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Fast-Tracking of the HIV Response: Do the Metros Lead the Way to Reaching 90-90-90 in South Africa?

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Abstract

Objective: This secondary data analysis determined how far the eight South African metropolitan municipalities have progressed in the expansion of HIV treatment. The framework of HIV care cascades (HCC) was used.

Methods: We collated data sources to understand the HCC in metro and non-metro populations including demographic, HIV prevalence and laboratory data (2014-2015) that we linked to unique individuals using a probabilistic matching algorithm. We defined the HCC using: number of persons living with HIV (PLHIV); total remaining on ART; numbers with a CD4 count and viral load (VL) test results in the past year and the number of suppressed VL tests.

Results: 37% of South Africa's PLHIV live in metros. Progress along the HCC for metro and non-metro populations was 53% of PLHIV in care and 45% on ART for both populations and 27% of metro/26% of non-metro populations virally suppressed. Achievement varied widely by metro, 35%-63% of PLHIV were on ART, 21%-48% of ART clients were virally suppressed. The largest treatment gap was in Ekurhuleni metro. The metros spend approximately US$383 million per year on ART. Annual VL testing of all ART clients in the eight metros would amount to approximately US$ 42 million or 11% of ART programme cost.

Conclusion: South Africa sees rapid growth of its urban centres which are chiefly affected by HIV. There are currently large gaps in the metro's 90-90-90 level of achievements. The District Implementation Plans offer a mechanism to focus investment on ART scale-up. Supporting factors are the existing expertise, service integration and infrastructure for large-scale ART, the close network of service delivery sites and service delivery solutions. Ensuring scale and quality of the HIV treatment programmes is vital for the metros' economic prosperity - and for South Africa as a whole.

Keywords: Viral load; HIV; Metropolitan municipality; Metro; Urbanisation; South Africa; Fast-track; 90-90-90 targets; Ending AIDS; HIV response; HIV care cascade

Introduction

South Africa remains a priority country for combatting HIV and AIDS with its estimated 6.3 million people living with HIV [1] and approximately 3.1 million on antiretroviral treatment (ART) by March 2015 [2]. The South African government has been providing ART at public health facilities through the comprehensive care, management and treatment programme which started in 2004. Throughout the epidemic, urban areas have had higher HIV prevalence and HIV incidence levels than the surrounding rural areas [3]. It is therefore of concern that the country's urban population is growing steadily (Figure 1) and that urbanisation increasingly involves population groups with high HIV infection rates – both potentially contributing to HIV epidemic dynamics. In 2014, there were 34.2 million urban residents in South Africa and the urbanisation rate was 64% [4]. It is projected by the United Nations that the country's urban population will exceed 40 million by 2030 [5]. All ethnic population groups except black Africans have consistently experienced urbanisation levels above the national average. However, the urbanisation of black Africans has in recent years been increasing at an accelerated pace, and it is in this population group that the HIV epidemic is most severe [3].

South Africa's Metros

The country has a system of metropolitan municipalities that was introduced so that cities could be governed as single entities. Local government reform after apartheid produced six Transitional Metropolitan Councils following the 1995/6 local government elections. In 2011, Buffalo City (East London) and Mangaung (Bloemfontein) were added to the category of metropolitan municipality ('metros'). Metros execute all the functions of local government for a city or conurbation [6]. The metros vary greatly in size; population density and growth rate (Table 1). The Cities of Johannesburg and Tshwane have experienced particularly high growth rates, over 3% in the last decade. A few have had relatively low growth, especially Buffalo City. The City of Johannesburg is the most densely populated metro with 2,696 people per km^2 and Mangaung, which became a metro in 2011, is the least densely populated with 119 people per km^2.

The eight metros only cover 2% of South Africa's territory but

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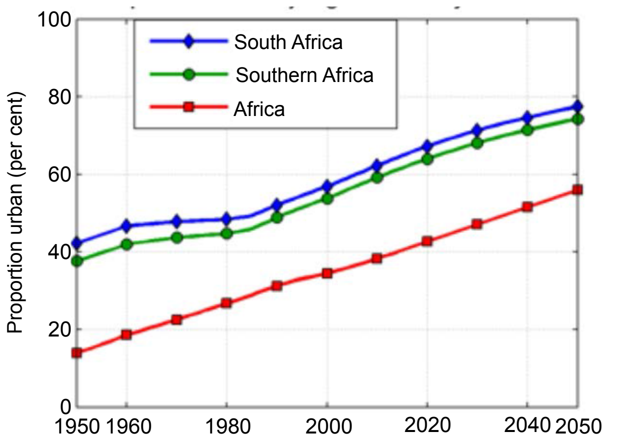
account for 39% of the country's population, 70% of its Gross Domestic Product (GDP), and half of all unemployed South Africans (Stat SA). The Integrated Urban Development Framework aims to develop urban areas towards better access to social and economic services by its residents and inclusive, sustainable economic growth in these areas [7]. The measures are expected to benefit the surrounding rural areas as well, as urban and rural areas are dynamically linked through flows of people and resources, helped by better transport, communication and migration [8]. Between 1996 and 2012, metros accounted for 75% of all net jobs created in South Africa, illustrating how important healthy and well populations are in these centres of economic growth and productivity (Ibid).



Source: World urbanization prospects 2014, http://esa.un.org/unpd/wup/Country-Profiles/ accessed 25 Nov 2016

Figure 1: Estimated proportion of urban population in South Africa, the region and the African continent (1950-2050).

The Metros' HIV Epidemics

The 2012 HIV prevalence and incidence survey demonstrated the importance of place of urban residence as a critical parameter for infection [3]. The HIV incidence rate in individuals aged two years or above was more than double in urban informal settlements (slums and squatter settlements, with informal street layouts, some with electricity; often in and around towns/cities or outskirts of townships) compared to urban formal areas (formal street layouts, with electricity and other services generally available such as flush toilets; these include formal townships and other residential areas with building structures are mainly made of brick) (2.5% vs. 1.1%). Equally, HIV prevalence differed by a factor of two (19.9% in informal areas and 10.1% in formal areas). This could not be explained by exposure to ART - which prolongs the lives of HIV infected people - as a similar proportion of PLHIV were on ART in the two areas (27.4% in informal areas and 28.3% in formal areas) [3].

The largest numbers of PLHIV are in the metros of Johannesburg, eThekwini and Ekurhuleni, due to the sizes of these cities and the high HIV prevalence levels (estimated based on 2011 census data and 2012 HIV prevalence data of the metros; accordingly, Johannesburg and eThekwini have an estimated 22% of the metros' total HIV burden, and Ekurhuleni 20%). In eThekwini and Ekurhuleni, nearly one in six adults is HIV infected, and in Johannesburg about 1 in 10. Due to HIV, the

Metropolitan municipality	Province	Capital	Area (km²)	Population (2011)	Population/km²	Growth rate p.a. (2001-2011)
Buffalo City*	Eastern Cape	East London	2,536	755,200	297.8	0.69
City of Cape Town	Western Cape	Cape Town	2,460	3,740,026	1,520.3	2.57
City of Johannesburg	Gauteng	Johannesburg	1,645	4,434,827	2,695.9	3.18
City of Tshwane	Gauteng	Pretoria	6,345	2,921,488	460.4	3.10
Ekurhuleni	Gauteng	Germiston	1,924	3,178,470	1,652.0	2.47
eThekwini	KwaZulu-Natal	Durban	2,292	3,442,361	1,501.9	1.08
Mangaung*	Free State	Bloemfontein	6,284	747,431	118.9	1.47
Nelson Mandela Bay	Eastern Cape	Port Elizabeth	1,959	1,152,115	588.1	1.36
All metros	-	-	25,445	20,371,918	800.6	
National				51,770,560		1.44

Sources: Municipal fact sheet http://www.statssa.gov.za/census/census_2011/census_products/Census_2011_Municipal_fact_sheet.pdf, accessed 8 Jan 2016
* Only gaining metropolitan municipality status in 2011

Table 1: Key demographic data on the South African metros (2011).

	HIV disease			Tuberculosis		
Metropolitan municipality	**% of notified deaths**	**Number**	**Rank**	**% of notified deaths**	**Number**	**Rank**
Buffalo City	5.8	497	2	9.0	778	1
City of Cape Town	6.1	1,644	2	4.8	1,304	5
City of Johannesburg	4.0	1,174	4	5.5	1,640	1
City of Tshwane	4.0	936	7	6.9	1,597	1
Ekurhuleni	2.2	524	10	7.4	1,749	1
eThekwini	4.8	800	5	10.5	1,744	1
Mangaung	5.4	569	2	5.4	572	1
Nelson Mandela Bay	7.7	780	2	7.6	769	3
All metros	4.7	6,924*		6.9	10,153[1)]	
National	4.8	21,938#	5	8.4	37,878[2]	1

Source: Mortality and causes of death in South Africa, 2014: Findings from death notification Statistics South Africa, Pretoria: Statistics South Africa, 2015. Compiled from appendices M and P1
* Of 147,829 total deaths notified from metros in 2014
# Of 453,360 total deaths notified in South Africa in 2014

Table 2: HIV disease and tuberculosis death notification data from metros, South Africa (2014).

tuberculosis (TB) burden in South Africa is also among the highest in the world with a TB incidence rate of 834/100,000 and a total of 314,193 TB cases notified in 2014 [9]. Despite large public sector treatment programmes, HIV and TB related mortality remain high with TB as the number one cause of death in six of the eight metros, and HIV taking rank 2 in four metros (Table 2). HIV and TB combined were responsible for about 12% of all notified deaths in metros in 2014 [10].

Fast-Tracking HIV Care and Treatment Scale-Up to End AIDS in 2030

In 2014, the United Nations Joint Programme on HIV/AIDS (UNAIDS) proposed a new international goal with the aim of ending the HIV epidemic by 2030. The goal is known as 90-90-90 and refers to three HIV care and treatment targets. The first is that 90% of PLHIV will know their HIV status; the second is that 90% of those diagnosed with HIV are on ART (i.e., 81% of all PLHIV); and the third is that 90% of those on ART will have a suppressed HIV RNA viral load (i.e., 73% of all PLHIV). Viral suppression in the South African context means having a viral load result of <400 viral RNA copies/ml in a laboratory test. Viral suppression is achieved through good adherence to antiretroviral medicine to which the virus is susceptible (no drug resistance). Viral suppression is associated with low HIV morbidity and mortality in the patient, and lower infectiousness to partners and the unborn child. The 90-90-90 targets should be met by 2020, with a further scale-up for another decade, to end the AIDS epidemic by 2030.

South Africa has adopted these targets and the HIV District Implementation Plans, from the financial year 2016/2017 onward, place strong emphasis on deploying significant effort to meet the three targets by 2020. As per the 2014 National ART guideline [11], several population groups were eligible for immediate ART once HIV diagnosed. These were a) those PLHIV with CD4 count <500 cells/µl irrespective of WHO clinical stage, b) all HIV-positive women who are pregnant, breastfeeding or within 1 year post-partum, regardless of CD4 cell count (immediate initiation of lifelong ART), c) all children under 5 years, regardless of their CD4 cell count or clinical staging, d) those with Hepatitis B or Cryptococcus meningitis, and e) all forms of TB, regardless of CD4 count or clinical staging.

Progress towards the UNAIDS 90-90-90 targets is often displayed as HIV care cascades (HCC) with four categories: HIV positive, HIV diagnosed, on ART and virally suppressed. It is essential for the metros to understand their progress towards the 90-90-90 targets, using all available viral loads (VL) data. We therefore embarked on a secondary data analysis, employing an innovative solution for record linkage between South Africa's health and laboratory information systems to address shortcomings in data flow and system integration between the National Health Laboratory Service (NHLS) and the data system at health facilities (Tier.Net is the National Department of Health's official patient HIV database which holds longitudinal patient demographic and clinical information about cohorts of patient started on HIV treatment). The objective was to assess the level of scale-up of the ART programme in the metros, using the HCC as an analysis framework, and determine the metros' progress in the scale-up of HIV care and treatment.

Methods

South Africa's public sector health facilities use test requisition forms that state the patient's name, date of birth, gender, and facility name. These requisition forms are sent to the NHLS, which stores all patients' laboratory test results in their Central Data Warehouse (CDW). Currently, only a small proportion of laboratory tests are associated with a national patient identification number in the CDW database. Without a unique patient identifier it is difficult to link all laboratory tests one patient may have in their lifetime to that one patient as patients may move between facilities and their personal information is often recorded differently on different requisitions.

Linkage Process of Patient, Laboratory and Clinic Data

Patient-level linking

To be able to track changes in VL and CD4 count data at the patient-level, a patient-linked cohort of laboratory test results stored in the CDW was created by linking patient-level information associated with each test result, to create a data base in which all test results for each individual patient were linked together. This patient-level cohort was created by linking VL test results for each individual using their names and date of birth. The creation of the patient level cohort was a multi-step procedure that used non-probabilistic and probabilistic ("fuzzy") linking procedures. Care was taken to create a unique identifier that simultaneously minimised over-matching (falsely combining records that should remain separate) and under-matching (falsely separating records that should be combined) [12].

Record-linkage procedure

The record linkage method consisted of five steps: data cleaning, exact-linking, pre-processing, fuzzy linking, and consolidation via network analysis. The methods were implemented using Boston University's Shared Computing Cluster, a network of high speed, multiprocessor computers that enabled the development of a comprehensive algorithm that could compare millions of records in less than 12 h per programme run. The final stage in the record linkage exercise was to validate it against a gold standard. In the case of the NHLS database, no gold standard exists that could capture the potential flow of patients across different sites within the national health system. Therefore, to validate the approach, a gold standard was constructed by manually matching 1,000 NHLS data to patient IDs.

Clinic-level linking

The National Department of Health (NDOH) and NHLS each have a list of facilities that use different names/identifiers for many health facilities. In order to develop the HCC it was important to know the number of patients on ART at each facility. This number is provided by the District Health Information System (DHIS), through their Total Remaining on ART (TROA) indicator for each health facility, using the facility names as cited by the NDOH list. Analysis and utilisation of NHLS' laboratory data to inform policy has been hampered by the lack of a single and unified clinic-level linking file matching NHLS facilities to NDOH facilities. Therefore, the analysis included a process of matching health facility names across existing NDOH and NHLS lists and using geo coordinates to verify facility names and locations.

Development of the HIV Care Cascade

The HCC was created using four categories: Number of PLHIV (the HIV positive); number of persons with a CD4 count or VL test result in the past 12 months ('in care', as a proxy for HIV diagnosed which was not available); Total remaining on ART (TROA); and Number of patient-linked VL tests that were suppressed [3] for the period from April 1, 2014 to March 31, 2015.

We calculated the number of PLHIV by multiplying mid-year population estimates (from Statistics South Africa) by the HIV prevalence estimates from the 2012 South African National HIV Prevalence, Incidence and Behaviour Survey. The mid-year population estimates were adjusted to the annual time point of our HCC estimates by linear interpolation. The HIV prevalence estimates were reported at a national level by all ages and in the eight metropolitan municipalities. We applied the 2012 HIV prevalence estimates to calculate the number of PLHIV with no adjustment.

We used the patient-linked cohort data to calculate the number of persons who had at least one HIV RNA viral load or CD4 count test in the previous 12 months, ensuring that each individual would only be counted once through removal of multiple tests.

The DHIS compiles reports of TROA for each facility recorded by geographic location and for all ages. TROA is not reported by sex. We used the mid-year TROA (for the April-March period), calculated as the mid-point between October and November 2014.

As with the CD4 tests, we used the NHLS CDW to calculate the number of persons who had a VL test in the previous 12 months and whether that test was virologically suppressed (VL result <400 copies/ml). Based on available South African unit costs for providing ART services, we conducted simple estimates of treatment and diagnostic costs for the metros.

Results and Discussion

ART client numbers and estimated treatment costs in the metros

The eight metros combined had an estimated 2.42 million PLHIV, of a total of about 6.47 million PLHIV in South Africa (37.4%) (Table 3). The metro health districts serve a large proportion of South Africa's ART clients - by October 2014, the ART programmes in the eight metros treated about 1.095 million PLHIV, or 37% of the country's ART clients. By far the largest HIV treatment programmes were in eThekwini (296 thousand clients) and Johannesburg (244 thousand clients), although Johannesburg had the largest number of PLHIV, at about 547 thousand. Table 3 also provides crude estimates of the ART programme cost to treat adult and pediatric clients for one year, using national average unit costs. All metros combined face a cost of approximately 383 million US dollars annually to provide ART to their HIV positive clients.

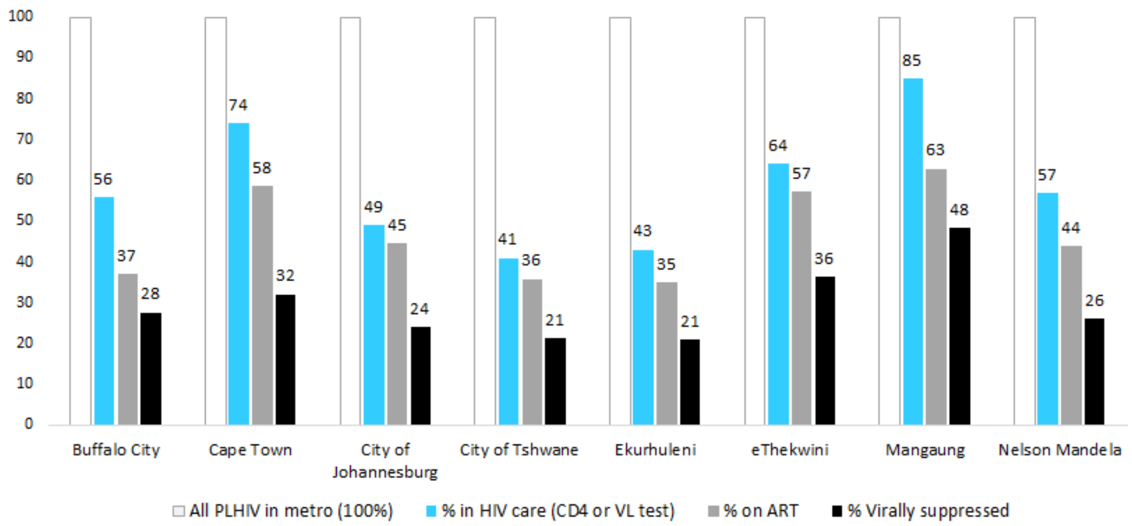
The HIV care cascade in the metros

The differentials across the metros at all stages of PLHIV's engagement in care were remarkable. Figure 2 summarizes the findings across the HCC for all metros. All metros have a proportion of HIV

Metropolitan municipality	Estimated number of PLHIV ('000)	All ART clients ('000)	ART clients 0-14 years	Approximate treatment cost per year, in million US$*
Buffalo City	105	39	2,247	13.62
City of Cape Town	212	124	5,639	43.36
City of Johannesburg	547	244	11,140	85.32
City of Tshwane	379	136	5,279	47.59
Ekurhuleni	494	173	8,190	60.48
eThekwini	517	296	14,864	103.45
Mangaung	62	39	2,294	13.62
Nelson Mandela Bay	100	44	2,762	15.36
All metros	2,416	1,095	52,415	382.78
All South Africa	6,473	2,952	383,000	1,022.56

Sources: South African National HIV Prevalence, Incidence and Behaviour Survey, 2012 and Stats SA Mid-year population estimates from Census 2011 Municipal Reports for PLHIV numbers; District Health Information System for patients on ART; SA investment case for estimated costs in 2014/15 (R3,879.26 per adult ART client per year and R3,451.05 per paediatric client). Using exchange rate R/US$=11.0385 (31st Oct 2014)

Table 3: PLHIV and ART client numbers in the metros and approximate ART cost per year (2014).



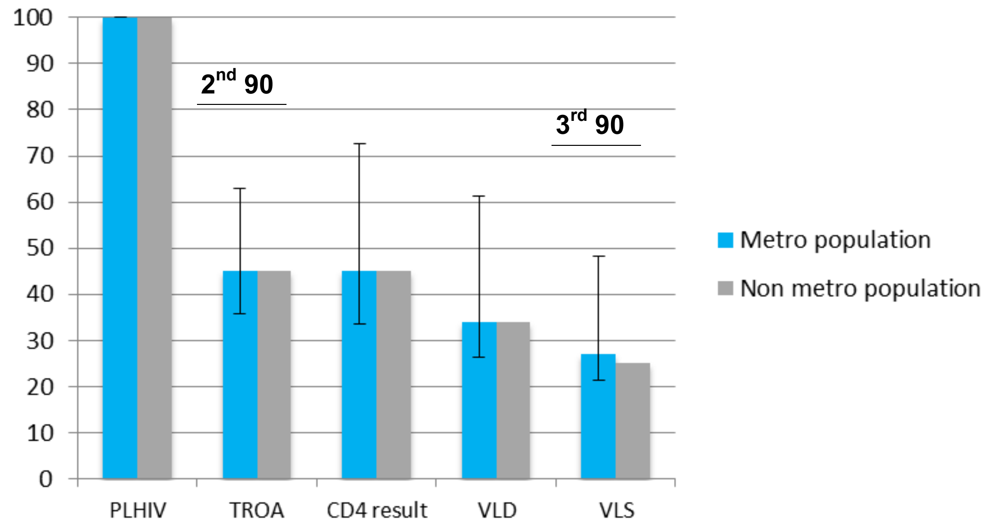
Sources: South African National HIV Prevalence, Incidence and Behaviour Survey, 2012 and Stats SA Mid-year population estimates from Census 2011 Municipal Reports for PLHIV; District Health Information System for patients on ART; National Health Laboratory Service Corporate Data Warehouse CD4 and VL test results

Figure 2: HIV care cascade of metropolitan municipalities in South Africa (2014/2015).

clients in care (having had either a CD4 or VL test over 12 months) but not on ART. PLHIV with CD4 count data and not yet meeting ART eligibility criteria fall into this group ("pre-ART clients"). Mangaung had the highest level of PLHIV in care at 85% and ART coverage and viral suppression were also highest in this metro. In contrast, Ekurhuleni had about half the levels of linkage to care and HIV treatment compared to Mangaung.

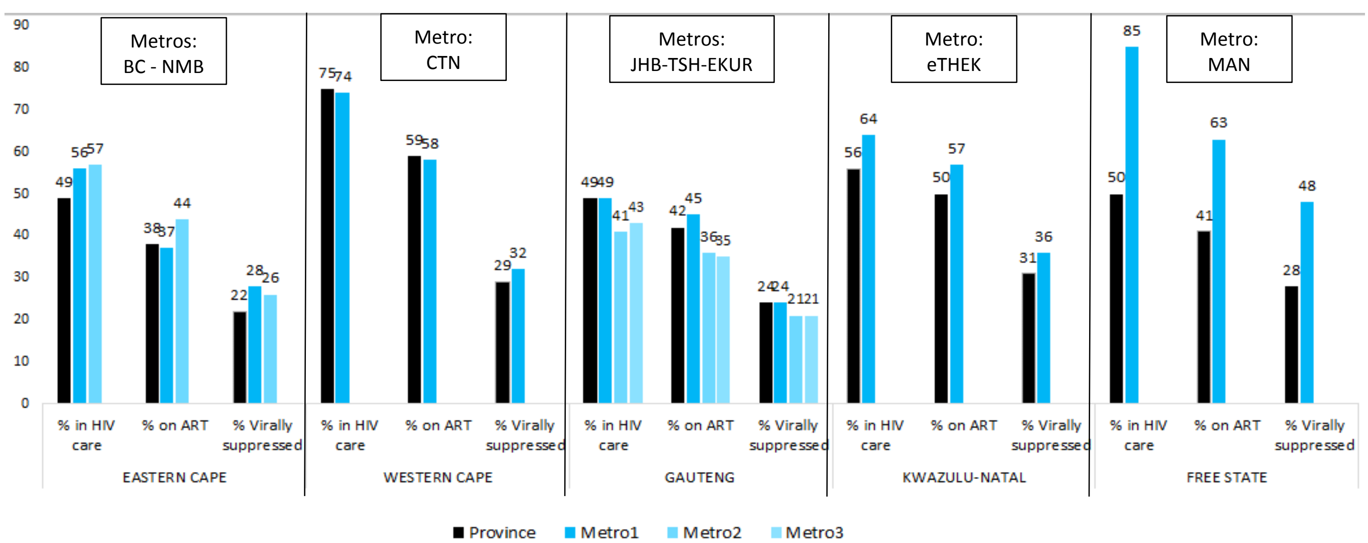
The proportion of PLHIV in care was the same in the metro and the non-metro populations of South Africa (at 53%) (Figure 3). Equally, ART coverage was the same in metro and non-metro populations (at 45%) and viral suppression was virtually the same (metro 27%, non-metro 26%).

Metros from the same province usually had similar levels of scale-up, with the exception of Mangaung metro and its province, Free State (Figure 4). Access to ART was comparatively low in the five metros of Gauteng and Eastern Cape, ranging from 35% of PLHIV on ART in Ekurhuleni to 44% in Nelson Mandela Bay and 45% in Johannesburg. ART coverage in Mangaung was at 63%, well above the average level in Free State. Cape Town and eThekwini (58% and 57%) also had comparatively high ART coverage but similar to their provinces as



Sources: South African National HIV Prevalence, Incidence and Behaviour Survey, 2012 and Stats SA Mid-year population estimates from Census 2011 Municipal Reports for PLHIV; District Health Information System for patients on ART; National Health Laboratory Service Corporate Data Warehouse CD4 and VL test results
Notes: PLHIV=People living with HIV, TROA=Total remaining on ART, VLD=viral load test done, VLS=viral load suppressed (<400 copies/ml)
2nd 90: refers to 90% of all PLHIV diagnosed and of these, 90% on ART (81%)
3rd 90: refers to 90% viral suppression of those on ART (73%)
Error bars indicate the range of values across the eight metros (min/max)

Figure 3: HIV care cascades in the metro and non-metro populations of South Africa (2014/2015).



Sources: South African National HIV Prevalence, Incidence and Behaviour Survey, 2012 and Stats SA Mid-year population estimates from Census 2011 Municipal Reports for PLHIV; District Health Information System for patients on ART; National Health Laboratory Service Corporate Data Warehouse CD4 and VL test results

Figure 4: HIV care cascades of metropolitan municipalities compared to their provinces (2014/2015).

Metropolitan municipality	VL tests done ('000)	VL test coverage (% of PLHIV on ART)	Estimated VL monitoring costs per year, million US$
Buffalo City	38	97.4	1.49
City of Cape Town	85	68.5	4.74
City of Johannesburg	169	69.3	9.33
City of Tshwane	100	73.5	5.20
Ekurhuleni	135	78.0	6.61
eThekwini	222	75.0	11.32
Mangaung	38	97.4	1.49
Nelson Mandela Bay	39	88.6	1.68
All metros	826	75.4	41.86

Sources: South African National HIV Prevalence, Incidence and Behaviour Survey, 2012 and Stats SA Mid-year population estimates from Census 2011 Municipal Reports for PLHIV; District Health Information System for patients on ART; National Health Laboratory Service Corporate Data Warehouse CD4 and VL test results; District planning tool (provided by Steve Cohen of Strategic Development Consultants) for VL monitoring cost=cost per VL test (R321/US$29.08)+laboratory processing costs (R101/US$9.15)

Table 4: VL monitoring, coverage, and approximate costs of universal VL monitoring in metros (2014/2015).

a whole. In order to achieve the second 90 target, the metros had a highly variable treatment gap: Mangaung needed to initiate about 11 thousand additional ART clients to reach the target, Nelson Mandela Bay 37 thousand, Buffalo City 46 thousand, Cape Town 48 thousand, eThekwini 122 thousand, Tshwane 171 thousand, and Johannesburg 199 thousand. Ekurhuleni needed to extend its ART programme to an extra 227 thousand PLHIV.

Equally, VL suppression showed large heterogeneity across the metros, with the three Gauteng and the two Eastern Cape metros having the lowest proportions of PLHIV with viral suppression at 21-28%. The gap to the third 90 target (73% of PLHIV virally suppressed) is large in these metros, and it is chiefly determined by the earlier stages of the cascade, especially ART coverage.

Viral load monitoring by the metros' health services

According to the HIV treatment guidelines, each ART client requires at least one VL monitoring test per year, to identify treatment failure due to poor treatment adherence or drug resistance. The compliance with viral suppression monitoring, indicated by the coverage of VL testing over a 12 month treatment period, was variable across the metros' health services (Table 4). Approximately three of four ART clients already received annual VL monitoring in 2014/2015. Going forward, the target for this indicator of treatment monitoring is 100%, i.e., all ART clients should have at least one VL test annually (National Department of Health, targets for District Implementation Plans, internal document). We therefore made a rough estimate of the costs the metros would incur if each ART client received one VL test per 12 months. In the eight metros, about US$ 42 million would need to be spent annually (approximately 11% of the ART cost per year, Table 3).

Conclusion

The main objective of this study was to determine how far the South African metros have progressed in the expansion of HIV treatment to their populations in relation to the overall progress in South Africa, the provinces in which they are based, and in comparison to each other.

The metropolitan districts share the common HIV goal of all of South Africa's health districts: to reach the 90-90-90 targets by 2020. Measuring progress towards these goals can prove challenging due the data requirements of knowing the metros' prevalence of HIV, the number of persons diagnosed, the number of persons on ART, and the number virally suppressed. Using 2012 South African National HIV Prevalence, Incidence and Behaviour Survey, the DHIS and the NHLS's CDW that stores HIV monitoring laboratory results, we were able to generate estimates for the HIV care cascades to better understand HIV burden and access to HIV services in these areas. A multi-step record linking process was necessary to associate patient data in Tier.Net with VL and CD4 test data from the CDW. We were unable to estimate the "first 90", the number of persons diagnosed, but we estimated the number of persons in HIV care, which we used as proxy for HIV diagnosed.

We estimated that there are approximately 2.4 million HIV infected inhabitants in South African metros, of which about 53% in care, 45% on ART and 27% virally supressed. This ART coverage costs the metros in excess of US$ 383 million per year. There was no evidence that metros are overall ahead of non-metro areas (or the national average) in the HIV care and treatment scale-up. The same proportion of PLHIV was in care and on ART in metro and non-metro populations. This was unexpected, as the geographic proximity of ART clients to treatment facilities in the urban areas could have been associated with better HIV service access and uptake.

This analysis is relevant to the 'Fast-track city initiative' (on World AIDS Day 2014, mayors from around the world gathered to launch the Paris Declaration on Fast-Track Cities and pledging to achieve the 90-90-90 targets by 2020 in participating cities). The South Africa fast-track movement aims to build upon and leverage existing HIV programmes and resources to strengthen city-wide responses by reaching 90-90-90 and zero discrimination targets. In South Africa, cities have united to meet these fast-track targets for "Ending the AIDS and TB epidemics by 2030". Reviewing progress and learning across the participating cities is a central aim of this initiative.

What is clear is that the metros need to make significant strides to meet the 2020 treatment target. Ekurhuleni had the largest treatment gap – approximately 227 thousand additional PLHIV need to be initiated and maintained on ART by 2020, a number similar to the total ART client population of Botswana, China or Thailand [13]. This could cost Ekurhuleni up to US$ 140 million per year based on 2014 ART unit costs, unless savings can be made in how the fully scaled-up ART programme is implemented. Despite these challenges, metro areas offer opportunities for rapid improvements in service delivery:

Opportunity for rapid scale up of HIV treatment coverage

The metros already run very large ART programmes. Larger ART facilities – which are predominantly found in urban settings - generally, achieve better viral suppression among their ART clients than smaller facilities [14]. This may be in part due to having more human and infrastructural resources and support targeted to large treatment sites, and the existing knowhow and resources can be mobilised for further expansion of the metros' ART programmes. The first ATMs for chronic medications have been set up in Soweto shopping malls in 2015 by Right to Care.

Opportunity for better linkage to HIV care

Although we determined linkage to care, we did not assess the first 90 (proportion of PLHIV who are HIV tested) in this study due to a lack of suitable data. The first 90 remains the biggest gap in the South African treatment cascade and many HIV testing service providers and health decision-makers are considering best approaches to reach different populations with HIV testing modalities and, upon diagnosis, link them to HIV treatment. Proximity of service delivery sites, close networks, better cell phone access and sheer volume of clients mean that better linkage to care modalities and doing so using innovative approaches, is possible in the metros.

Opportunity for more functional integration of HIV services

Because of the existence of several HIV services (male circumcision, prevention of mother-to-child transmission, provider-initiated HIV testing, etc.), economies of scope are most likely in urban areas where functional integration of HIV services with each other, and within an integrated clinic model, is possible. This will address for instance the barriers to patients' treatment adherence of transport costs to clinics for drug refills [15,16].

Opportunity for technical efficiency gains

Technical efficiency gains, in areas where large volumes of patients are to be served is feasible to gain economies of scale and thus reduce the minimum cost of delivering a specific service. Technically efficient ART programmes are not only cost-effective, but also cost-saving [17].

Opportunity for better health outcomes

The latter part of our HIV care cascades pointed to large differences in viral suppression achieved in the metros. Among the many consequences are impaired HIV transmission reduction through ART (as more ART clients remain infectious while not virally suppressed), and lower cost savings (as unsuppressed ART clients are more likely to fall ill and generate care costs). One South African study in the private sector found that greater ART adherence, as assessed by pharmacy claims, was associated with lower overall direct health care expenditures among ART clients enrolled in a private-sector managed care programme [18].

Opportunity for more rapid implementation of the new national chronic disease adherence guidelines

Large urban ART sites risk having long waiting times due to the sheer number of ART clients. To address this, the NDOH and partner organisations like Médecins Sans Frontières (MSF) have recognised the need to decongest health facilities, especially the high volume ones in densely populated areas. The aim is to introduce HIV treatment support models that require little clinic contact for stable clients, so that health facility staff can focus on unstable and complex clients (described in the 2016 South Africa National Chronic Disease Adherence Guidelines [19], which includes TB, NCDs and mental health conditions). These system reforms all intend to improve public sector care by clinic decongestion, down-referral, decentralisation, community-based monitoring and assisted self-monitoring by chronic clients. Urban areas offer an ideal opportunity to harness these different strategies.

Opportunity for better use of laboratory data to track and optimise ART scale-up

The secondary data analysis described in this paper debuts the South African patient-level laboratory cohort and demonstrates its ability to provide comprehensive information on linkage to care and viral suppression in the metros. Drawing from VL and CD4 test data archived at the CDW rather than Tier.Net provides a more comprehensive picture as a large proportion of the test data never gets captured in Tier.Net. For the financial year 2014/2015, Tier.Net reported 46% VLD for adults (Tier update of Oct 2015, NDOH internal document), whereas the methodology used in this project found that 75% of ART clients had at least one VL test in the 12 month period [14]. This comprehensive information can be used to identify successes (and failures) – health districts or facilities that have high (or low) VL testing coverage, and high (or low) proportion of virologically suppressed. Learning and investments in the metros' ART programmes can then happen in the right places.

Ensuring scale and quality of the HIV treatment programmes is vital for the metros' economic prosperity - and for South Africa as a whole given the metros account for 70% of the country's GDP. ART not only prolongs lives (one South African study reported life expectancy increased by an average of 11.3-years following the introduction of mass HIV treatment) [20], it also impacts productivity and labour supply. In KwaZulu-Natal, economic spill-over effects were documented in households where HIV infected household members were on ART [21]. Other studies have identified aggregate effects of ART scale-up on economic outcomes at the community level [22]. The effects of ART on labor market outcomes is particularly strong where work opportunities are present, indicating the need to pair health, development and investment strategies as envisaged in South Africa's Integrated Urban Development Framework. Better health indeed equals more wealth. Getting health service delivery right in urban areas in an era of prolonged and increasing urbanization is vital not only for the individuals who live there, but the economies as a whole.

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