BMJ Open

Cohort profile: the Right to Care Clinical HIV Cohort, South Africa

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To cite: Fox MP, Maskew M, Brennan AT, *et al*. Cohort profile: the Right to Care Clinical HIV Cohort, South Africa. *BMJ Open* 2017;**7**:e015620. doi:10.1136/bmjopen-2016-015620

► Prepublication history and additional material are available. To view these files please visit the journal online (http://dx.doi.org/ 10.1136/bmjopen-2016-015620).

Received 20 December 2016
Revised 26 February 2017
Accepted 3 April 2017

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ABSTRACT

Purpose The research objectives of the Right to Care Clinical HIV Cohort analyses are to: (1) monitor treatment outcomes (including death, loss to follow-up, viral suppression and CD4 count gain among others) for patients on antiretroviral therapy (ART); (2) evaluate the impact of changes in the national treatment guidelines around when to initiate ART on HIV treatment outcomes; (3) evaluate the impact of changes in the national treatment guidelines around what ART regimens to initiate on drug switches; (4) evaluate the cost and cost-effectiveness of HIV treatment delivery models; (5) evaluate the need for and outcomes on second-line and third-line ART; (6) evaluate the impact of comorbidity with non-communicable diseases on HIV treatment outcomes and (7) evaluate the impact of the switch to initiating all patients onto ART regardless of CD4 count.

Participants The Right to Care Clinical HIV Cohort is an open cohort of data from 10 clinics in two provinces within South Africa. All clinics include data from 2004 onwards. The cohort currently has data on over 115 000 patients initiated on HIV treatment and patients are followed up every 3–6 months for clinical and laboratory monitoring.

Findings to date Cohort data includes information on demographics, clinical visit, laboratory data, medication history and clinical diagnoses. The data have been used to identify rates and predictors of first-line failure, to identify predictors of mortality for patients on second-line (eg, low CD4 counts) and to show that adolescents and young adults are at increased risk of unsuppressed viral loads compared with adults.

Future plans Future analyses will inform national models of HIV care and treatment to improve HIV care policy in South Africa.

Strengths and limitations of this study

- The biggest strength of the Right to Care Clinical cohort is its size. With over 115 000 patients ever initiated onto HIV treatment, precise evaluations can be conducted. This is particularly important when describing outcomes among subsets of the cohort that could not be conducted with much precision using individual clinic data.
- Second, while the clinics use a similar treatment protocol and data collection strategies, they show geographic variation. While other cohort collaborations do have such geographic variation, few were designed to encompass clinics which shared a common software and approach to data collection. Further because we link the data to the National Health Laboratory Service and the National Population Registry, we have high-quality, nearly complete data on mortality (for citizens who provide an ID), viral load and CD4 counts as well as laboratory tests for antiretroviral monitoring such as haemoglobin and creatinine.
- The main weakness of the data is the lack of standardised follow-ups. Because the cohort follows changing national guidelines and because specific research-based efforts to get patients to adhere to treatment visit schedules are not performed, we do not always have standard monitoring points for all patients within the cohort. This can make interpretation of results difficult and requires careful consideration of the meaning of missing data.

INTRODUCTION

As we enter the second decade of large-scale access to antiretroviral therapy (ART) in sub-Saharan Africa, there is little question about the role that clinical cohorts have played in both evaluating and shaping HIV policy within the continent.[1–3] South Africa, with the largest HIV treatment programme in the world and over 3 million people on ART, has been a leader in this area. The numerous clinical cohorts that were established since 2004[4–7] have been used to evaluate the changes in national treatment policy. One of these cohorts, the Themba Lethu Clinical Cohort[8] was established at the Helen Joseph Hospital in Johannesburg and has led to numerous insights into the effectiveness of the treatment roll-out and also participates in larger country-wide and region-wide evaluations through the International Epidemiologic Database to Evaluate AIDS (IeDEA) network.[7 9] However, the Themba Lethu cohort is based at a large urban tertiary hospital and as the responsibility for HIV care and treatment shifts from hospital based programs to primary

Table 1 Routinely collected data for patients in the Right to Care Clinical HIV Cohort, South Africa

Data fields	
Demographics	Clinic ID, name, national ID number, contact details, gender, date of birth, employment status, alcohol use, smoking history, ethnicity, education level
Clinical visit data	Date of visit (scheduled and actual), TB screening, urine analysis, vital signs, height, weight, description and duration of new symptoms, systems based clinical examination (eg, cardiology, neurology, respiratory, etc)
Laboratory results	ART initiation and monitoring bloods including CD4 count, HIV viral load, full blood counts, liver function tests, renal function tests, TB microscopy and culture results, pap smear screening results, lactate levels, glucose and lipid profiles
Medication history	Date of start and stop of ART and non-ART medications, reasons for treatment discontinuation, self-reported treatment adherence
Clinical diagnoses	Pregnancy, opportunistic infections including TB, hepatitis, PCP, AIDS-related malignancies including Kaposi sarcoma and cervical cancer, ART toxicities including peripheral neuropathy, anaemia, hyperlactataemia/lactic acidosis, lipoatrophy

ART, antiretroviral therapy; TB, tuberculosis; PCP pneumocystis pneumonia.

healthcare clinics, it has become clear that the Themba Lethu Clinical cohort is not sufficient for describing the HIV treatment programme in South Africa in its entirety. As such, the Right to Care Clinical Cohort, which includes the Themba Lethu cohort, has been established to provide a broader, more representative perspective on South Africa's HIV care and treatment programme.

COHORT DESCRIPTION

The Right to Care Clinical Cohort is a network of 10 clinical cohorts all established or expanded around 2004 as part of the public-sector roll-out of ART in South Africa under support from the US Agency for International Development from the President's Emergency Plan for AIDS Relief programme. The clinics have all been supported by Right to Care, a South African NGO which partners with clinic-based HIV care and treatment programs throughout South Africa. As part of their support to clinics, Right to Care has provided both data entry and an electronic data capturing and patient management system called Therapy-Edge-HIV (TM). Thus, each clinic within the network follows a common data entry protocol and uses a standard database for data capture. Table 1 shows the major data fields captured within the database. To oversee the data and conduct analyses, Right to Care partners with both the individual clinics and the Health Economics and Epidemiology Research Office in South Africa, part of the Wits Health Consortium which functions as a collaboration between the University of the Witwatersrand and Boston University. Analysis of anonymised data has been approved by the University of the Witwatersrand Human Research Ethics Committee and the Boston University Institutional Review Board.

Among the individual clinics within the Right to Care Clinical Cohort, two are stand-alone HIV clinics while the remaining eight are primary healthcare clinics, which have an HIV treatment programme. While the individual clinics provide fertile ground for evaluating the effects of specific drug regimens,[10–14] treatment outcomes,[15–21] opportunistic infections[22–24] and adverse drug events,[10 25] because the cohort is large and the clinics are diverse in location and staff mix but provide care according to a standard protocol,[26–29] they also create an excellent environment for evaluating large policy changes like the recent move to treatment for all, South Africa's national adherence strategy and South Africa's national decanting strategy. In addition, such large collaborations are needed both to triangulate the results of other large collaborations such as IeDEA[30] and to create cohorts large enough to evaluate future needs. These include the coming wave of patients failing first-line[31] and second-line treatment[12 32–34] and needing access to expensive third-line regimens or the needs of key populations such as pregnant women[35] and adolescents in HIV care.[17]

The Right to Care Clinical Cohort is an open cohort and includes all patients enrolled at one of the participating clinics since April 2004. The clinics included in the cohort are located in Gauteng and Mpumalanga provinces within South Africa as shown in figure 1. Of these, nine are urban sites while one is in a rural site. All the clinics follow the most recent version of the South African National HIV Treatment Guidelines,[28] though the clinics vary in their staffing models.

As of June 2016, across the 10 clinics, 155 144 patients have been enrolled, of which 116 490 have initiated ART. Currently, 46 241 are actively on ART. The clinics range in size from 4332 to 39 297 current patients. Table 2 summarises the demographic and clinical characteristics of the cohort stratified by last treatment regimen. About two-thirds of the cohort (63%) are female; most are black or of African ethnicity (95%) and the patients have a median age of 35 years (IQR 29–42 years). Average CD4 counts at ART initiation have been increasing over time as the treatment thresholds have increased from ≤200 cells/mm^3 in 2004 to ≤350 cells/mm^3 in 2011 to ≤500 cells/mm^3 in 2015 to treatment for all in 2016. During that

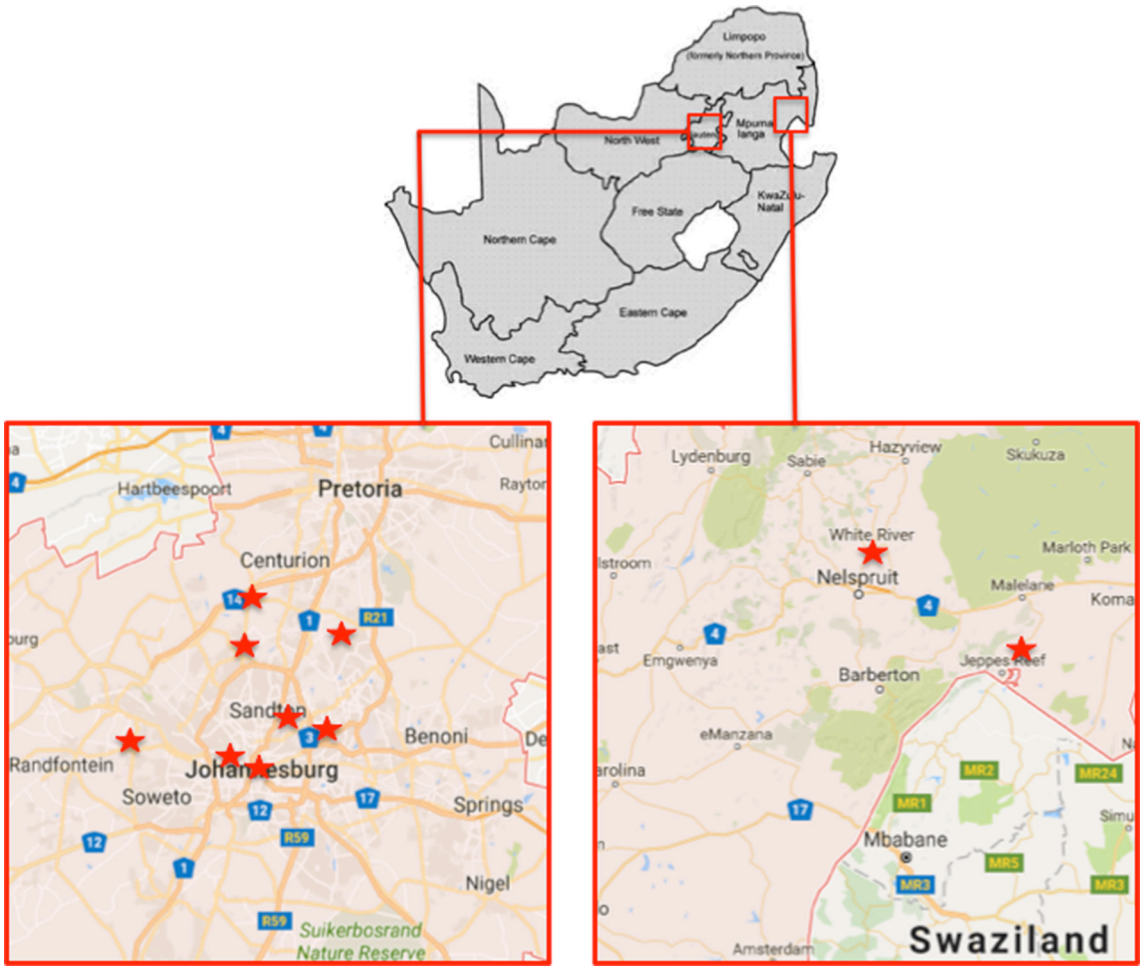

Figure 1 Location of clinics in Right to Care Clinical Cohort.

time, the median (IQR) CD4 count at ART initiation has increased from 118 (49–188 cells/mm^3) to 241 (97–394 cells/mm^3). South Africa has recently removed CD4 eligibility thresholds in line with recent WHO recommendations.

Since the large-scale roll-out of ART in South Africa in 2004, the recommended drug regimens for both first-line and second-line ART have evolved (first-line regimens shown in figure 2). Within the cohort, 39 244 patients are currently on first-line ART. Since 2004, three-drug first-line therapy has been non-nucleoside reverse transcriptase inhibitor (NNRTI) based, with efavirenz preferred, but nevirapine is also available. In addition to lamivudine, stavudine was the favoured nucleoside reverse transcriptase inhibitor in the early years but in 2010 tenofovir was recommended.

South Africa monitors the effectiveness of HIV treatment using viral loads. For patients who have documented first-line failure (defined as two consecutive viral loads≥1000 copies/mL^3 at least 2 weeks apart), switching to second-line protease inhibitor-based therapy (typically lopinavir-ritonavir) is recommended. A total of 5909 patients are currently on second-line ART, making it one of the largest second-line cohorts in Africa. More recently, access to third-line ART has become available for patients failing second-line. Access is managed by application to a national third-line committee that will order resistance testing and prescribe an appropriate third-line regimen based on the results. Third-line consists of any of darunavir, raltegravir and etravirine. Currently, 129 patients have been initiated on third-line within the cohort.

Follow-up measures

Protocols for follow-up of patients on ART within the clinics follow national HIV treatment guidelines that have changed over the years. While initially patients were required to be seen each month to collect antiretrovirals (ARVs), as the programme has matured, patients who have been demonstrated to be adherent and stable on treatment can be prescribed 2 or 3 months of ART at a time, allowing for fewer visits, a reduced burden on the patient and lower clinic volume on a daily basis. A total of 116 490 patients who had ART within the cohort have contributed a total of 3 42 931 person-years on ART. The median (IQR) duration of follow-up per person has been 2.17 (0.81–4.41) person-years with a range of 0.04 to 12.5 person-years. This equates to 1 597 690 total medical and 2 262 626 pharmacy visits at a rate of 6.6 per year.

Table 2 Characteristics of patients in the Right to Care Clinical HIV Cohort in South Africa by last treatment regimen

Demographic characteristics		First line (N=1 10 452)	Second line (N=5909)	Third line (N=129)
Gender	Female, n (%)	70 590 (63.9)	3822 (64.7)	65 (50.4)
	Male, n (%)	39 860 (36.1)	2087 (35.3)	64 (49.6)
	Missing, n (%)	2 (0)	0 (0)	0 (0)
Nationality	South African, n (%)	96 977 (88.0)	5354 (90.6)	109 (84.5)
	Non-South African, n (%)	13 176 (12.0)	555 (9.4)	20 (15.5)
	Missing, n (%)	299 (0)	2 (0)	0 (0)
Education level	No education, n (%)	7372 (6.7)	384 (6.5)	1 (0.8)
	Primary, n (%)	18 520 (16.8)	886 (15.0)	33 (25.6)
	Secondary, n (%)	56 156 (50.8)	3058 (51.8)	66 (51.2)
	Tertiary, n (%)	2179 (2.0)	124 (2.1)	1 (0.8)
	Missing, n (%)	26 225 (23.7)	1457 (24.7)	28 (21.7)
Employment status	Unemployed, n (%)	58 862 (53.3)	3378 (57.2)	48 (37.2)
	Employed, n (%)	43 261 (39.2)	2274 (38.5)	74 (57.4)
	Missing, n (%)	8329 (7.5)	257 (4.3)	7 (5.4)
Characteristics at ART initiation				
Age (years)	Median (IQR)	35.6 (29.4–42.3)	33.9 (28.4–40.1)	36.1 (29.8–41.2)
Body mass index (kg/m^2)	<18.5, n (%)	12 640 (11.4)	754 (12.8)	14 (10.9)
	18.5–24.9, n (%)	36 258 (32.8)	1948 (33.0)	35 (27.1)
	25–29.9, n (%)	13 289 (12.0)	650 (11.0)	9 (7.0)
	30, n (%)	7394 (6.7)	340 (5.8)	11 (8.5)
	Missing	40 871 (37.0)	2217 (37.5)	60 (46.5)
	Median (IQR)	22.2 (19.4–25.8)	22.0 (19.1–25.3)	22.2 (18.9–26.2)
CD4 count category (cells/mm^3)	<50, n (%)	18 651 (16.9)	1344 (22.7)	20 (15.5)
	50–100, n (%)	13 915 (12.6)	858 (14.5)	16 (12.4)
	100–200, n (%)	26 426 (23.9)	1227 (20.8)	17 (13.2)
	200–350, n (%)	17 046 (15.4)	578 (9.8)	15 (11.6)
	>350, n (%)	7573 (6.9)	262 (4.4)	10 (7.8)
	Missing, n (%)	26 841 (24.3)	1640 (27.8)	51 (39.5)
	Median (IQR)	137 (58–222)	97 (36–180)	113 (43–257)
HIV viral load (copies/mL^3)	≤1 00 000, n (%)	17 710 (16.0)	1100 (18.6)	28 (21.7)
	>1 00 000, n (%)	10 087 (9.1)	786 (13.3)	12 (9.3)
	Missing*, n (%)	82 655 (74.8)	4023 (68.1)	89 (69.0)
Haemoglobin level (g/dL)	Median (IQR)	11.5 (10.0–13.0)	11.4 (10.0–12.8)	11.9 (10.7–13.2)
Tuberculosis	Yes, n (%)	9871 (8.9)	632 (10.7)	9 (6.9)
	No, n (%)	1 00 381 (91.1)	5258 (89.3)	120 (93.1)
Current status	Alive and in care, n (%)	42 542 (38.5)	3605 (61.0)	94 (72.9)
	Deceased, n (%)	10 561 (9.6)	261 (4.4)	2 (1.6)
	Lost to follow-up, n (%)	28 561 (25.9)	1010 (17.1)	25 (19.4)
	Transferred out, n (%)	28 788 (26.1)	1033 (17.5)	8 (6.2)

*HIV viral load was only completed at baseline in the early years of the programme.

Laboratory investigations for all the clinics in the cohort are conducted by the National Health Laboratory Service (NHLS). While NHLS sends back individual reports to the clinics with the results of each investigation, within the cohort, data from the NHLS are downloaded directly and are integrated into the individual patient database on a daily basis, allowing complete and accurate data on lab investigations.

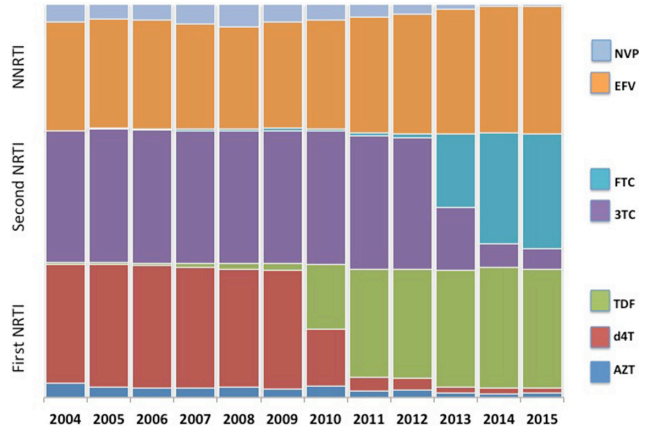

Figure 2 Distribution of first-line antiretroviral therapy regimen component drugs by calendar year. 3TC, lamivudine; AZT, zidovudine; d4T, stavudine; EFV, efavirenz; FTC, emtricitabine; NRTI, nucleoside reverse transcriptase inhibitor; NVP, nevirapine; TDF, tenofovir.

Since the beginning of the programme, CD4 counts have been used to determine ART eligibility, with the first viral load monitoring being conducted at between 4 and 6 months on treatment. The interval for monitoring has changed from every 6 months after the initial viral load, to a 6-month and 12-month viral load and then a repeat viral load every year as of 2013. Cohort patients had a median (IQR) of 2.1 (0.48–4.6) viral loads per year and a median (IQR) of 3 (2–7) viral loads per person. Figure 3 shows the increase in numbers on ART and the proportion of patients virally suppressed with changes in the national guidelines.

Because of the richness and size of the cohort, the data have been used to conduct important evaluations of the impact of second-line treatment,[13 36] of transfer between clinics,[15] of the impact of changes in CD4 thresholds on clinic crowding,[37] as well as of the impacts of the shift to tenofovir in replacement of stavudine[11 38] in the national programme. In addition, when warranted, analyses of subsets of the data are used to conduct urgent evaluations such as the impact of pregnancy on retention,[35] outcomes within patients on second-line ART[33] and outcomes for adolescents on ART.[39] The data have also been successfully used by doctoral students for dissertation work.[37]

Data collection

As noted, all clinics within the cohort have employed a common patient data collection system since 2004, the TherapyEdge-HIV (TM) patient management system. The system is a longitudinal database designed to capture essential information from all HIV-related clinic visits.[40] Data are captured on patients both prior to ART initiation and after. While the CD4 threshold for ART initiation has changed over time, the protocol for patients prior to initiation has been 6-monthly monitoring of CD4 count until eligibility is established.

For each patient interaction at a cohort clinic, the date of the encounter is recorded allowing for longitudinal follow-up. At the first visit, demographics data are collected including key identifiers and information on age, sex, race, education, alcohol use and smoking. When possible national identifiers are collected to allow linkage with national registries and phone numbers are collected to allow for patient tracing should patients become lost to follow-up. At each follow-up visit, data on clinical conditions that are identified (such as side effects, TB and so on) are captured. At each visit, information is also

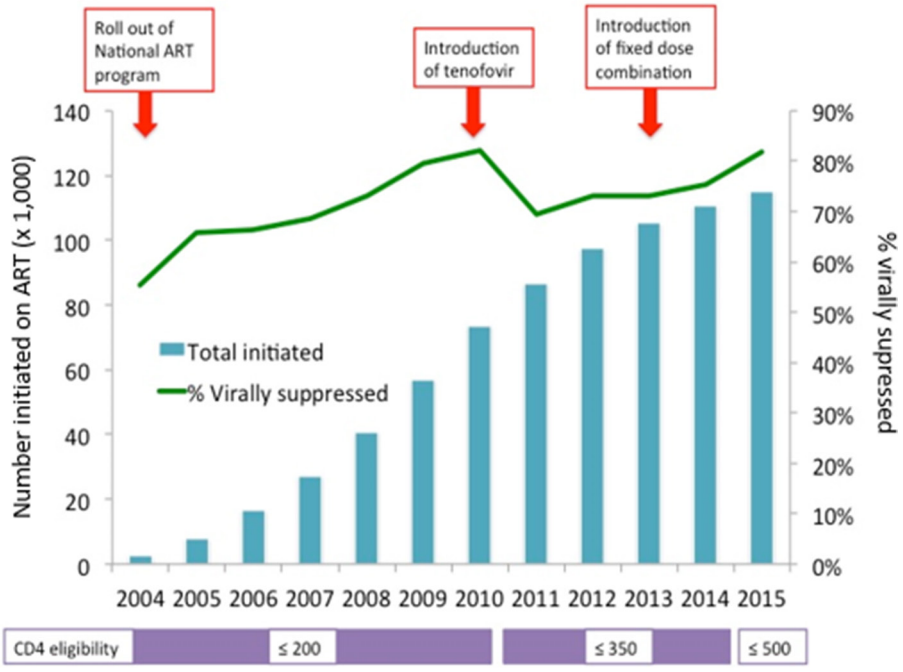

Figure 3 Numbers on antiretroviral therapy and viral load suppression over time in the Right to Care HIV Cohort. This analysis was cross-sectional, and missing viral loads are not included.

recorded on any medication dispensed including ARVs and other medications.

Overall retention in HIV care in sub-Saharan Africa is less than ideal.[41–43] Because one of the main uses of these data has been to describe the cascade of HIV care,[44 45] no attempts are made to influence retention for research purposes. Instead, all measures are taken to reduce attrition as part of usual clinical care. All the clinics within the cohort attempt to trace patients who are lost to follow-up, though with differing intensities. Each clinic uses its own definition of loss for triggering tracing activities, though a common definition of 3 months late for an appointment is used for research purposes and standardising loss rates across clinics. At all clinics, tracing is initially done through calling the phone number collected at enrolment. Some of the clinics also employ tracers or use community outreach workers to attempt to trace patients who do not return to care.

Mortality is ascertained in multiple ways within the cohort. All sites use passive follow-up to identify patients who have died and record the information when it is reported back by a family member or friend. In addition, data on all patients who have provided a national identification number and who are lost to follow-up are cross-referenced with South Africa's National Population Register[15] (NPR) to determine final outcomes. The proportion of patients who are either in possession of, or report their national ID number varies from clinic to clinic, ranging from 35% to 74%. Prior to the initial linkage between Themba Lethu Clinic and the NPR, 17% of patients within the clinic were considered lost to follow-up and 4% were known to have died. After linkage, the proportion who were considered to be lost dropped to 10% and the proportion who were recorded to have died increased to 11%.[15]

Another way patients leave the cohort is through transfer to another treatment facility. When the patient formally requests this it is noted in the database as a patient outcome. The rate of transfer within the cohort is 12% and varies from 11% to 50%, though those at the higher end see this as intentional transfers of patients who are 'down-referred' to smaller clinics once stable.[46 47] However, as is common within HIV treatment programmes within the region, transfers are often 'silent transfers' where patients transfer without informing their current clinic. Patients who transfer to a new clinic outside our network without informing us will appear as lost to follow-up. We have shown that this can bias estimates of retention in care,[48] and therefore the clinics within the cohort request patients notify the clinic if they wish to receive care elsewhere so that care can be coordinated.

FINDINGS TO DATE

The Right to Care Clinical Cohort is used to monitor the continued roll-out of ART in South Africa and to evaluate the impact of changes in the national treatment programme as they are made. Current areas of research include: (1) monitoring treatment outcomes (including death, loss to follow-up, viral suppression, CD4 count gain, etc) for patients on ART; (2) evaluating the impact of changes in the national treatment guidelines around when to initiate ART on HIV treatment outcomes; (3) evaluating the impact of changes in the national treatment guidelines around what ART regimens to initiate on drug switches; (4) evaluating the cost and cost-effectiveness of HIV treatment delivery models; (5) evaluating the need for and outcomes on second-line and third-line ART; (6) evaluating the impact of comorbidity with non-communicable diseases on HIV treatment outcomes and (7) evaluating the impact of the switch to initiating all patients onto ART regardless of CD4 count.

To date, we have used the Right to Care cohort to evaluate various aspects of the national HIV treatment programme. Three examples of this work include:

- *Treatment outcomes.* While numerous models have found important predictors of failing first-line therapy, few have had the size to be able to develop a precise predictive model of treatment failure.[49] Using data on 71 154 individuals, we showed that age, sex, interactions between age and sex, first-line NNRTI, CD4 count, mean corpuscular volume, haemoglobin level, history of TB and missed visits during the first 6 months on ART were predictive of failure. After stratifying into risk groups, failure in the highest risk group was 24.4% over 5 years on ART but only 9.4% among the lowest risk group, allowing stratification of risk for clinics.[49]
- *Second-line ART outcomes.* The need for second-line treatment has been growing as treatment scale up has continued, but there is little robust data on outcomes among patients who have already failed a first-line regimen.[34] With data on 1435 patients on second-line ART between 2004 and 2013, we found that a low CD4 count (<50 cells/mm^3) at the time of switch was strongly predictive of mortality (adjusted HR (aHR) vs ≥200 cells/mm^3: 3.76; 95% CI: 1.87 to 7.57) as was a high viral load (≥50 000 copies/mL vs 1000–4999 copies/mL aHR: 2.01; 95% CI: 1.07 to 3.77).[33] The results suggest that earlier switch would likely benefit patients failing first-line before disease progresses to severe immunosuppression.
- *Outcomes for adolescents on HIV treatment.* While having been identified as a key population for ending the AIDS epidemic, few cohorts have been able to measure outcomes among adolescents on HIV treatment in resource-limited settings because there are not sufficient numbers. Comparing 310 adolescents 10–14 years, 342 adolescents 15–19 and 1599 young adults 20–24 years to adults ≥25 years, we found both older adolescents (adjusted risk ratio (RR) 1.75 95% CI 1.25 to 2.47) and young adults (RR 1.33 95% CI 1.10 to 1.60) were at increased risk of an unsuppressed viral load compared with adults[17] suggesting they need to be targeted for additional intervention.

Perhaps the biggest strength of the Right to Care Clinical cohort is its size. With over 115 000 patients ever initiated onto HIV treatment, precise evaluations can be conducted. This is particularly important when describing outcomes among subsets of the cohort that could not be conducted with much precision using individual clinic data. For example, by pooling data across 10 clinics, we are able to conduct precise analyses on a large cohort of patients initiating second-line therapy.

Second, while the clinics use a similar treatment protocol and data collections strategies, they show geographic variation. While other cohort collaborations do have such geographic variation, few were designed to encompass clinics which shared a common software and approach to data collection. Further because we link the data to the NHLS and the National Population Registration, we have high-quality, nearly complete data on mortality (for citizens who provide an ID), viral load and CD4 counts as well as ARV monitoring labs such as haemoglobin and creatinine.

Perhaps the main weakness of the data is the lack of standardised follow-ups. Because the cohort follows changing national guidelines and because specific research-based efforts to get patients to adhere to treatment visit schedules are not performed, we do not always have standard monitoring points for all patients within the cohort. This can make interpretation of results difficult and requires careful consideration of the meaning of missing data. It also calls for the use of missing data methods[50] and formal quantitative bias analysis[51–54] to explore the impact of any systematic errors. In addition, because the cohort is not designed as a research cohort, biological samples are not collected at routine intervals (beyond what is required for clinical care) and these samples are not stored. Therefore, we cannot use the cohort to study topics such as molecular epidemiology or biomarker research. Because the cohort is meant to reflect what is happening in actual clinic care, such samples will continue to not be stored going forward.

COLLABORATIONS

Investigators wishing to work with the data should contact the team at the Health Economics and Epidemiology Research Office (information@heroza.org) and send a concept sheet for the analyses they are interested in performing and the variables that would be required. Anyone wishing to work with the data from the Right to Care Cohort must seek Institutional Review Board approval from both their own institutions and from the Human Research Ethics Committee (Medical) of the University of the Witwatersrand. After receiving such approvals, those wishing to work with the data must sign a data-use agreement. Those wishing to find out more about the Right to Care cohort can visit the website of the Health Economics and Epidemiology Research Office in Johannesburg, South Africa, at http://www.heroza.org/.

Correction notice This paper has been amended since it was published Online First. Owing to a scripting error, some of the publisher names in the references were replaced with 'BMJ Publishing Group'. This only affected the full text version, not the PDF. We have since corrected these errors and the correct publishers have been inserted into the references. Mhairi Maskew was correctly listed as the second author but then listed again at the end of the author list. This has been corrected so he only appears once in the author list.

Acknowledgements The authors wish to thank Babatyi Malope-Kgokong for her efforts and input in developing the database. We also thank Ms. Imogen Jaffray and the TherapyEdge-HIV team as well as the data capturers who helped collect the data. Most importantly, we thank the patients who contributed to this cohort.

Contributors MPF and MM conceptualised the study. MPF and MM wrote the first draft. GM conducted the data analysis. MPF, MM, ATB, DE, DO, GM, PM, JB, OE, DM, SM, LL and IS contributed to interpreting the data and to the writing and revising of the manuscript.

Funding This study is made possible by the generous support of the American people through Cooperative Agreement AID 674-A-12-00029 from the US Agency for International Development (USAID).

Disclaimer The contents are the responsibility of the authors and do not necessarily reflect the views of USAID or the US Government. The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript.

Competing interests None declared.

Ethics approval Boston University Institutional Review Board, University of the Witwatersrand Human Research Ethics Committee.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Investigators wishing to work with the data should contact the team at the Health Economics and Epidemiology Research Office and send a concept sheet for the analyses they are interested in performing and the variables that would be required. Anyone wishing to work with the data from the Right to Care Cohort must seek IRB approval from both their own institutions and from the Human Research Ethics Committee (Medical) of the University of the Witwatersrand. After receiving such approvals those wishing to work with the data must sign a data-use agreement. Those wishing to find out more about the Right to Care cohort can visit the website of the Health Economics and Epidemiology Research Office in Johannesburg, South Africa at.

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