Privacy preserving-probabilistic record linkage to assess cancer outcomes in people living with HIV in South Africa

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Abstract

Background: Privacy-preserving probabilistic record linkage (PPPRL) methods were developed and applied in high-income countries to link records within and between organizations under strict privacy protections. PPPRL has not yet been used in African settings.

Methods: We used HIV-related laboratory records from National Health Laboratory Services (NHLS) in South Africa to construct a cohort of HIV-positive patients and link them to the National Cancer Registry (NCR) with PPPRL. The study was restricted to Gauteng province from 2004 to 2014. We used records with national IDs (gold standard) to determine precision, recall, and f-measure of the linkages. We included all patients with ≥ 2 HIV-related lab records measured in the cohort and assessed the number of cancers diagnosed in people living with HIV (PLWH).

Results: We included 11,480,118 HIV-related laboratory records and 664,869 cancer records in the linkage. We included 1,173,908 persons in the HIV cohort; 66.6% were female and median age at first HIV-related lab test was 33.9 years (IQR 27.4-41.3). Of the patients in the cohort, 26,348 were diagnosed with at least one cancer and 8,329 of these cancers were diagnosed before or on the date of the patient's first HIV-related record; 18,019 were diagnosed after their first HIV-related record. For all linkages, precision, recall, and f-measures were high.

Conclusion: Our study showed it is feasible to use PPPRL in an African setting to link routinely collected health records from different data sources and create a longitudinal HIV cohort with cancer outcomes while strictly protecting patient privacy. This work served as the foundation to create a nationwide population-based cohort including all South African provinces which will be used to inform cancer control programs.

INTRODUCTION

Privacy-preserving probabilistic record linkage (PPPRL) methods were developed and are applied in high-income countries to link records within and between organizations while strictly protecting patients' privacy [1][2], but we found no evidence PPPRL has been used in African settings. To study cancer related morbidity in people living with HIV (PLWH), HIV and cancer registry match studies have linked data from patients in HIV cohorts to cancer registry records based on plain names [3–7]. But HIV cohorts in sub-Saharan Africa (SSA) are often small groups of children and adults who are treated in specialized HIV clinics in urban settings; these groups do not represent the HIV population of the whole country [5–7]. Two-thirds of the world's HIV-positive population lives in SSA and we need large, representative, population-based cohort studies of PLWH in this region to inform cancer epidemiology and policy.

South Africa is an ideal place to use population-based health records from routine care to create a population-based HIV cohort with cancer outcomes. The South African National Health Laboratory Services (NHLS) runs a network of laboratories and is the main diagnostic pathology service supporting the national and provincial health departments that deliver healthcare to over 84% of the South African population [8][9]. The South African National Cancer Registry (NCR) is South Africa's primary cancer surveillance system [10][11]. The NHLS and NCR do not use unique patient identifiers, and both strictly protect patient privacy.

We used PPPRL to construct a cohort of PLWH with cancer outcomes by linking population-based HIV and cancer records in South Africa and to assess the PPPRL's recall and precision.

METHODS

Data sources

We retrieved NCR records for all South African provinces and NHLS records for Gauteng Province, covering the period 2004 to 2014. We limited this study to Gauteng province, which is the most populous province in South Africa. For a detailed description of the two data sources, see supplement (supp **Box 1**). From the NHLS Corporate Data Warehouse (CDW) we extracted all HIV-related lab records: HIV ELISA (enzyme linked immunosorbent assay) test; HIV Western blot test; HIV rapid test; HIV RNA viral load; CD4 count/percentage, date of test (specimen registration). Within

NHLS, each sample taken from a patient is assigned a unique Episode number; one Episode number can include several laboratory tests if they were performed on the sample.

Privacy preserving probabilistic record linkages (PPPRL)

The main steps in PPPRL are identifying linkage variables, pre-processing and encrypting data, de-duplicating and linking data, evaluation and clerical review of linkages, and constructing analysis files.

Identification of linkage variables

We used the following patient-identifying information as linkage variables for NHLS records: Episode number; national ID; given name(s); surname(s); sex; precise or estimated date of birth; facility that provided care; and the corresponding district and sub-district. We used these linkage variables for NCR records: given name; surname; sex; precise date of birth or, where not available birth year or patient's age.

Data pre-processing and encryption

We pre-processed NHLS and NCR records with Python scripts and standardized linkage variables for format, structure, and content. We created regular expression templates to handle titles, prepositions, special characters, hyphens, blanks, one or more given names and surnames, etc. We checked dates for plausibility and standardized their format. We excluded records with missing or implausible surnames, records with age > 100 years at test date, records in which National ID or Episode number deviated from standard length, and all HIV tests with negative, missing, or inconclusive test results. After pre-processing, we used the P3RL encryption tool to encrypt names [2]. We generated specific hash functions using the same key word and the same length of string for encrypting the two datasets, thus ensuring data privacy and irreversibility of encryption. The P3RL encryption tool still allowed us to compare strings within and between data bases. We transformed every name into a 250-digit hexadecimal string. We validated encryption, with a test word encrypted at the same time as the names. We recoded National IDs and dropped original national IDs and unencrypted names from the dataset before deduplicating and linking. We assessed completeness of linkage variables, patient characteristics, and facility/geographic location and compared records with and without national IDs.

Deduplication and linkage

We deduplicated NHLS records (one table linkage mapping one-to-many records) and linked NHLS and NCR records (one-to-many mapping) with G-Link (G-Link 3.3 Rel 5.2 [12]). First, we deterministically deduplicated pre-processed NHLS records using the Episode number, and then we used encrypted first names and surnames, sex, date, and year of birth. Thereafter, we probabilistically linked records using encrypted first names, encrypted surnames, sex, precise birth date (if not available, then birth year), facility that provided care, and geographic location of the facility (district and sub-district). Next, we probabilistically linked the deduplicated NHLS data with the NCR dataset using the following linkage variables: encrypted first names; encrypted surnames; sex; and precise birth date or, if unavailable, birth year. During deduplication, if we found discrepancies in the linkage variables of records assigned to the same person, we created dummy variables that coded the alternative information. For example, if there were discrepancies in the birth date of a person in NHLS records, we compared them to NCR records for each of the birth date records assigned to that person. We thus used all the information in the NHLS data set. Finally, we used a one-to-many mapping method to map the data (G-Link 3.3 Rel 5.2 user guide). We were able to link the two databases and deduplicate the NCR records at the same time. The technical linkage details, including blocking, matching, and grouping, are in the **supplement Box 2**.

Evaluation and clerical review

We determined optimal cut-offs and evaluated linkage accuracy, using NHLS and NCR records with national ID (gold standard). First, we used deterministic record linkages based on national IDs to identify records that belonged to the same patient in the two data sets. Next, we probabilistically linked records (as described above) using the same set of linkage variables, without national IDs so we could identify correct matches (true positive), incorrect matches (false positive), and missed matches (false negative). We derived recall (true positive / [true positive + false negative]), precision (true positive / [true positive + false positive]), and the f-measure (the harmonic mean of precision and recall, see **Box 1).** We assessed and plotted linkage accuracy at 16 different cut-offs for the total weight (increments of 20 from -80 to 220) for deduplication within NHLS records and linkage between NHLS and NCR records. For the clerical review, we checked for matched and mismatched birth dates and birth years, and assessed the size of record clusters.

Cohort construction

For linked cases, we retrieved and merged this information from the NCR: ethnicity; International Statistical Classification of Diseases and Related Health Problems (ICD)-10 and International Classification of Diseases for Oncology (ICD-O)-3 code; test date (specimen registration); facility where the pathological examination was conducted, and corresponding province, district, and sub-district. We included in the cohort all patients who had at least two HIV-related lab records at a minimum of two different time points. We excluded patients with missing information for age and sex. We used percentages, medians, and interquartile ranges (IQR) to describe patient characteristics (age, sex, and ethnicity), disease characteristics (CD4 and HIV RNA measurements) and utilization of health care (number of lab records, number of facilities attended, type of care provided for cancer, calendar period of entering care).

Ethics, privacy, data protection and access arrangements

The study was granted ethical approval by the Human Research Ethics Committee of the University of the Witwatersrand, Johannesburg (ID M190594) and the Cantonal Ethics committee in Bern (ID 2016–00589). Data pre-processing with full access to patient names was performed by NCR staff on the NCR's premises in Johannesburg. Encrypted data were sent to the Institute of Social and Preventive Medicine (ISPM), University of Bern. ISPM staff used PPPRL methods to deduplicate and link records. Encrypted names and recoded IDs were removed for analyses.

RESULTS

Data preparation and data quality

We retrieved 13,665,095 HIV-related lab records from the NHLS CDW for Gauteng province for the years 2004 – 2014 (**Figure 1**). During preprocessing, we excluded 4.23% of records because of missing or invalid names or birth dates and 12.3% with negative, invalid, or missing HIV test results; 34.6% of excluded HIV test records belonged to children aged <10 years (**Supp Table 1)**. We retained 11,480,118 NHLS records for the linkages (**Figure 1**). We retrieved 664,869 unique cancer cases from the NCR for South Africa for the study period; no records were removed from this data set during pre-processing. **Supp Table 2** shows the characteristics of retained NHLS and NCR records. Sex, at least one given name, and one surname was available for almost all NHLS and NCR records. Precise birthdates (day, month, and year) were available for 88% of NHLS and 73% of NCR records. For 26%

of NCR records, only the birth year was available; 12% of NHLS records contained an estimated birth date. Unique Episode numbers existed for all NHLS records but were not available for NCR records. National IDs were available for a fraction of NHLS and NCR records (Supp Table 2). When we compared NHLS and NCR records with and without national IDs we found no difference in the completeness of given names, surnames, or sex, and the distribution of sex and age was similar (**Supp Table 2)**. Precise birthdates were more complete in NHLS and NCR records with national ID than in records without national ID. Facility was available for all NHLS records (with and without national ID). For NCR records, Hospital information was available for 97% of NCR records with national ID, but only for 80% without national ID.

Optimal linkage thresholds and linkage evaluation

To determine optimal linkage thresholds and to assess linkage accuracy we used the subset of records described in **Supp Table 2** (138,365 NHLS and 99,250 NCR records with National IDs). Of these, 87,248 NHLS records and 96,643 NCR records were unique; there were 871 matching IDs and 863 matching unique IDs between the data sets. We estimated precision, recall, and f-measures at different thresholds of total weight for linkages within NHLS and between NHLS and NCR records, see **Supp Table 3**. For linkages within the NHLS, precision, recall, and f-measure was highest (0.97 each) at a threshold of 20, but to avoid to large record clusters, we raised the threshold to 200. At that threshold, precision was 0.99, recall 0.89 and f-measure 0.94. For the linkage between NHLS and NCR records, we set the threshold to 0 and found precision was 0.98, recall 0.96, and f-measure 0.97**.**

Deduplication and linkage

With the one-table linkage procedure (G-Link) and the optimal linkage thresholds we had determined, we deduplicated 11,480,118 NHLS records (**Figure 1**) to 3,772,187 unique entities. Using the one-to-many linkage procedure (G-Link), we linked 54,235 cancer cases to the HIV records (**Figure 1**).

HIV cohort and cancer diagnoses

To construct the HIV cohort, we excluded records with missing information on birth date or sex and patients without follow-up time (patients with only one record or patients whose linked records all had the same date). Included and excluded patients were similar in age and sex (Supp **Table 4)**. Finally, we included 1,173,908 patients with ≥ 2 HIV-related lab records at ≥ 2 different test dates

(**Table 1**). Of these, 225,454 (19.2%) had a positive HIV test. In patients without a positive HIV test, 88% had CD4 measurements, 40% had HIV RNA tests, and 27% had both CD4 and HIV RNA measurements recorded as evidence for HIV infection; 66.6% of patients were female and median age at first HIV-related lab test was 33.9 years (IQR 27.4-41.3) (**Table 1**); 5% of the population was younger than 10 years. Median CD4 cell count at first encounter was 264 cells/µL (IQR 135-431) and increased with calendar years **(Figure 2**). HIV RNA viral loads were available for 55% of patients: median viral load was log 2.7 (IQR 2.0 – 4.6). The median number of HIV-related lab records per person was 4 (IQR 3-7) and median follow-up time was 602 days (IQR 212-1,365).

Overall, 26,348 patients in the cohort had been diagnosed with at least one cancer: 8,329 were prevalent cases (occurring before or on the date of the first HIV-related record) and 18,019 were incident cases (**Table 1**). Patients with prevalent or incident cancer were older (43.3 years for prevalent and 39.4 years for incident versus 33.7 years) as compared to patients who did not develop cancer. They tended to have lower CD4 cell counts at first encounter (239 cells/µl and 206 cells/µl versus 265 cells/µl) and were more likely to have had an HIV test than patients who did not develop cancer. The sex distribution was similar in patients with and without cancer.

Discussion

Our study established the feasibility of using PPPRL to link routinely collected health records from different sources and use them to construct a longitudinal HIV cohort with cancer outcomes in South Africa. We successfully used encrypted patient names for linkages within and across organizations that strictly protect patient privacy and we used the linked data set to identify cancer diagnoses in PLWH in Gauteng Province, South Africa.

To our best knowledge, this is the first study using PPPRL methods in an African setting. The study is population-based and includes all records from patients who were receiving care in the public health care sector in Gauteng Province, South Africa, during the study period.

As in previous studies [13], we were limited by the fact birth dates were poorly captured. Many records only listed age and did not contain precise birth dates, which makes linkage less accurate. We assessed linkage accuracy using records with National IDs (gold standard) and found both precision and recall were high, but few records contained national IDs. Those records with a National ID were more likely to have precise birth dates than records without national IDs, so they do not accurately represent the whole data set; linkage accuracy for records without national ID should be lower. There were few linkage variables, so we had limited ability to improve the accuracy of our linkages. The study had a few other limitations. We used encrypted patient names to protect patient

privacy, but this limited clerical review of linkages. For example, we could not determine the extent to which different names for the same patent (e.g., anglicized first names/African first names or married/maiden names) in different data sources affected our linkages [13]. Since HIV status is not generally recorded in NCR records, we could not use it to validate our linkages [10]. And, as we expected, we were also limited by incomplete reporting of cancer cases to the NCR, especially for patients attending care in the public health care sector; we may thus have underestimated the true burden of disease, especially in those patients [11]. Since the South African NCR only recently began collecting information on cancer stage, this data was not available for the current study. At NHLS and NCR data sets, clinical information, as well as treatment and treatment outcome information is generally unavailable [10][11]. Since we restricted this study to PLWH who received care in Gauteng province, we will have missed measurements for any patient who lives in Gauteng province but who was treated or received tests elsewhere.

The demographics of our HIV cohort, which we constructed based on HIV related lab records, are similar to those of the HIV epidemic in South Africa, where more than 60% of PLWH are women and about 5% are children [14]. The increase in average CD4 count measurements since the rollout of ART in 2004 [15] and is also apparent in our study. A previous record linkage study that used NHLS HIV-related lab records to create a population-based HIV cohort in South Africa, reached similar findings [16]. When the tested their linkage algorithm against National IDs, their recall rate was 98.5%, while ours was 97% [16]. Like them, we found about 55% of patients had only one record. Single records may belong to people who were tested only once and never entered care or they might have been unlinked through error (undermatches). We found patient demographics were similar for linked and unlinked records as were CD4 trajectories and calendar year of first HIV-related lab record. It is thus likely that these records are predominantly unlinked rather than signifying a patient did not enter care.

This study laid the foundation for linking records from routine health care from different data sources that strictly protect privacy in an African setting. Using the privacy preserving record linkages established in the current study, we have since included HIV records from all nine provinces in South Africa stored at NHLS and created a national longitudinal cohort with cancer outcomes [17][18]. This national cohort will allow to estimate cancer incidence in PLWH, which would not have been possible with the two data bases in isolation [13]. The methods we used in this study allow data linkage without compromising patient privacy. They can in principle also be used to link with Statistics South Africa (Stats SA) so we can obtain vital status to assess cancer related mortality.

Conclusion

Our study showed it is feasible to use PPPRL in an African setting to link routinely collected health records from different data sources and create a longitudinal HIV cohort with cancer outcomes while strictly protecting patient privacy. This work served as the foundation to create a nationwide population-based cohort including all South African provinces which will be used to inform cancer control programs in South Africa and other countries in SSA.

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Author contributions

ME, ES, and JB are co-PIs of the study and were involved in the study's conception, supervision and obtaining funding. MM and JB wrote the first draft of the manuscript. LB, VO and AS were involved in data cleaning and record linkages; LB and FC performed data analyses. All authors commented on the paper and approved the final version.

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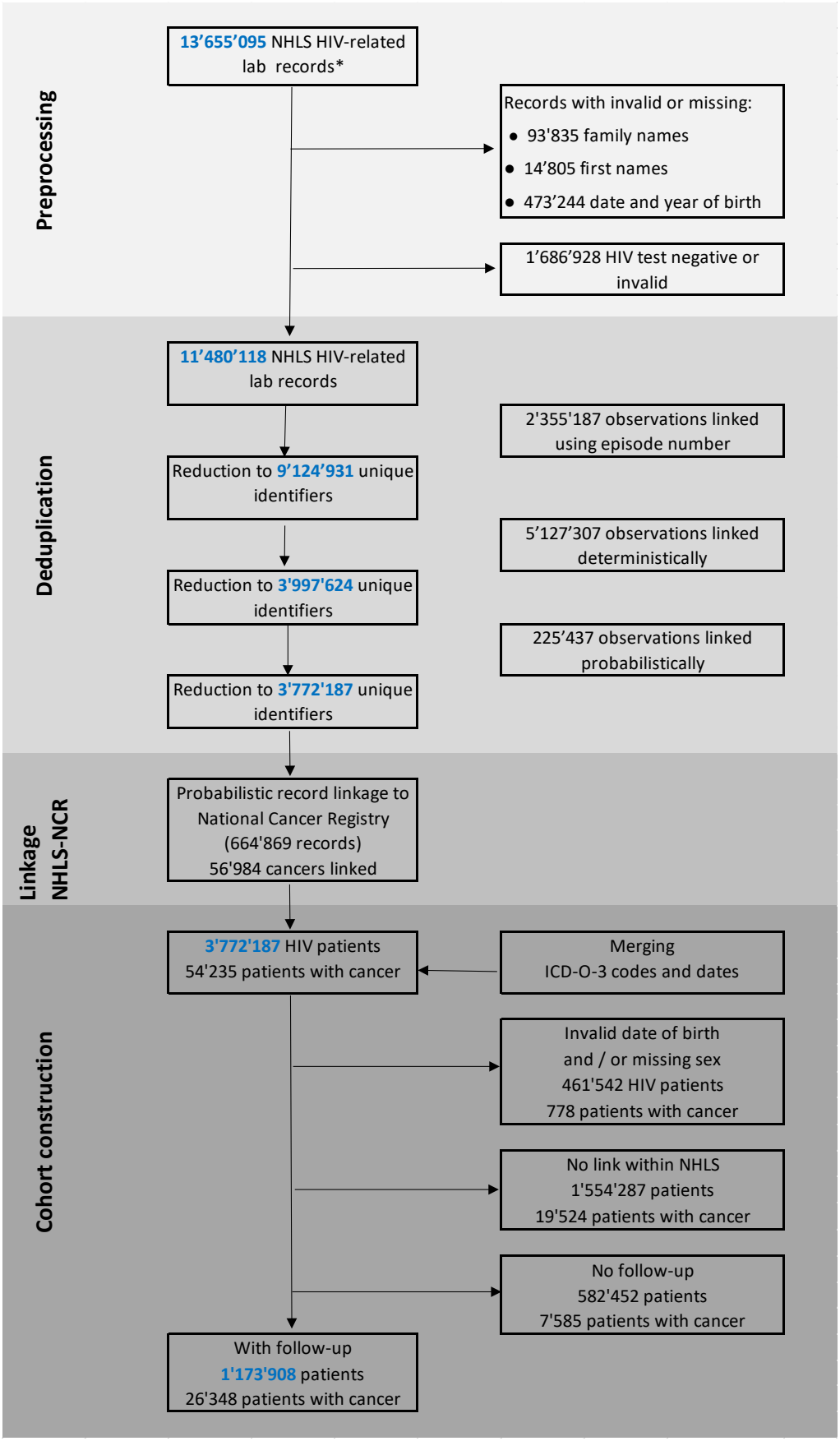
Figure 1: From records to patients: data flow diagram



*HIV-related lab records defined as: positive HIV tests, CD4 cell and HIV RNA measurements

Box 1: In a nutshell: evaluating linkage algorithms and optimal cut-offs

To evaluate linkage algorithms, matches are compared against a gold standard; in our study, we used NHLS and NCR records with national IDs so we could identify correct matches where two records belonged to the same person (true positive), incorrect matches where two records belonged to the same person when they should not (false positive), and missed matches where two records do not belong to the same person when they should (false negative). Measures to quantify linkage quality are recall (true positive / (true positive + false negative)), also known as sensitivity, and precision (true positive / (true positive + false positive)), also known as positive predictive value. The f-measure combines precision and recall:

$$f= 2 * \frac{(precision*recall)}{precision+recall})$$

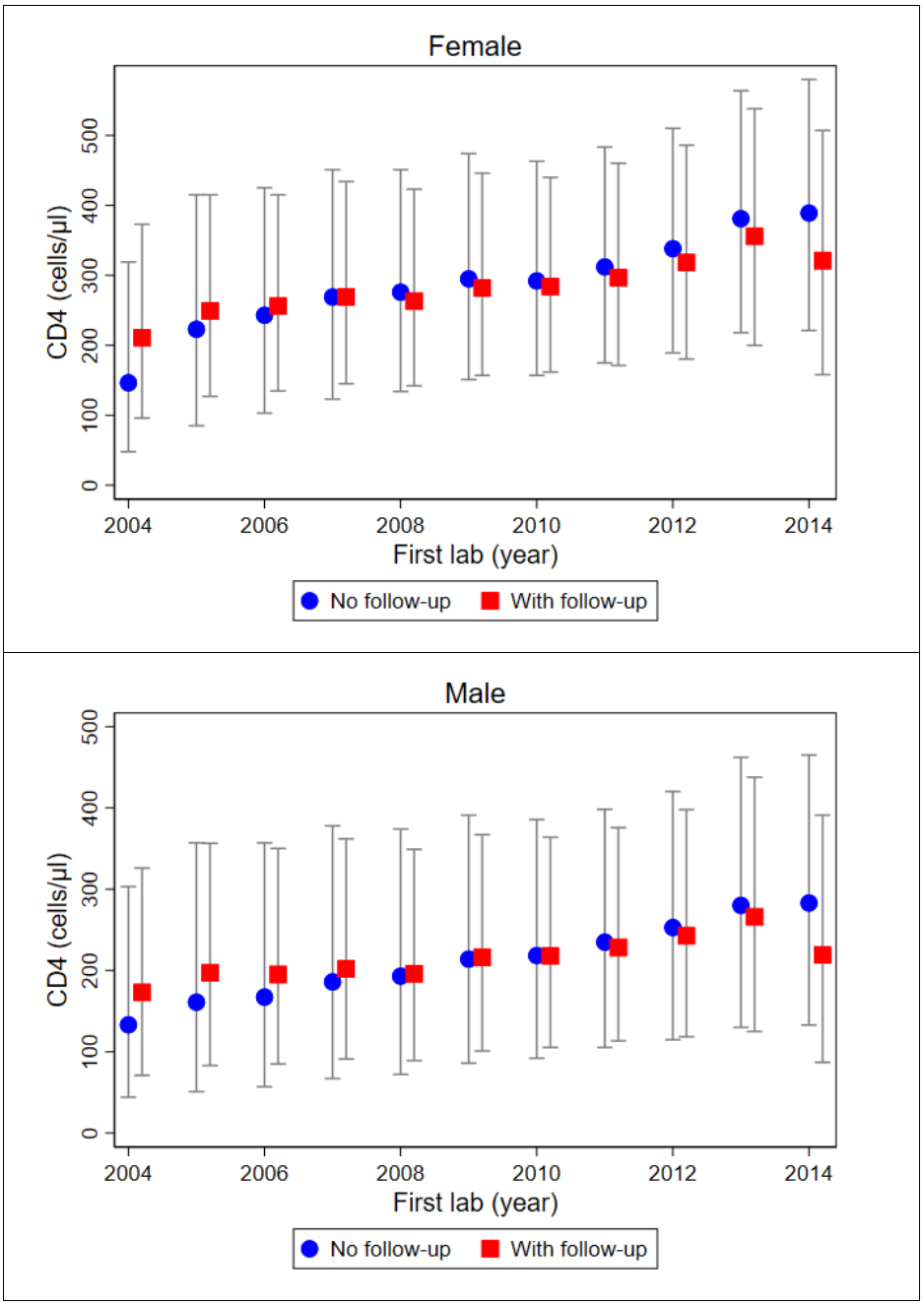
Different thresholds (or cut-offs) divide potential pairs into definite and rejected pairs. Depending on the cut-offs, precision and recall of the linkage change. The higher the chosen cut-off, the higher the precision and the lower the recall. In theory, the optimal cut-off is the point at which the f-measure is the highest and precision is equal (or near equal) to the recall. In practice, cut-offs can be adapted after clerical review to avoid, e.g., very large clusters of records.

Table 1: Characteristics of patients included in cohort

	Patients with prevalent cancer	Patients with incident cancer	Patients without cancer	Total
	N (%)	N (%)	N (%)	N (%)
ALL PATIENTS	8329 (100)	18019 (100)	1147560 (100)	1173908 (100)
PATIENT CHARACTERISTICS				
Gender				
Female	5352 (64.3)	11679 (64.8)	765165 (66.7)	782196 (66.6)
Male	2977 (35.7)	6340 (35.2)	382395 (33.3)	391712 (33.4)
Race				
Black	6577 (79.0)	149174 (82.8)	NA	155751 (11.9)
Colored	521 (6.3)	872 (4.8)	NA	1393 (0.11)
White	913 (11.0)	1808 (10.0)	NA	2721 (0.21)
Asian	57 (0.7)	101 (0.6)	NA	158 (0.01)
Missing	261 (2.0)	321 (1.8)	1147560 (100)	1148142 (87.8)
Age at first lab record				
Median age [years], IQR	43.3 (35.9-51.7)	39.4 (32.3-47.6)	33.7 (27.3-41.1)	33.9 (27.4-41.3)
DISEASE CHARACTERISTICS				
Median CD4 cell count at first CD4 lab record (IQR) [cells/µl]	239 (120-399)	206 (95-361)	265 (136-432)	264 (135-431)
Missing or below 5 years old	2 (0.02)	14 (0.08)	6359 (0.55)	6375 (0.54)
Median HIV RNA at first HIV RNA lab record (IQR) [log10 copies/ml]	2.6 (1.9-4.5)	4.0 (2.5-5.1)	2.6 (2.0-4.6)	2.7 (2.0-4.6)
Missing	3709 (44.5)	8396 (46.6)	513087 (44.7)	525192 (44.7)
HEALTH CARE UTILIZATION				
Calendar period of first lab record*				
2004 - 2006	1052 (12.6)	7410 (41.1)	195109 (17.0)	203571 (17.3)
2007 - 2009	2384 (28.6)	6166 (34.2)	363487 (31.7)	372037 (31.7)
2010 - 2014	4893 (58.9)	4443 (24.7)	588964 (51.3)	598300 (51.0)
Median number of lab records (IQR)	5 (3-8)	6 (3-12)	4 (3-7)	4 (3-7)
Total number of lab records	62983	205669	6797442	7066094
Median follow-up time [days] (IQR)	440 (141-1107)	965 (216-2169)	600 (212-1357)	602 (212-1365)
Gauteng sub-districts				
City of Johannesburg Metro	3415 (41.0)	8227 (45.7)	443784 (38.7)	455426 (38.8)
City of Tshwane Metro	1967 (23.6)	4205 (23.3)	236730 (20.6)	242.902 (20.7)
Ekurhuleni Metro	1812 (21.8)	3413 (18.9)	271994 (23.7)	277219 (23.6)
Sedibeng	574 (6.9)	1067 (5.9)	95785 (8.4)	97426 (8.3)
West Rand	561 (6.7)	1107 (6.1)	99267 (8.7)	100935 (8.6)

HIV, human immunodeficiency virus; IQR, interquartile range; *National ART guidelines were released in 2004 and updated in 2010

Figure 2: First median CD4 cell count over time, female and male, stratified by follow-up



Supplement Box 1: NHLS and NCR data bases

The South African NHLS is the largest diagnostic service in the country and supports national and provincial health departments in the delivery of healthcare (http://www.nhls.ac.za/). NHLS was established in 2004 and serves the public health care sector, covering 84% of the population of 59 million South Africans (http://www.statssa.gov.za/?cat=15) through a national network of 265 laboratories. Each laboratory has its own information system, but all systems are connected to a single electronic data repository: the NHLS Corporate Data Warehouse (CDW) located in Modderfontein in Johannesburg. This electronic repository includes the data of all diagnostic tests conducted in the public health care sector in South Africa. Data include results of HIV tests, CD4 cell counts, HIV RNA viral loads, and all other laboratory tests and results. Demographic patient data is also recorded, including first name(s) and surname(s), sex, precise date of birth or estimated data of birth derived from patient age at time of diagnostic procedure, the facility that provided care, and its province, district and sub-district. For patients whose precise date of birth is not recorded but whose age is listed, birth date was back calculated from their age at a specific test date. CDW performed the calculation and informed us whether birth dates were precise or back calculated were provided. Data are organized by Episode numbers: each sample sent to the lab with a request for analyses is assigned a unique Episode number. Unique patient identifiers (national ID), are available for about 5% of patients nationally. Data are recorded across lifespan, regardless of the facility providing care. For example, patients diagnosed with HIV in infancy will have their data recorded at each health care facility that provides care and this data will be sent to the repository in Johannesburg.

The National Cancer Registry (NCR) of South Africa is a division of the NHLS and is located on NHLS premises in Modderfontein, Johannesburg. It was established in 1986 and is South Africa's primary and largest cancer surveillance system. The NCR includes over 1.2 million cancer records and the registry receives between 90,000 to 100,000 cancer notifications annually. The NCR collates and analyzes cancer cases diagnosed in pathology laboratories nationwide and reports annual cancer incidence rates stratified by sex, age, and ethnicity, but not by HIV status. Data have been obtained from the NHLS for many years, and it provides 100% notification from public sector laboratories. Since 2011, is has been obligatory to report all confirmed cancer diagnoses from all laboratories, both public and private, to the registry (Regulation 380 of the National Health Act 61). At NCR, cancer diagnoses are validated: the reports for a given cancer case are read and then manually coded according to ICD-10 and the International Classification of Disease for Oncology (ICD-O-3). For patients with multiple cancer diagnoses, the primary cancer and any additional cancers are determined and unique cancer case identifiers assigned. Unique patient identifiers do not generally not exist, and national ID is available for only 15% of cancer records. Demographic information includes first name, surname, sex, birth date (if not available, then birth year), hospital and province.

Supplement Box 2: Technical details for probabilistic deduplication and record linkages

Probabilistic deduplication and record linkage within NHLS and between NHLS and NCR included creating initial criteria (blocking), applying rules and weights to potential record pairs, grouping (choice of cut-off), and mapping.

Blocking: creating initial criteria

To reduce the number of potential pairs we determined initial criteria, which defined linkage blocks (pockets). Every pocket included rules to determine if potential pairs were selected for the next procedure. At minimum, a potential pair had to meet the criteria of one of pocket to be chosen. For NHLS deduplication and probabilistic record linkage we used these pockets:

1) Exact match on last encrypted names, not missing dates of birth and exact match on dates of birth; OR

2) Exact match on first names, not missing date of birth and exact match on date of birth; OR

3) Exact match of first name and last name, match on sex and not missing sex; OR

4) Exact match on last name and exact match on first name.

Matching: applying rules and weights to the potential record pairs

We applied a set of rules to the chosen pairs and weighted them according to the outcomes of these rules. Encrypted given names and surnames were compared with Dice-coefficients (Schnell et al, 2009). A rule also comparing first and family names to check whether they were swapped. If two or more given or family names existed and none matched exactly, we used a rule to compare the names to each other. A special rule compared the full dates of birth if they were present. It also checked for typos and ensured numbers were not swapped. A conditional rule was invoked if full dates of birth were missing and compared birth years. Rules compared sex and geographical characteristics of the facilities. The table below lists our matching rules.

Matching rules and their order used in probabilistic record linkages

Order	Linkage Rules	Description
1	Compare encrypted first names	Calculates the similarity index of encrypted first names (Dice coefficient) and differentiates depending on similarity of encrypted character strings: 8 outcomes with different outcome weights.
2	Compare all encrypted first names	This rule is applied if a person has more than one first name. It determines if the first name matches the second or third first name.
3	Compare encrypted last names	Calculates the similarity index of encrypted last names (Dice coefficient) and differentiates depending on similarity of encrypted character strings: 8 outcomes with different outcome weights.
4	Compare all encrypted last names	This rule is applied if a person has more than one last name. It compares the first last name to the second last name.
5	Check if the encrypted first name and the encrypted last name are swapped	Calculates the similarity index of encrypted first name and encrypted last name (Dice coefficient) and differentiates based on similarity of encrypted character strings: 8 outcomes with different outcome weights.
6	Compare dates of birth	Compares full dates of birth if they are not missing. It also checks for typos and that the numbers are not swapped. It calculates age difference.
7	Compare years of birth	Conditional rule applied if the full date of birth is missing; it compares birth years.
8	Compare sex	Compares sex.
9	Compare geographical information of facilities, sub-districts and districts	This rule discriminates into different outcomes depending if lab tests were taken at the same or different facilities, and in the same or different districts and sub-districts.

Grouping: choosing of cut-offs

We attributed weights to the outcomes of the rules according to M- and U-Probability of any given outcome. M-Probability is the probability that we observe a match in the rule outcomes and it is a true match. U-probability is the probability we observe a match even if it is not a true match.

Reference

Schnell R, Bachteler T, Reiher J. Privacy-preserving record linkage using Bloom filters. BMC Med Inform Decis Mak. 2009;9:41.

Supplement Table 1: Characteristics of datasets, 2004 - 2014

Data sets included	Gauteng NHLS data set								National Cancer Registry	
	Retained records		Excluded records				Total		Total	
			Poor data quality		HIV test result negative or missing					
	Number	%	Number	%	Number	%	Number	%	Number	%
Number of tests / records	**11'480'118**	**83.50**	**581'884**	**4.23**	**1686928**	**12.27**	**13'748'930**	**100.00**	**664'869**	**100**
Type of tests										
CD4 measurement	6'035'876	52.58	167'213	28.74	0	0.00	6'203'089	45.12	NA	NA
HIV RNA viral loads	3'047'731	26.55	67'247	11.56	0	0.00	3'114'978	22.66	NA	NA
HIV tests	2'396'511	20.88	167'213	59.69	1‘635‘231	96.94	4'198'955	30.54	NA	NA
Missing	0	0.00	77	0.01	51‘697	3.06	51'774	0.38	NA	NA
Invasive cancer	NA	NA	NA	NA	NA	NA	NA	NA	664'869	100
Unique Episode numbers	**9'124'931**	**83.58**	**391'366**	**3.58**	**1400747**	**12.83**	**10'917'044**	**100.00**	**NA**	**NA**
Sex										
Female	7'450'937	64.90	301'090	51.74	955'211	56.62	8'707'238	63.33	339'757	51.10
Male	3'913'875	34.09	198'424	34.10	696'447	41.28	4'808'746	34.98	324'391	48.79
Missing	115'306	1.00	82'370	14.16	35'270	2.09	232'946	1.69	721	0.11
Age										
Age reported	**11'480'118**	**100.00**	**79'076**	**13.59**	**1'686'928**	**100.00**	**13'246'122**	**96.34**	**652'434**	**98.13**
Age calculated using date of birth	10'135'262	88.29	54'969	9.45	1‘305‘906	77.41	11'496'137	86.79	482'378	72.55
Age calculated using year of birth	1'344'856	11.71	24'107	4.14	381‘022	22.59	1'749'985	13.21	182'491	27.45
Missing	0	0.00	502'808	86.41	0	0.00	502'808	3.66	12'435	1.87
Age groups in years										
<10	589'615	5.14	18'197	3.13	583‘252	34.57	1'191'064	8.99	5'016	0.75
10-19	352'872	3.07	4'471	0.77	85‘089	5.04	442'432	3.34	5'030	0.76
20-29	2'183'795	19.02	19'965	3.43	318‘894	18.90	2'522'654	19.04	16'735	2.52
30-39	4'258'843	37.10	21'325	3.66	277‘352	16.44	4'557'520	34.41	52'765	7.94
40-49	2'716'886	23.67	10'103	1.74	185‘311	10.99	2'912'300	21.99	90'993	13.69
50-59	1'086'424	9.46	3'758	0.65	131‘433	7.79	1'221'615	9.22	136'043	20.46
60-69	244'739	2.13	947	0.16	68‘962	4.09	314'648	2.38	160'246	24.1
70+	46'944	0.41	310	0.05	36‘635	2.17	83'889	0.63	185'606	27.92

Table 1 shows the characteristics of the two data bases after pre-processing, NHLS records stratified by retained and excluded records

Supplement Table 2: Completeness of main linkage variables, 2004 – 2014

	Gauteng NHLS records			NCR records		
	Total N (%)	with national ID N (%)	without national ID N (%)	Total N (%)	with national ID N (%)	without national ID N (%)
Names						
Surname 1	11,480,118 (100)	179,212 (100)	11,300,906 (100)	664,869 (100)	99,250 (100)	565,619 (100)
Surname 2	1,579 (0.0)	30 (0.0)	1,549 (0.0)	NA	NA	NA
First name 1	11,480,118 (100)	179,212 (100)	11,300,906 (100)	644077 (96.9)	97,225 (98.0)	546,852 (96.7)
First name 2	242,161 (2.1)	7,354 (4.1)	234,807 (2.1)	88262 (13.3)	11,642 (11.7)	76,620 (13.6)
First name 3	457 (0.0)	16 (0.0)	441 (0.0)	NA	NA	NA
Age						
Precise date of birth	10,135,260 (88.3)	177,742 (99.2)	9,957,518 (88.1)	482378 (72.6)	99,249 (100)	383,129 (67.7)
Only year of birth	NA	NA	NA	170,056 (25.6)	1 (0)	170,055 (30.1)
Date of birth estimated	1,344,856 (11.7)	1,470 (0.8)	1,343,386 (11.9)	NA	NA	NA
Median age [years](IQR)*	35 (28-43)	37 (30-44)	35 (28-43)	60 (48-70)	63 (53-73)	59 (47-69)
Sex	11,364,812 (99.0)	177,935 (99.3)	11,186,877 (98.9)	664,148 (99.9)	99,244 (100)	564,904 (99.9)
Male	3,913,875 (34.1)	57,129 (31.9)	3,856,746 (34.1)	324,391 (48.8)	54,041 (54.0) 45,203	270,350 (47.8)
Female	7,450,937 (64.9)	120,806 (67.4)	7,330,131 (64.9)	339,757 (51.1)	(45.5)	294,554 (52.1)
Episode number	11,480,118 (100)	179,212 (100)	11,300,906 (100)	NA	NA	NA
Location						
Facility/hospital	11,480,118 (100)	179,212 (100)	11,300,906 (100)	547,273 (82.3)	96,437 (97.2)	450,836 (79.7)
Province	11,480,118 (100)	179,212 (100)	11,300,906 (100)	574,792 (86.5)	96,555 (97.3)	478,237 (84.6)
District	11,480,118 (100)	179,212 (100)	11,300,906 (100)	NA	NA	NA
Sub-district	11,480,118 (100)	179,212 (100)	11,300,906 (100)	NA	NA	NA

*Median age at HIV related laboratory record for NHLS data and cancer record for NCR data

Supp Table 2 shows the completeness of the linkage variables in the NHLS and NCR data sets stratified by availability of national ID

Supplement Table 3: linkage thresholds and precision, recall and f-measure for NHLS deduplication and linkage with NCR data

	NHLS deduplication			Linkage with NCR data		
Threshold	**Precision**	**Recall**	**F-Measure**	**Precision**	**Recall**	**F-Measure**
-80	0.94	0.98	0.96	0.25	0.97	0.4
-60	0.95	0.98	0.96	0.77	0.97	0.86
-40	0.95	0.98	0.96	0.93	0.97	0.95
-20	0.97	0.98	0.97	0.97	0.97	0.97
0	0.97	0.97	0.97	0.98	0.96	0.97
20	0.97	0.97	0.97	0.98	0.95	0.96
40	0.97	0.96	0.97	0.97	0.55	0.7
60	0.98	0.94	0.96	0.97	0.54	0.69
80	0.98	0.94	0.96	0.97	0.52	0.68
100	0.98	0.92	0.95	0.97	0.48	0.64
120	0.98	0.90	0.94	1	0.48	0.65
140	0.98	0.90	0.94	-	-	-
160	0.99	0.90	0.94	-	-	-
180	0.99	0.90	0.94	-	-	-
200	0.99	0.89	0.94	-	-	-
220	0.99	0.89	0.94	-	-	-

Supplement Table 3 shows precision, recall, and measures for NHLS deduplication and NCR linkages at different thresholds. Grey area indicates the threshold with highest precision, recall, and f-measure.

Supplement Table 4: Patient characteristics stratified by follow-up

	Patients without follow-up		Patients with follow-up			Total
	Patients with cancer	Patients without cancer	Patients with prevalent cancer	Patient with incident cancer	Patients without cancer	Total
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
All patients	27109 (100)	2109630 (100)	8329 (100)	18019 (100)	1147560 (100)	3310647 (100)
PATIENT CHARACTERISTICS						
Gender						
Female	16318 (60.1)	1377363 (65.3)	5352 (64.2)	11679(64.7)	765165 (66.7)	2175877 (65.7)
Male	10791 (39.9)	732267 (34.7)	2977 (35.8)	6340 (36.3)	382395 (33.3)	1134770 (34.3)
Ethnicity						
Black	20229 (74.6)	NA	6577 (79.0)	149174 (82.8)	NA	41723 (1.3)
Colored	1837 (6.8)	NA	521 (6.3)	872 (4.8)	NA	3230 (0.1)
White	3960 (14.6)	NA	913 (11.0)	1808 (10.0)	NA	6681 (0.2)
Asian	866 (3.2)	NA	57 (0.7)	101 (0.6)	NA	375 (0.0)
Missing	866 (3.2)	2109630 (100)	261 (2.0)	321 (1.8)	1147560 (100)	3258638 (98.4)
Age at first lab record [years]						
Median age* [years], (IQR)	44.2 (35.6-53.5)	33.8 (27.3-41.6)	43.3 (35.9-51.7)	39.4 (32.3-47.6)	33.7 (27.3-41.1)	33.9 (27.4-41.6)
Age groups in years						
< 10	147 (0.5)	90106 (4.3)	40 (0.5)	133 (0.7)	57150 (5.0)	147576 (4.5)
10 – 19	221 (0.8)	70431 (3.3)	63 (0.8)	202 (1.1)	35777 (3.1)	106694 (3.2)
20 - 29	2696 (10.0)	579289 (27.5)	713 (8.6)	2838 (15.8)	308420 (26.9)	893956 (27.0)
30 - 39	7222 (26.6)	755271 (35.8)	2445 (29.4)	6265 (34.8)	425556 (37.1)	1196759 (36.2)
40 - 49	7587 (28.0)	406168 (19.3)	2626 (31.5)	5139 (28.5)	224704 (19.6)	646224 (19.5)
50 - 59	6171 (22.8)	162023 (7.7)	1808 (21.7)	2772 (15.4)	79955 (7.0)	252729 (7.6)
60 - 69	2396 (8.8)	35911 (1.7)	530 (6.4)	592 (3.3)	13830 (1.2)	53259 (1.6)
≥ 70	669 (2.5)	10431 (0.5)	104 (1.3)	78 (0.4)	2168 (0.2)	13450 (0.4)
DISEASE CHARACTERISTICS						
CD4 cell count at first lab record * [cells/µl], Median (IQR)	270 (118-884)	292 (140-479)	239 (120-399)	206 (95-361)	265 (136-432)	264 (135-431)
< 50	2726 (10.1)	188334 (8.9)	854 (10.3)	2418 (13.4)	105877 (9.2)	300209 (9.1)
50-99	2313 (8.5)	145400 (6.9)	822 (9.9)	2179 (12.1)	97332 (8.5)	248046 (7.5)

100-199	4009 (14.8)	291169 (13.8)	1767 (21.2)	4022 (22.3)	213148 (18.6)	514115 (15.5)
200-349	5125 (18.9)	433091 (20.5)	2148 (25.8)	4319 (24.0)	300155 (26.2)	744838 (22.5)
350-499	3461 (12.8)	328680 (15.6)	1257 (15.1)	2398 (13.3)	192702 (16.8)	528498 (16.0)
500-699	2602 (9.6)	237357 (11.3)	778 (9.3)	1353 (7.5)	120569 (10.5)	362659 (11.0)
≥ 700	2888 (10.7)	175737 (8.3)	518 (6.2)	929 (5.2)	84599 (7.4)	264671 (8.0)
Missing	3985 (14.7)	309862 (14.7)	185 (2.2)	401 (2.2)	33178 (2.9)	347611 (10.5)
Aged < 5 years old	41	34227	2	14	6359	40643
First HIV RNA lab record, median (IQR) [log10 copies/ml]	2.6 (1.4-4.4)	2.6 (1.3-3.9)	2.6 (1.9-4.5)	4.0 (2.5-5.1)	2.6 (2.0-4.6)	2.6 (1.7-4.4)
First HIV RNA [log10 copies/ml]						
< 2.7	2494 (9.2)	286516 (13.6)	2447 (29.4)	3387 (18.8)	323184 (28.2)	618028 (18.7)
2.7-3.9	492 (1.8)	58219 (2.8)	687 (8.3)	1302 (7.2)	91721 (8.0)	152421 (4.6)
4.0-4.9	587 (2.2)	51690 (2.5)	655 (7.9)	2061 (11.4)	97983 (8.5)	152976 (4.6)
≥ 5.0	795 (2.9)	61354 (2.9)	831 (10.0)	2873 (16.0)	121585 (10.6)	187438 (5.7)
Missing	22741 (83.9)	1651851 (78.3)	3709 (44.5)	8396 (46.6)	513087 (44.7)	2199784 (66.5)
HEALTH CARE UTILISATION						
Calendar period of first lab record*						
2004 - 2006	4493 (16.6)	225242 (10.7)	1052 (12.6)	7410 (41.1)	195109 (17.0)	433306 (13.1)
2007 - 2009	7699 (28.4)	476124 (22.6)	2384 (28.6)	6166 (34.2)	363487 (31.7)	855860 (25.9)
2010 - 2014	14917 (55.0)	1408264 (66.8)	4893 (58.9)	4443 (24.7)	588964 (51.3)	2021481 (61.2)
Median number of lab records* (IQR)	1 (1-2)	1 (1-2)	5 (3-8)	6 (3-12)	4 (3-7)	2 (1-4)
Total number of lab records	70791	3105026	62983	205669	6797442	10241911
Median number of CD4 records (IQR)	1 (1-1)	1 (1-1)	2 (2-4)	3 (2-6)	2 (2-4)	1 (1-2)
Total number of CD4 records	23303	1813694	27243	86633	3561384	5512257
Median number of HIV RNA (IQR)	1 (1-1)	1 (1-1)	2 (1-3)	2 (1-5)	2 (1-4)	1 (1-3)
Total number of HIV RNA	5035	521922	14685	40414	2324027	2906083
Median number facilities attended (IQR)	2 (2-2)	1 (1-1)	2 (2-3)	3 (2-4)	1 (1-2)	1 (1-1)
Type of facilities attended						
Only public sector	21333 (78.7)	2109630 (100)	6785 (81.5)	14737 (81.8)	1147560 (100)	3300045 (99.7)

Both public and private sector	5776 (21.3)	NA	1544 (18.5)	3282 (18.2)	NA	10602 (0.3)
Median follow-up time (IQR) [days]	NA	NA	440 (141-1107)	965 (216-2169)	600 (212-1357)	602 (212-1365)
Gauteng sub-districts						
City of Johannesburg Metro	9977 (36.8)	786981 (37.3)	3415 (41.0)	8227 (45.7)	443784 (38.7)	1252384 (37.8)
City of Tshwane Metro	6657 (24.6)	406799 (19.3)	1967 (23.6)	4205 (23.3)	236730 (20.6)	656358 (19.8)
Ekurhuleni Metro	6230 (23.0)	546988 (25.9)	1812 (21.8)	3413 (18.9)	271994 (23.7)	830437 (25.1)
Sedibeng	1993 (7.4)	167639 (8.0)	574 (6.9)	1067 (5.9)	95785 (8.4)	267058 (8.1)
West Rand	2252 (8.3)	201223 (9.5)	561 (6.7)	1107 (6.1)	99267 (8.7)	304410 (9.2)

HIV, human immunodeficiency virus; IQR, interquartile range; *National ART guidelines were released in 2004 and updated in 2010, NA not available