Title

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Journal

AIDS, 33(9)

ISSN

0269-9370

Authors

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Publication Date

2019-07-15

DOI

10.1097/qad.0000000000002220

Peer reviewed

HHS Public Access

Author manuscript

AIDS. Author manuscript; available in PMC 2020 July 15.

Published in final edited form as:

AIDS. 2019 July 15; 33(9): 1491–1500. doi:10.1097/QAD.0000000000002220.

Heterogeneity in the costs of medical care among people living with HIV/AIDS in the United States

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Abstract

Objective: The costs of medical care for people with HIV/AIDS (PWH) vary substantially across demographic groups, stages of disease progression and regionally across the US. We aimed to estimate medical costs for PWH and examine the heterogeneity in costs within key patient groups typically distinguished in cost-effectiveness analyses.

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Conflicts of Interest: None to declare

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Design: Retrospective cohort study using health administrative databases for diagnosed PWH in care at 17 HIV Research Network (HIVRN) sites across the US.

Methods: We estimated mean quarterly costs for key patient groups using multivariable generalized linear mixed effects models. We used quantile regression to highlight differences in the effect of covariates within each patient group (difference between covariate estimates at the mean versus the 90th percentile of quarterly costs), identifying covariates with a larger effect among the highest cost PWH, or generating greater uncertainty in mean cost estimates.

Results: Our sample included 40,022 patients with a median age of 39 years. Mean quarterly costs were highest for people who inject drugs (PWID) with advanced disease progression and for PWH on antiretroviral treatment (ART). Within patient groups, we found the most heterogeneity at different levels of resource use for PWH on ART and PWH off ART with CD4<200, PWID, as well as PWH in the South.

Conclusions: This study quantifies heterogeneity in costs both across and within key PWH patient groups. Our results highlight the need for sensitivity analysis on cost estimates and may inform decisions on model structure in cost-effectiveness analyses on HIV/AIDS treatment and prevention strategies.

Background

Life expectancy of people living with HIV (PWH) has increased due to advances in the clinical care of HIV/AIDS [1], screening [2], earlier ART initiation and delayed disease progression [3]. As a result, the economic burden of HIV has evolved, with PWH living longer, and accumulating higher medical costs over their lifetime [4, 5]. Immediate access to combination antiretroviral therapy (ART) provides individual and public health benefits [6], while suboptimal ART uptake challenges efforts to reduce HIV-related morbidity, mortality and transmission [7]. High costs of scaling-up treatment and prevention strategies, largely attributable to antiretroviral medications, future uncertainty in ART costs due generic medications [8], and newer branded regimens [9] present additional challenges to reducing the public health and economic burden of HIV [4, 10].

The US HIV epidemic features substantial geographic variation and is best characterized as a set of diverse microepidemics, dispersed mostly across large urban centers [11]. Among six major US cities, HIV transmission risk group composition for PWH varied from 28–77% for men who have sex with men (MSM), 4–42% for people who inject drugs (PWID), and 10–38% for heterosexuals (HET), and race/ethnicity composition varied from 9–78% Black, 3–43% Hispanic/Latino, and 15–70% white [11]. These cities also had wide differences in provision and funding of HIV care, including Medicaid funding per PWH (e.g. $1,488 in Miami vs. $17,122 in New York), as well as state-level Medicaid eligibility [12, 13]. Prior to the affordable care act, the national percentage of uninsured individuals under 65 was 13.9% for whites, 21.6% for blacks and 33.3% for Hispanics [14], though expansion of coverage has begun to reduce these disparities [15]. HIV disease progression [4, 16–19], as well as geographic variation in demographics and clinical practice have contributed to differences in the costs of medical care for PWH across the US [20]. In a climate of uncertainty in healthcare funding and delivery, analysis on how medical costs differ across geographic

region, risk group, and disease progression should be an area of scrutiny by researchers and policymakers alike.

Model-based cost-effectiveness analysis provides a framework to quantify the health and economic value of strategies to address HIV microepidemics while accounting for the synergistic effects of different combinations of public health interventions [21–23]. A review of cost-effectiveness studies on the treatment and prevention of HIV/AIDS from 1991–2011 noted that most assumed a uniform cost per patient [24], meaning that population heterogeneity in PWH was not captured in cost projections. Recent studies of the lifetime cost savings from preventing HIV have incorporated population heterogeneity by using cost inputs that varied across transmission risk group, age, sex and race/ethnicity [4]; however, these national estimates did not account for regional heterogeneity in group composition.

Focusing on the mean effect of covariates can obscure potentially large heterogeneity within patient groups, where differences in mean costs are driven by a small percentage of high-intensity health resource users [25]. Quantile regression analysis can reveal how estimates for a particular patient group may vary depending on the intensity of resource use for an individual, relative to others within the same group [25, 26]. For cost-effectiveness analysis, cost inputs for PWH patient groups derived from coefficient estimates with large variation in effect size are subject to greater uncertainty. There is thus potential to under- or over-estimate the cost-effectiveness of a given intervention, depending on the case-mix of patients it is designed to reach.

We aimed to estimate medical costs for PWH, attributable to health resource use intensity, and examine heterogeneity in costs across (using standard multiple regression techniques) and within (using quantile regression) geographic region, transmission risk group, and CD4 cell count. We estimated the effect of covariates at different cost quantiles to identify covariates with the greatest heterogeneity within patient groups.

Methods

Study design and data sources

The HIV Research Network (HIVRN) is a consortium of 17 adult and pediatric HIV care providers located in the northeastern (n=8), southern (n=5), and western United States (n=4) [20, 27]. HIVRN sites abstracted data elements from patients' medical records, and data were assembled into a single database after quality assurance review [19]. HIVRN data included demographic data, length of inpatient visits, number of outpatient and emergency visits, laboratory tests (including CD4 and plasma viral load (pVL) tests), as well as dates and durations for ART and non-ART prescription drugs. All sites participating in the HIVRN for all years between 2002 and 2015 were included in the analysis. We limited our analyses to patients over 15 years of age, observed in care for at least one quarter between 2010–2015 (defined as at least one record of any healthcare utilization for a given person-quarter), and those with complete demographic information.

Study measures

The primary outcome for our analysis was total quarterly healthcare costs, including costs for inpatient, outpatient, and emergency care, lab tests, ART and non-ART prescription drugs. Unit costs for inpatient, outpatient and emergency visits were derived from McCollister et al. (2017) [28]. Costs for prescription drugs were derived from Veterans Affairs (VA) Federal Supply Schedule (FSS) prices that we adjusted upward by 21% according to the recommended adjustment for FSS pricing relative to the usual cost to the US healthcare system [29]. For unit costs of prescription drugs, we assumed that the average FSS price represented the average monthly supply cost for each drug, and we derived medication costs of from VA FSS price lists, using brand-specific drug prices where indicated in our utilization data and generic prices if available. Costs for CD4 and pVL tests were derived from Schackman et al. (2015) [4], and all other laboratory testing unit costs were derived from Medicare clinical laboratory fee schedules [30]. We calculated costs from the perspective of a large-scale purchaser of services, such as national Medicaid or Medicare programs, and presented estimates in 2018 USD.

The primary independent variables included CD4-based disease progression, ART status (based on ART quarterly prescriptions), geographic region (northeast, south, west), gender and HIV risk groups, including MSM, MSM who inject drugs (MWID), male and female PWID and male and female HET. We categorized disease progression by quarterly median CD4 cell count per microliter (cells/μL) as <200, 200–499, ≥500, and missing. We imputed missing CD4 results by carrying forward results from an individual's most recent test for a maximum of two quarters, after which we classified these measures as missing.

We controlled for race/ethnicity (Black, Hispanic/Latino, and non-Hispanic white/others), age (categorized as <30, 30–39, 40–49, and 50+), calendar year, plasma viral load (pVL) suppression and insurance coverage. We categorized pVL measures as: at least one test ≤200 copies/mL, all tests >200 copies/mL, and missing. We imputed missing pVL measures by carrying forward results from an individual's most recent test for a maximum of two quarters, after which we classified these measures as missing. We derived insurance status from medical records and categorized coverage as: private insurance, Medicare and/or Medicaid, and other coverage/uninsured/missing.

Statistical Analysis

We estimated mean quarterly medical costs using a generalized linear model (GLM) with a log link and gamma distribution. We chose this model given that our data were non-negative and right-skewed, a case in which ordinary least-squares regression (OLS) estimates can be biased and where re-transformations of log-transformed costs are sensitive to model misspecification [31, 32]. We selected a multilevel GLM with individual-level random intercepts to account for intra-individual correlation from repeated measurements, and did not include clinic-level random intercepts due to insufficient variation after including individual-level random intercepts.

We estimated mean regional quarterly medical expenditures by HIV risk group, CD4 category and ART status, controlling for covariates listed above. We presented stratified quarterly costs averaged over patient groups within each region.

As a secondary analysis, we used quantile regression to investigate within-group differences of covariate effects for individuals at different cost quantiles. Quantile regression fits a multivariable regression at each conditional quantile of the dependent variable, and residuals are weighted based on the chosen quantile [33]. The coefficient for a 90th percentile quantile regression refers to the effect of a covariate on costs for the individual in the 90th percentile of the cost distribution for a given person-quarter [34]. Because quantiles are based on the distribution of the outcome variable over the entire sample, individuals may appear in different quantiles throughout the study period. We log-transformed quarterly healthcare costs and display estimates for conditional quantiles, highlighting relative to the reference group within each category.

While estimates of covariate effects on the mean provide only one estimate, covariates may influence the conditional distribution of the outcome variable by expanding dispersion, stretching or compressing one tail, or inducing multimodality [33]. We investigated the impact of key covariates across the cost distribution, by estimating a set of coefficients at different quantiles and comparing these to the effect on the mean. This allowed us to identify coefficient estimates that were larger in magnitude at higher cost quantiles, highlighting where mean cost estimates applied to a particular patient subgroup in cost-effectiveness analysis were subject to greater uncertainty.

Due to greater uncertainty in non-ART prescription drug costs, we conducted sensitivity analysis by removing these costs from total medical costs. We also re-estimated our primary regression model with site-level, instead of regional, indicators, and removed individual-level random intercepts.

We created our analytic sample in SAS v9.4, and conducted statistical analysis in Stata v14.1. Quantile regression analyses were performed using the Stata package “qreg2”, which allowed us to derive standard errors which were valid under intra-cluster correlation [35].

Results

Descriptive statistics

Our sample included 40,022 PWH (24% female, median age: 39 years) with a median 3.25 (IQR: 1.5, 5.5) years of follow-up and 13 (6, 22) observations per individual from 2010 and 2015. PWH in the West were 63% MSM, and PWH in the South were 58% Black (Table 1). Unadjusted total mean costs per person-quarter ranged from $8,825 in the Northeast to $10,382 in the South. ART drug costs among all PWH, both on and off ART, were the largest component of total mean costs, ranging from 72% in the West to 82% in the South (Fig.1). Diagnostic testing and outpatient costs were a substantial portion of costs for those in the 10^{th} percentile (Fig.2A), while ART costs represented the majority for those in the 50^{th} and 90^{th} percentiles (Fig.2A-C). Inpatient and emergency department visits represented

a larger proportion of costs for those in the 90th percentile (Fig.2C), particularly in the Northeast and West.

GLM regression results

We derived mean quarterly costs within our sample, using coefficient estimates from our multilevel GLM model to generate fitted values for PWH stratified by HIV risk group, CD4 category, geographic region, and ART receipt. Costs for individuals off ART ranged from $1,208 (95% CI: 1,192–1,224) for MSM in the Northeast with CD4 ≥500 to $4,274 (4,114–4,434) for female PWID in the West with CD4 <200. For individuals on ART, costs ranged from $10,534 (10,414–10,654) for MSM in the Northeast with CD4 ≥500, to $15,787 (15,229–16,345) for female PWID in the West with CD4 <200 (Table 2).

Quantile regression results

Differences in CD4 cell count and ART status had the largest overall effect on costs, across patient groups, relative to risk groups and regions. Using quantile regression, we highlighted within-group differences in coefficient estimates across cost quantiles (Fig.3). For PWH off ART with CD4 200–499 and CD4 <200, coefficient estimates were higher for those at the 90th percentile, relative to the mean estimate (142% and 168%, respectively). Within PWH on ART, estimates for individuals at the 90th percentile were lower relative to the mean for all CD4 categories. Within male and female PWID, estimates for those at the 90th percentile were 69% and 66% higher, respectively, relative to the mean estimates. Estimates for female heterosexuals, MSM and MWID were similar in magnitude across quantiles. Finally, for PWH in the South, coefficient estimates were more than double (230%) for those at the 90th percentile, relative to the mean, while estimates for those in the West were relatively consistent across quantiles.

Sensitivity analysis

Removing individual-level random effects increased coefficient estimates for CD4 <500 relative to CD4 ≥500 among PWH off ART, and decreased estimates for all CD4 categories for individuals on ART relative to those off ART. Replacing indicators for regions to site-level attenuated coefficient estimates for transmission risk groups relative to HET, while coefficient estimates on disease progression were essentially unchanged. Removing non-ART prescription drug costs increased coefficient estimates for those with a CD4 of less than 500 relative to CD4 ≥500. None of these changes affected the statistical significance of coefficient estimates for our primary covariates, or changed the relative rank order of effect sizes within each PWH patient group (Appendix Table 1).

Discussion

Main findings

This study provides regional estimates for medical costs among PWH, stratified by HIV risk group, HIV disease progression, and ART receipt. We identified heterogeneity in mean quarterly costs across PWH patient groups, and in the effects of covariates for individuals within these groups, at different levels of resource use intensity. Using quantile regression, we identified the most substantial heterogeneity among key PWH patient groups, at different

levels of total costs, for those in the South, those with low CD4 cell counts, and among PWID.

Disease progression accounted for the largest cost differences for all PWH. For MSM off ART, the difference in mean costs between CD4 <200 and ≥500 was $1,892, $2,039 and $2,065 for those in the Northeast, South, and West respectively. Among MSM on ART, this difference was $917, $989 and $1,001 in the Northeast, South and West respectively. Gebo et al. (2010) estimated cost differences between CD4 ≥500 and those with CD4 ≤50 and 50–200 to be $8,062 and $2,813 respectively among all PWH (adjusted to quarterly costs in 2018 USD) [19]. Fleishman et al. (2016) estimated cost differences among PWH enrolled in Medicaid to be $6,838 higher for PWH with CD4 <200 compared to CD4 ≥500 (adjusted to quarterly costs in 2018 USD) [36]. The disparity in cost estimates by disease progression between our results and previous studies likely reflect differences in CD4 categories, driven by inclusion of a separate category for CD4≤50 in Gebo et al. (2010) [19], indicative of very poor health. Furthermore, costs in both studies were estimated by pooling all PWH, both on and off ART, and PWH in Fleishman et al. (2016) were enrolled in Medicaid with higher overall medical costs across all patient groups [36]. Given substantially higher costs of PWH with advanced disease progression, this reinforces the importance of early engagement on ART in reducing medical costs by delaying disease progression among PWH [4]. Higher cost estimates for female PWH, were consistent with trends in overall US healthcare spending, where estimated spending per person was 25% higher for women than men in 2013, excluding pregnancy-related expenses [37].

Mean quarterly costs also varied by risk group, with PWID having the highest costs among risk groups, and MSM the lowest. Among PWH off ART with CD4 <200, quarterly cost differences between male PWID and MSM were $652 in the Northeast, $702 in the South and $711 in the West regions. Cost differences among male PWID and MSM on ART were $2,409 in the Northeast, $2,596 in the South and $2,628 in the West regions, respectively. This was consistent with previous findings of high costs associated with complications due to injection drug use [38], as well as PWID having the highest costs among risk groups in previous cost estimates for PWH [19, 36].

Our quantile regression analysis demonstrated disparate patterns of the effect of ART receipt on total costs. Coefficient estimates by CD4 category for PWH off ART were increasing, and estimates for those on ART were decreasing for PWH at higher cost percentiles (Fig. 3). The convergence in estimates between PWH on and off ART with low CD4 cell counts suggested that the high cost of ART medications played a diminishing role in how PWH in the highest cost quantiles accumulated costs, relative to other components such as inpatient and emergency costs. This interpretation is consistent with previous findings that inpatient costs were the largest component of medical costs for those with CD4 cell counts <50 [19]. In the context of cost-effectiveness analysis, costs for PWH on ART were better captured by mean estimates for a representative individual, compared to mean estimates for PWH off ART, which could be subject to greater bias, as mean cost estimates were driven by individuals with the highest costs. It has been noted elsewhere that differences in coefficient effects at lower quantiles may reflect differential access and preferences for preventative care, while differences at higher quantiles result from individuals with more critical health

issues [34, 39]. Our results for PWH off ART likely reflect this utilization pattern, where individuals were not engaging in preventative care (smaller effects for individuals at lower quantiles) but incurring higher costs due to complications from untreated HIV disease progression (larger effects for individuals at higher quantiles).

Our quantile regression results also demonstrated variation in coefficient estimates among PWID (Fig. 3). Smaller coefficient estimates for those in the lower quantiles of medical costs may reflect lower levels of engagement in HIV care among PWID [40], while larger effects among those with the highest resource use intensity could reflect higher costs resulting from complications of injection drug use [38, 41]. Cost estimates for interventions targeting the highest-cost PWID could potentially be underestimated if they were able to target individuals with the highest intensity of resource use, such as syringe exchanges, or opioid agonist treatment programs aimed at PWID hospitalized for injection drug use-related infections [38]. Similarly, costs among PWID could be underestimated if an intervention re-engaged individuals with low levels of engagement in care and low medical costs, but had little effect on reducing costs for those with high utilization.

Quantile regression analysis also highlighted disparate patterns in the effect of receiving care in a particular region. Controlling for demographic differences, insurance coverage, and disease progression, coefficient estimates for residence in the South were negative for PWH at the lowest cost quantiles and increasing for PWH at higher cost quantiles compared to the Northeast (Fig. 3), indicating that higher mean costs in the South were skewed by the highest cost individuals. In this case, relatively similar differences in mean costs between the South and West, compared to the Northeast, obscured a different underlying pattern of effects for PWH with different levels of health resource use. For PWH with lower CD4 cell counts and PWID, differences in coefficient estimates across quantiles for PWH in the South may have reflected barriers to accessing care, resulting in a negative effect among PWH at lower quantiles of medical costs and a positive and increasing effect among those with the highest costs (Fig. 3).

Our study had several limitations. We calculated prescription drug costs from prescribed medications, not purchase records, so we could not determine if individuals had purchased all prescribed medication. As a result, we may have overestimated prescription drug costs, however, our results in sensitivity analysis were robust to the exclusion of non-ART prescription drug costs. While our study represents a comprehensive assessment of medical costs among key PWH patient groups in the US, our analysis was limited to geographic regions of HIVRN clinics. Thus, our estimates are regional averages and may not fully capture heterogeneity in medical costs for individual cities within regions. Furthermore, while we had individual utilization records, we did not have access to billing records or clinic/region-specific unit costs. Thus, cost differences likely understate variation in prices across geographic regions and should be interpreted as differences in costs from health resource use intensity, rather than differences in prices for the same services across regions or by different payers. While we did not estimate the effects of hepatitis-HIV co-infection on health resource costs, the higher prevalence of HIV/HCV co-infection among PWID/MWID relative to other risk groups [42] likely contributed to higher estimates for these risk groups. HIVRN sites are experienced in the treatment of HIV and costs may differ for individuals at

sites with less provider experience or smaller caseloads of PWH. Finally, given the ability of individuals to receive care from providers outside of HIVRN clinics, as well as care that was not captured in HIVRN data [19], particularly among those enrolled in Medicaid [36], costs of medical care in this cohort can be considered a lower bound, particularly for those not on ART.

Our study estimated the regional costs of medical care among key PWH patient groups, and heterogeneity within these groups at different quantiles of the cost distribution. We found considerable variation in mean estimates of quarterly costs by transmission risk group, disease progression and geographic region, confirming the need to explicitly model key PWH patient groups in cost-effectiveness analysis. Our results also highlight the need to consider heterogeneity when using mean costs as inputs in cost-effectiveness analysis, either by incorporating wider bounds on cost estimates with substantial heterogeneity in sensitivity analysis, or by including additional strata within key PWH populations informed by differences in medical costs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements:

The content is solely the responsibility of the authors and does not necessarily represent the official views of the funders. The funders had no direct role in the conduct of the analysis or the decision to submit the manuscript for publication. The funders had no role in the study design, data collection, interpretation, or writing of the report. The corresponding author had final responsibility for the decision to submit for publication and full access to all the data.

Funding: This study was supported by funding from US National Institutes of Health, National Institute on Drug Abuse (number R01DA041747–02S1) as well as the Agency for Healthcare Research and Quality (HHSA290201100007C), the Health Resources and Services Administration (HHSH250201600009C).

References

1. Palella FJ Jr, Baker RK, Moorman AC, Chmiel JS, Wood KC, Brooks JT, et al. Mortality in the highly active antiretroviral therapy era: changing causes of death and disease in the HIV outpatient study. J Acquir Immune Defic Syndr 2006,43:27–34. [PubMed: 16878047]
2. Paltiel A, Walensky RP, Schackman BR, et al. Expanded hiv screening in the united states: Effect on clinical outcomes, hiv transmission, and costs. Annals of Internal Medicine 2006,145:797–806. [PubMed: 17146064]
3. Günthard HF, Saag MS, Benson CA, et al. Antiretroviral drugs for treatment and prevention of hiv infection in adults: 2016 recommendations of the international antiviral society–usa panel. JAMA 2016,316:191–210. [PubMed: 27404187]
4. Schackman BR, Fleishman JA, Su AE, Berkowitz BK, Moore RD, Walensky RP, et al. The lifetime medical cost savings from preventing HIV in the United States. Med Care 2015,53:293–301. [PubMed: 25710311]
5. Sloan CE, Champenois K, Choisy P, Losina E, Walensky RP, Schackman BR, et al. Cost-Effectiveness of Preventing AIDS Complications (CEPAC) investigators. Newer drugs and earlier treatment: impact on lifetime cost of care for HIV-infected adults. AIDS 2012,26:45–56. [PubMed: 22008655]
6. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med 2011,365:493–505. [PubMed: 21767103]

7. Skarbinski J, Rosenberg E, Paz-Bailey G, Hall HI, Rose CE, Viall AH, et al. Human immunodeficiency virus transmission at each step of the care continuum in the United States. JAMA Intern Med 2015,175:588–596. [PubMed: 25706928]
8. Hill A, Hill T, Jose S, Pozniak A. Predicted savings to the UK National Health Service from switching to generic antiretrovirals, 2014–2018. J Int AIDS Soc 2014,17.
9. Gulick R HIV treatment 2020: what will it look like? J Int AIDS Soc 2014,17.
10. Farnham PG, Holtgrave DR, Gopalappa C, Hutchinson AB, Sansom SL. Lifetime costs and quality-adjusted life years saved from HIV prevention in the test and treat era. JAIDS Journal of Acquired Immune Deficiency Syndromes 2013,64:e15–e18. [PubMed: 24047975]
11. Panagiotoglou D, Olding M, Enns B, Feaster DJ, del Rio C, Metsch LR, et al. Building the Case for Localized Approaches to HIV: Structural Conditions and Health System Capacity to Address the HIV/AIDS Epidemic in Six US Cities. AIDS and Behavior 2018.
12. Families USA. A 50-State look at medicaid expansion. In. Washington, DC: Families USA; 2016.
13. Kates J, Dawson L, Undem T, Perry K. Health insurance coverage for people with HIV under the Affordable Care Act: Experiences in five states. In. Kaiser Family Foundation: Kaiser Family Foundation; 2014.
14. Clemans-Cope L, Kenney GM, Buettgens M, Carroll C, Blavin F. The Affordable Care Act's Coverage Expansions Will Reduce Differences In Uninsurance Rates By Race And Ethnicity. Health Affairs 2012,31:920–930. [PubMed: 22566430]
15. Chen J, Vargas-Bustamante A, Mortensen K, Ortega AN. Racial and Ethnic Disparities in Health Care Access and Utilization Under the Affordable Care Act. Med Care 2016.
16. Chen RY, Accortt NA, Westfall AO, Mugavero MJ, Raper JL, Cloud GA, et al. Distribution of health care expenditures for HIV-infected patients. Clin Infect Dis 2006,42:1003–1010. [PubMed: 16511767]
17. Fleishman JA, Gebo KA, Reilly ED, Conviser R, Christopher Mathews W, Todd Korthuis P, et al. Hospital and outpatient health services utilization among HIV-infected adults in care 2000–2002. Med Care 2005,43:III40–52. [PubMed: 16116308]
18. Hutchinson AB, Farnham PG, Dean HD, Ekwueme DU, del Rio C, Kamimoto L, et al. The economic burden of HIV in the United States in the era of highly active antiretroviral therapy: evidence of continuing racial and ethnic differences. J Acquir Immune Defic Syndr 2006,43:451–457. [PubMed: 16980906]
19. Gebo KA, Fleishman JA, Conviser R, Hellinger J, Hellinger FJ, Josephs JS, et al. Contemporary Costs of HIV Health Care in the HAART Era. AIDS (London, England) 2010,24:2705–2715.
20. Yehia BR, Gebo KA, Hicks PB, Korthuis PT, Moore RD, Ridore M, et al. Structures of care in the clinics of the HIV Research Network. AIDS Patient Care STDS 2008,22:1007–1013. [PubMed: 19072107]
21. Briggs A, Sculpher M, Claxton K. Decision modelling for health economic evaluation: OUP Oxford; 2006.
22. Garnett GP. An introduction to mathematical models in sexually transmitted disease epidemiology. Sexually transmitted infections 2002,78:7–12. [PubMed: 11872850]
23. Garnett GP, Cousens S, Hallett TB, Steketee R, Walker N. Mathematical models in the evaluation of health programmes. The Lancet 2011,378:515–525.
24. Meyer-Rath G, Over M. HIV treatment as prevention: modelling the cost of antiretroviral treatment--state of the art and future directions. PLoS Med 2012,9:10.
25. Le Cook B, Manning WG. Thinking beyond the mean: a practical guide for using quantile regression methods for health services research. Shanghai Arch Psychiatry 2013,25:55–59. [PubMed: 24948867]
26. Smith J, Banks H, Campbell H, Douglas A, Fletcher E, McCallum A, et al. Parameter Heterogeneity In Breast Cancer Cost Regressions - Evidence From Five European Countries. Health Econ 2015,2:23–37.
27. Yehia BR, Agwu AL, Schranz A, Korthuis PT, Gaur AH, Rutstein R, et al. Conformity of pediatric/adolescent HIV clinics to the patient-centered medical home care model. AIDS Patient Care STDS 2013,27:272–279. [PubMed: 23651104]

28. McCollister K, Yang X, Sayed B, French MT, Leff JA, Schackman BR. Monetary conversion factors for economic evaluations of substance use disorders. Journal of Substance Abuse Treatment.
29. VA Health Economics Resource Center (HERC). Determining the Cost of Pharmaceuticals for a Cost-Effectiveness Analysis. In; 2016.
30. Centers for Medicare and Medicaid Services. Clinical laboratory fee schedule. 2017.
31. Buntin MB, Zaslavsky AM. Too much ado about two-part models and transformation? Comparing methods of modeling Medicare expenditures. J Health Econ 2004,23:525–542. [PubMed: 15120469]
32. Blough DK, Madden CW, Hornbrook MC. Modeling risk using generalized linear models. J Health Econ 1999,18:153–171. [PubMed: 10346351]
33. Koenker R, Hallock K. Quantile regression: An introduction. Journal of Economic Perspectives 2001,15:43–56.
34. Candon MK, Barry CL, Epstein AJ, Marcus SC, Kennedy-Hendricks A, Xie M, et al. The Differential Effects of Insurance Mandates on Health Care Spending for Children's Autism Spectrum Disorder. Med Care 2018,56:228–232. [PubMed: 29287035]
35. Machado JAF, Parente PMDC, Silva JMCS. QREG2: Stata module to perform quantile regression with robust and clustered standard errors. In. S457369 ed: Boston College Department of Economics; 2011.
36. Fleishman JA, Monroe AK, Voss CC, Moore RD, Gebo KA. Expenditures for Persons Living With HIV Enrolled in Medicaid, 2006–2010. J Acquir Immune Defic Syndr 2016,72:408–415. [PubMed: 26977747]
37. Dieleman JL, Baral R, Birger M, Bui AL, Bulchis A, Chapin A, et al. US Spending on Personal Health Care and Public Health, 1996–2013. JAMA 2016,316:2627–2646. [PubMed: 28027366]
38. Tookes H, Diaz C, Li H, Khalid R, Doblecki-Lewis S. A Cost Analysis of Hospitalizations for Infections Related to Injection Drug Use at a County Safety-Net Hospital in Miami, Florida. PLoS One 2015,10.
39. Cook BL, Manning WG. Measuring racial/ethnic disparities across the distribution of health care expenditures. Health Serv Res 2009,44:1603–1621. [PubMed: 19656228]
40. Des Jarlais DC, Bramson HA, Wong C, Gostnell K, Cepeda J, Arasteh K, et al. Racial/ethnic disparities in HIV infection among people who inject drugs: an international systematic review and meta-analysis. Addiction 2012,107:2087–2095. [PubMed: 22823178]
41. Takahashi TA, Maciejewski ML, Bradley K. US hospitalizations and costs for illicit drug users with soft tissue infections. J Behav Health Serv Res 2010,37:508–518. [PubMed: 19381818]
42. Spradling PR, Richardson JT, Buchacz K, Moorman AC, Finelli L, Bell BP, et al. Trends in hepatitis C virus infection among patients in the HIV Outpatient Study, 1996–2007. J Acquir Immune Defic Syndr 2010,53:388–396. [PubMed: 19738485]

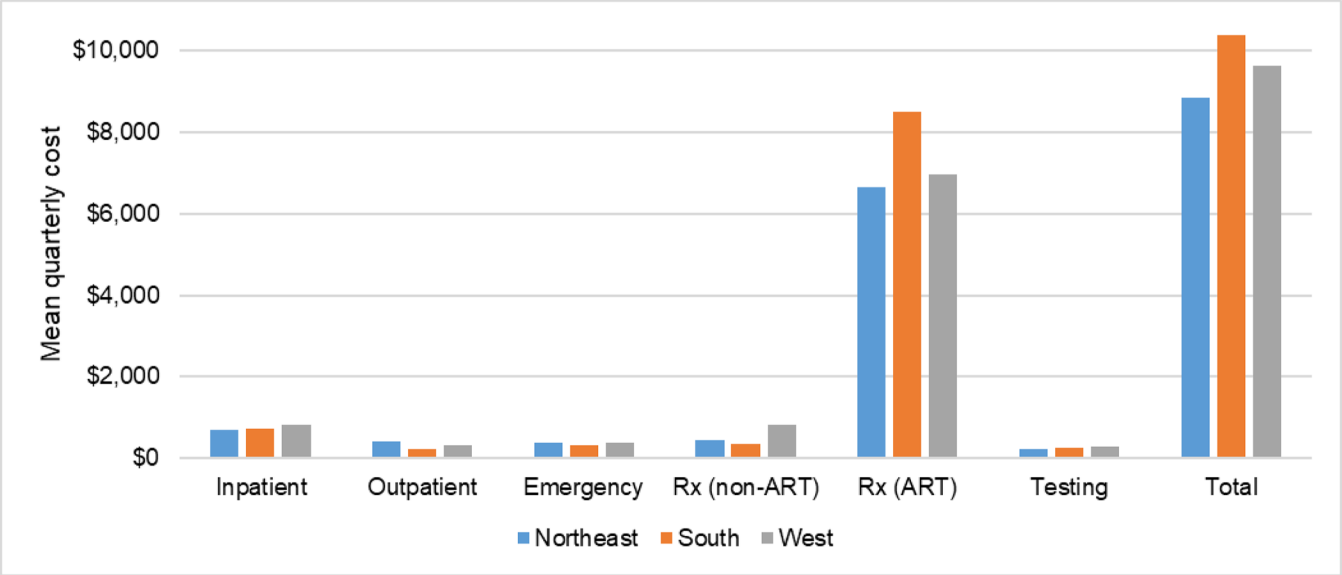

Fig 1. Unadjusted mean quarterly costs per person-quarter by component and region (2018 USD)

Rx: Prescription medication; ART: Antiretroviral therapy

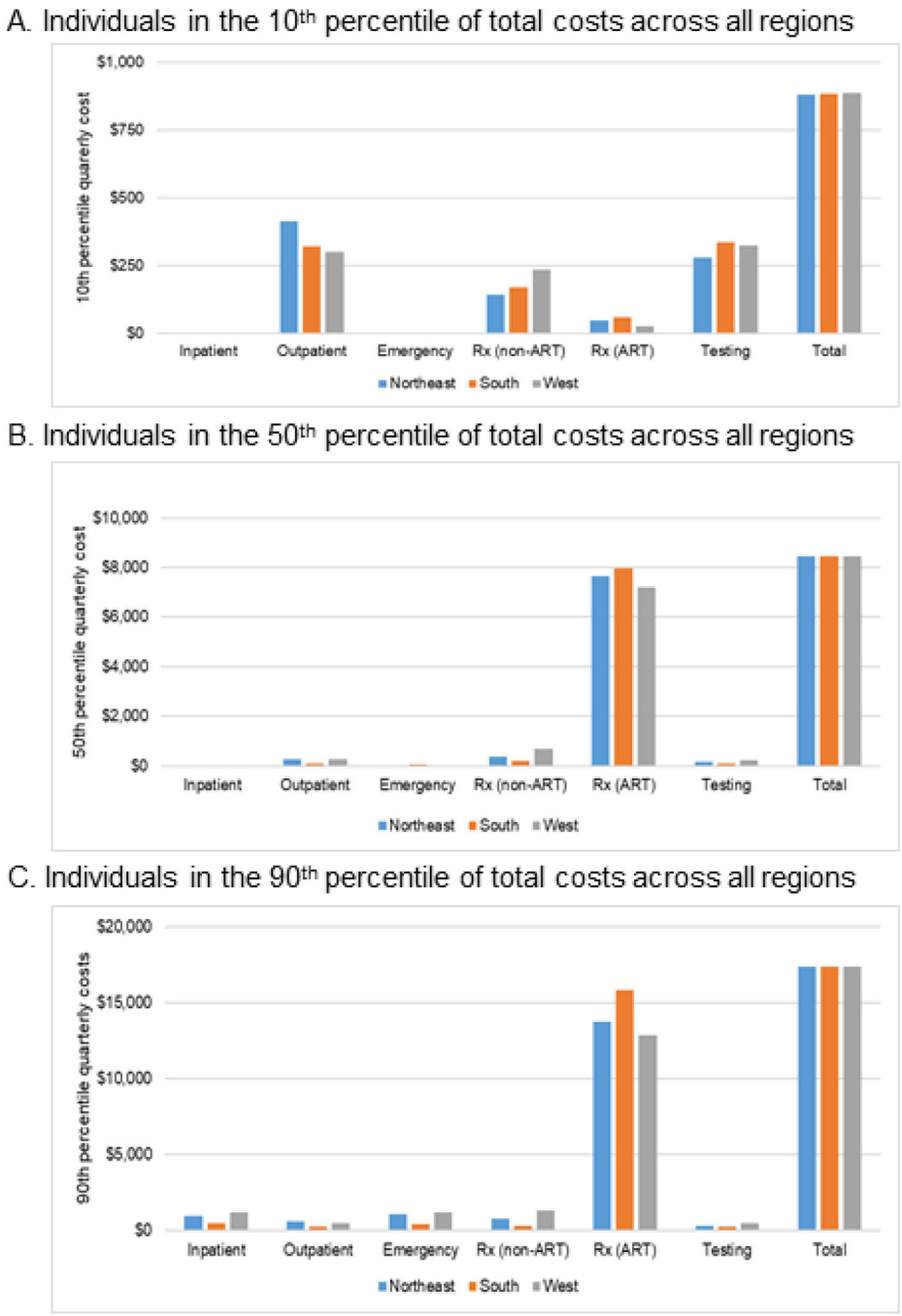

Fig. 2. Unadjusted costs per person-quarter at selected quantiles by component and region (2018 USD)

Rx: Prescription medications; ART: Antiretroviral therapy

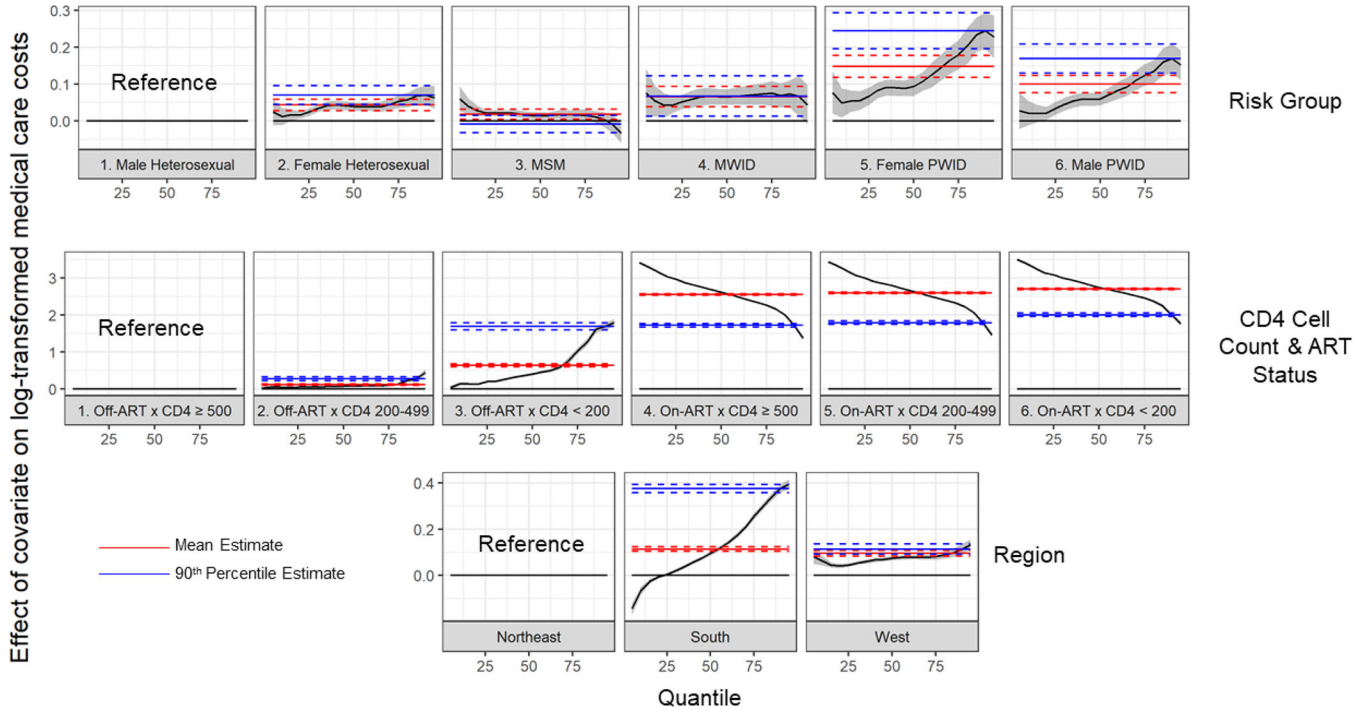

Figure 3. Quantile regression estimates for individual covariates at conditional quantiles of the log-transformed total quarterly costs distribution (2018 USD)

PWID: People who inject drugs; MSM: Men who have sex with men; MWID: MSM who inject drugs; ART: Antiretroviral therapy. Quantile regression coefficient estimates are presented for every 5th percentile between the 5th and 95th percentile of log-transformed total quarterly medical costs. The solid line represents the point estimates of the coefficient for a given conditional quantile ranging from 0.05 to 0.95, and the shaded area shows the 95% confidence band. 95% confidence intervals were derived from clustered standard errors (shown as grey shading around quantile regression estimates), which adjusts standard errors to account for within-individual correlation of observations due individuals having multiple observations in our data set. The horizontal red line represents the cluster-robust ordinary least squares estimate of the mean effect, and the blue line represents the estimated effect at the 90th percentile, with dashed lines indicating the 95% confidence interval for each coefficient.

Table 1.

Summary statistics of sample cohort at baseline by geographic region

	Northeast	South	West
Individuals (N)	17432	16074	6516
Risk group			
Male			
HET	2861 (16.4%)	3378 (21%)	811 (12.4%)
MSM	8758 (50.2%)	6804 (42.3%)	4090 (62.8%)
PWID	1315 (7.5%)	980 (6.1%)	289 (4.4%)
MWID	338 (1.9%)	357 (2.2%)	447 (6.9%)
Female			
HET	3557 (20.4%)	4000 (24.9%)	717 (11%)
PWID	603 (3.5%)	555 (3.5%)	162 (2.5%)
Race/Ethnicity			
White/Other†	5049 (29%)	3949 (24.6%)	3621 (55.6%)
Black	7557 (43.4%)	9257 (57.6%)	1343 (20.6%)
Hispanic	4826 (27.7%)	2868 (17.8%)	1552 (23.8%)
Age (median)	40.7	37	39.4

HET: Heterosexual; MSM: Men who have sex with men; PWID: People who inject drugs; MWID: MSM who inject drugs; ART: Antiretroviral therapy;

† Includes Asian, Pacific Islander and Aboriginal.

Table 2.

Predicted mean quarterly medical costs derived from multilevel generalized linear model (2018 USD)

		Predicted Total Quarterly Costs Per PLHIV[†]					
		Northeast		South		West	
Risk Group	**CD4**	**Off ART**	**On ART[‡]**	**Off ART**	**On ART[‡]**	**Off ART**	**On ART[‡]**
MSM	*≥ 500*	$1208 [1192, 1224]	$10534 [10414, 10654]	$1302 [1284, 1320]	$11350 [11209, 11491]	$1318 [1295, 1341]	$11494 [11314, 11674]
	200–499	$1456 [1436, 1476]	$10696 [10572, 10820]	$1569 [1546, 1592]	$11526 [11383, 11669]	$1589 [1561, 1617]	$11671 [11488, 11854]
	< 200	$3100 [3044, 3156]	$11451 [11296, 11606]	$3341 [3279, 3403]	$12339 [12164, 12514]	$3383 [3312, 3454]	$12495 [12281, 12709]
PWID	*≥ 500*	$1526 [1476, 1576]	$13310 [12879, 13741]	$1645 [1590, 1700]	$14342 [13876, 14808]	$1666 [1607, 1725]	$14523 [14019, 15027]
(Female)	*200–499*	$1840 [1779, 1901]	$13515 [13077, 13953]	$1983 [1917, 2049]	$14563 [14090, 15036]	$2008 [1937, 2079]	$14747 [14235, 15259]
	< 200	$3917 [3779, 4055]	$14469 [13990, 14948]	$4221 [4073, 4369]	$15591 [15075, 16107]	$4274 [4114, 4434]	$15787 [15229, 16345]
PWID	*≥ 500*	$1462 [1426, 1498]	$12750 [12445, 13055]	$1576 [1536, 1616]	$13738 [13403, 14073]	$1595 [1550, 1640]	$13911 [13532, 14290]
(Male)	*200–499*	$1762 [1718, 1806]	$12946 [12637, 13255]	$1899 [1851, 1947]	$13950 [13612, 14288]	$1923 [1869, 1977]	$14126 [13742, 14510]
	< 200	$3752 [3649, 3855]	$13860 [13517, 14203]	$4043 [3931, 4155]	$14935 [14562, 15308]	$4094 [3970, 4218]	$15123 [14701, 15545]
MWID	*≥ 500*	$1330 [1282, 1378]	$11598 [11187, 12009]	$1433 [1381, 1485]	$12497 [12053, 12941]	$1451 [1398, 1504]	$12655 [12204, 13106]
	200–499	$1603 [1545, 1661]	$11777 [11359, 12195]	$1728 [1665, 1791]	$12690 [12239, 13141]	$1749 [1685, 1813]	$12850 [12392, 13308]
	< 200	$3413 [3283, 3543]	$12608 [12152, 13064]	$3678 [3538, 3818]	$13586 [13096, 14076]	$3724 [3581, 3867]	$13757 [13258, 14256]
HET	*≥ 500*	$1306 [1285, 1327]	$11389 [11218, 11560]	$1407 [1384, 1430]	$12272 [12091, 12453]	$1425 [1395, 1455]	$12426 [12180, 12672]
(Female)	*200–499*	$1574 [1547, 1601]	$11564 [11389, 11739]	$1696 [1668, 1724]	$12461 [12277, 12645]	$1718 [1681, 1755]	$12618 [12367, 12869]
	< 200	$3352 [3283, 3421]	$12380 [12174, 12586]	$3612 [3539, 3685]	$13340 [13124, 13556]	$3657 [3568, 3746]	$13509 [13225, 13793]
HET	*≥ 500*	$1260 [1238, 1282]	$10990 [10813, 11167]	$1358 [1335, 1381]	$11842 [11655, 12029]	$1375 [1346, 1404]	$11992 [11749, 12235]
(Male)	*200–499*	$1519 [1492, 1546]	$11160 [10980, 11340]	$1637 [1609, 1665]	$12025 [11837, 12213]	$1658 [1622, 1694]	$12177 [11931, 12423]
	< 200	$3235 [3167, 3303]	$11948 [11740, 12156]	$3485 [3413, 3557]	$12874 [12657, 13091]	$3529 [3443, 3615]	$13036 [12759, 13313]

MSM: Men who have sex with men; PWID: People who inject drugs; MWID: MSM who inject drugs; HET: Heterosexual; ART: Antiretroviral therapy

[†]Quarterly cost predictions derived from GLM model in Appendix Table 1. Cost predictions based on fitted values for each individual, averaged over person quarters in sample, holding all other covariates fixed at their observed values (including: age, year, race/ethnicity, viral suppression, and insurance status).

[‡]On ART defined as prescription of ART drugs in a given person-quarter