(19–29), these are limited in the South African setting and do not make use of linked individuated data. Several WHO guidance documents support the transition to routine data for HIV surveillance, however these guidelines expect countries to have met specific quality standards before this transition(30–32). These quality standards include agreement between sentinel surveillance HIV testing and programmatic testing as well as quality of data collection(32). Recent studies in South Africa continue to show weaknesses in implementation of HIV rapid testing practices, but improved performance in PEPFAR-supported facilities(33,34). It should be emphasised that in this thesis the focus is not on the validity of antenatal HIV test results, but rather the validity of HIV ascertainment for antenatal HIV surveillance estimates such as prevalence and treatment coverage.

In chapters 2 and 3, I demonstrate the validity and utility of routine CBS data for HIV prevalence and ART coverage estimates. Given that antenatal and HIV testing coverage in the Western Cape is high(35,36) and all clinical decisions at individual level are based on the results of routine PoCT, I argue that in such settings, routine individuated data (whether HIV testing data or other forms of HIV ascertainment data) should be preferable for surveillance as they provide a clearer picture of the HIV care cascade at both individual and population level, initiated by a positive test result from routine PoCT. The assessment of data collection processes described in the WHO guidelines refers more to register-based aggregated programme data, rather than linked consolidated individuated data from multiple data sources(32). The availability of such a CBS system should therefore negate the need for detailed readiness assessments previously described in the context of register-based aggregate data systems.

In Chapters 4 and 5, I demonstrate the opportunity to strengthen CBS through digitisation of PoCT. While other forms of HIV ascertainment from routine data may be reliably used to estimate HIV prevalence, digitisation of PoCT within a CBS system is particularly useful in quantifying new diagnoses and linkage to care after a positive test result by distinguishing retesting from first-time testing. Beyond direct surveillance gains, digitisation further allows improved monitoring and support of staff involved in testing. This is achieved through recognising gaps in training (e.g., capturing of patient details), highlighting where testing protocols were not correctly followed (e.g., test sequence for discordant results), quantifying staff workload (e.g., number of tests conducted per counsellor), and reducing staff workload by enabling more efficient consultations through elimination of unnecessary retesting. Despite these gains, implementation of digitised PoCT is challenging, as described in Chapter 4, but amenable to scale up with appropriate resources and leadership.

In contrast to the challenges of digitisation of adult PoCT, chapter 6 describes the utility of available routine HIV testing data in children for whom laboratory-based HIV PCR tests are conducted. In this chapter, the added utility of electronic records of negative HIV tests in the context of prevention is highlighted. The availability of negative HIV PCR results in children serves as the outcome of prevention efforts in maternal HIV care, facilitating monitoring and surveillance of vertical transmission prevention. In adults, negative HIV results are not captured on any system unless laboratory-based tests are conducted for in-patients or for discordance as part of the POCT algorithms. Digitisation of these results, inclusive of negative results, may enhance efforts at developing an HIV prevention cascade within CBS systems and better evaluating interventions such as pre-exposure prophylaxis, to prevent HIV transmission and acquisition.

Interestingly HIV PCR results were not available for all the children evaluated in this study as expected per policy guidelines, however the availability of other routine HIV data points facilitated HIV ascertainment where testing data were missing. This again highlights the utility of integrated data systems where proxies for variables are available. The unavailability of PCR

test results may be further explored to understand whether guidelines were followed correctly, again emphasizing the utility of case-based systems for a wide range of monitoring activities. Similarly concerns around the unintended consequences of birth PCR testing in later years (as per testing guidelines) resulting in decreased likelihood for follow-up testing may be better evaluated where linked data are available and records are not limited to only one electronic platform such as the laboratory information system(37).

HIV trends in the Western Cape province using a CBS lens

Each of the results chapters provide insights into HIV testing, prevalence and treatment trends in the Western Cape province using a CBS system, revealing the unique contribution of individuated datasets in province-wide surveillance and monitoring of targets. Additionally, since all chapters focus primarily on the antenatal care setting, trends in access and utilisation of antenatal care services were also described.

In Chapter 2 and 3, the limitations of sentinel surveillance in providing sub-district level antenatal HIV prevalence and ART coverage trends are described. Similarly routine aggregate data estimates are limited to specific indicators, for example only if indicators include specific age categories can temporal trends in different age groups be assessed using routine aggregate data. In contrast, CBS captures age as a numerical variable which can be categorised according to surveillance needs for epidemiological analyses. Since CBS includes the entire population without the need for sampling, granular estimates at district and sub-district level are also presented. Using CBS, granular estimates can be further explored and interrogated at community or facility level, providing a richer understanding of contextual factors impacting trends and thereby facilitating more directed interventions.

In Chapter 2, differences in HIV prevalence estimates between PHDC and DHIS are considerably larger in Northern and Tygerberg sub-districts compared to other sub-districts where prevalence estimates are closely aligned. These differences would be overlooked if

only district-level estimates are available and the opportunity for further investigation and remediation would be lost.

Similarly, in Chapter 3, I illustrate how ART coverage before pregnancy has increased over time in different age groups. This trend is important to understand from an epidemiological perspective as vertical transmission of HIV is less likely if maternal ART is initiated pre-conception(38). As detailed in Chapter 6, evaluating this indicator in adolescents and young women is particularly important as pregnancy is indicative of recent unprotected sexual activity with a high risk of HIV acquisition and consequent vertical transmission(39). Younger women however may not engage with health services as much as older women and therefore may not access HIV testing at health services until seeking antenatal care(40). From a health services perspective, understanding ART initiation both *before* and *during* pregnancy is important to ensure that service opportunities for initiation of ART during pregnancy and thereby prevention of vertical transmission are utilised optimally. Using CBS systems, I was able to demonstrate how ART initiation before and during pregnancy is above 90% in most districts of the Western Cape. CBS therefore allows deeper insight into maternal ART initiation and data are available for further exploration of epidemiological and service-related questions emerging from these findings.

In Chapters 3 and 6, I further illustrate how CBS allows the options of restricting analyses to specific groups in order to determine impact on temporal trends. In Chapter 3, for example, ART coverage is higher over time when restricting to pregnancies with live birth outcomes compared to all outcomes. Similarly, in Chapter 6, I was able to assess the impact of child death on HIV ascertainment and HIV trends to determine potential biases when evaluating risk factors for vertical transmission. CBS systems can therefore be used to address various objectives and allow more nuanced understanding of surveillance indicators and the relevant biases, to efficiently inform responses.

In Chapters 4 and 5, the inclusion of PoCT for HIV enhances CBS, providing greater insight for the interpretation of trends. For example, the discrepancies between self-reported HIV status and CBS HIV ascertainment leading to retesting, despite records of positive HIV diagnoses was a notable finding in Chapter 4. Similarly, duplication of records is a well-documented concern in routine aggregate data systems(41). Through linkage of individuated data, CBS may uncover phenomena such as retesting and recognise duplicate records, thereby allowing more accurate interpretation of prevalence trends and testing targets(41).

Lastly chapter 6 highlights the in-depth longitudinal analysis of vertical transmission using CBS that traditionally would only be possible with data from explicit bespoke observational studies(42). Such studies are both costly and time-consuming. Routine individuated data enabled a province-wide 10-year analysis of vertical transmission including multivariable risk factor analysis without the logistical, administrative and cost-related challenges of bespoke observational studies. These data further suggested higher vertical transmission than programme-reported rates based on HIV-PCR alone, emphasising the value of multiple data points within CBS to infer HIV(41,42). Although ascertainment of timing of HIV transmission requires improved digitised testing data for both mother and child, CBS systems enabled a better understanding of trends in timing of diagnosis. For example, the lower proportion of late diagnosis of children in later years suggests improved access to HIV testing as testing policy changed.

All five results chapter clearly emphasise the contribution of CBS in enriching our epidemiological understanding of HIV over time by providing reliable, granular estimates to evaluate policy and programmes timeously and inform action at both individual and population level.

Challenges in HIV CBS in the Western Cape

The strengths of CBS have been discussed thus far, however the challenges in implementation and utilisation of CBS should be explored and addressed in order to optimise CBS systems.

Firstly, the CBS system described in this thesis is developed using routine public health sector data consolidated within the PHDC. Those with limited access to public health services and those using the private healthcare sector will therefore be excluded. Efforts to improve access to health services as well as screening opportunities should be considered to ensure that all people living with HIV can be tested and results appropriately digitised and linked to existing health information system for further management. Collaboration with the private sector to consolidate data on a unified platform should be considered to improve population wide health surveillance, with appropriate data governance mechanisms in place to protect patient privacy.

While province-wide CBS offers a wealth of data, it should be noted that no real gold standard exists with which to validate these data. In Chapters 2 and 3, HIV prevalence estimates are compared to sentinel survey prevalence estimates, routine aggregate data and Thembisa modelling estimates. In Chapter 5, PoCT data are compared to routine aggregate data. Although sentinel surveys are historically a major component of HIV surveillance and used in many studies to validate routine data estimates, these data are not necessarily the gold standard(19,21,22,24–29,43). Additionally, numerators and denominators differ in the various datasets, further complicating comparisons. The Thembisa model makes use of multiple data sources including survey and routine data. While modelling estimates do provide a good indicator of current prevalence estimates, these cannot be considered the gold standard given that the estimates are reliant on good quality data from multiple data sources, and often include the data source being validated as one of those sources. Validation of PHDC data against patient clinical notes at facility level may be possible, but this would not be possible at province level for logistical reasons. Furthermore, clinicians themselves make use of routine electronic data such as laboratory data and even consolidated linked electronic data from the

PHDC user platform, Single Patient Viewer, when compiling patients' medical history(15). This means that even source documents such as paper-based clinical notes are interlinked with other routine electronic data making it difficult to validate individual data points separately against a gold standard.

The advantages of CBS in providing data timeously, efficiently and cost-effectively have been emphasised throughout this thesis. However, the challenges of routine individuated data are also highlighted in the limitations section of all chapters of this thesis, including completeness, data quality, capturing quality, varying use of electronic systems, staff turnover and limited variables for analysis of associations with outcomes(41). In Chapters 2 and 3, challenges in distinguishing first and follow-up antenatal visits are shown, however linkage prevents duplication of records so that multiple visits are still consolidated under one identifier. In Chapter 3, treatment interruption was another factor that could not be adequately described with the available data. The unavailability of detailed patient characteristics and appropriate proxies such as socio-economic status, education level, and infant feeding methods are also recognised in all thesis chapters. These issues may be addressed in the long-term through improved data collection on routine administrative systems. Regular engagement with available data helps to highlight these gaps and develop strategies to improve data.

While the transition to routine data from regular sentinel surveys and large observational cohorts may reduce the costs and administrative burden of running large studies, the limitations of routine data described require close attention. The consolidation of routine data requires regular iterations and checking to ensure that data are correctly linked and inferences are accurate. On a routine platform, such checks are reliant on competent staff teams with both technical and clinical expertise who may then develop comprehensive protocols to protect against human error. Furthermore, as more systems become digitised over time, more data are consolidated on a unified platform. This requires robust infrastructure and technical know-how(44). From a research perspective, prospective observational studies, though challenging, offer more control over data quality and completeness, and consequently more confidence in

the accuracy of results. Routine data, however, require thorough interrogation and iteration before analysis and interpretation to inform action(32,41,45). From a personal research perspective, the management of primary data described in Chapters 4 and 5 was more straightforward than the management of secondary data from routine platforms that were used in Chapters 2, 3 and 6. However, this is likely as routine individuated data systems are still in early development in our setting. As routine individuated data systems mature, the accuracy and completeness improve as also shown in Chapters 2, 3 and 6. Lessons learnt from high-income settings, such as the UK, show that mature CBS systems in themselves become tools for data quality improvement(5).

Chapter 4 highlights the complex relationships between frontline staff and health information systems, underscoring the need for adequate engagement of staff and robustly designed, implemented and routinely evaluated protocols, when implementing and using health information interventions. For example, improved completion of paper-based forms in antenatal care was noted, which may be driven by an awareness of what data are used for and better feedback to persons collecting data(46–48). Similarly, a consistent intervention champion was shown to strengthen sustainability and ownership of new health information interventions, in keeping with other studies(49,50). In the face of increasing budget cuts and consequent higher workload within the public sector, retention of staff, regular training and availability of champions are all constrained, directly impacting systems strengthening. However, mature data systems can themselves contribute to reducing workload and supporting overburdened staff once adequately embedded within services. A thorough stakeholder analysis (including all cadres of clinical, technical, administrative and managerial staff) considering stakeholder needs, values and conflicting priorities is needed when planning health information strengthening initiatives(51,52). This may be time-consuming initially and require strong leadership. Once established, however, a robust CBS system may be used beyond disease surveillance to also identify staff training gaps and service inefficiencies (such

as retesting), quantify workload estimates more accurately and thereby facilitate more evidence-based resource allocation in under-resourced settings.

Recommendations and impact

While this thesis has focussed on the last decade (2010 – 2020) during which major changes to HIV policy took place, an **updated analysis** of the current decade is recommended for continuous monitoring of trends. Further surveillance analyses, beyond the standard reporting elements is also possible through digitisation and linkage.

This study affirms the WCDHW decision to **discontinue the provincial antenatal survey** given that routine provincial data provide reliable estimates for antenatal HIV prevalence and ART coverage. While the national antenatal survey continues in the province as part of a standardised survey approach across the country, the value in routine individuated data replacing costly, time-consuming surveys is highlighted as one of the many advantages of strengthening routine individuated data.

Going forward, the existing HIV cascade within a CBS system in the Western Cape can be improved through **scaled up digitisation of PoCT** and more complete data capturing on electronic platforms at all healthcare facilities. This may require improvements to infrastructure and networking capabilities in all clinical environments and regular training of staff(41). Alternative testing capture solutions such as mobile devices, facility-based laboratories or direct digital capture can be considered if resources allow(53,54).

Regular insightful **feedback** to frontline staff on the utility of collected data may strengthen data collection by demonstrating the value of quality data for monitoring of health programmes and health services management(47,48). Regular feedback should be provided either during existing governance-related meetings or when appropriate within clinical schedules. Alerting systems may be incorporated within CBS to further assist services in identifying persons in need of greater support, for example those who test HIV positive but are not linked to care, those with treatment non-initiation or interruption and children with HIV exposure who are not

tested at the recommended intervals. These alerting systems can then be evaluated and improved using CBS and feedback from frontline staff members.

While this thesis has focussed only on the Western Cape province where CBS is possible within a routine information system, it is imperative to consider **sharing best practices** to develop similar systems in other parts of the country and continent. Firstly, it should be acknowledged that development and use of CBS within routine information systems is complex and requires time, stakeholder engagement, resources and political commitment. Until sufficient completeness of electronic systems is achieved, an absolute shift to individuated data is not recommended. This does however perpetuate a continued reliance on routine aggregate data systems rather(55). Even without completeness of a data point, the ability to use multiple sources of data to ascertain a health care concept, if data are linked on a unique identifier, creates utility of CBS in advance of complete coverage of source systems. This, in turn, can help catalyse energy to improve completeness as the utility and gaps become evident.

Some systems, such as the laboratory system, are already fully digitised and generalisable immediately in countries like South Africa(44). To enable linkage between existing electronic systems, the first step is to **implement a unique patient identifier** that may be used across the country to facilitate linkage and consolidation on an integrated platform(44,55,56). Countries in Africa are at different stages of implementing unique patient identification, for example Eswatini makes use of national ID numbers, while South Africa is implementing a 10-digit system generated identifier linked to the national ID number or passport number(55). Challenges in implementing unique identifiers are many and need to be addressed thoroughly for CBS to be successfully implemented. The challenges include, among others, multiple identifiers assigned to one person, inconsistent recording of identifiers, poor infrastructure, unreliable electricity-supply and poor internet connectivity(55). Addressing these issues must be prioritised in order to achieve CBS. The current move towards the National Health Insurance in South Africa may provide the political catalyst for greater government

commitment in strengthening information systems that form the backbone of implementation of universal health coverage(55).

Lastly, the findings of research such as this should be **presented and discussed** with relevant stakeholders to enable knowledge translation and impactful action. At the time of submission of this thesis, published findings relating to the feasibility and utility of digitisation of HIV testing were presented to key stakeholders at WCDHW. These findings also contributed to the WHO Consolidated Guidelines on Person-Centred HIV Strategic Information published in 2022(57). It is hoped that this research may continue to spur further research and development of routine data systems for improved surveillance and monitoring of HIV and serve as an exemplar for the establishment and use of other disease cascades embedded in routine information systems.

Conclusion

In this thesis I have shown the validity of a CBS system, established through linked, individuated routine data. Additionally, I demonstrated the feasibility of improving HIV CBS from point of diagnosis and the utility of CBS in providing timely, reliable and granular estimates of temporal trends in antenatal HIV prevalence, linkage to care, ART coverage and vertical transmission. Further development of CBS in the Western Cape through digitisation of all sentinel events within the HIV cascade, improved completeness of capturing within electronic systems and closing the feedback loop from capturing to sharing of relevant information, are necessary to improve the utility of CBS. Sharing expertise may facilitate the establishment of CBS in other provinces of South Africa and similar low-and-middle income settings. This collaborative approach may enhance the monitoring and surveillance of targets and facilitate the timely implementation of evidence-based interventions to effectively prevent and manage HIV at both individual and population levels.

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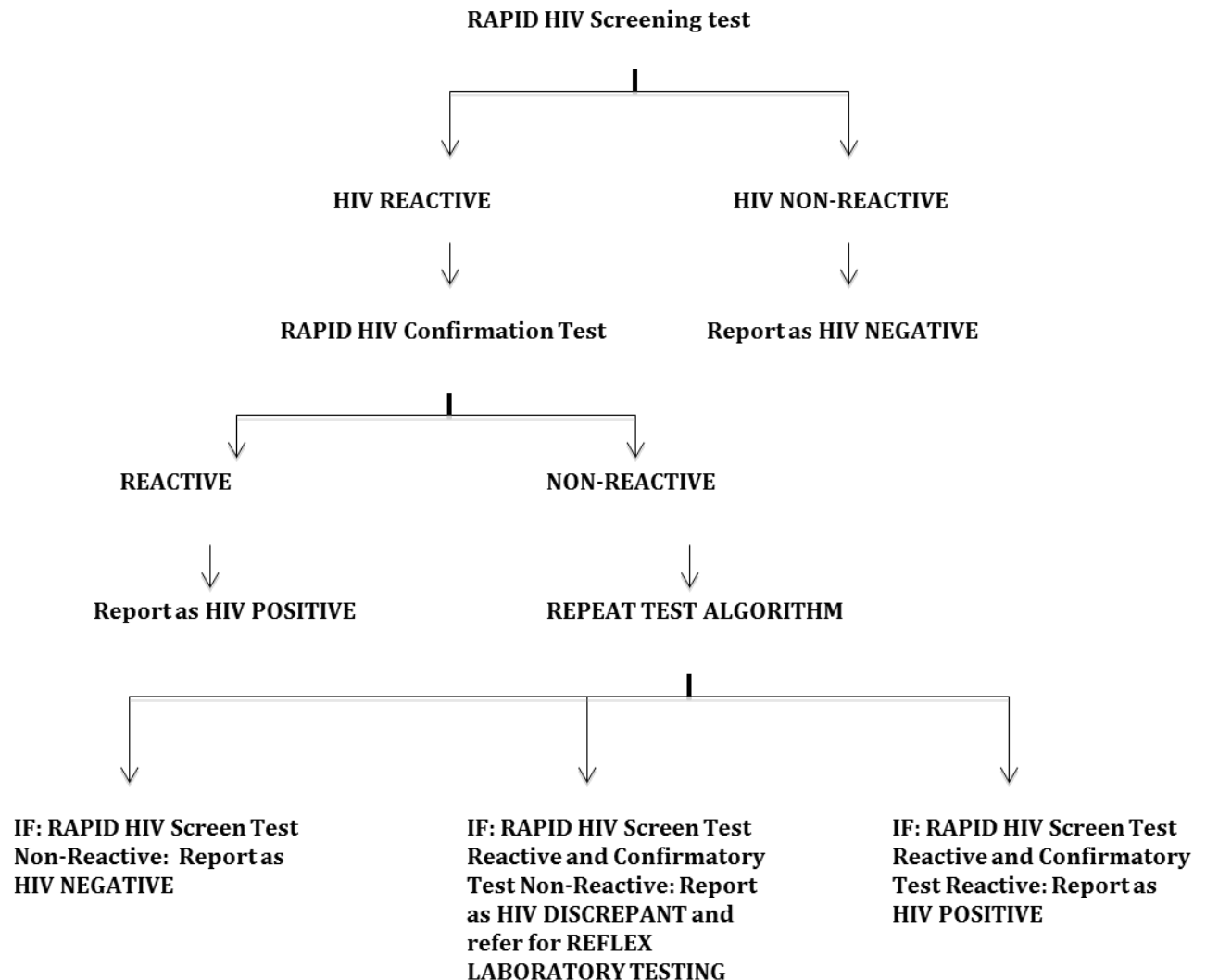
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Appendices

Appendix A: HIV Testing Algorithm



National Department of Health, South Africa. National HIV Testing Services Policy: 2016.
Available at: <https://sahivsoc.org/Files/HTS%20Policy%2028%20July%20final%20copy.pdf>
(Accessed 30 May 2019)

Appendix B: HIV Testing Services (HTS): Consent & Testing Record for Adults & Children

HIV TESTING SERVICES (HTS): CONSENT & TESTING RECORD FOR ADULTS & CHILDREN													
Place Patient Sticker Here										If HTS done as part of outreach activity indicate event/site:			
Name of Client:													
Folder Number:												Individual	Couple
Age:										Date: dd / mm / yyyy		Male	Female
Reason for Accessing Service													
PMTCT/HIV exposed	ANC 1st test	20 w k rpt	32 w k rpt	Perinatal (delivery)	Maternal (breastfeeding)	Baby birth	Baby 10w k PCR	Baby 9 mth	Baby other	Baby 18mth			
PICT (Provider initiated) TB		PICT (Provider initiated) other than PMTCT/TB (e.g. STI, FP, IMCI, CDL)				Self Referred							
ADVISE CLIENT TO HAVE AN HIV TEST (If involved in vaccine trial which may give false positive result refer to study site)													
Accept HIV Test:	Yes	No	If accept:	First Ever HIV Test	Repeat HIV Test (last test less than 1 yr ago)			Repeat HIV Test (last test more than 1 yr ago)					
If previously tested:		Date of test dd / mm / yyyy			HIV test result:		Positive		Negative				
If refuses testing/referred to another site, specify reason:													
CONSENT TO HIV TESTING (Consent of caregiver or parent is required if <12yrs)													
I hereby consent to having an HIV test.													
Ndiyavuma okokuba igazi lam lingahlolelwa isifo sengculazi (HIV/AIDS)													
Ek verleen hiermee toestemming vir 'n MIV toets.													
Name/Igama/Naam					Client			Parent		Caregiver			
Signature/Usayine/Handtekening:					Date/Umhla/Datum:								
TEST CLIENT (NR = nonreactive; R = reactive; INV = invalid) Rapid Test/s performed by:													
Screening rapid test:		name		Batch No:		Expiry date:		NR	R	INV			
Confirmatory rapid test:		name		Batch No:		Expiry date:		NR	R	INV			
If screening test and confirmatory test are discordant, or an invalid result is obtained, repeat test/s:													
Screening rapid test:		name		Batch No:		Expiry date:		NR	R	INV			
Confirmatory rapid test:		name		Batch No:		Expiry date:		NR	R	INV			
Rapid HIV Test outcome			HIV NEGATIVE			HIV POSITIVE			DISCORDANT (needs lab testing)				
Elisa / PCR (circle)		Date to return for Elisa/PCR result: dd / mm / yyyy				Outcome after Elisa/PCR:		HIV NEGATIVE		HIV POSITIVE			
SCREENING/EDUCATION AT HTS													
PMTCT Education				Sexual & Reproductive Health (SRH)/ Family Planning (FP) Screen (Men & Women)									
Transmission to baby		ARVs for baby		Using FP method:		Yes	No	Method:		Next FP appt:			
Feeding options		ARVs for mother		Referred for FP:		Yes	No	N/A		Using condoms:		Yes No	
Cotrimoxazole baby		Testing of baby		Pap smear Ever:		Yes	No	Referred to PN:					
TB Screen				STI Symptom Screen									
Cough for more than 2 weeks:		Yes	No	Engage in vaginal / anal / oral sex:		Vaginal		Anal		Oral			
Weight loss more than 1.5kg last mth:		Yes	No	Discharge/"drop" from vagina/penis:		Yes	No	Sores on vagina/penis:		Yes	No		
Fever:		Yes	No	Discharge/"drop" blood from anus:		Yes	No	Sores on anus:		Yes	No		
TB contact in house:		Yes	No	Women: Lower abdominal pain:		Yes	No	Burning on passing urine:		Yes	No		
Referred to PN:				Referred to PN:									
MEDICAL MALE CIRCUMCISION (MMC)													
MMC Education (MEN & WOMEN)				Yes	No	Site client referred to:							
SUPPORT [Post Test]													
		Indeterminate			Negative			Positive					
Importance of returning for Elisa/PCR test result													
Partner Testing, Disclosure													
Risk Reduction Plan													
Condoms Issued													
Latex compatible lubricant issued (anal sex)													
Importance of linkage to care													
DATE FOR FOLLOW UP: dd / mm / yyyy													

Appendix C: UCT Human Research Ethics Approval Letter



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



Room G50- Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: hrec-enquiries@uct.ac.za

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

16 February 2021

HREC REF: 083/2021

Prof A Boule

School of Public Health & Family Medicine
Level 4, Falmouth Building
Email: andrew.boule@uct.ac.za
Student: Nisha.jacob@uct.ac.za

Dear Prof Boule

PROJECT TITLE: FEASIBILITY, VALIDITY AND UTILITY OF HIV TESTING DATA AS KEY COMPONENTS OF HIV CASE-BASED SURVEILLANCE- PHD- CANDIDATE DR NISHA JACOB

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

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

This approval is subject to strict adherence to the HREC recommendations regarding research involving human participants during COVID -19, dated 17 March 2020 & 06 July 2020.

Approval is granted for one year until the 28 February 2022.

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)

The HREC acknowledge that the student: Dr Nisha Jacob will also be involved in this study.

Please quote the HREC REF 083/2021 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, where necessary, before the research may occur.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FACULTY OF HEALTH SCIENCES HUMAN RESEARCH ETHICS COMMITTEE

HREC/REF 083/2021sa

Ethics approval renewed until 28 February 2025. Latest renewal included in Thesis Ethics submission file.

Appendix D: Directed acyclic graph (DAG) – Risk factors for vertical transmission of HIV

