Using HIV Surveillance Data for Public Health Evaluations and Interventions: Common Challenges & Proposed Methodological Solutions

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Abstract

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Epidemiology

In the United States (U.S.), the purpose of HIV surveillance and related data systems is changing. Evolving programmatic priorities and complicated care needs of an aging population has led to greater demand for timely, accurate, and detailed data. My dissertation evaluates three prominent data systems: (1) National HIV Surveillance System (NHSS), (2) Medical Monitoring Project (MMP), and (3) CFAR Network of Integrated Clinical Systems (CNICS). Identification and management of data limitations were goals underlying each aim.

My first aim evaluates the burden of diabetes, chronic kidney disease, and hypertension in MMP, a nationally representative sample, and CNICS, a clinical cohort. We encountered and addressed the following challenges: selection bias, missing data, non-standardized case definitions, and dissimilar patient populations. After using a standardized analytic approach, MMP and CNICS

yielded similar sub-group specific prevalence estimates. Both data sources suggest considerable disease burden among older adults in HIV care.

My second aim used NHSS and US census data to project the demographic composition of the U.S. population of people living with diagnosed HIV (PLWDH) through 2045. The model developed for this aim projects that the US PLWDH population will continue to grow in absolute size and will increasingly be comprised of racial/ethnic minorities; the number of PLWDH 55 years and older is projected to more than double between 2013 and 2045.

My final aim used King County HIV surveillance data to explore the origins of NHSS data and how surveillance data is used for HIV control interventions. We discovered that the number of in-migrants with HIV is increasing concurrently with a decrease in the number of new diagnoses; that 12% of cases reported to CDC as newly diagnosed had evidence of a prior HIV diagnosis; and integration of patient care and HIV control activities improved key program metrics.

In conclusion, existing data systems to monitor the U.S. PLWDH population have limitations, some of which can be addressed through statistical adjustment and some can only be resolved through adaptation of the data system's design. As demands on HIV care programs are projected to grow, the programmatic utility of HIV surveillance systems should be enhanced.

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I am so grateful for the guidance and advice provided by my committee members on my dissertation. They provided invaluable input on my initial dissertation proposal, providing direction for the entire dissertation journey. While pursuing my dissertation research, my committee helped me troubleshoot analytical (and political!) challenges, provided detailed feedback on numerous manuscript drafts, and provided hours of their time. Under their mentorship, I received training on more sophisticated analytical approaches and scientific writing -- skills that I will carry with me the rest of my career as an epidemiologist.

While pursuing my doctoral research, I have been employed by Public Health- Seattle & King County as an HIV epidemiologist. This position has provided so much more than salary support: it has provided on-the-job training in evaluation design and implementation, data management, data analysis, and reporting of results to diverse audiences. Through this position, I have observed how surveillance programs operate locally and in-conjunction with state and federal partners, providing valuable insight for my dissertation.

Countless people at CDC went out of their way to set-up my remote access to a CDC computer, which was necessary to access the data for the first and second aims of my dissertation. In particular, I'm grateful to Heather Bradley, Dawn Gnesda, Renee Dawkins, and Shelia Coggins for their assistance navigating security protocols, CITGO access, and clearance processes.

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Contents

List of Figures

List of Tables

Chapter 1: Introduction

The first AIDS cases in the United States were first recognized by the Centers for Disease Control and Prevention (CDC) in 1981.[1] By 1995, 429,582 (78%) of the 551,515 individuals that had been diagnosed with AIDS had died.[2] In June 1995, the Food and Drug Administration approved the first protease inhibitor, ushering in the era of highly active antiretroviral therapy.[3] Soon after, AIDS-related mortality rates plummeted in the United States.[4] In the last twenty years (e.g. 1996-2016), treatment of HIV has become more effective (and tolerable), resulting in tremendous gains in life expectancy.[5, 6] My dissertation focuses entirely upon the current and future context of the HIV/AIDS epidemic in the United States, specifically the demographic characteristics and health status of people living with HIV, and the data systems in place to monitor key indicators of the domestic HIV/AIDS epidemic.

Currently, the population of people who live with diagnosed HIV (PLWDH) in the U.S. is comprised of nearly 1 million individuals and is disproportionately comprised of men who have sex with men (MSM) and racial/ethnic minority groups.[7] In 2013, the U.S. PLWDH population was 76% male, and 43%, 32%, and 20% non-Hispanic Black, non-Hispanic White, and Hispanic/Latino, respectively.[8] Over half of PLWDH were estimated to have contracted HIV through male-to-male sexual contact; one-quarter through heterosexual sexual contact; and over 15% through injection drug use (IDU).[8] By 2013, one-quarter of the PLWDH population was 55-years and older[7]. The growing numbers of older adults with HIV have received considerable attention[9-18], in part because their care is more costly[19] and often complicated by multi-morbidity and poly-pharmacy.[20-38]

The role of HIV surveillance data in HIV control efforts is expanding. With evidence demonstrating that antiretroviral therapy (ART) prevents HIV transmission[39, 40], HIV control efforts are increasingly focused on identifying cases with undiagnosed HIV, linking new diagnoses to care, and ensuring people with diagnosed HIV are retained in care and achieve viral suppression. These endeavors rely upon surveillance data to identify potential new cases, monitor linkage and retention in care, and to validly estimate the underlying size of the PLWDH population, the denominator of many key programmatic indicators.[41]

Without a single-payer healthcare system and central repository of healthcare data, population-based estimates of patient characteristics and health status are difficult to validly measure. The National HIV Surveillance System (NHSS) is managed by CDC, but implemented by a vast network of state and local health departments. As a census of all diagnosed cases in the U.S., plays a central role in program planning and resource allocation decisions. There is considerable heterogeneity, across jurisdiction and over time, with regard to reporting requirements, approach to data collection, and data completeness and quality. Although all persons with diagnosed HIV have been reportable, by name, to local and state health departments since April 2008[42], only de-identified data is reported to CDC. Jurisdictions maintain their own surveillance registries. Cross-jurisdictional migration of PLWDH greatly complicates estimates of the underlying PLWDH population size, as it is difficult to discern which cases have emigrated out of a jurisdiction (as opposed to poorly engaged in care) and which cases new to the surveillance system are in-migrants (as opposed to new diagnoses).[43, 44] It is likely that the size of the PLWDH population, as measured by case reports submitted to CDC, is overestimated.[45] The inflated denominator likely biases downward estimates of the percent retained in care and

percent virally suppressed.[43, 46] The overly pessimistic estimates of these key programmatic could potentially misdirect program priorities and program targets.

The infrastructure underlying NHSS allows for a limited set of data elements to be collected on *all* PLWDH at the time of their diagnosis, including: residence, age at diagnosis, sex at birth, race/ethnicity, and risk transmission category. The latter is assigned in a hierarchical order of probability of the most likely route of HIV acquisition: male-to-male sex, injection drug use, male-to-male sex and injection drug us, heterosexual sex, and unknown/unreported.[47] Additionally, all states have enacted laws requiring laboratory reporting of CD4 and HIV viral load results, though not all states require *complete* CD4/viral load reporting.[48] For example, some states may only require that unsuppressed viral load results be reported. Reported lab results enable public health agencies to monitor, on an ongoing basis, linkage and retention in care, viral suppression, and potential re-location.

More nuanced data about the health status of PLWDH is collected through other systems. CDC designs and oversees the implementation of the Medical Monitoring Project, a supplemental surveillance project that relies upon complex survey design to generate population-based estimates of hundreds of health indicators pertaining to socioeconomic status, quality of life measures, mental and physical health issues, access to health and social services, sexual behaviors, drugs use, immunizations, reproductive health care, and co-morbidities. Similar types of data are collected in large clinical cohort studies. The CFAR Network of Integrated Clinical Systems (CNICS) is an example of a large clinical cohort that operates at eight large, university-affiliated HIV care clinics in sever U.S. states.

My dissertation utilizes these and other data systems to describe the current burden of co-morbidities among PLWDH (Chapter 2), project the future demographic composition of the US

PLWDH population (Chapter 3), and to evaluate how integration of HIV surveillance and field services activities in King County influences surveillance data quality and program metrics (Chapter 4). These aims allowed for the limitations of three prominent data systems to be explored. Where possible, we developed analytic strategies and made programmatic recommendations on how identified limitations could be addressed. Thus, this dissertation simultaneously evaluates three large U.S. data systems, as it forecasts how demands on HIV care programs will shift in the future in light of the changing demographic composition of the U.S. PLWDH population.

Chapter 2: Reconciling the Evaluation of Co-Morbidities among HIV Care Patients in Two Large Data Systems: the Medical Monitoring Project and CFAR Network of Integrated Clinical Systems

Abstract

The estimated burden of chronic disease among people living with HIV (PLWH) varies considerably by data source, due to differences in case definitions, analytic approaches, and underlying patient populations. We evaluated the burden of three chronic conditions [diabetes (DM), chronic kidney disease (CKD), and hypertension (HTN)] in two large data systems that are commonly queried to evaluate health issues affecting HIV care patients: the Medical Monitoring Project (MMP), a nationally representative sample, and the *Centers for AIDS Research Network of Integrated Clinical Systems (*CNICS), a clinical cohort. In order to reconcile these two data sources, we addressed issues common to observational data, including selection bias, missing data, and development of case definitions. The overall adjusted estimated prevalence of DM, CKD, and HTN in MMP was 12.7%, 7.6%, and 33.3%, respectively, and the overall prevalence of DM, CKD, and HTN in CNICS was 9.9%, 8.3%, and 38.1%, respectively. Prevalence of all three conditions increased with age in both data sources. After reconciling the approach to analyzing MMP and CNICS data, sub-group specific prevalence estimates of DM, CKD, and HTN was generally similar in both data sources. Both data sources suggest a considerable burden of disease among older adults in HIV care.

Introduction

Although the majority of adults receiving HIV care in high income countries are virally suppressed[49-51], people living with HIV (PLWH) are nonetheless disproportionately affected by cancer[28, 29], cardiovascular disease[29-33], kidney disease[29, 34-36], liver disease[29, 36], metabolic disorders[37, 38], and other chronic diseases[29]. The excess burden of chronic disease among people living with HIV (PLWH) is attributable to HIV infection, its treatment, and greater exposure to traditional chronic disease risk factors, including smoking, drug and alcohol use, and chronic viral infections. The high prevalence of chronic disease among PLWH has implications for how HIV medical care is organized, the training of HIV medical providers, and the costs of medical care.

Large-scale surveillance systems and clinical cohorts have been established in the United States to monitor the health of PLWH, though their design, representativeness of the PLWH population, and approach to analyses vary widely. Not surprisingly, the estimated burden of disease varies substantially by data source. For example, the estimated prevalence of kidney disease was 3% among Veterans Administration patients (measured by ICD-9 codes)[36], 8% among Medicare beneficiaries (measured by ICD-9 codes)[52], and 15% in a CDC cohort study (measured by medical record data on diagnoses, medications, and lab results)[53]. The extent to which these differences in estimated prevalence are attributable to differences in patient population, study design, or analytical approach is difficult to discern.

The Medical Monitoring Project (MMP) and the Centers for AIDS Research Network of Integrated Clinical Systems (CNICS) are two of ten data systems considered by the Institute of Medicine as the "most useful for tracking the impact of the NHAS [National HIV/AIDS

Strategy] and the ACA [Affordable Care Act] on HIV care".[54] Though MMP and CNICS collect similar data elements and are frequently analyzed and described in the published literature[55, 56], they have never been closely compared. Our primary objective is to demonstrate methodological tactics that can be employed to enhance the comparability of data collected by separate entities. Our secondary objective is to estimate and compare the prevalence of diabetes (DM), chronic kidney disease (CKD), and hypertension (HTN) in MMP and CNICS, given our rigorous approach to reconciling these two data sources.

Methods

Data Sources

Medical Monitoring Project (MMP)

MMP is a Centers for Disease Control and Prevention-funded HIV surveillance project that collects annual cross-sectional clinical, socio-demographic, and behavioral data on a national probability sample of adults in HIV care. Prior to the 2015 data collection cycle, MMP used a three-stage sampling design to generate samples representative of adults receiving HIV care in the US. The three hierarchical levels of sampling were states/territories, HIV care facilities (in selected jurisdictions), and patients who received care at participating facilities in January–April in a given year. Data collection for MMP is conducted by health departments in 16 states and Puerto Rico. During face-to-face or telephone interviews, information on demographic characteristics, adherence to HIV medication regimens, behavioral risk factors, and service utilization is collected. Medical record abstractions (MRA) are conducted to collect clinical data pertaining to diagnoses, medications, laboratory results, and health service utilization. Data are

weighted for unequal selection probabilities and non-response. A more detailed description of the MMP methodology is available elsewhere.[57]

For this analysis, we analyzed MRA records from the 2013 MMP cycle (data collected June 2013–May 2014). All sampled jurisdictions participated in MMP. Of the 598 sampled facilities, 480 (85%) facilities participated. Of the 9,371 sampled patients, MRAs were completed for 6,412 patients (70% of eligible, sampled patients). Clinical records dated within two years before the MMP interview were abstracted for MRA data collection. In some jurisdictions, MRAs could be completed under surveillance authority. For MRAs conducted under surveillance authority without corresponding interview data, records dated within two years before the date of first contact attempt were abstracted.

Centers for AIDS Research Network of Integrated Clinical Systems (CNICS)

CNICS is a research network involving eight large CFAR clinics that prospectively collects comprehensive patient data at point-of-care through a repository of electronic medical record data and other sources. The eight CFAR clinics participating in CNICS are University of Alabama (Birmingham), University of Washington (Seattle), University of California San Diego, University of California San Francisco, Case Western Reserve University (Cleveland, OH), Johns Hopkins University (Baltimore, MD), Fenway Health/Harvard (Boston, MA), and University of North Carolina (Chapel Hill).

Patients who receive HIV care at the eight clinics are included in the CNICS cohort; the median follow-up for each patient is 49 months. Approximately 1400 patients are newly enrolled each year; <10% of patients leave the CFAR clinical sites (and thus CNICS) annually.[58] For this

analysis, we created a cohort of CNICS patients who had a visit in 2013 (n=13,842) and analyzed records dated within the two years preceding each patient's last visit in 2013.

National HIV Surveillance System (NHSS)

To illustrate how MMP and CNICS participants compare to the US PLWH population, we included data from the NHSS in Table 2.2. The NHSS data presented corresponds to PLWH diagnosed, reported, and presumed living in 2013, and were adjusted for reporting delays.[47]

Analysis

A key goal of this project was to standardize our analytic approach to augment the comparability of MMP and CNICS data. To this end, we applied identical case definitions to MMP and CNICS data, accounted for missing data, stratified all analyses by sex, age, and race, and evaluated the influence of MMP's sampling frame on our results in a sensitivity analysis (described hereafter).

Case Definitions

For this analysis, we applied case definitions developed and validated by CNICS investigators to MMP and CNICS datasets. The case definitions are described in Table 2.1.

Management of Missing Data

All case definitions rely upon biological measurements: the DM definition relies upon HbA1c and glucose measurements, the CKD definition relies upon creatinine measurements, and the HTN definition relies upon blood pressure measurements. If a patient did not have the measures

specified by the case definition in the two year observation period, and did not otherwise meet the case definition, their disease status was set to missing. The percent missing for each condition is listed in Table 2.3.

We considered three approaches to managing missing data: (1) assume that patients with missing values for a given condition did *not* have the condition, (2) exclude patients with a missing value for a given condition from analyses of that condition ("complete case" analysis), and (3) impute disease status for patients with missing values. In 1.3, we contrast how these three approaches impacted the estimates of overall CKD, DM, and HTN prevalence.

Ultimately, we decided to implement multiple imputation (MI) for all subsequent analyses. The MI models were implemented separately in MMP and CNICS. The data were assumed to be missing at random – that is, missingness was conditional only on the variables included in the imputation model[i]. We used IVEware Version 0.2, a SAS-callable macro, to perform multiple imputation by chained equations (MICE) (also called "sequential regression multivariate imputation"). MICE formulates separate regression models for each variable with missing data and uses regression appropriate for the variable type (e.g. linear regression for continuous variables and logistic regression for dichotomous variables). We imputed ten datasets and estimated the mean prevalence across the 10 imputed datasets. Standard error was calculated

[i] The following variables were included in the MMP imputation models that assessed CKD, DM, and HTN: age, sex, race, ethnicity, nativity, risk transmission category, years since HIV diagnosis, history of male-to-male sex, history of injection drug use, region, project area, body mass index, average eGFR, average systolic blood pressure, average diastolic blood pressure, dialysis, CKD status, DM status, HTN status, and dyslipidemia status. The following variables were included in the CNICS imputation models that assessed CKD, DM, and HTN: age, sex race, ethnicity, risk transmission category, region, body mass index, site, average eGFR, average systolic blood pressure, average diastolic blood pressure, CKD status, DM status, HTN status, and dyslipidemia status.

using Rubin's Rules[59]; the Taylor Series approach was used to obtain variance estimates for MMP, accounting for its survey design.

Estimation of Diabetes, Chronic Kidney Disease, and Hypertension Prevalence

Stratum, cluster, and weighting design variables were included in all analyses of MMP data. All analyses were stratified by sex at birth, race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, and other), and age group (18–34, 35–54, ≥55 years). Age group categories were determined so as to allow comparability and linkage with other data sources. DM, CKD, and HTN prevalence was estimated separately for MMP and CNICS patients. For each stratum, we calculated a Z statistic to test whether the proportion classified as having DM, CKD, or HTN significantly differed between MMP and CNICS.

Sensitivity Analysis: Addressing Potential Selection Bias in MMP

To be included in the MMP sampling frame, patients must have had an HIV care visit during January –April of the sampling year. Using CNICS data, we evaluated whether the relative risk of meeting the CKD, DM, and HTN case criteria differed between CNICS patients who did and did not have a visit during January – April. We estimated the adjusted relative risk (aRR) of each condition given the presence or absence of visit during January – April, controlling for age, sex, race, and BMI, by implementing a Poisson regression model with robust error variance. If a significant association was observed, then we calculated a modified prevalence estimate based upon the following input parameters: mean and standard error (SE) of disease by sub-group among MMP participants, aRR and SE of disease given presence or absence of January – April visit among CNICS patients, and percent of CNICS patients with a January – April visit. To account for uncertainty in the point estimates, we ran 1000 simulated observations in Stata

drawing from the prevalence and log(aRR) distributions, assuming normal distributions within the indicated mean and standard errors, and then applied the following equation to the simulated observations:

$$Prevalence_{PDP\ correction\ factor} = prevalence*(\%\ with\ PDP\ visit + (\%\ without\ PDP\ visit* (aRR_{disease|No\ PDP\ visit}))$$

To obtain the overall adjusted point prevalence, we estimated the mean adjusted prevalence across the 1,000 simulations. The corresponding standard error was the standard deviation of the simulated mean adjusted prevalence estimates.

Results

Patient Demographic Characteristics

This analysis included clinical records from 6,412 MMP participants and 13,842 CNICS patients. Age was similarly distributed in MMP and CNICS, with more than half of patients between the ages of 35 and 54. The age distribution is older in MMP and CNICS than that of all HIV cases reported to the National HIV Surveillance System (NHSS) (see Table 2.2). The distribution of sex at birth, race/ethnicity, and region of current residents among MMP participants was more similar to NHSS data than that of CNICS patients. Compared to MMP and NHSS data, a larger proportion of CNICS patients were male, non-Hispanic (NH) White, and residents of the western region of the US.

Comparison of Overall Prevalence Estimates Yielded by Three Approaches to Managing Missing Data

The percent missing values for CKD, DM, and HTN was similar between MMP and CNICS (Table 2.3). Missingness was highest for CKD (10% in MMP and 13% in CNICS) and lowest for HTN (4% in MMP and 5% in CNICS). For all conditions, the percent missing was highest in the youngest age group and lowest in the oldest age group.

In both MMP and CNICS, there was a tendency for estimated prevalence to be lowest when patients with missing values were assumed to be free of disease and highest when patients with missing values were excluded from analyses. The estimates yielded by the MI models tended to be closer in value to estimates yielded by the complete case analysis. The overall prevalence of DM, CKD, and HTN (estimated through MI) in MMP was 12.7%, 7.6%, and 33.3%, respectively. The overall prevalence of DM, CKD, and HTN (estimated through MI) in CNICS was 9.9 %, 8.3%, and 38.1%, respectively.

Chronic Kidney Disease (CKD)

The estimated CKD prevalence increased with age (Table 2.4, Figure 2.1). Across MMP and CNICS, the CKD prevalence ranged from 0–2.4% in the youngest age group (<35 years); 1.2–10.8% in the middle age group (35–54 years); and 7.5–31.9% in the oldest age group (≥55 years). Among NH-White and NH-Black patients, the estimated prevalence was greater for women than men. Significant differences in age- and sex-specific prevalence estimates were observed between MMP and CNICS among NH-Blacks ≥35 years old, with greater prevalence observed in CNICS than in MMP. Thus, in CNICS the CKD burden appeared considerably greater among NH-Black patients than NH-White and Hispanic patients; in MMP, age- and sex-specific prevalence estimates were more consistent across racial groups.

Diabetes (DM)

Among patients classified as diabetic in MMP and CNICS, respectively, 66% and 76% had ≥1 HbA1c measures > 6.5%, 63% and 60% had a DM-specific medication, 36% and 18% had a DM diagnosis and a DM-related medication, and 31% and 44% had ≥2 random glucose tests ≥200 mg/dL. Only 3% of CNICS cases and 5% of MMP cases met the glucose criteria and no other diabetes case criteria. The estimated DM prevalence increased with age (Table 2.5, Figure 2.2). In the youngest age group (<35 years), the DM prevalence ranged from 1.6–8.1%; in the middle age group (35–54 years), the DM prevalence ranged from 6.9–14.9%; in the oldest age group (≥55 years) the DM prevalence ranged from 12.7–40.4%. Within demographic strata, prevalence estimates were fairly consistent between MMP and CNICS. In the youngest age group, DM prevalence tended to be higher among women than men; in the older age groups DM prevalence was more similar between men and women. There was a pattern suggesting that prevalence tended to be lowest for NH-Whites and highest for Hispanics.

Hypertension (HTN)

Among patients classified as hypertensive in MMP and CNICS, respectively, 82% and 88% had a recorded HTN diagnosis and anti-hypertensive medication prescription, and 45% and 42% had high blood pressure measurements. The overall HTN prevalence was 33.7% (95% CI: 31.6%, 35.8%) for MMP participants and 38.1% (95% CI: 37.9, 39.0%) for CNICS participants (Table 2.6, Figure 2.3). The estimated HTN prevalence increased with age. In the youngest age group (<35 years), the prevalence ranged from 3.1%–19.9%; in the middle age group (35–54 years), the prevalence ranged from 16.6–51.2%; in the oldest age group (≥55 years) the prevalence ranged from 41.2–76.0%. Significant differences in prevalence estimates were observed between MMP and CNICS among non-Hispanic Blacks ≥35 years old and NH-White men ≥55 years, with greater prevalence observed in CNICS than in MMP. Regardless of data source, sex, and age

group, the prevalence was highest for NH-Blacks/African Americans relative to NH-Whites and Hispanics.

Sensitivity Analysis: Addressing Potential Selection Bias in MMP

Accounting for differences in patients with and without a January – April visit, the adjusted relative risk of CKD, DM, and HTN was 0.82 (95% CI= 0.71, 0.95), 0.93 (95% CI= 0.82, 1.07), and 1.03 (95% CI= 0.99, 1.08), respectively. Since a significant association existed between having a January – April visit and CKD, we re-estimated the CKD prevalence, adjusting for MMP's sampling design, and compared the adjusted prevalence estimates to the original estimates presented in Table 2.4. The adjusted estimates differed by less than 1 percentage point from the original MMP prevalence estimates (Supplementary Table 2.S1).

Discussion

In our effort to reconcile measurement of the burden of DM, CKD, and HTN in MMP and CNICS, we encountered several common challenges non-standard case definitions, missing data, and potential for selection bias. We detailed how we decided to manage these issues and how these decisions influenced our results. After reconciling our approach to analyzing MMP and CNICS data, we demonstrated a considerable burden of DM, CKD, and HTN among older adults receiving care at facilities included in these two prominent data systems.

MMP and CNICS differ dramatically in their design. MMP is a probability sample of HIV care patients who receive care from clinics located in geographically diverse areas across the United States; clinical data is manually abstracted from medical records by trained health department

staff. CNICS is a census of almost all patients receiving care at eight, large university-affiliated clinics that use integrated electronic medical record systems that ensures that data entered at point-of-care can be readily deposited into a central repository. Given these differences, one would expect our analysis to yield prevalence estimates that varied widely by data source. However, the estimated prevalence of DM, CKD, and HTN was generally similar across MMP and CNICS, which is likely attributable to our concerted effort to reconcile how DM, CKD, and HTN are defined and statistically evaluated.

We have several recommendations for evaluating DM, CKD, HTN, and other chronic conditions in the context of HIV. First, analysts should be cautious about how disease status is assigned for patients without complete documentation corresponding to the case criteria. In our analysis, patients without biological measures specified by the case definition who did not otherwise meet the case definition were assigned missing values for disease status; their probable disease status was subsequently assigned through multiple imputation. However, this was a departure from the norm in the literature which has most commonly assumed that patients lacking documentation corresponding to the case definition are free of disease, [29, 36, 52, 53, 60,61] or excluded patients without documentation from analyses.[62] While the absence of biological data (and no other diagnostic or medication data) might connote for many patients that the laboratory test was not clinically indicated, for some patients, the absence of a laboratory test, diagnostic, and prescription data could reflect other issues, such as sub-optimal engagement in care. In summary, we suspect that treating the absence of documentation as being indicative of being free of disease may cause the burden of disease to be underestimated for prevalent co-morbidities. A second methodological recommendation is that standard and existing case definitions be employed, so that studies can be more easily compared. We reported the proportion of patients

classified as being a DM or HTN case that met each specific component of the case definition, illustrating the sensitivity of disease status classification to decisions about case definitions. Finally, we recommend that prevalence estimates applied to a heterogeneous group be interpreted cautiously, as it might reflect the underlying demographics rather than the actual burden of disease.

With the number of PLWH over 55 years old increasing in the United States[63], HIV care programs should anticipate a growing number of their patients requiring services related to DM, CKD, and HTN, and likely other chronic diseases. While data sources like MMP and CNICS allow for the prevalence and risk factors of various chronic conditions to be routinely monitored, determining how best to concurrently treat and manage HIV and common chronic conditions requires intensive investigation. For example, how to interrupt the causal links between HIV, HIV-associated inflammation, and development of chronic conditions; how antiretroviral therapies (ART) interact with the numerous drugs that treat common chronic diseases; how the various ART regimens might differentially impact chronic conditions; what strategies to managing multi-morbidity will be feasible for patients to consistently adopt; and the degree to which PLWH are adherent to clinical recommendations pertaining to chronic disease management.[20, 22, 23]

There are limitations shared by MMP and CNICS, limitations unique to each data source, and limitations of our analytic approach. Both MMP and CNICS are unlikely to capture information about care received outside of patients' primary facility. CNICS and MMP are vulnerable to different types of selection bias. CNICS represents patients who receive care at large, public, university-affiliated clinics in urban settings. MMP represents these patients, as well as patients who receive care at clinics that vary with regard to predominant funding base, size, and

urbanicity. Perhaps consequently, the distribution of sex, race/ethnicity, and regional distribution among MMP participants is more similar to the census of all adults with diagnosed HIV (per NHSS data) than that of CNICS. However, only 70% of patients sampled for MMP in 2013 contributed data to this analysis. Although the analyses are weighted to adjust for non-response bias, the effect of non-response is unlikely to be eliminated. Prior to 2015, MMP sampled from a list of patients who had a visit in January–April. In a sensitivity analysis, we used CNICS data to explore whether this sampling approach might affect the estimated prevalence of CKD, DM, and HTN. Although we observed a significant association between presence or absence of a January – April visit and meeting the CKD case criteria, it did not appear to substantially affect the estimated prevalence of CKD (Supplementary Table 2.S1).

Our analytical approach had limitations. As noted above, we used multiple imputation to assign disease status to patients without any documentation corresponding to the case definition. Although we included many demographic and clinical variables in our imputation models, it is unlikely that we fully accounted for all factors that affect missingness, compromising the 'missing at random' assumption that underlies MI procedures. A separate limitation is that a small subset of patients (about 5%) contributed data to both MMP and CNICS, as there are four clinics that participate in both MMP and CNICS. A final limitation of our analysis is that we did not rigorously evaluate racial disparities. Based on the existing literature[34], we expected the CKD prevalence to be considerably greater among NH-Black participants than participants of other racial/ethnic backgrounds. This pattern was evident in CNICS, but not MMP. The root cause of these discordant findings is unknown.

In conclusion, after we methodically reconciled how CKD, DM, and HTN were defined and statistically evaluated in MMP and CNICS, we observed sub-group specific prevalence estimates

that were fairly consistent across data sources. The consistency between the two data sources may perhaps allay some concerns regarding the limitations of both data sources. MMP and CNICS can provide reliable data to monitor HIV co-morbidities in the US.

Table 2.1 Case Definitions Applied to Medical Monitoring Project (MMP) and CFAR Network of Integrated Clinical Systems (CNICS) data.

Condition	Case Criteria
Chronic Kidney Disease	Two eGFR[#] values <60 ml/min 90 or more days apart without an intervening normal value.
Diabetes	1. HbA1c ≥6.5%; OR 2. "Diabetes-specific" medication^; OR 3. Diabetes diagnosis AND "diabetes-related" medication*; OR 4. ≥ 2 random glucose tests ≥200 mg/dL
Hypertension	1. A diagnosis of hypertension AND the presence of any antihypertensive medication. OR 2. The average of at least 2 systolic blood pressure (SBP) measurements ≥140 mmHg or diastolic blood pressure (DBP) measurements ≥90 mmHg.

Note: All criteria assessed in a 2 year observation period.

[#]eGFR= Estimated Glomerular Filtration Rate. eGFR is routinely used to assess kidney function. We applied the CKD-EPI creatinine equation[64] to MMP and CNICS data to estimate participants' GFR.

^DM-specific medications: Alogliptin, Canagliflozin, Chlorpropamide, Exenatide, Glimepiride, Glipizide, Glipizide, Glyburide, Insulin, Linagliptin, Liraglutide, Nateglinide, Pramlintide, Repaglinide, Saxagliptin, Sitagliptin, Tolazamide, Tolbutamide.

*DM-related medications: Acarbose, Metformin, Miglitol, Pioglitazone, Rosiglitazone, Troglitazone.

Table 2.2: Characteristics of Medical Monitoring Project (MMP) and CFAR Network of Integrated Clinical Systems Patients (CNICS) Participants, Relative to People with an HIV Diagnosis Reported to the National HIV Surveillance System (NHSS), United States, 2013.

	MMP (n=6,412) % (95% CI)	CNICS (n=13,842) %	NHSS[47] %
Age Group			
18–34	14.6 (13.3, 16.0)	14.4	18.4
35–54	57.3 (55.5, 59.1)	58.4	56.5
≥55	28.1 (26.3, 29.9)	27.2	25.1
Race/Ethnicity			
Non-Hispanic White	31.0 (24.5, 37.5)	44.4	31.8
Non-Hispanic Black	42.8 (33.9, 51.7)	38.6	42.7
Hispanic	21.1 (14.7, 27.7)	13.5	20.3
Other	5.0 (3.6, 6.3)	3.4	5.1
Sex at birth			
Male	72.9 (70.7, 75.1)	81.9	75.7
Female	26.9 (24.7, 29.1)	18.1	24.3
Region^			
Midwest	13.9	6.6	11.7
Northeast	18.7	8.3	24.7
South	38.9	40.3	42.7
West	23.1	44.8	18.8
US Territories	5.4	0.0	2.0

^"Region"= the unweighted percent of the MMP and CNICS sample receiving HIV care in the five listed regions. Regions are defined by the US Census Bureau and used in CDC's National HIV Surveillance System:
Northeast: CT, ME, MA, NH, NJ, NY, PA, RI, VT
Midwest: IL, IN, IA, KS, MI, MN, MO, NE, ND, OH, SD, WI
South: AL, AR, DE, DC, FL, GA, KY, LA, MD, MS, NC, OK, SC, TN, TX, VA, WV
West: AK, AZ, CA, CO, HI, ID, MT, NV, NM, OR, UT, WA, WY.

US Territories: PR, AS, GU, MP.

Table 2.3: Overall Prevalence of Diabetes, Chronic Kidney Disease, and Hypertension among MMP and CNICS Participants, Estimated by Three Different Approaches to Addressing Missingness

		Disease Prevalence when Participants with Missing Values were…		
	% Missing	Assumed to NOT have condition % (95% CI)	Excluded from Analysis ("Complete Case") % (95% CI)	Assigned Disease Status Given Demographic and Health Characteristics[^] ("Multiple Imputation") % (95% CI)
Diabetes				
MMP	9.1	10.6 (10.1, 11.1)	13.2 (12.7, 13.7)	12.7 (12.0, 13.3)
CNICS	11.7	8.3 (7.8, 8.7)	9.4 (8.9, 9.9)	9.9 (9.2, 10.5)
Chronic Kidney Disease				
MMP	10.3	7.3 (6.9, 7.6)	7.6 (7.2, 7.9)	7.6 (7.2, 8.0)
CNICS	13.2	7.5 (7.1, 8.0)	8.7 (8.2, 9.2)	8.3 (7.8, 8.8)
Hypertension				
MMP	4.2	32.6 (30.7, 34.6)	34.1 (32.0, 36.2)	33.3 (31.6, 35.8)
CNICS	4.9	36.4 (35.6, 37.2)	38.3 (37.5, 39.2)	38.1 (37.9, 39.0)

Abbreviations: MMP = Medical Monitoring Project; CNICS= Centers for AIDS Research Network of Integrated Clinical Systems

Notes: Patients with less than 2 creatinine measures (separated by 90 days) in the 2 year observation period were considered missing CKD status. Patients without a single HbA1c or two glucose measures in the two year observation period who did not otherwise meet the case criteria, were assigned missing values for diabetes status. Patients without at least two blood pressure measurements in the two year observation period, and did not otherwise meet the case criteria, were assigned missing values for HTN status.

[^] The following variables were included in the MMP imputation models that assessed CKD, DM, and HTN: age, sex, race, ethnicity, nativity, risk transmission category, years since HIV diagnosis, history of male-to-male sex, history of injection drug use, region, project area, body mass index, average eGFR, average systolic blood pressure, average diastolic blood pressure, dialysis, CKD status, DM status, HTN status, and dyslipidemia status. The following variables were included in the CNICS imputation models that assessed CKD, DM, and HTN: age, sex race, ethnicity, risk transmission category, region, body mass index, site, average eGFR, average systolic blood pressure, average diastolic blood pressure, CKD status, DM status, HTN status, and dyslipidemia status.

Table 2.4: Prevalence of Chronic Kidney Disease among Adults in HIV Care in 2013, Estimated with MMP and CNICS Data

	MMP	CNICS
	Prevalence % (95% CI)	Prevalence % (95% CI)
Overall	7.6 (7.2, 8.0)	8.3 (7.8, 8.8)
NH-White Men		
18–34	0.1 (0, 3.5)	0.5 (0.0, 2.3)
35–54	4.1 (2.6, 5.6)	3.0 (2.4, 3.6)
≥55	16.8 (13.4, 20.3)	12.7 (11.0, 14.4)
NH-Black Men		
18–34	0.4 (0, 2.3)	2.4 (0.0, 6.0)
35–54	6.6 (4.4, 8.8)†	9.7 (8.3, 11.0)†
≥55	15.4 (12.2, 18.7)†	20.8 (18.3, 23.3)†
Hispanic Men		
18–34	1.4 (0, 3.8)	0.5 (0.0, 1.6)
35–54	2.9 (1.3, 4.4)	1.2 (0.5, 1.8)
≥55	17.8 (11.3, 24.3)	12.7 (8.5, 16.9)
NH-White Women		
18–34	2.2 (0, 7.1)	0 (0, 0)
35–54	9.1 (3.6, 14.5)	8.8 (5.7, 12.0)
≥55	23.8 (14, 33.6)	23.2 (16.5, 30.0)
NH-Black Women		
18–34	2.0 (0, 8.1)	1.4 (0.0, 3.4)
35–54	5.6 (3.8, 7.3)‡	10.8 (8.9, 12.8)‡
≥55	20.2 (16, 24.4)‡	31.9 (27.9, 35.9)‡
Hispanic Women		
18–34	0.3 (0, 3.6)	0 (0, 0)
35–54	4.6 (0, 9.1)	2.8 (0.1, 5.6)
≥55	17.0 (9.1, 24.8)	7.5 (0.0, 15.8)

Abbreviations: MMP = Medical Monitoring Project; CNICS= Centers for AIDS Research Network of Integrated Clinical Systems; "NH"=Non-Hispanic.
Notes: The CKD case criterion was two eGFR values <60, which were ≥ 90 days apart without an intervening normal value. Prevalence estimates presented reflect the results from multiple imputation model; across all strata and data sources, the difference between the point estimates estimated from complete case (not presented) and MI analyses was <1%. MMP prevalence estimates were adjusted for MMP's sampling frame (see Methods section). Significant differences in prevalence estimated by MMP and CNICS are indicated with † ($p<.05$) and ‡ ($p<.01$).

Table 2.5: Prevalence of Diabetes among Adults in HIV Care in 2013, Estimated with MMP and CNICS Data

	MMP	CNICS
	Prevalence % (95% CI)	Prevalence % (95% CI)
Overall	12.7 (12.0, 13.3)	9.9 (9.2, 10.5)
NH-White Men		
18–34	1.8 (0, 5.1)	1.8 (0.2, 3.4)
35–54	7.6 (5.2, 10)	6.9 (5.8, 7.9)
≥55	14.4 (10.6, 18.2)	15.0 (12.8, 17.1)
NH-Black Men		
18–34	1.6 (0, 5.1)	1.9 (0.9, 2.9)
35–54	11.2 (8.1, 14.3)	10.1 (8.7, 11.5)
≥55	22.1 (16.6, 27.5)	18.0 (15.7, 20.3)
Hispanic Men		
18–34	3.4 (0, 8.9)	1.6 (0.1, 3.0)
35–54	12.8 (9.4, 16.3)†	7.9 (6.0, 9.7)†
≥55	28.2 (19, 37.3)	20.1 (15.0, 25.2)
NH-White Women		
18–34	5.3 (0, 18.1)	3.2 (0.0, 7.5)
35–54	8.9 (2.7, 15.1)	10.3 (7.0, 13.5)
≥55	17.4 (6.6, 28.2)	12.7 (7.4, 18.0)
NH-Black Women		
18–34	3.4 (0, 8.8)	6.7 (2.4, 10.9)
35–54	11.9 (7.5, 16.3)	11.7 (9.7, 13.7)
≥55	25.2 (17.6, 32.9)	18.2 (14.9, 21.5)
Hispanic Women		
18–34	8.1 (0, 20.4)	4.4 (0.0, 12.7)
35–54	14.9 (5.9, 23.8)	7.7 (3.0, 12.3)
≥55	40.4 (25.9, 54.9)	22.5 (9.4, 35.6)

Abbreviations: MMP = Medical Monitoring Project; CNICS= Centers for AIDS Research Network of Integrated Clinical Systems; "NH"=Non-Hispanic.
Notes: The DM case criteria include (1) HbA1C ≥6.5% OR (2) diabetes-specific medication OR (3) diabetes diagnosis AND "diabetes-related" medication OR (4) ≥ 2 random glucose tests ≥200 mg/dL . Prevalence estimates presented reflect the results from multiple imputation model; across all strata and data sources, the difference between the point estimates estimated from complete case (not presented) and MI analyses was <1%. MMP prevalence estimates were adjusted for MMP's sampling frame (see Methods section). Significant differences in prevalence estimated by MMP and CNICS are indicated with † ($p<.05$) and ‡ ($p<.01$).

Table 2.6: Prevalence of Hypertension among Adults in HIV Care in 2013, Estimated with MMP and CNICS Data

	MMP	CNICS
	Prevalence % (95% CI)	*Prevalence % (95% CI)*
Overall	33.3 (31.6, 35.8)	38.1 (37.9, 39.0)
NH-White Men		
18–34	13.1 (3.6, 22.6)	12.9 (10.2, 15.6)
35–54	25.0 (19.7, 30.3)	28.1 (26.6, 29.7)
≥55	41.2 (35.7, 46.8) ‡	50.5 (48.0, 53.0) ‡
NH-Black Men		
18–34	14.8 (9.0, 20.6)	19.9 (17.0, 22.9)
35–54	39.7 (35.8, 43.7) ‡	48.1 (45.8, 50.4) ‡
≥55	58.4 (52.3, 64.5) ‡	67.8 (65.0, 70.7) ‡
Hispanic Men		
18–34	11.1 (4.1, 18.1)	6.5 (3.4, 9.6)
35–54	21.1 (16.7, 25.4)	21.3 (18.8, 23.7)
≥55	51.6 (40.2, 62.9)	47.8 (41.5, 54.1)
NH-White Women		
18–34	7.6 (0.0, 24.0)	7.2 (0.6, 13.9)
35–54	17.9 (8.5, 27.2)	30.7 (25.4, 36)
≥55	50.1 (35.5, 64.6)	50.9 (42.2, 59.5)
NH-Black Women		
18–34	12.8 (4.5, 21.1)	19.5 (11.8, 27.3)
35–54	38.8 (33.7, 43.9) ‡	51.2 (47.9, 54.5) ‡
≥55	65.2 (58.6, 71.8) ‡	76.0 (72.3, 79.6) ‡
Hispanic Women		
18–34	7.5 (0.0, 18.0)	3.1 (0.0, 9.2)
35–54	23.7 (14.2, 33.1)	16.6 (10.1, 23.1)
≥55	55.4 (40.0, 70.8)	50.5 (34.6, 66.4)

Abbreviations: MMP = Medical Monitoring Project; CNICS= Centers for AIDS Research Network of Integrated Clinical Systems; "NH"=Non-Hispanic.

Notes: The HTN case criteria include (1) A diagnosis of hypertension AND the presence of any antihypertensive medication OR (2) the average of at least 2 systolic blood pressure (SBP) measurements ≥140 mmHg or diastolic blood pressure (DBP) measurements ≥90 mmHg over a 2 year period. Prevalence estimates presented reflect the results from multiple imputation model; across all strata and data sources, the difference between the point estimates estimated from complete case (not presented) and MI analyses was <1%. Significant differences in prevalence estimated by MMP and CNICS are indicated with † ($p<.05$) and ‡ ($p<.01$).

Supplemental Table 2.S1: Comparison of MMP Chronic Kidney Disease Prevalence Estimates, adjusted and unadjusted for presence or absence of January – April visit.

	Chronic Kidney Disease % (95% CI)	
	Unadjusted	Adjusted
NH-White Men		
18–34	0.1 (0, 3.5)	0 (0, 3.3)
35–54	4.1 (2.6, 5.6)	3.9 (2.4, 5.4)
≥55	16.8 (13.4, 20.3)	16.1 (12.8, 19.5)
NH-Black Men		
18–34	0.4 (0, 2.3)	0.4 (0, 2.1)
35–54	6.6 (4.4, 8.8)	6.2 (4.2, 8.2)
≥55	15.4 (12.2, 18.7)	14.8 (11.7, 17.8)
Hispanic Men		
18–34	1.4 (0, 3.8)	1.3 (0, 3.5)
35–54	2.9 (1.3, 4.4)	2.8 (1.3, 4.3)
≥55	17.8 (11.3, 24.3)	17.6 (11.2, 23.9)
NH-White Women		
18–34	2.2 (0, 7.1)	2.1 (0, 6.4)
35–54	9.1 (3.6, 14.5)	8.6 (3.5, 13.7)
≥55	23.8 (14, 33.6)	22.3 (12.9, 31.8)
NH-Black Women		
18–34	2.0 (0, 8.1)	1.8 (0, 7.5)
35–54	5.6 (3.8, 7.3)‡	5.3 (3.6, 7.1)
≥55	20.2 (16, 24.4)‡	19.2 (15.2, 23.3)
Hispanic Women		
18–34	0.3 (0, 3.6)	0.3 (0, 3.5)
35–54	4.6 (0, 9.1)	4.3 (0, 8.6)
≥55	17.0 (9.1, 24.8)	16.7 (8.9, 24.5)

Abbreviations: MMP = Medical Monitoring Project; "NH"=Non-Hispanic.
Notes: The CKD case criterion was two eGFR values <60, which were ≥ 90 days apart without an intervening normal value. Prevalence estimates presented reflect the results from multiple imputation model; across all strata and data sources, the difference between the point estimates estimated from complete case (not presented) and MI analyses was <1%.

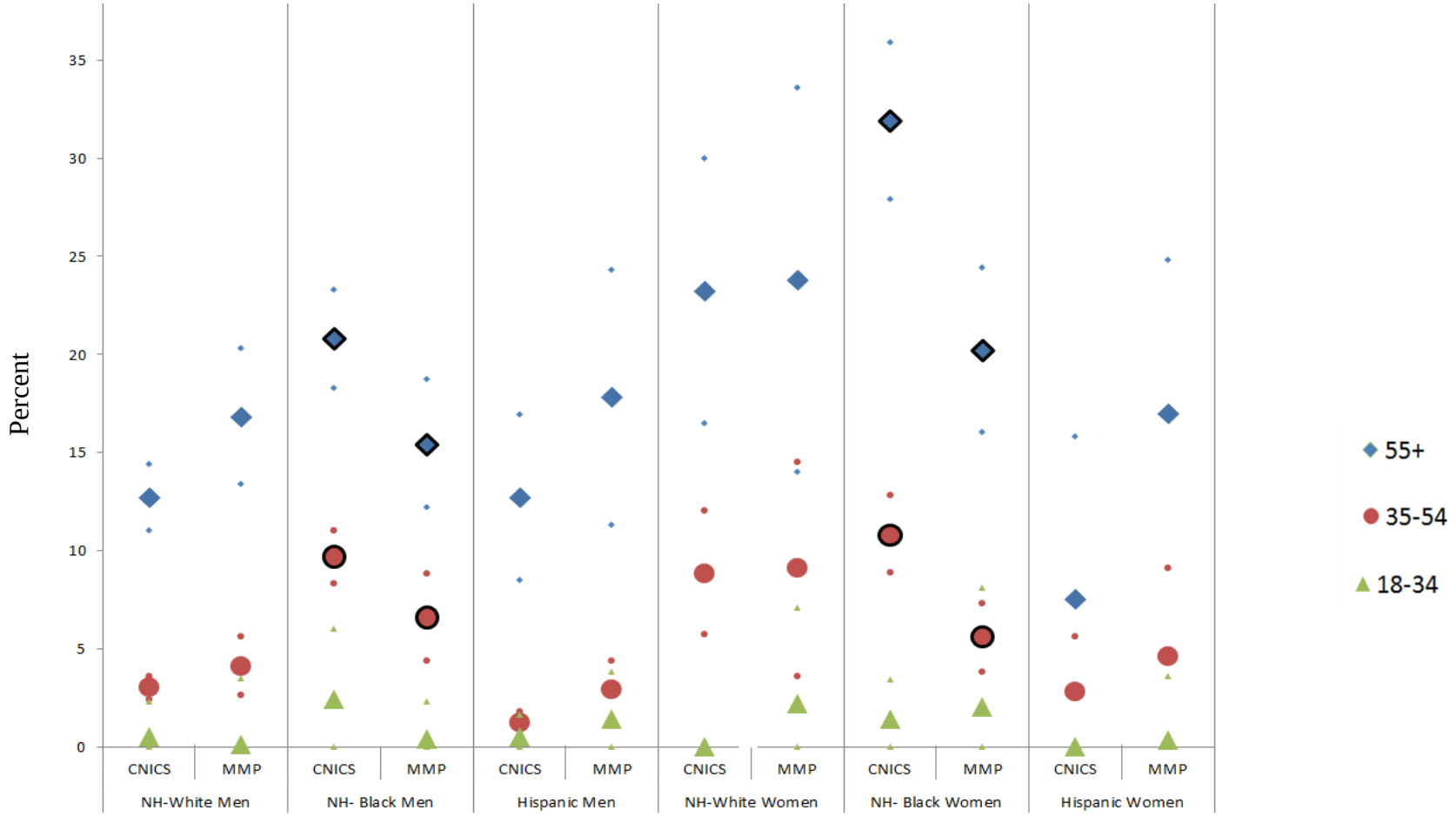


Figure 2.1: Prevalence of Chronic Kidney Disease among Adults in HIV Care in 2013, Stratified by Age, Sex, and Race/Ethnicity and Estimated with MMP and CNICS Data.

Note: Large symbols connote point estimate and small symbols connote 95% confidence intervals. Symbols outlined in black connote a significant difference between MMP and CNICS.

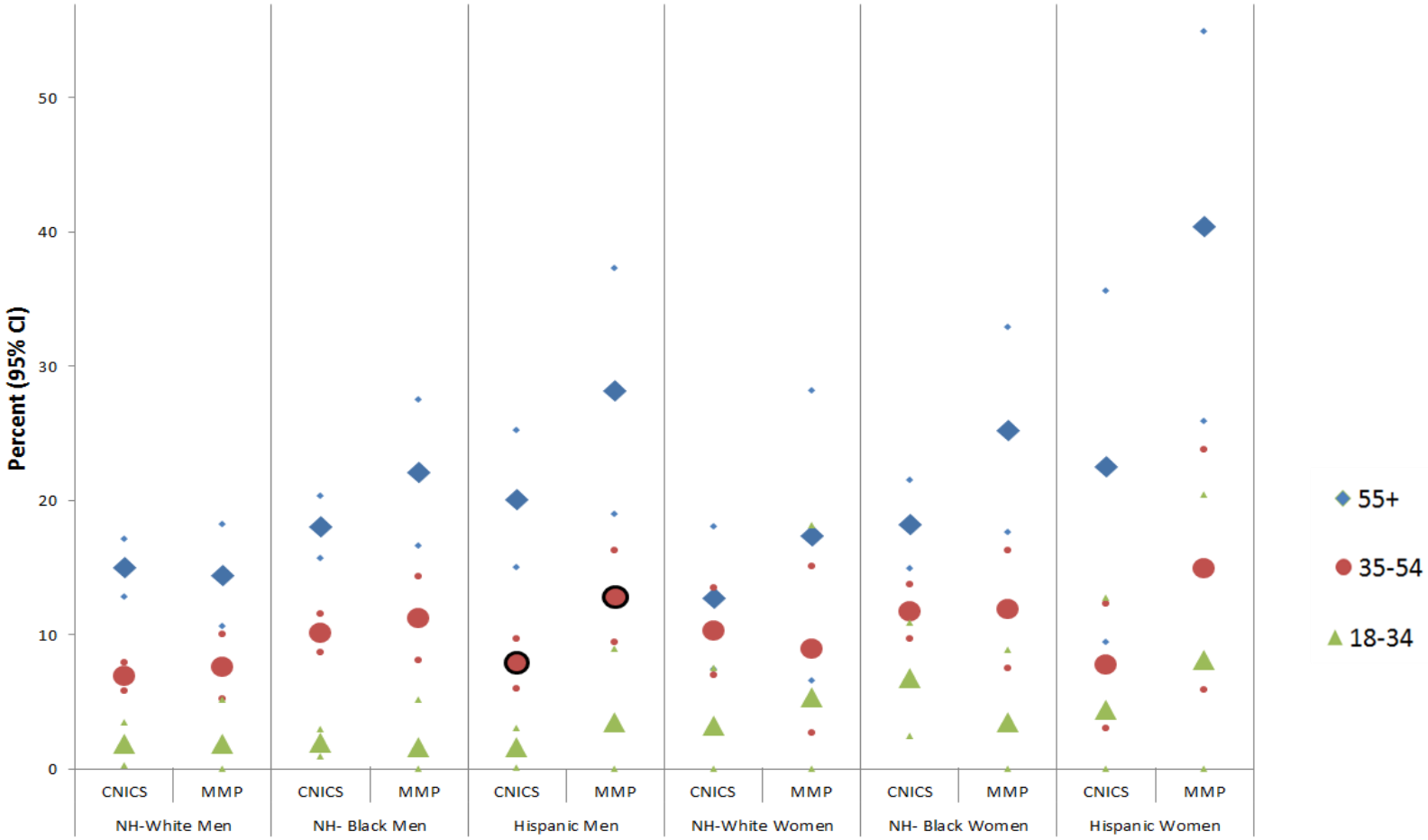


Figure 2.2: Prevalence of Diabetes among Adults in HIV Care in 2013, Stratified by Age, Sex, and Race/Ethnicity and Estimated with MMP and CNICS Data.

Note: Large symbols connote point estimate and small symbols connote 95% confidence intervals. Symbols outlined in black connote a significant difference between MMP and CNICS.

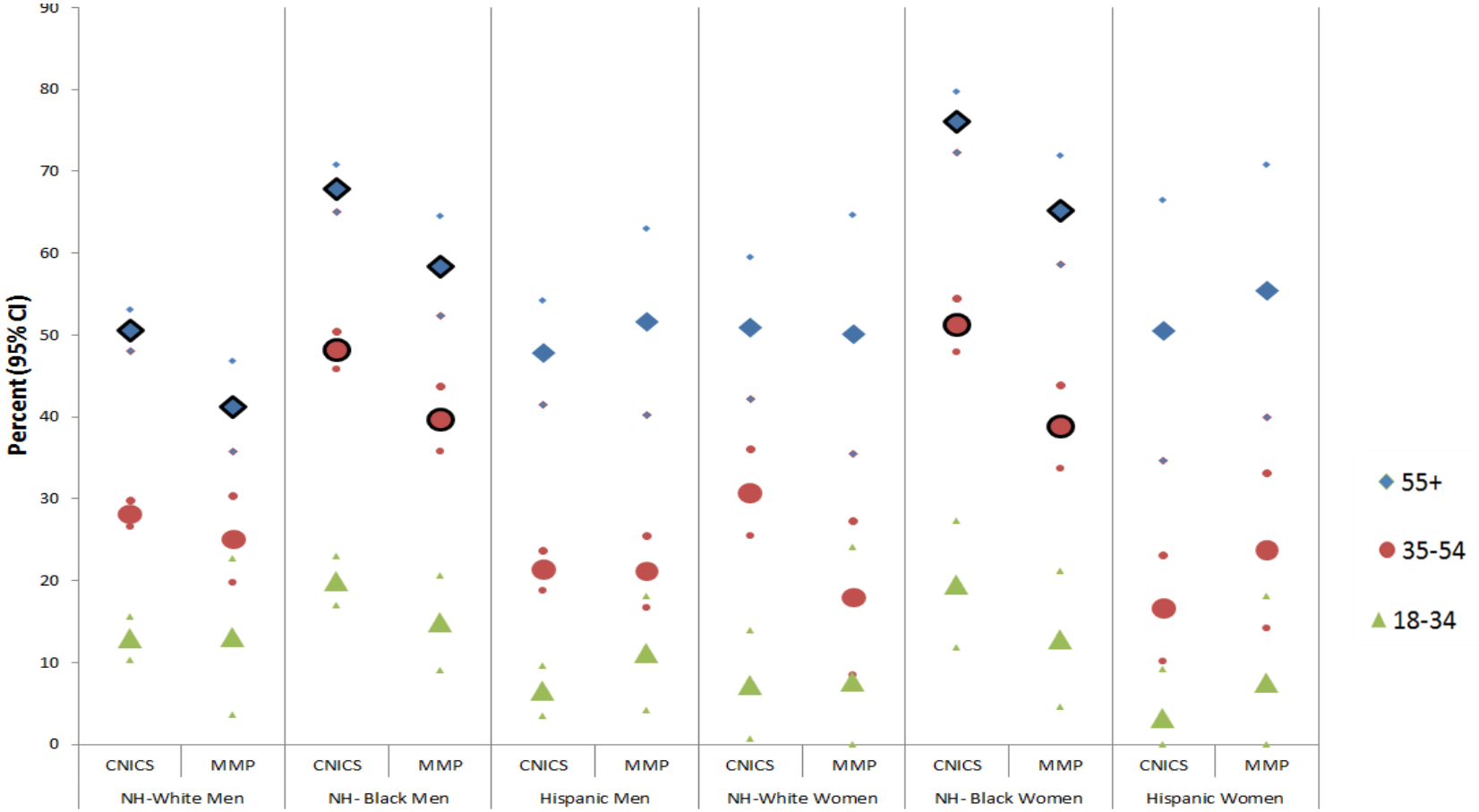


Figure 2.3: Prevalence of Hypertension among Adults in HIV Care in 2013, Stratified by Age, Sex, and Race/Ethnicity and Estimated with MMP and CNICS Data.

Note: Large symbols connote point estimate and small symbols connote 95% confidence intervals. Symbols outlined in black connote a significant difference between MMP and CNICS.

Chapter 3: Projected Demographic Composition of the United States Population of People Living with Diagnosed HIV

Abstract

Introduction: The transformation of HIV from a fatal disease to lifelong disease has resulted in an HIV-infected population that is growing and aging, placing new and increasing demands on public programs and health services. We used National HIV Surveillance System and US census data to project the demographic composition of the population of people living with diagnosed HIV (PLWDH) in the United States through 2045.

Methods: The input parameters for the projections include: (1) census projections, (2) number people with an existing HIV diagnosis in 2013, (3) number of new HIV diagnoses in 2013, and (4) death rate within the PLWDH population in 2013. Sex-, risk group-, and race-specific projections were estimated through an adapted Leslie Matrix Model for age-structured populations.

Results: Projections for 2013-2045 suggest that the number of PLWDH in the U.S. will consistently grow, from 917,294 to 1,232,054, though the annual growth rate will slow from 1.8% to 0.8%. The number of PLWDH aged 55 years and older will increase from 232,113 to 470,221. The number of non-Hispanic (NH) African Americans/Blacks and Hispanics is projected to consistently grow, shifting the racial/ethnic composition of the US PLWDH population from 32 to 23% NH-White, 42 to 38% NH-Black, and 20 to 32% Hispanic between 2013 and 2045.

Conclusions: Given current trends, the composition of the PLWDH population is projected to change considerably. Public health practitioners should anticipate large shifts in the age and racial/ethnic structure of the PLWDH population in the United States.

Introduction

In settings where antiretroviral therapy (ART) is widely accessible, HIV has transitioned from being a debilitating and fatal disease to being a lifelong chronic disease.[54] This transformation has caused the population of persons living with diagnosed HIV (PLWDH) to consistently grow in size[63] and for the age distribution to shift to older age groups.[8]

These demographic shifts are evident in the annual HIV surveillance reports published by the Centers for Disease Control and Prevention (CDC).[7, 65-68] Between 2008 and 2013, the proportion of the US PLWDH population that was over-55 increased from 16% to 25%.[8] Other demographic characteristics, such as race/ethnicity and risk transmission category, remained more stable in this six-year period. In 2013, 76% of the PLWDH population was male, and 43%, 32%, and 20%, respectively, was non-Hispanic Black, non-Hispanic White, and Hispanic/Latino.[8] Over half of PLWDH were estimated to have contracted HIV through male-to-male sexual contact; one-quarter through heterosexual sexual contact; and over 15% through injection drug use (IDU).[8]

Several publications have explored how effective HIV prevention and care promotion initiatives could impact the future number of incident cases, prevalent cases, and mortality among PLWDH in the United States.[69-71] However, the future demographic profile of the US PLWDH population has received limited attention, despite its considerable implications for HIV prevention and care programs. We used National HIV Surveillance System and US census data to project the demographic composition of the PLWDH population in the United States through 2045.

Methods

Data source and Input Parameters

The input parameters for the projections are derived entirely from two data sources: National HIV Surveillance System (NHSS) and the US Census Bureau Population Projections. NHSS is a population-based surveillance system that collects data on PLWDH in the United States.[72] It is the primary data source for monitoring trends in HIV/AIDS diagnosis, size and composition of the PLWH population, and mortality rates within the PLWDH population in the United States.[73] The United States Census Bureau produces projections of the US resident population by age, sex, race, and Hispanic origin by applying a cohort-component method to 2010 Census data and making assumptions about future births, deaths, and net international migration rates.[74]

Our projection model of the demographic composition of the US PLWDH population was based upon four types of input parameters: (1) census projections of the general US population, (2) estimated number of people known to be living with HIV, (3) estimated number of newly reported HIV diagnoses in 2013, and (4) estimated mortality rates within the PLWDH population in 2013. To minimize the influence of random year-to-year variation on estimates of parameters (3) and (4), we applied multivariate regression models to 2008-2013 data to predict sub-group specific 2013 diagnosis and mortality rate estimates.[ii] Observed versus predicted diagnosis mortality rates are illustrated in Supplemental Figures 3.1 and 3.2. When very high mortality rates were observed (e.g. 7-10% annual mortality), the prediction model tended to yield more

[ii] For all sub-groups in 2008-2013, we estimated the annual diagnosis and mortality rates, according to these equations:
$Annual\ Dx\ Rate_{Year} = (\#\ of\ New\ Diagnoses)_{Year}/(\#\ in\ General\ Population - Estimated\ \#\ of\ PLWDH)_{Year}$
$Annual\ Mortality\ Rate_{Year} = (\#\ of\ Deaths\ among\ PLWDH)_{Year}/(Estimated\ \#\ of\ PLWDH)_{Year}$
Then we used linear regression to estimate trends in estimated new diagnosis rates, using these equations:
$log(Diagnosis\ Rate) = Year + Sex + Race/Ethnicity + Age\ Group + Risk\ Transmission\ Category + (AgeXRace\ interaction\ term)$
$log(Mortality\ Rate) = Year + Sex + Race/Ethnicity + Age\ Group + Risk\ Transmission\ Category + (AgeXRace\ interaction\ term)$
We used results from the regression models to predict the estimated diagnosis rate and mortality rate in 2013.

modest annual mortality rates (e.g. 6% annual mortality); otherwise the observed and predicted mortality and diagnosis rates were similar. Migration was accounted for in all input parameters: census projections account for assumptions about future trends in migration and immigrants with HIV who enter the United States are reported as new diagnoses and are subsequently treated as prevalent diagnosed cases.

Our projection model was implemented separately for 24 sub-groups, corresponding to (4 race/ethnicity groups X 4 transmission categories for men) and (4 race/ethnicity groups X 2 transmission categories for women). Within each of these 24 sub-groups, the model was structured by 5-year age groups for MSM and 10-year age groups for the other risk groups. The four race/ethnicity groups modeled were Non-Hispanic (NH) White, NH-Black/African American, Hispanic/Latino, Other race/ethnicity groups. The six risk groups were men who have sex with men (MSM), MSM who inject drugs (MSM-IDU), non-MSM male and female persons who inject drugs (PWID), and heterosexual men and women. Transmission category was assigned in hierarchical order of probability; for example, men who reported having male and female sex partners prior to HIV diagnosis were assigned to the MSM category.[47] For reported cases without an identified risk factor, CDC uses multiple imputation to assign a plausible transmission category based upon other characteristics.[75] The future population size of MSM, PWID, MSM-IDU, and heterosexuals was estimated by applying current risk group estimates[76-79] to 2012 census projections[80] of the US general population (Table 3.1). All parameters derived from NHSS were statistically adjusted for reporting delays, accounting for patient-level, facility-level, and jurisdictional-level factors that affect reporting delays.[47]

Assumptions and Sensitivity Analyses

The base model assumes that the HIV diagnosis rate and mortality rate will remain constant between 2013 and 2045. Acknowledging that the diagnosis rate could decline in the future if transmission rates decline (e.g. if HIV prevention interventions, including treatment as prevention and pre-exposure prophylaxis, achieved higher efficacy and/or uptake), we conducted a sensitivity analysis that illustrated how an annual 1% reduction in diagnosis rates among MSM and a 0.5% reduction in diagnosis rates among all other risk groups, uniformly applied to all races and age groups, would impact the projected demographic composition of the PLWDH population in the United States. This modest reduction was applied relative to the preceding year (e.g. the diagnosis rate for MSM in 2015 was 99% that in 2014), resulting in a 27.5% and 14.8% decline in diagnosis rates among MSM and non-MSM, respectively, over the 32 year projection period.

Model Mechanics

The count of PLWDH in each projected year is a summation of the count of PLWDH in each age group. The latter corresponds to (1) prevalent cases from the prior time period who were already in the age group or aged into the age group; and (2) newly diagnosed cases who were already in the age group or aged into the age group, less the newly cases who died, as described in this equation:

$$H_{a,t} = \left[H_{a,t-1} \times \left(1 - \frac{1}{n_a}\right) \times (1 - M_a)\right] + \left[H_{a-1,t-1} \times \frac{1}{n_{a-1}} \times (1 - M_{a-1})\right] + \left[(C_{a,t-1} - H_{a,t-1}) \times \left(1 - \frac{1}{n_a}\right) \times D_a\right] + \left[(C_{a-1,t-1} - H_{a-1,t-1}) \times \frac{1}{n_{a-1}} \times D_{a-1}\right]$$

Where the notation is defined as:

$H_{a,t}$	number of individuals with HIV ($H_{a,t}$) in an age category a at year t
n_a	number of years in age category a (e.g. for an age category of 25 to 34, n_a =10)
M_{a-1}	annual mortality rate of HIV-diagnosed individuals in age category $a - 1$
D_{a-1}	annual HIV diagnosis rate of individuals in age category $a - 1$
$C_{a,t} - H_{a,t}$	number individuals **not** diagnosed with HIV, which equals

[Census projections of the total number of individuals ($C_{a,t}$)] -
[number of individuals with HIV ($H_{a,t}$)]

The model was implemented in Stata, Version 14.

Results

Projections for 2013-45 suggest that the number of PLWDH in the U.S. will consistently grow, from 917,294 to 1,232,054, while the annual growth rate will slow from 1.8% to 0.8% (Figure 3.1). Figure 3.2 depicts the age distribution among men and women with diagnosed HIV observed in 2013 and projected in 2025, 2035, and 2045. The number of PLWDH aged 55 years and older will more than double between 2013 and 2045, from 232,113 to 470,221. The largest shift in age structure will occur between 2013 and 2025, when the proportion of PLWDH aged 55 years and older will increase sharply from 25% to 38%. Thereafter, the relative age distribution remains fairly stable, while the absolute number of PLWDH in each age group will consistently grow.

While the size of the non-Hispanic (NH)-White PLWDH population is projected to peak in 2021 and thereafter decline, the number NH-African Americans/Blacks, Hispanics, and people of other racial/ethnic backgrounds is projected to consistently grow throughout the period 2013-2045 (Figure 3.3). These dynamics will shift the PLWDH population between 2013 and 2045 from 32% to 23% NH-White, 42% to 38% NH-Black/African American, 20% to 32% Hispanic/Latino, and 5% to 7% other racial/ethnic background. This shift among PLWDH is somewhat parallel to projected demographic trends in the general population, the percent of which is anticipated to shift between 2013 and 2045 from 65% to 50% NH-White, 12 to 13%

NH-African American/Black, 15% to 25% Hispanic, and 7% to 11% other race/ethnic group. Because our demographic projections of the PLWDH population apply constant diagnosis rates to census estimates of the general population, the estimated prevalence of diagnosed HIV is projected to remain stable. In all projected years, the number PLWDH per 1000 people in the general population was 2.1 to 2.2 for NH-Whites, 13.1 to 15.1 for NH-Blacks, 5.7 to 5.9 for Hispanics.

Figure 3.4 details how the PLWDH population age structure currently varies by race/ethnicity group, and how the age population structure is projected to shift over time. In 2013, the age distribution for men and women in all four race/ethnicity groups is normally distributed, centered around the 45-54 year old age group. By 2045, the age distribution of women with diagnosed HIV is skewed toward older age groups in all race/ethnic groups. Among men with diagnosed HIV, the age distribution remains fairly normally distributed for NH-Blacks/African Americans and Hispanics, but is skewed toward older age groups among NH-Whites; specifically, 48% of NH-Whites, 37% of NH-Blacks/African Americans, and 35% of Hispanics are projected to be ≥55 years old in 2045. The percent of PLWDH ≥55 years old is slightly older than that projected for the general population in 2045 (per US Census projections), which estimates that 44% of NH-Whites, 35% of NH-African American/Blacks, and 29% of Hispanics will be ≥55 years old in 2045.

The results presented in Figures 3.1-4 were given by the base model, which assumed the estimated HIV diagnosis rate in 2013 would remain constant over time. In Figure 3.5, we compare the projected number of PLWDH from the base model to the number given by a model that allowed for the diagnosis rate to moderately decline over time (an annual reduction of 1% for MSM and 0.5% for non-MSM). Whereas the base model projected that the PLWDH

population in 2045 would be 34% larger than the PLWDH population in 2013, the model in the sensitivity analysis estimated that the PLWDH population in 2045 would be 19% larger than the population in 2013. The relative distribution across racial groups did not change in the sensitivity analysis; however, the age distribution was proportionally older in the sensitivity analysis compared to the base model.

Discussion

Given current trends, we project that the size of the PLWDH population will increase and its demographic composition will change considerably. Our model projects that the US PLWDH population will be increasingly comprised of ethnic minorities. While non-Hispanic Blacks will comprise the largest proportion of the PLWDH population in all projected years, the number of Hispanics/Latinos with HIV is expected to considerably increase in the coming decades. For Hispanics/Latinos, the rapid population growth is largely driven by the population dynamics in the US general population. In contrast, the growth of the non-Hispanic Black PLWDH population reflects disparities in HIV incidence. These results underscore the importance of expanding coverage of HIV care, treatment, and prevention programs to ethnic/racial minorities, ensuring such programs are culturally and linguistically appropriate, and developing an HIV medical and social services for older patients.

Our model projects that the number of PLWDH 55 years and older will more than double between 2013 and 2045. An older PLWDH population has many implications for the provision of HIV care, treatment, and prevention programs. Chronic disease and polypharmacy will become more prevalent in an older PLWDH population, further complicating the delivery of HIV care. HIV care providers will need to be more skilled in the care of chronic conditions

affecting older populations and how those conditions interact with HIV infection and its treatment; and clinical research will be needed to inform the changing demands of HIV care. Budget analysts will need to forecast how care costs will change given increasing number of elderly PLWDH. HIV prevention campaigns and programs may need to be adapted to ensure that older people at risk for acquiring and transmitting HIV are reached by prevention messages and services.

The projections made by our model are vulnerable to uncertainty around the input parameter estimates and limitations of our modeling approach. The model is built upon three types of input parameters: (1) US Census Bureau population projections, (2) estimates of the proportion of the general population that is comprised of MSM, PWID, MSM-IDU, and at-risk heterosexuals, and (3) 2013 National HIV Surveillance System (NHSS) estimates of prevalent HIV cases, new HIV diagnoses, and deaths among PLWDH. US Census population projections are vulnerable to a number of sources of error, most notably, unforeseen future departures from historical trends in birth rates, mortality rates, and migration rates. The population estimates of MSM, MSM-IDU, PWID, and high risk heterosexuals are crude and derived from national probability surveys, which have their own sources of limitations. We applied these population estimates to all demographic sub-groups, though the prevalence of risk behaviors could vary by age and race/ethnicity and could vary over time. Indeed, existing population estimates suggest that injection drug use (IDU) is more prevalent among NH-Whites and NH-Blacks/African Americans than Hispanics and people of other racial/ethnic backgrounds[81], and that IDU is trending downward over time for most sub-groups, except young people who are increasingly engaging in IDU.[82]

There are several limitations of NHSS data, perhaps most notably duplicate case reporting. A recent comparison of PLWDH population estimates based upon case reports versus an alternative approach based upon HIV laboratory reports yielded findings that suggested that the former approach considerably overestimated the number of people with diagnosed HIV in the United States.[45] The authors explain that duplicate case-reports can arise if out-of-state migration and deaths are improperly accounted for within the surveillance system.[45] Since our model relied heavily upon NHSS case report data, our projections might have amplified this bias, yielding projections that over-estimate the future population size of the PLWDH population.

There are several limitations of our modeling approach. We used a static model that might inadequately capture complex processes that could affect the demographic composition of the US PLWDH population. In particular, the base model's assumption that new diagnosis rates and annual mortality rates would remain constant over time might be unrealistic. We compared results from the base model to that of a model that allowed declining diagnosis rates, and found that the results from the two models diverged over time. This sensitivity analysis serves as a reminder that uncertainty tends to grow with each projected year. Indeed, major technological advancements in HIV prevention (e.g. vaccines) and cure could occur in future decades, potentially nullifying the applicability of our projections to the future context of HIV population parameters. The projections made by this model did not account for children and adolescents with HIV, adults who contracted HIV through some other route besides sexual contact and injection drug use, and r people who died the same year they were diagnosed with HIV. However, these groups would comprise a very small proportion of the PLWDH population and would thus have little influence on the composition of the overall PLWDH population.[47]

Although the projections yielded by our demographic model may be imperfect, they are based upon the best data available on the population structures of the US general and PLWDH populations, and thus provide insight into how the demographics of the PLWDH population may change in the future. HIV care and prevention programs in the United States should anticipate the increasing size of the US PLWDH population and its considerable shift in age and racial/ethnic composition. These changing population dynamics should be considered in current decisions about resource allocation, human resource needs, HIV-prevention programs, and design of research studies.

Table 3.1: Estimated Proportion of the US Adults in Each HIV Risk Group

Sub-Group	Percent of General Population	Assumption	Source
Men			
MSM (non-IDU)	3.63%	3.9% of general male population are MSM 93.1% of MSM population is non-IDU [.931 X .039] = .0363	[83]
IDU (non-MSM)	3.22%	3.6% of general male population are IDU 89.5% of male IDU population is non-MSM [.895 X .036] = .0322%	[77, 78]
MSM-IDU	0.27%	6.9% of MSM population are IDU [.069 X .039] = 0.0027	[77]
Heterosexual	84.1%	84.1% of men have had sex, but never had sex with a man or injected drugs.	[79]
Women			
IDU	1.6%	1.6% of female population has history of IDU	[78]
Heterosexual	89.4%	89.4% of women have had sex with a man, but never injected drugs.	[79]

Note: A five-year recall period was used for MSM estimate; report of 'ever' injecting drugs was used for IDU estimate. Percentages do not sum to 100%, because it is assumed that some adults do not engage in any behaviors that pose HIV risk.

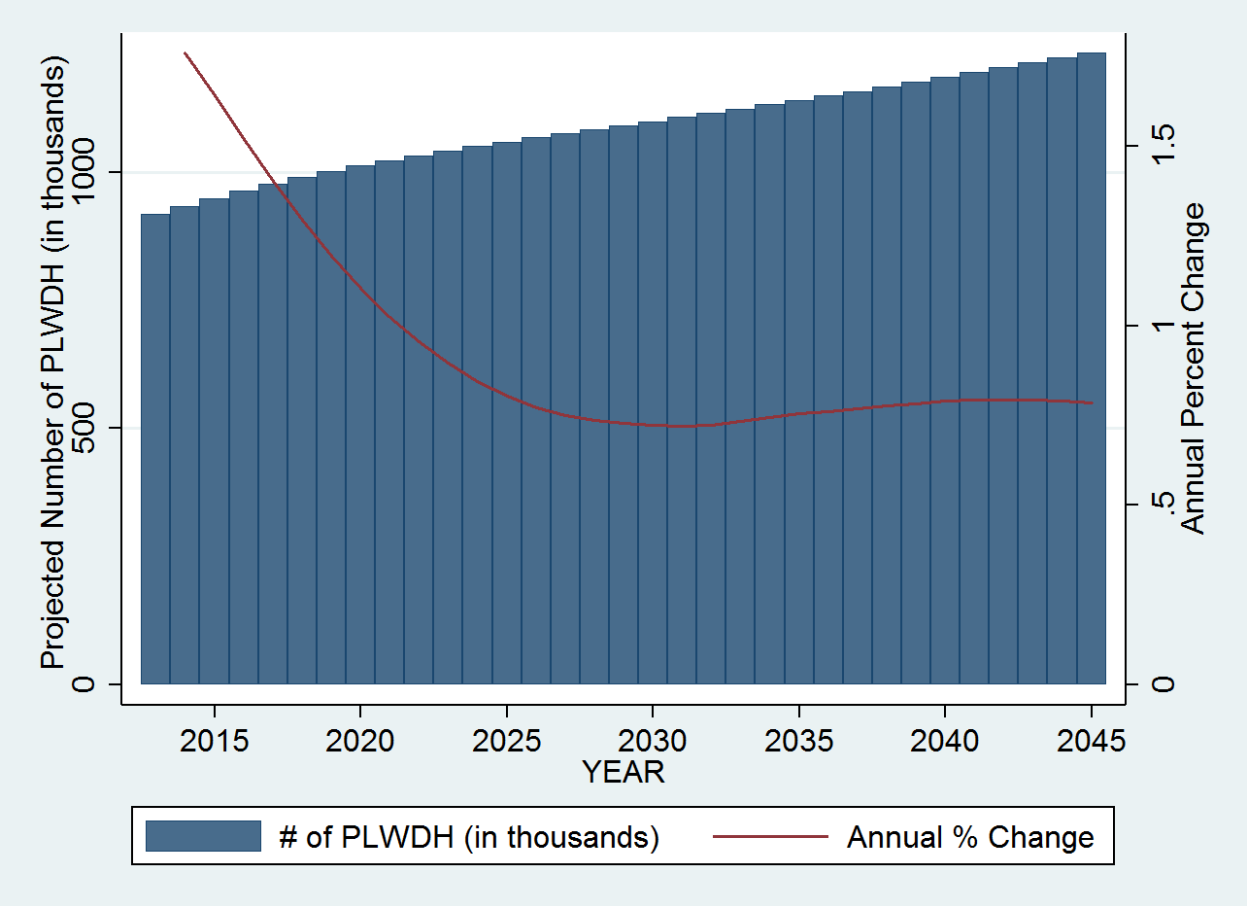


Figure 3.1: Projected Growth of the Population of People Living with Diagnosed HIV in the United States in 2013-2045

Figure 3.2: Current and Projected Population Age Pyramid Corresponding to People Living with Diagnosed HIV in the United States in 2013, 2025, 2035, and 2045.

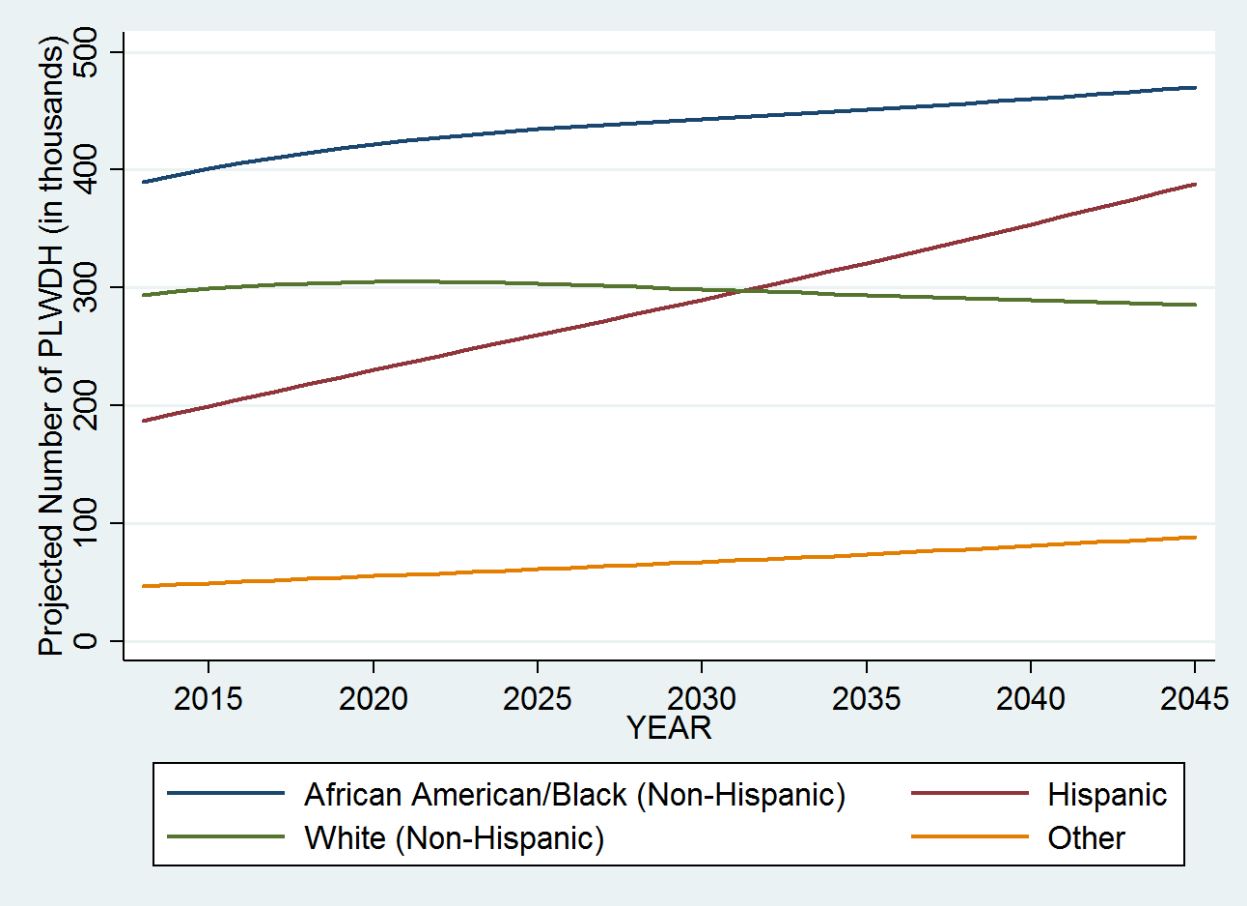


Figure 3.3: Projected Number of People Living with Diagnosed HIV in the United States in 2013-2045, by Race/Ethnicity

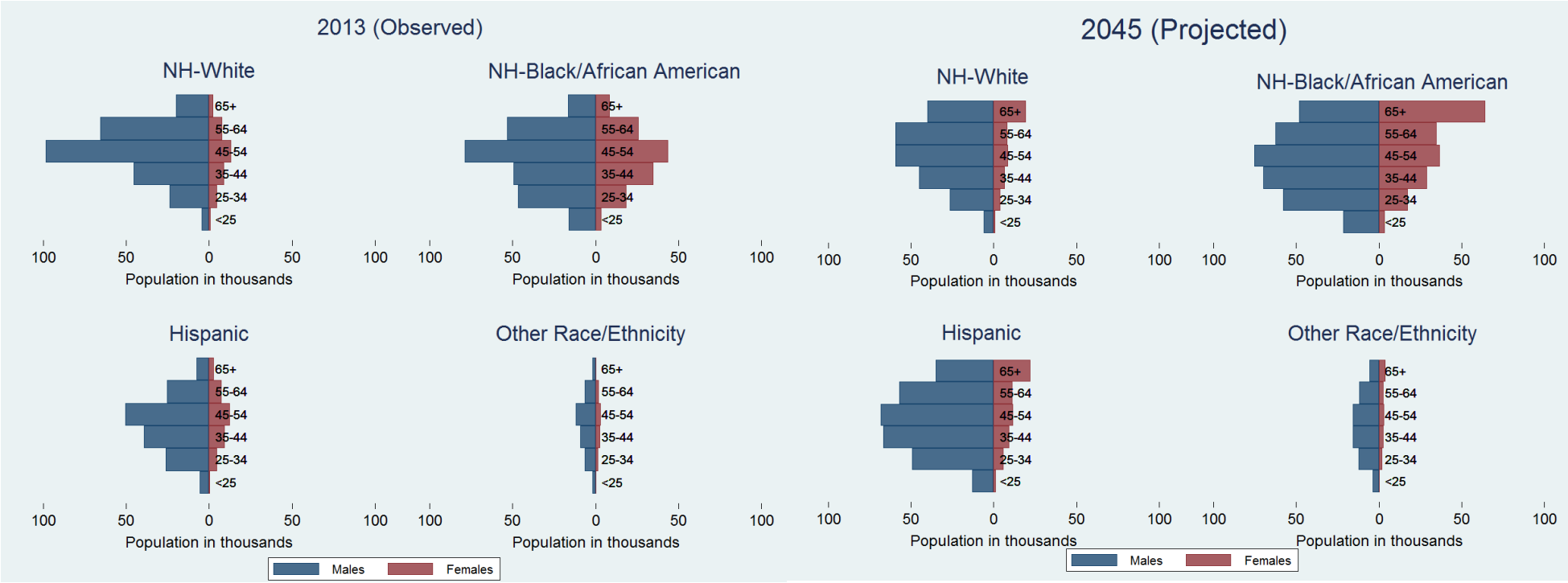


Figure 3.4: Projected Population Pyramids, by Race/Ethnicity, Corresponding to People Living with Diagnosed HIV in the United States in 2013 and 2045.

Abbreviations: NH=Non-Hispanic

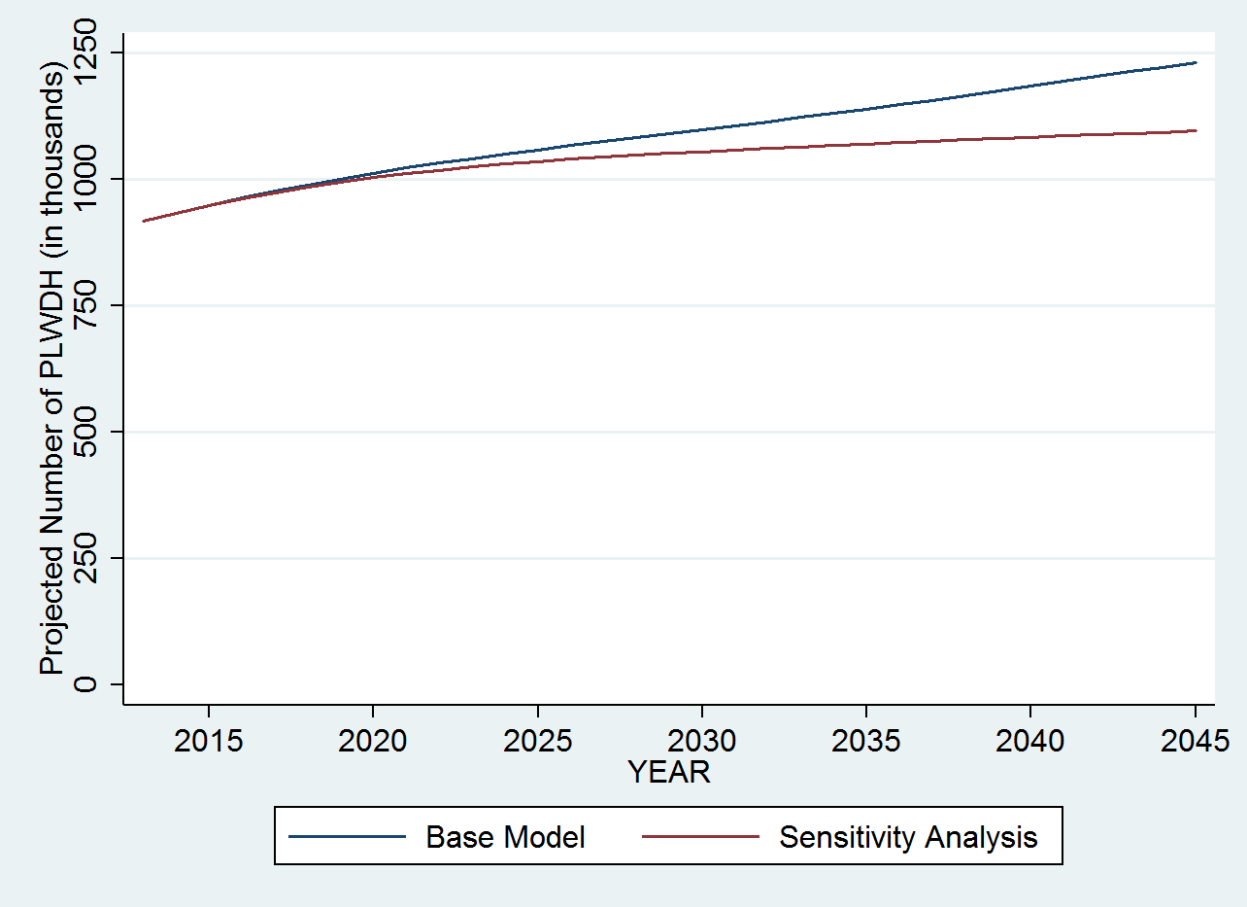
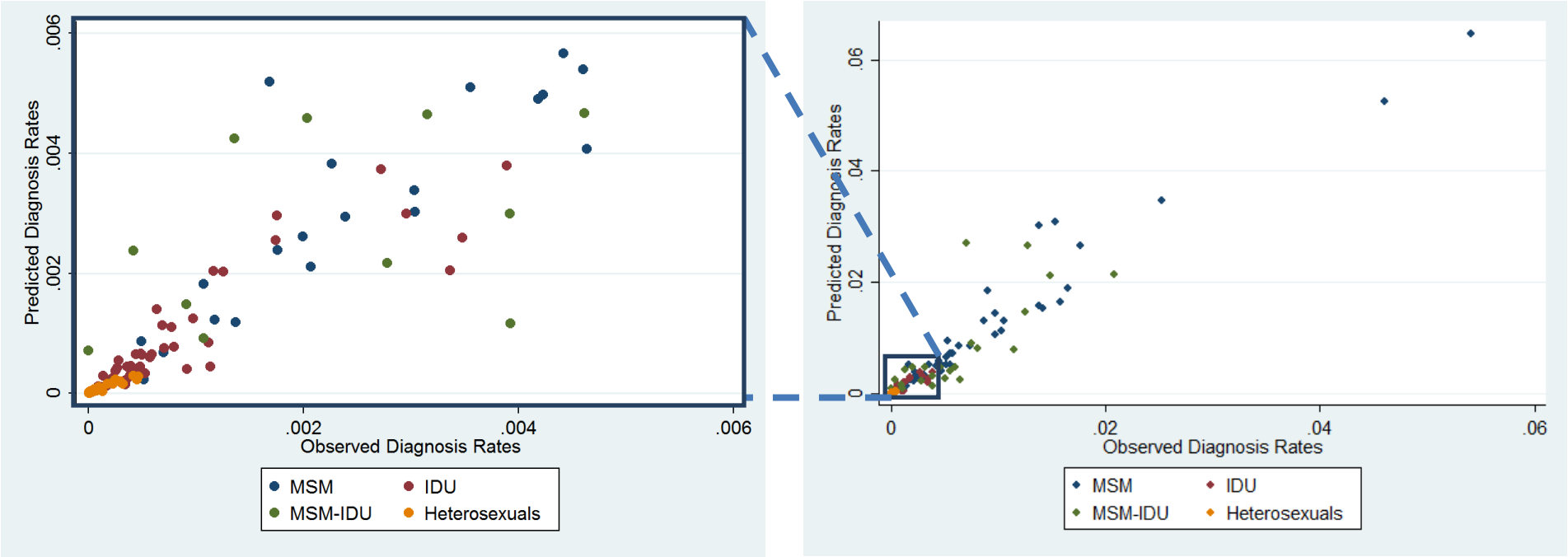


Figure 3.5: Evaluating the Influence of the Assumption of Constant Diagnosis Rates on the Projected Number of People Living with Diagnosed HIV: Comparison of Base Model (in blue) to Model that Allows Diagnosis Rates to Decline* Over Time (in red).

Notes: The model corresponding to the blue line assumed that estimated diagnosis rates in 2013 would remain constant across all projected years; the model corresponding to the red line assumed that the diagnosis rates would decline annually by 1% for MSM and 0.5% for all other risk groups.



Panel A **Panel B**

Supplementary Figure 3.1: Comparison of Diagnosis Rates Observed in 2013 (X-axis) to Diagnosis Rates Estimated through Prediction Models, by Risk Transmission Category.

Note: Panel A and Panel B differ in terms of scale: Panel A presents data corresponding to sub-groups with observed diagnosis rates less than 5 per 1000 people, whereas Panel B presents data for all sub-groups included in the model. Each point represents one of the sub-groups included in the model (e.g. Hispanic MSM ages 15-19).

Supplemental Figure 3.2: Comparison of Annual Mortality Rates among People Living with Diagnosed HIV in 2013 (X-axis) to Mortality Rates Estimated through Prediction Models, by Risk Transmission Category.

Note: Each point represents one of the sub-groups included in the model (e.g. Hispanic MSM ages 15-19). A mortality rate of .06 corresonds to 6 deaths per 100 PLWDH.

Chapter 4: Integration of HIV Surveillance & HIV Control Interventions: Impact on Data Quality and Program Metrics

Abstract

Objectives: The purpose of HIV surveillance in the United States is evolving. We describe Public Health- Seattle & King County's processes for investigating newly reported cases and integrating HIV surveillance and field services, and we evaluate how integration affects data quality and program indicators.

Methods: We analyzed HIV case reports, reported laboratory records, medical records, and partner services databases; estimated program metrics; and assessed the relationship between partner services and timely linkage to care using multivariate Poisson regression models.

Results: In 2010-2015, 2850 people entered the King County surveillance system, of whom 52% were newly diagnosed, 41% had a confirmed prior diagnosis in another state, and 7% had an unconfirmed prior diagnosis. The number of in-migrants increased, while the number of new diagnoses decreased over time ($p<.0001$). Participation in partner services was associated with linking to care within 30 and 90 days of diagnosis ($aRR_{30\ days}=1.11$, 95%CI=1.03-1.19; $aRR_{90\ days}=1.10$, 95%CI=1.05-1.16).

Conclusions: Integration of HIV surveillance, partner services, and linkage to care efforts facilitated the identification of in-migrants with HIV and delivery of a comprehensive outreach package to newly diagnosed cases.

Introduction

The purpose of HIV surveillance in the United States is changing. For almost three decades, state and local health departments in the U.S. have used HIV surveillance data to monitor the growth of the HIV epidemic and define the populations most affected by HIV/AIDS. Scientific evidence demonstrating that effective treatment prevents HIV transmission[39] , that early treatment initiation improves clinical outcomes[84], and that a large number of persons living with HIV are not engaged with care[47] have led to fundamental changes in HIV prevention, with a new emphasis on case-finding and treatment. This emphasis has also changed the role of surveillance as many health departments increasingly rely on surveillance data to direct public health interventions, a strategy the Centers for Disease Control and Prevention (CDC) has called Data-to-Care.[85] In this new paradigm, surveillance data are needed that track specifically which individuals are currently living in-jurisdiction and their current health status, rather than just case numbers and demographic descriptions.

Surveillance data with protected health information (PHI) are collected and managed by local and state health departments, and these departments submit data without names to CDC. CDC then uses non-name identifiers to attempt to de-duplicate cases. However, without a centralized repository of truly identifiable case surveillance data, cross-jurisdictional migration can result in duplicate case reporting.[45] To varying extents, health department HIV programs investigate each case that newly enters their local surveillance system with the goals of 1) determining if a newly reported case is a new diagnosis and to characterize the epidemiologic features of that case; 2) ensuring that newly diagnosed cases successfully link to medical care; and 3) providing partner services, an intervention designed to deliver HIV testing, other prevention services (including

PrEP referrals[86]), and treatment (if needed) to the sex and needle sharing partners of newly diagnosed HIV cases.

In many areas, these three goals are not well integrated. In some instances, separate surveillance, partner services, and linkage to care teams address each goal with minimal coordination or communication. Starting in 2001, the Public Health – Seattle & King County (PHSKC) HIV/STD Program began integrating surveillance and field services with the objective of more efficiently achieving each of the above goals.[87] We have previously described the outcomes of partner services efforts in identifying new cases of HIV infection in King County.[88, 89] Here we describe our approach to managing newly reported cases and evaluate how integrating HIV surveillance with field services affects surveillance data quality and linkage to care and partner services indicators.

Methods

Description of PHSKC's Approach to HIV Surveillance and Outreach Programs

HIV/AIDS reporting requirements in Washington State have evolved over time. Prior to 1999, only AIDS and symptomatic HIV were reportable by name. From 1999 to 2006, new HIV diagnoses were reportable, but Public Health used a confidential code instead of names to identify cases. Since 2006, Washington State law has required that health care providers report all new HIV and AIDS diagnoses by name and that laboratories report tests confirming HIV infection, HIV viral load (detectable and undetectable), and CD4+T-lymphocyte test results of any value by name.[90] While the Washington Administrative Code (WAC) calls for all diagnoses of HIV disease to be reported to local health authorities within 3 working days of diagnosis, the majority of all cases are found initially through receipt of an HIV-indicative laboratory test

result. Most laboratories and healthcare facilities in Washington State submit laboratory data electronically using either a delimited flat file or via the Public Health Reporting of Electronic Data (PHRED) system, which is managed by the Washington State Department of Health (DOH). All data received are formatted for upload into the HIV Laboratory Tracking Database at DOH and matched bimonthly against the Enhanced HIV/AIDS Reporting System (eHARS), a web-based platform that enables HIV surveillance data to be securely entered, stored, managed, and reported to the CDC. Laboratory data that match previously existing cases are retained in the Laboratory Tracking Database with a corresponding identifier and subsequently uploaded into EHARS and linked to existing records corresponding to the case. Laboratory results that do not match a known case are returned to Local Health Jurisdictions (LHJs), such as PHSKC, for follow up investigation based on the geographic location of ordering provider/facility.

The PHSKC field services unit is divided into specialty teams assigned to specific infections and populations. The HIV partner services team, which is also tasked with ensuring that persons with newly diagnosed HIV link to HIV medical care, is one of these, and consists of two Disease Intervention Specialists (DIS) (1.4 fulltime equivalent) and a surveillance coordinator. The DIS with primary responsibility for the team's work is jointly funded using HIV surveillance and partner services grant funding and shares an office with the HIV surveillance coordinator in the PHSKC STD Clinic.

When a potentially new case of HIV is identified, the team initially determines whether the case was previously recorded in Washington State eHARS. If the case does not already exist in eHARS, staff members review the case's medical records to retrieve contact and demographic information, diagnostic and clinical data surrounding their diagnosis, and ascertainment of risk exposure and reasons for testing. PHSKC has an agreement with the majority of the large

healthcare organizations in King County that provides surveillance and field services staff remote access to electronic medical records (EMRs) for case reporting and other disease control efforts. For smaller facilities in the area, PHSKC DIS complete case reporting activities either via telephone conversations with staff or with onsite chart reviews. If in the course of chart review or other investigation activities staff find evidence suggesting that a case moved to Washington after being diagnosed in another state, staff call the surveillance team in the other state to determine the case's earliest HIV diagnosis date and residence at diagnosis, resolve missing or conflicting case data, and discuss likely current residence.

The field services team attempts to contact all persons without evidence of a prior HIV diagnosis and all previously diagnosed cases that are not known to be virally suppressed. DIS only routinely provide partner services to persons with newly diagnosed HIV infection, but seek to ensure linkage to care for all unsuppressed persons with newly reported HIV infection. DIS in King County have not undergone any formal training in linkage to care, nor do they employ a defined behavioral intervention to promote linkage to care. They do not close investigations of persons with newly reported HIV infection until they have confirmed that a case has linked to care or until the DIS, DIS supervisor, and program medical officer determine that additional efforts to promote linkage are futile. We define confirmed linkage based on the presence of a laboratory test result in surveillance that was ordered by an HIV medical provider or medical record review or direct communication with a healthcare facility demonstrating attendance at a visit with an HIV medical provider. Most newly diagnosed cases are invited to participate in the PHSKC One on One program, which allows patients to be seen by a public health medical provider for a clinical assessment, initial laboratory evaluation (CD4 lymphocyte count and HIV

RNA), and counseling, usually within several days of diagnosis.[91] Ensuring that all patients link to care is a central goal of the One on One program.

The HIV program's medical officer, surveillance epidemiologists, field services supervisor, and DIS who provide HIV partner services meet monthly to discuss the status of all newly reported cases, facilitating the exchange of information between field services, surveillance and medical staff, and allowing the team to develop strategies to assist persons with HIV infection thought to be at high risk for treatment failure or HIV transmission and partners who are at high risk for HIV acquisition.

Evaluation Overview

We hypothesize that the integrative processes described above have improved (1) surveillance data quality, specifically in terms of distinguishing newly diagnosed cases from imported cases (e.g. cases that move into jurisdiction after being diagnosed with HIV in another state or country), and (2) linkage to care and partner services metrics. These hypotheses are explored using programmatic and surveillance data.

Data Sources

Several data sources were used in our analyses: eHARS, reported laboratory records, STD Clinic records, EMRs, and partner services databases. The following elements in eHARS were utilized in the analysis: year case entered the King County surveillance system, date of HIV diagnosis (and corresponding facility), date of birth, sex at birth, and risk transmission category. Date of specimen collection on reported laboratory records was assumed to be a marker for an HIV care visit and was used to evaluate linkage to care. STD Clinic records corresponding to the One on One program were used to identify cases who had participated in this program. Since the results

from CD4 and viral load tests ordered for One-on-One are often subsequently shared with HIV treating clinicians who may not immediately repeat the tests, we abstracted date of first care visit (as indicated in EMR) for a subset of One-on-One participants (n=132) who receive care at a facility that permits PHSKC EMR access for surveillance purposes, rather than relying on reported laboratory result to approximate date of care initiation.

PHSKC has used a series of locally developed partner services databases designed to meet programmatic needs. The partner services databases have been used to capture both partner services interview data, as well as investigative notes. In 2014, we started assigning a disposition to each newly reported case indicating whether the case was newly diagnosed or had confirmed or unconfirmed evidence of being diagnosed within or outside the U.S. Prior to 2014, this information was captured less systematically in other fields.

Analysis

Our analysis describes cases that entered the King County surveillance system between 2010 and 2015. For the purposes of national HIV surveillance, cases with evidence of a prior diagnosis that is unconfirmed by another jurisdiction's HIV surveillance program are classified as newly diagnosed. In this analysis, cases with unconfirmed evidence of a prior diagnosis (obtained through self-report or medical record review) are differentiated from cases that appear to be true new diagnoses.

Our analysis has multiple components. First, we illustrate trends in the number of new diagnoses and imported cases between 2010 and 2015 and show how the classification of cases with unconfirmed evidence of a prior diagnosis affects estimated trends. Second, we compare characteristics of cases reported as new diagnoses for the purposes of national HIV surveillance,

cases that were newly diagnosed without any evidence of a prior diagnosis, and cases that had unconfirmed evidence of a prior diagnosis; differences between the two latter groups were assessed with chi-squared tests. All subsequent analyses were restricted to newly diagnosed cases without any evidence of a prior diagnosis. Third, we report the percent of newly diagnosed cases that participated in partner services and One-on-One and other program metrics corresponding to these programs. Finally, we determined the proportion of newly diagnosed King County cases that appeared to link to HIV care, outside the context of a One-on-One session, within 30, 60, 90, and 365 days of diagnosis overall and by receipt of partner services. We used multivariable Poisson regression with robust error variance to assess the relationship between receiving partner services and linking to care within 30 and 90 days of diagnosis, adjusting for year of diagnosis, diagnosing facility type, age at diagnosis, sex at birth, race/ethnicity, nativity status, and risk transmission category. All analyses were performed in Stata 13 (StataCorp, College Station, TX).

Results

Between 2010 and 2015, 2850 people newly entered the King County HIV Surveillance System. Of those persons, 1677 (60%) were classified as new HIV diagnoses for the purposes of national HIV surveillance, 204 (12%) of whom self-reported a prior HIV diagnoses or had information recorded in their medical record indicating that they had previously been diagnosed with HIV. Of cases classified as newly diagnosed for the purposes of national HIV surveillance, 87% were male and 5% non-Hispanic White; 59% were between the ages of 20 and 40 at time of diagnosis; 73% were known to be men who have sex with men (MSM); and 28% were known to have been

born outside the United States (Table 1). The 204 cases that were reported as new diagnoses in 2010-2015 but had evidence of a prior diagnosis were more likely to be female, a racial/ethnic minority, foreign-born, heterosexual, and to have entered the King County Surveillance system in 2014 than cases that did not have evidence of a prior diagnosis.

Figure 1 presents trends in the number of previously reported imported cases and new HIV diagnoses in King County, 2010 to 2015, separating new diagnoses into those reported as new for the purposes of national surveillance (regardless of local evidence of a previous diagnosis) and those that were new diagnoses according to all available data sources, including unconfirmed self-report. The number of new diagnoses declined from 2010 to 2015, concurrent with an increase in the number of imported cases. The percentage of all cases entering the surveillance system that PHSKC reported as being new for the purposes of national surveillance declined from 67% in 2010 to 51% in 2015. The proportion of cases entering the surveillance system that were newly diagnosed without any evidence of a prior diagnosis declined from 59% in 2010 to 45% in 2015.

All subsequent analyses excluded cases with confirmed or unconfirmed evidence of a prior HIV diagnosis. A total of 390 newly diagnosed persons (27%) participated in the One on One program at the STD Clinic, 56% of whom were seen in One on One within one week of the date their blood was obtained for HIV testing. After participating in One-on-One, 89% linked to HIV care within 90 days of their diagnosis. Nearly all (98%) newly diagnosed cases were initiated for partner services, 84% were successfully contacted, and 80% were interviewed. DIS inability to locate the case and the case refusing partner services were the most common reasons for not receiving partner services.

The percentage of newly diagnosed cases that linked to care within 30 days of diagnosis significantly increased between 2010 and 2015 (72% to 90%, p<.0001). A modest increase was observed in the percent linking to care within 90 days of diagnosis (88% to 94%, p=0.213). In unadjusted analyses, the percent that had linked to care within 30 and 90 days of diagnosis was greater among cases that had received partner services versus those that had not (30 days: 80% vs. 76%, RR: 1.05 (95% CI= 0.98, 1.13) p=0.21; 90 days: 92% vs. 86%, RR: 1.09 (95% CI= 1.03, 1.15), p<.0001). Controlling for demographic characteristics and other factors, linkage to care within 30 and 90 days of diagnosis was significantly greater among cases that had received partner services compared to those that had not ($aRR_{30\ days}$,=1.11, 95% CI=1.03-1.19, p=.004; $aRR_{90\ days}$,=1.10, 95% CI=1.04-1.16, p=.001). None of the demographic characteristics were significantly associated with linking to care within 90 days, though cases diagnosed in 2015 were significantly more likely to link to care within 30 and 90 days of diagnosis compared to cases diagnosed in 2010 ($aRR_{30\ days}$,=1.25, 95% CI=1.15-1.36, p<.0001; $aRR_{90\ days}$,=1.07, 95% CI=1.02-1.14, p=.008).

Discussion

Over the course of the last decade, PHSKC has increasingly integrated HIV surveillance investigations with HIV partner services and efforts to promote linkage to HIV medical care. This process has improved HIV surveillance data, and our findings suggest that, along with improvements in national data and surveillance processes, our approach has allowed our health department to better estimate the true number of new HIV diagnoses in our jurisdiction. It has

also allowed us to achieve near universal linkage to HIV care through a process that relies primarily on DIS to coordinate, monitor and assure patients' entry into medical care.

Our findings suggest that integrating surveillance and field services improves HIV surveillance. The growing ratio of in-migrants with prior diagnoses ("imported cases") to new diagnoses in King County likely reflects population growth in King County[92], much of which is a result of in-migration[93], increased ascertainment of in-migration as HIV surveillance staff have increased their focus on this disposition, and improved quality of national surveillance data. While our ratio of imported cases to new diagnoses might be greater than elsewhere, it is plausible that the ratio of imported cases to new diagnoses is increasing throughout the United States. Newly diagnosed HIV cases comprise a small and decreasing percentage of all people living with diagnosed HIV (PLWDH).[8] Assuming that the rate of annual out-of-state migration among PLWDH is fairly constant, the number of prevalent cases that move across state boundaries in a given year is likely increasing and might soon surpass the number of new diagnoses.

The increase in imported cases has implications for health department surveillance data quality and the workload associated with new case investigation. Thorough investigation of each case entering the surveillance system is needed to prevent duplicate case reporting, a data quality issue that is difficult to resolve[94] and threatens the validity of surveillance data[45], and to improve the efficiency of outreach programs designed for people newly diagnosed with HIV. In our experience, strategies that improve a surveillance program's ability to distinguish imported cases from new diagnoses include: dedicated staffing, negotiating electronic access to medical record systems, establishing routine calls with jurisdictions with large PLWDH populations and integrating surveillance with HIV partner services. A separate, related issue is that cases likely to have been diagnosed outside the U.S. before immigrating to the U.S. are classified as new

diagnoses for surveillance purposes. In King County, this led to an almost 12% overestimate of new diagnoses and an overestimate of the proportion of new diagnoses comprised of non-Hispanic Blacks, women, and heterosexuals. Although imported cases of HIV need to be included in surveillance data, efforts to evaluate local transmission patterns and prevention programs would ideally exclude such cases as they are not avertable through local prevention activities.

Our findings highlight the feasibility and value of integrating linkage to care with HIV partner services and public health clinical services. In many areas of the U.S., persons newly diagnosed with HIV must interact with multiple people from different agencies before seeing an HIV medical provider, a trying process that contributes to delays in linkage to care. PHSKC strives to streamline this process. DIS discuss both partner services and linkage to care topics when they meet with newly diagnosed cases, and One on One enables newly diagnosed cases to receive immediate clinical evaluation. These activities occur at the PHSKC STD Clinic, illustrating how such clinics can play a larger role in high impact HIV prevention and can facilitate an integrated approach to management of newly diagnosed cases of HIV. Program metrics, including time to linkage to care, appear to have improved after PHSKC integrated its approach to patient care and HIV control activities (i.e. partner services). The higher level of linkage we observed among partner services recipients is consistent with a prior report from New York City[95] and adds to the evidence that field services can be an effective population-based approach to promoting linkage to care. This approach may complement individual level interventions, like the Antiretroviral Treatment Access Study (ARTAS)[96], and are consistent with ongoing efforts in other parts of the U.S. designed to rapidly initiate antiretroviral therapy among persons with newly diagnosed HIV.[97]

There are limitations to the surveillance data included in these analyses and perhaps to the generalizability of our experience. The observed trends in number of new diagnoses and imported cases might be, to an unknown extent, influenced by changes in surveillance practices. Many analyses relied upon the date of HIV diagnosis, a field in eHARS that might imperfectly align with actual diagnosis date. Similarly, date of first reported CD4 or viral load result may imperfectly align with date of care initiation.[98] For example, incomplete laboratory reporting of CD4 counts and viral loads and care visits without laboratory orders may cause the time from diagnosis to linkage to care to be overestimated. Also, the multivariate model we used to assess the relationship between partner services and linkage might have inadequately controlled for all sources of confounding. Finally, King County has a relatively well funded HIV/STD program and a relatively small number of new HIV cases compared to many other U.S. jurisdictions. Some aspects of our approach may prove difficult to implement in areas with more limited resources or larger epidemics, though DIS responsible for investigating new HIV cases in King County carry relatively large caseloads compared to many jurisdictions with larger epidemics. It should also be noted that despite high levels of linkage to care, 19% of PLWDH in King County are not suppressed, highlighting the need to address each step on the HIV care continuum.

In summary, we found that integrating surveillance and field staff into a team responsible for investigating new cases of HIV, providing partner services and ensuring PLWDH link to care was feasible. This approach allowed us to integrate new data elements into case investigations that are relevant to understanding our local epidemic (i.e. prior HIV diagnosis, nativity and timing of immigration), and resulted in near universal linkage to HIV care. Our system of integration also included an important role for our STD clinic as a site for rapid evaluation of persons with newly diagnosed HIV infection, further illustrating the benefits of deploying an

interdisciplinary team that utilizes diverse public health resources to efficiently respond to new HIV cases. CDC is now encouraging state and local public health HIV/STD programs to better integrate their surveillance and prevention activities. Our experience supports this direction and may be a model for some other jurisdictions.

Table 4.1: Characteristics of Newly Diagnosed Cases Reported in King County, 2010-15

		Of Reported New Diagnoses:		
	Reported New Diagnosis (n=1677) # (%)	No Evidence of Prior Diagnosis (n=1473) # (%)	Had Evidence of Prior Diagnosis (n=204) # (%)	p-value
Sex at Birth				
Male	1454 (87)	1310 (90)	144 (71)	<.0001
Female	223 (13)	163 (11)	60 (29)	
Age at HIV diagnosis				
13-19	36 (2)	31 (2)	5 (3)	0.172
20-29	474 (28)	430 (29)	44 (22)	
30-39	523 (31)	456 (31)	67 (33)	
40-49	382 (23)	331 (23)	51 (25)	
50-59	201 (12)	176 (12)	25 (12)	
60+	61 (4)	49 (3)	12 (6)	
Race/Ethnicity				
White	915 (55)	859 (58)	56 (28)	<.0001
Black	333 (20)	241 (16)	92 (45)	
Hispanic	238 (14)	219 (15)	19 (9)	
Asian	123 (7)	88 (6)	35 (17)	
Am. Indian/Alaskan Native	12 (0.7)	12 (0.8)	0 (0.0)	
Pacific Islander	13 (0.8)	12 (0.8)	1 (0.5)	
Multi-Racial	43 (3.0)	42 (3)	1 (0.5)	
Nativity				
US born	1097 (65)	1033 (70)	64 (31)	<.0001
Foreign born	471 (28)	338 (23)	133 (65)	
Unknown	109 (7)	102 (7)	7 (3)	
Risk Transmission Category				
MSM	1102 (66)	1023 (70)	79 (39)	<.0001
IDU	57 (3)	51 (4)	6 (3)	
MSM- IDU	118 (7)	112 (8)	6 (2.9)	
Heterosexual	251 (15)	175 (12)	76 (37)	
Other	6 (0.4)	2 (0.1)	4 (2)	
Not Reported	143 (9)	110 (8)	33 (16)	
Year of Diagnosis				
≤2009^	70 (4)	39 (3)	31 (15)	
2010	320 (19)	293 (20)	27 (13)	<.0001
2011	269 (16)	248 (17)	21 (10)	
2012	281 (17)	256 (17)	25 (12)	
2013	247 (15)	218 (15)	29 (14)	
2014	270 (16)	222 (15)	48 (24)	
2015	220 (13)	197 (13)	23 (11)	
Diagnosing Facility*				
Outpatient clinic	696 (42)	625 (42)	71 (35)	<.0001
PHSKC STD Clinic	351 (21)	336 (23)	15 (7)	
HIV/MSM Specialty Clinic†	300 (18)	209 (14)	91 (45)	
Inpatient	140 (8)	127 (9)	13 (6)	
HIV Community Based Org.	102 (6)	102 (7)	0 (0)	
ED/Urgent Care	56 (3)	50 (3)	6 (3)	
Other	32 (2)	24 (2)	8 (4)	

^Cases diagnosed in 2009 were included in the analysis if they entered the KC surveillance system in 2010.

*As indicated in eHARS

†Refers to clinics that provide HIV care, including the Harborview Madison Clinic, as well as private practices that are known to explicitly serve the LGBT community.

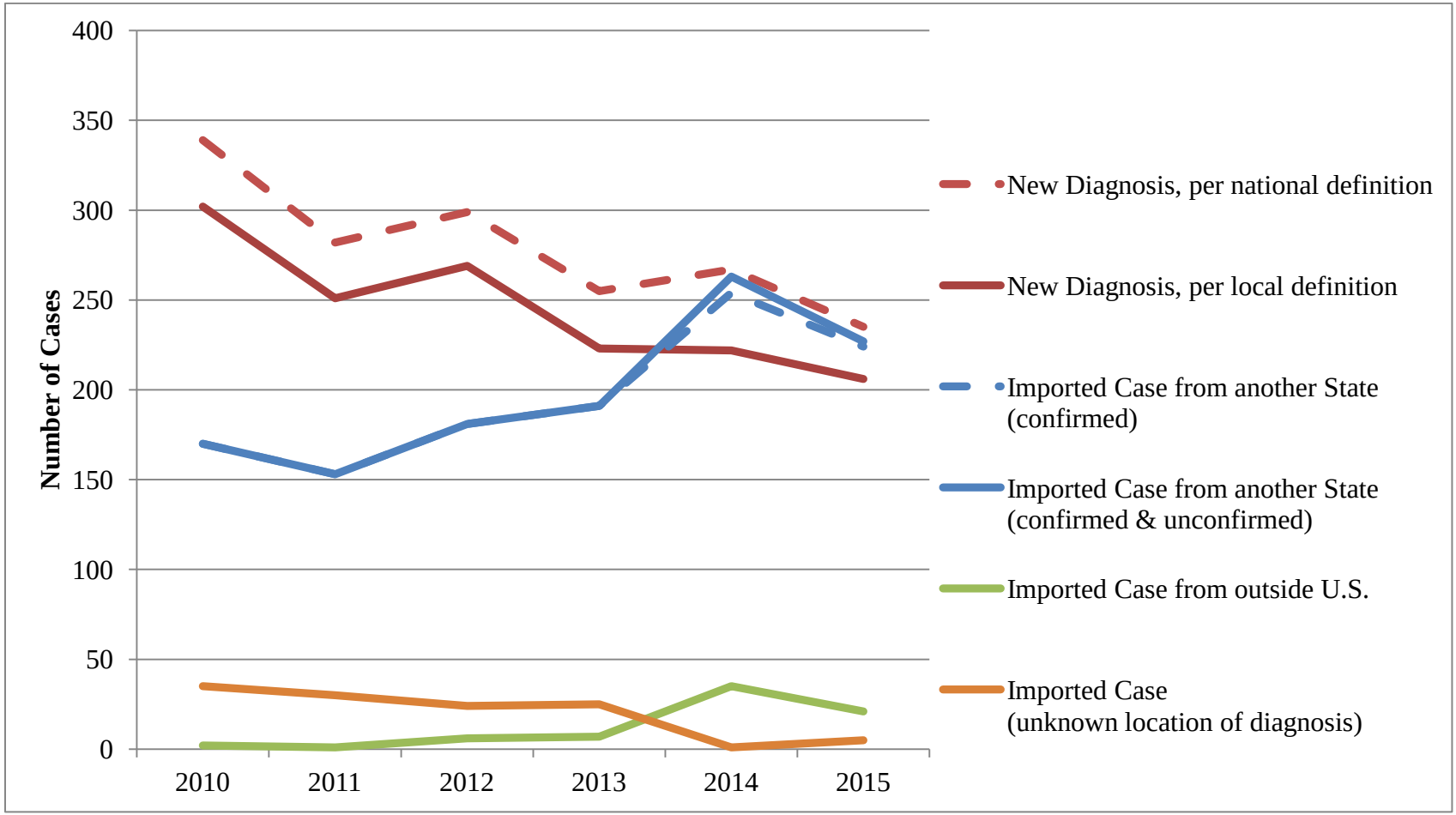


Figure 4.1: Number of Cases Newly Entering King County HIV Surveillance System, by Jurisdiction at Diagnosis
The dashed lines represent what PHSKC reported to CDC. The solid lines represent PHSKC's classification of cases per locally available data. Information about prior diagnoses was more systematically collected after 2013.

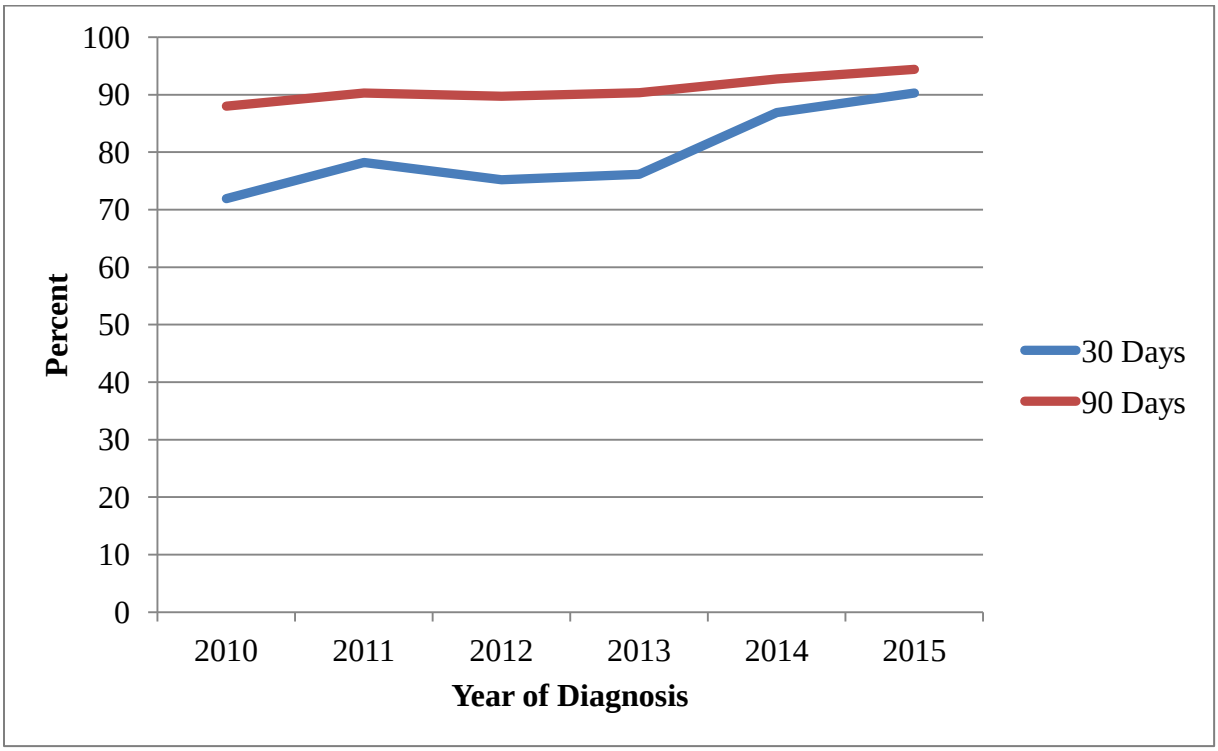


Figure 4.2: Time between Diagnosis and Linkage to Care among 1429 HIV Cases Diagnosed between 2010 and 2015 in King County, Washington
Excludes cases with evidence of a prior diagnosis (n=204), cases diagnosed in correctional settings (n=5), and cases diagnosed in 2009 that entered the King County surveillance system in 2010 (n=70).

Table 4.2: Time from Diagnosis to Linkage to HIV Care, Overall and by Partner Services Status, among 1468 People Newly Diagnosed with HIV in King County, 2010-2015[#]

	Percent Linked to Care within:				Linked to care within:	
	30 Days	60 Days	90 Days	365 Days	30 Days aRR^ (95% CI)	90 Days aRR^ (95% CI)
All New Cases	79.0	87.7[+]	90.8‡	96.1‡		
Received Partner Services	79.7	88.7	92.2	97.5	1.11 (1.03, 1.19)*	1.10 (1.04, 1.16)‡
No Partner Services received	76.4	83.8	85.5	90.5	1.00	1.00

[#] Excludes 209 cases that had evidence of an unconfirmed prior diagnosis (n=204) or were diagnosed in a correctional setting (n=5)

[+]p≤.05, *p≤.01, †p≤.001, ‡ p≤.0001

^Adjusted for age, sex, race/ethnicity, nativity, diagnosis year, risk transmission category, and facility type.

Chapter 5: Conclusion

This dissertation utilized data from a number of different sources to describe the current burden of co-morbidities among PLWDH, project the future demographic composition of the US PLWDH population, and to evaluate how programmatic integration influences surveillance data quality and program metrics. Evaluating surveillance data, identifying its limitations, and developing analytic strategies to addressing identified limitations were key goals of each aim. The description of this process was intentionally detailed in order to inform others who evaluate HIV surveillance data at the local, state, and federal U.S. government levels.

MMP and CNICS, despite the considerable differences in their design, yielded generally similar estimates of the prevalence of diabetes, chronic kidney disease, and hypertension after the definition and statistical evaluation of these conditions were reconciled between the two data sources. Both data systems suggest a considerable burden of diabetes, hypertension, and chronic disease among older adults with HIV. This analysis demonstrated the sensitivity of the disease prevalence estimates to (1) case definitions, (2) assignment of disease status for people without complete documentation corresponding to case definitions, and (3) the underlying demographics of the study population.

The demographic model illustrated that the demographic composition of the U.S. PLWDH population will continue to grow in size and will be increasingly comprised of ethnic minorities. The model forecasts that the number of older PLWDH will increase while their proportion relative to other age groups will stabilize by 2025.

Findings from these first two aims have considerable implications for HIV programs and planning. The demands of the HIV care population will grow in the future, both in terms of the number of patients needing services and the nature of the services and care needed. While observational data, like NHSS, MMP, and CNICS, allow for the demographic and health status of PLWH to be routinely monitored, determining how best to incorporate the interconnected issues of aging, co-morbidity, racial/ethnic health disparities, population growth into HIV health service planning needs to be informed by rigorous study. Additional research is needed on how antiretroviral therapies (ART) interact with the numerous drugs that treat common chronic diseases; how the various ART regimens might differentially impact chronic conditions; what strategies to managing multi-morbidity will be feasible for patients to consistently adopt; the degree to which PLWDH are adherent to clinical recommendations pertaining to chronic disease management; and how all of the above might differ by patient characteristics.

The analysis of King County surveillance data was motivated by concerns that the validity of the results from the demographic model might be threatened by duplicate case reporting. We used local surveillance data to illustrate how program integration can improve data quality - and vice versa - how surveillance data can be used to improve program metrics. Our thorough description of PHSKC's approach to investigating newly reported cases of HIV and the collaboration between the HIV surveillance, field services, and clinical services teams might serve as a model for other HIV control programs looking for strategies to improve program integration. Our analysis revealed that more than half of cases new to the King County HIV surveillance system were in-migrants (as opposed to new diagnoses), and the ratio of in-migrants to newly diagnosed cases is increasing over time. This trend is unlikely unique to King County, as the number of PLWDH migrating across state boundaries each year is likely growing concurrently with the

growth of the US PLWDH population. In addition to underscoring the importance of case investigations as a means to prevent duplicate case reporting, this conclusion raises an important question of whether the current surveillance system, at least as it's currently designed, is capable of effectively addressing the growing number of migrants with HIV.

In conclusion, the systems in place to monitor the characteristics and health status of the U.S. PLWDH population are complex and may need to be adapted in light of the projected growth of the PLWDH population. Existing data suggest that chronic disease is currently prevalent among PLWDH, though more research is need to inform how best to manage patients affected by HIV and other chronic conditions. Given current population parameters, the PLWDH population is projected to grow more disproportionately comprised of racial/ethnic minorities. Structural interventions are needed to address health disparities and promote care engagement among all PLWDH.

Bibliography

1. Pneumocystis pneumonia--Los Angeles. *MMWR Morb Mortal Wkly Rep.* Jun 5 1981;30(21):250-252.

2. Epidemiology of HIV/AIDS--United States, 1981-2005. *MMWR Morb Mortal Wkly Rep.* Jun 2 2006;55(21):589-592.

3. James JS. Saquinavir (Invirase): first protease inhibitor approved--reimbursement, information hotline numbers. *AIDS Treat News.* Dec 22 1995(no 237):1-2.

4. CDC. Slide Set: HIV Mortality (through 2010). http://www.cdc.gov/hiv/pdf/statistics_surveillance_HIV_mortality.pdf. Accessed [June 1, 2014.

5. Nakagawa F, May M, Phillips A. Life expectancy living with HIV: recent estimates and future implications. *Curr Opin Infect Dis.* Feb 2013;26(1):17-25.

6. Life expectancy of individuals on combination antiretroviral therapy in high-income countries: a collaborative analysis of 14 cohort studies. *Lancet.* Jul 26 2008;372(9635):293-299.

7. Centers for Disease Control and Prevention. HIV Surveillance Report, 2014; vol. 26. http://www.cdc.gov/hiv/library/reports/surveillance/. Published November 2015. Accessed 24JULY2016.

8. CDC. NCHHSTP Atlas. http://www.cdc.gov/nchhstp/atlas/. Accessed 24JULY2016.

9. Avelino-Silva VI, Ho YL, Avelino-Silva TJ, Santos Sde S. Aging and HIV infection. *Ageing Res Rev.* Jan 2011;10(1):163-172.

10. Bakanda C, Birungi J, Mwesigwa R, et al. Association of aging and survival in a large HIV-infected cohort on antiretroviral therapy. *AIDS.* Mar 13 2011;25(5):701-705.

11. Ball SC. Increased longevity in HIV: caring for older HIV-infected adults. *Care Manag J.* 2014;15(2):76-82.

12. Cahill S, Valadez R. Growing older with HIV/AIDS: new public health challenges. *Am J Public Health.* Mar 2013;103(3):e7-e15.

13. Cardoso SW, Torres TS, Santini-Oliveira M, Marins LM, Veloso VG, Grinsztejn B. Aging with HIV: a practical review. *Braz J Infect Dis.* Jul-Aug 2013;17(4):464-479.

14. Chambers LA, Wilson MG, Rueda S, et al. Evidence Informing the Intersection of HIV, Aging and Health: A Scoping Review. *AIDS Behav.* Nov 2 2013.

15. Effros RB, Fletcher CV, Gebo K, et al. Aging and infectious diseases: workshop on HIV infection and aging: what is known and future research directions. *Clin Infect Dis.* Aug 15 2008;47(4):542-553.

16. Ghidei L, Simone MJ, Salow MJ, et al. Aging, antiretrovirals, and adherence: a meta analysis of adherence among older HIV-infected individuals. *Drugs Aging.* Oct 2013;30(10):809-819.

17. Mills EJ, Barnighausen T, Negin J. HIV and aging--preparing for the challenges ahead. *N Engl J Med.* Apr 5 2012;366(14):1270-1273.

18. Shah S, Mildvan D. HIV and aging. *Curr Infect Dis Rep.* May 2006;8(3):241-247.

19. Guaraldi G, Zona S, Menozzi M, et al. Cost of noninfectious comorbidities in patients with HIV. *Clinicoecon Outcomes Res.* 2013;5:481-488.

20. Edelman EJ, Gordon KS, Glover J, McNicholl IR, Fiellin DA, Justice AC. The next therapeutic challenge in HIV: polypharmacy. *Drugs Aging.* Aug 2013;30(8):613-628.

21. Greene M, Justice AC, Lampiris HW, Valcour V. Management of human immunodeficiency virus infection in advanced age. *JAMA.* Apr 3 2013;309(13):1397-1405.

22. Justice AC, Braithwaite RS. Lessons learned from the first wave of aging with HIV. *AIDS.* Jul 31 2012;26 Suppl 1:S11-18.

23. Nachega JB, Hsu AJ, Uthman OA, Spinewine A, Pham PA. Antiretroviral therapy adherence and drug-drug interactions in the aging HIV population. *AIDS.* Jul 31 2012;26 Suppl 1:S39-53.

24. Justice AC ea. Overview of Ageing: How Can We Optimize Care in the Context of Multimorbidity? Paper presented at: The Royal Society of Medicine HIV Conference. 2011.

25. Kim DJ, Westfall AO, Chamot E, et al. Multimorbidity patterns in HIV-infected patients: the role of obesity in chronic disease clustering. *J Acquir Immune Defic Syndr.* Dec 15 2012;61(5):600-605.

26. Salter ML, Lau B, Go VF, Mehta SH, Kirk GD. HIV infection, immune suppression, and uncontrolled viremia are associated with increased multimorbidity among aging injection drug users. *Clin Infect Dis.* Dec 2011;53(12):1256-1264.

27. Schafer I, von Leitner EC, Schon G, et al. Multimorbidity patterns in the elderly: a new approach of disease clustering identifies complex interrelations between chronic conditions. *PLoS One.* 2010;5(12):e15941.

28. Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. *Lancet.* Jul 7 2007;370(9581):59-67.

29. Rasmussen LD, May MT, Kronborg G, et al. Time trends for risk of severe age-related diseases in individuals with and without HIV infection in Denmark: a nationwide population-based cohort study. *The lancet. HIV.* Jul 2015;2(7):e288-298.

30. Triant VA, Lee H, Hadigan C, Grinspoon SK. Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. *J Clin Endocrinol Metab.* Jul 2007;92(7):2506-2512.

31. Freiberg MS, Chang CC, Kuller LH, et al. HIV infection and the risk of acute myocardial infarction. *JAMA Intern Med.* Apr 22 2013;173(8):614-622.

32. Womack JA, Chang CC, So-Armah KA, et al. HIV Infection and Cardiovascular Disease in Women. *J Am Heart Assoc.* 2014;3(5).

33. Lang S, Mary-Krause M, Cotte L, et al. Increased risk of myocardial infarction in HIV-infected patients in France, relative to the general population. *AIDS.* May 15 2010;24(8):1228-1230.

34. Abraham AG, Althoff KN, Jing Y, et al. End-stage renal disease among HIV-infected adults in North America. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America.* Mar 15 2015;60(6):941-949.

35. Guaraldi G, Orlando G, Zona S, et al. Premature age-related comorbidities among HIV-infected persons compared with the general population. *Clin Infect Dis.* Dec 2011;53(11):1120-1126.

36. Goulet JL, Fultz SL, Rimland D, et al. Aging and infectious diseases: do patterns of comorbidity vary by HIV status, age, and HIV severity? *Clin Infect Dis.* Dec 15 2007;45(12):1593-1601.

37. Samaras K. Prevalence and pathogenesis of diabetes mellitus in HIV-1 infection treated with combined antiretroviral therapy. *J Acquir Immune Defic Syndr.* Apr 15 2009;50(5):499-505.

38. Monroe AK, Glesby MJ, Brown TT. Diagnosing and managing diabetes in HIV-infected patients: current concepts. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America.* Feb 1 2015;60(3):453-462.

39. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med.* Aug 11 2011;365(6):493-505.

40. Cohen MS, McCauley M, Gamble TR. HIV treatment as prevention and HPTN 052. *Curr Opin HIV AIDS.* Mar 2012;7(2):99-105.

41. Gardner EM, McLees MP, Steiner JF, Del Rio C, Burman WJ. The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. *Clin Infect Dis.* Mar 15 2011;52(6):793-800.

42. CDC. Surveillance Overview. 2015; http://www.cdc.gov/hiv/statistics/surveillance/. Accessed 20SEPT2016.

43. Buskin SE, Kent JB, Dombrowski JC, Golden MR. Migration distorts surveillance estimates of engagement in care: results of public health investigations of persons who appear to be out of HIV care. *Sex Transm Dis.* Jan 2014;41(1):35-40.

44. Lesko CR, Sampson LA, Miller WC, et al. Measuring the HIV Care Continuum Using Public Health Surveillance Data in the United States. *J Acquir Immune Defic Syndr.* Dec 15 2015;70(5):489-494.

45. Xia Q, Braunstein SL, Wiewel EW, Eavey JJ, Shepard CW, Torian LV. Persons Living With HIV in the United States: Fewer Than We Thought. *J Acquir Immune Defic Syndr.* Aug 15 2016;72(5):552-557.

46. Xia Q, Kersanske LS, Wiewel EW, Braunstein SL, Shepard CW, Torian LV. Proportions of patients with HIV retained in care and virally suppressed in New York City and the United States: higher than we thought. *J Acquir Immune Defic Syndr.* Mar 1 2015;68(3):351-358.

47. Bradley H, Hall HI, Wolitski RJ, et al. Vital Signs: HIV diagnosis, care, and treatment among persons living with HIV--United States, 2011. *MMWR Morb Mortal Wkly Rep.* Nov 28 2014;63(47):1113-1117.

48. CDC. State Laboratory Reporting Laws: Viral Load and CD4 Requirements. 2015; http://www.cdc.gov/hiv/policies/law/states/reporting.html. Accessed 20SEPT2016.

49. Althoff KN, Buchacz K, Hall HI, et al. U.S. trends in antiretroviral therapy use, HIV RNA plasma viral loads, and CD4 T-lymphocyte cell counts among HIV-infected persons, 2000 to 2008. *Ann Intern Med.* Sep 4 2012;157(5):325-335.

50. Bradley H MC, Beer L, Huang H, Shouse L., CROI. Increased HIV Viral Suppression among US Adults Receiving Medical Care, 2009-2013. Paper presented at: CROI2016; Boston.

51. Raymond A, Hill A, Pozniak A. Large disparities in HIV treatment cascades between eight European and high-income countries - analysis of break points. *Journal of the International AIDS Society.* 2014;17(4 Suppl 3):19507.

52. Gilden DE, Kubisiak JM, Gilden DM. Managing Medicare's HIV caseload in the era of suppressive therapy. *Am J Public Health.* Jun 2007;97(6):1053-1059.

53. Buchacz K, Baker RK, Palella FJ, Jr., et al. Disparities in prevalence of key chronic diseases by gender and race/ethnicity among antiretroviral-treated HIV-infected adults in the US. *Antivir Ther.* 2013;18(1):65-75.

54. *IOM (Institute of Medicine). 2012. Monitoring HIV Care in the United States: Indicators and Data Systems. Washington, DC: The National Academies Press.*

55. MMP. MMP Bibliography as of January 10, 2014. http://www.cdc.gov/hiv/pdf/research_mmp_bibliography.pdf. Accessed 7Dec2014.

56. CNICS. Ongoing Projects. http://www.uab.edu/cnics/ongoing-projects. Accessed 7Dec2014.

57. Watkins CC, Treisman GJ. Neuropsychiatric complications of aging with HIV. *J Neurovirol.* Aug 2012;18(4):277-290.

58. Kitahata MM, Rodriguez B, Haubrich R, et al. Cohort profile: the Centers for AIDS Research Network of Integrated Clinical Systems. *Int J Epidemiol.* Oct 2008;37(5):948-955.

59. RubinD.B. *Multiple Imputation for Nonresponse in Surveys.* . New York: John Wiley & Sons; 1987.

60. Schoffelen AF, Smit C, van Lelyveld SF, et al. Diminished impact of ethnicity as a risk factor for chronic kidney disease in the current HIV treatment era. *The Journal of infectious diseases.* Jul 15 2015;212(2):264-274.

61. Willig AL, Westfall AO, Overton ET, et al. Obesity is associated with race/sex disparities in diabetes and hypertension prevalence, but not cardiovascular disease, among HIV-infected adults. *AIDS research and human retroviruses.* Sep 2015;31(9):898-904.

62. Mocroft A, Lundgren JD, Ross M, et al. Development and validation of a risk score for chronic kidney disease in HIV infection using prospective cohort data from the D:A:D study. *PLoS medicine.* Mar 2015;12(3):e1001809.

63. Justice AC. Overview of ageing: how can we optimize care in the context of multimorbidity? R Soc Med 2012 Nov; 120-127.

64. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med.* May 5 2009;150(9):604-612.

65. Centers for Disease Control and Prevention. HIV Surveillance Report, 2011; vol. 23.

http://www.cdc.gov/hiv/topics/surveillance/resources/reports/. Published February 2013. .

66. Centers for Disease Control and Prevention. HIV/AIDS Surveillance Report, 2005. Vol. 17. Rev ed. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; 2007]. Available at: http://www.cdc.gov/hiv/topics/surveillance/resources/reports/.

67. Centers for Disease Control and Prevention. HIV Surveillance Report, 2009; vol. 21. http://www.cdc.gov/hiv/topics/surveillance/resources/reports/. Published February 2011. .

68. CDC. HIV Surveillance Report, vol. 25, 2013. Available at: http://www.cdc.gov/hiv/topics/surveillance/resources/reports/.

69. Shah M, Risher K, Berry SA, Dowdy DW. The Epidemiologic and Economic Impact of Improving HIV Testing, Linkage, and Retention in Care in the United States. *Clin Infect Dis.* Jan 15 2016;62(2):220-229.

70. Shah M, Perry A, Risher K, et al. Effect of the US National HIV/AIDS Strategy targets for improved HIV care engagement: a modelling study. *Lancet HIV.* Mar 2016;3(3):e140-146.

71. Hall HI, Green TA, Wolitski RJ, et al. Estimated future HIV prevalence, incidence, and potential infections averted in the United States: a multiple scenario analysis. *J Acquir Immune Defic Syndr.* Oct 2010;55(2):271-276.

72. Chen M, Rhodes PH, Hall IH, Kilmarx PH, Branson BM, Valleroy LA. Prevalence of undiagnosed HIV infection among persons aged >/=13 years--National HIV Surveillance System, United States, 2005-2008. *MMWR Morb Mortal Wkly Rep.* Jun 15 2012;61 Suppl:57-64.

73. CentersforDiseaseControlandPrevention. HIV Surveillance Report, 2011; vol. 23. 2013; http://www.cdc.gov/hiv/topics/surveillance/resources/reports/. Accessed [Accessed on 2/25/2014.

74. US Census Bureau. Projected Population by Single Year of Age, Sex, Race, and Hispanic Origin for the United States: 2012 to 2060. https://www.census.gov/population/projections/data/national/2012/downloadablefiles.html.

75. Harrison KM, Kajese T, Hall HI, Song R. Risk factor redistribution of the national HIV/AIDS surveillance data: an alternative approach. *Public Health Rep.* Sep-Oct 2008;123(5):618-627.

76. Purcell DW, Johnson CH, Lansky A, et al. Estimating the population size of men who have sex with men in the United States to obtain HIV and syphilis rates. *Open AIDS J.* 2012;6:98-107.

77. Estimated percentages and characteristics of men who have sex with men and use injection drugs--United States, 1999-2011. *MMWR Morb Mortal Wkly Rep.* Sep 20 2013;62(37):757-762.

78. Amy Lansky TF, Christopher Johnson, Deborah Holtzman, Cyprian Wejnert, Andrew Mitsch, Deborah Gust, Robert T. Chen, Yuko Mizuno, Nicole Crepaz. Estimating the Number of Injection Drug Users in the United States to Calculate National Rates of HIV Infection. Paper presented at: 2012 National Summit on HIV and Viral Hepatitis Diagnosis, Prevention, and Access to Care.2012; Washington DC.

79. Lansky A, Johnson C, Oraka E, et al. Estimating the Number of Heterosexual Persons in the United States to Calculate National Rates of HIV Infection. *PloS one.* 2015;10(7):e0133543.

80. United States Census Bureau (2012). 2012 National Population Projections.

http://www.census.gov/population/projections/data/national/2012.html. Accessed 24JULY2016.

81. Lansky A, Finlayson T, Johnson C, et al. Estimating the number of persons who inject drugs in the united states by meta-analysis to calculate national rates of HIV and hepatitis C virus infections. *PLoS One.* 2014;9(5):e97596.

82. Tempalski B, Pouget ER, Cleland CM, et al. Trends in the population prevalence of people who inject drugs in US metropolitan areas 1992-2007. *PLoS One.* 2013;8(6):e64789.

83. !!! INVALID CITATION !!!

84. Lundgren JD, Babiker AG, Gordin F, et al. Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection. *N Engl J Med.* Aug 27 2015;373(9):795-807.

85. Frieden TR, Foti KE, Mermin J. Applying Public Health Principles to the HIV Epidemic--How Are We Doing? *N Engl J Med.* Dec 3 2015;373(23):2281-2287.

86. Chan G, Katz D, Golden M, Dombrowski J (2015).Utilizing STD Partner Services to Target High-Risk Men Who Have Sex with Men for Pre-Exposure Prophylaxis Referral: Programmatic Experience in King County, Washington. National HIV Prevention Conference, Atlanta, GA.

87. Golden MR, Hopkins SG, Morris M, Holmes KK, Handsfield HH. Support among persons infected with HIV for routine health department contact for HIV partner notification. *J Acquir Immune Defic Syndr.* Feb 1 2003;32(2):196-202.

88. Golden MR, Stekler J, Kent JB, Hughes JP, Wood RW. An evaluation of HIV partner counseling and referral services using new disposition codes. *Sex Transm Dis.* Feb 2009;36(2):95-101.

89. Katz DA, Dombrowski JC, Kerani RP, et al. Integrating HIV Testing as an Outcome of STD Partner Services for Men Who Have Sex with Men. *AIDS Patient Care STDS.* May 2016;30(5):208-214.

90. PHSKC. Summary of Washington State HIV/AIDS Reporting Requirements and Regulations. 2014; http://www.kingcounty.gov/healthservices/health/communicable/hiv/epi/legal.aspx. Accessed 28AUG2016.

91. PHSKC. One on One: Health services for people newly diagnosed with HIV. 2013; http://www.kingcounty.gov/healthservices/health/communicable/hiv/resources/OneOnOne.aspx. Accessed 30OCT2016.

92. KingCounty. King County experiences strong population growth according to 2010 census results. 2011; http://www.kingcounty.gov/elected/executive/constantine/News/release/2011/February/24Census.aspx. Accessed 30AUG2016.

93. State of Washington: 2015 Population Trends. In: Forecasting&ResearchDivision-OfficeofFinancialManagement, ed2015.

94. Ocampo JM, Smart JC, Allston A, et al. Improving HIV Surveillance Data for Public Health Action in Washington, DC: A Novel Multiorganizational Data-Sharing Method. *JMIR Public Health Surveill.* Jan-Jun 2016;2(1):e3.

95. Bocour A, Renaud TC, Udeagu CC, Shepard CW. HIV partner services are associated with timely linkage to HIV medical care. *AIDS.* Nov 28 2013;27(18):2961-2963.

96. Gardner LI, Metsch LR, Anderson-Mahoney P, et al. Efficacy of a brief case management intervention to link recently diagnosed HIV-infected persons to care. *AIDS (London, England).* Mar 4 2005;19(4):423-431.

97. Pilcher CD, Ospina-Norvell C, Dasgupta A, et al. The Effect of Same-Day Observed Initiation of Antiretroviral Therapy on HIV Viral Load and Treatment Outcomes in a U.S. Public Health Setting. *Journal of acquired immune deficiency syndromes (1999).* Jul 16 2016.

98. Keller SC, Yehia BR, Eberhart MG, Brady KA. Accuracy of definitions for linkage to care in persons living with HIV. *J Acquir Immune Defic Syndr.* Aug 15 2013;63(5):622-630.