

Effect of Race and/or Ethnicity in Use of Antiretrovirals and Prophylaxis for Opportunistic Infection: A Review of the Literature

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SYNOPSIS

Objective. The authors performed a systematic and critical review of published studies investigating potential associations between race and/or ethnicity and use of HIV-related medications, including antiretroviral medications and medications used for prophylaxis of opportunistic infections.

Methods. The authors conducted a Web-based search of the University of California MEDLINE/HealthSTAR database for articles published from January 1, 1985, to October 31, 2001. References cited in articles were used to identify potential additional articles for this review. The authors reviewed articles published in peer-reviewed scientific journals that analyzed race/ethnicity as a predictor of antiretroviral or HIV-related prophylactic medication use.

Results. The authors identified 28 reports, including: (a) 26 studies published in 1991–2001 that addressed antiretroviral use, spanning data collection periods from 1984 to 1999; (b) 11 studies published in 1994–2001 that addressed prophylaxis for *Pneumocystis carinii* pneumonia (PCP), reporting on data collected from 1989 to 1998; and (c) three studies published from 1998 to 2001 that addressed prophylaxis for other opportunistic infections, reporting on data collected from 1993 to 1998. Among the studies that addressed antiretroviral use, 14 found a negative association between non-white race and at least one measure of antiretroviral use, three studies found a positive association, and 16 studies found no association; seven studies found mixed results across several measures of antiretroviral use. Only four of 11 studies found a negative association between race/ethnicity and PCP prophylaxis; the remainder found no association. Two out of three studies found a negative association between race/ethnicity and prophylaxis for other infections.

Conclusions. There is evidence of racial/ethnic disparities in utilization of antiretrovirals, which are known to be strongly associated with positive HIV health outcomes. It is now imperative for researchers and policy makers to better understand the causes of these disparities, evaluate programs that affect the delivery of HIV medications, and implement program and policy changes necessary to address the disparities.

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Many studies across a variety of disciplines have identified differences in health status, health care access, and health care utilization by race/ethnicity.¹⁻⁵ During the past few years, however, there has been an effort by public health organizations and government agencies to call increased national attention to the importance of addressing issues of racial/ethnic disparities in health in a systematic fashion. There is increased national attention explicitly focused on the goal of *eliminating*, not simply reducing, health disparities between segments of the population, including members of racial and ethnic groups.⁶ At the same time, there has also been a virtual revolution in the treatment options available to HIV-infected people in the United States. Given the substantial evidence that use of HIV-related medications strongly predicts health outcomes among both individuals and populations, it is important to understand what determines medication access. A good deal of research has focused on determining whether access to or utilization of HIV-related medications differs by race/ethnicity.

In an effort to gain a broader understanding of racial/ethnic differences in utilization of antiretroviral medications and prophylactic medications, we performed a systematic literature review. In this article, we first present a brief history of the introduction of antiretroviral medications and the evolution of HIV treatment guidelines. We then describe the results of our literature search and review of studies examining the possible link between race/ethnicity status and utilization of HIV medications.

Background

In 1987, zidovudine (AZT) became the first antiretroviral drug to be approved by the Food and Drug Administration (FDA) for the treatment of HIV disease, specifically for the treatment of advanced disease. Additional nucleoside analogs to receive FDA approval were didanosine in 1991, zalcitabine in 1992, stavudine in 1994, lamivudine in 1995, and abacavir in 1998. The first protease inhibitor to be approved was saquinavir, in 1995, with subsequent approvals for ritonavir and indinavir in 1996, nelfinavir in 1997, amprenavir in 1999, and a lopinavir/ritonavir combination in 2000. In the mid-1990s, non-nucleoside reverse transcriptase inhibitors (NNRTIs) received FDA approval, starting with nevirapine in 1996, followed by delavirdine in 1997, and efavirenz in 1998 (see FDA website for detailed information on approval dates).⁷

Early published HIV treatment guidelines⁸ recommended initiating therapy with zidovudine in symptomatic individuals with CD4 cell counts <500 cells/mm³ and asymptomatic individuals with CD4 counts

<200 cells/mm³. No antiretroviral therapy was recommended for asymptomatic individuals with CD4 cell counts in the 200–500 cells/mm³ range, and no antiretroviral therapy was suggested for asymptomatic individuals with CD4 cell counts >500 cells/mm³. Monotherapy with zidovudine or another nucleoside analog remained the recommended standard until 1996, when the International AIDS Society-USA Panel recommended combination nucleoside therapy, with the addition of protease inhibitors reserved for individuals at higher risk of progression.⁹ These were the first consensus panel guidelines to include HIV RNA (viral load) level as a criterion for initiation and modification of antiretroviral therapy. The Panel on Clinical Practices for the Treatment of HIV, convened in 1996 by the Department of Health and Human Services and the Henry J. Kaiser Family Foundation, published its antiretroviral guidelines for adults and adolescents in 1998.¹⁰ These guidelines are updated regularly, with the most recent information available electronically on the HIV/AIDS Treatment Information Service website.¹¹

In the late 1990s, clinical trials demonstrated the high efficacy of triple combination therapies containing a protease inhibitor or an NNRTI, now widely referred to as highly active antiretroviral therapy (HAART).¹²⁻¹⁵ Surveillance data showed declines in both AIDS incidence and mortality in the United States from 1996 to 1998,¹⁶ a trend that coincided with increased availability of HAART. Furthermore, several observational studies provided important data on the effectiveness of antiretrovirals, measured as a decrease in AIDS incidence and mortality.¹⁷⁻²⁰

In 2000, revised guidelines from the Department of Health and Human Services recommended treatment for all symptomatic individuals (regardless of CD4 cell count or viral load) and an option to treat asymptomatic individuals with <500 CD4 cells/mm³ or a viral load >10,000 copies/mL.²¹ Due to accumulating evidence about treatment side effects, guidelines published more recently have adopted a more conservative approach, with explicit recognition that “clinical benefit has been demonstrated in controlled trials only for patients with CD4+ T cells <200/mm³.²² These guidelines recommend initiating treatment only to symptomatic patients and to asymptomatic individuals with CD4 counts <200 cells/mm³. The guidelines state that “treatment should generally be offered, though controversy exists,” for asymptomatic individuals with CD4 cell counts in the 200–350 cells/mm³ range (regardless of viral load), and the guidelines urge a frank discussion of the lack of consensus among experts with respect to treatment for asymptomatic individu-

als with CD4 counts >350 cells/mm³ and viral loads $<30,000$ copies/mL.²³ Recommended treatment regimens include two specified nucleoside analogs plus either a protease inhibitor, a protease inhibitor combination, or an NNRTI.²³ The 2000 guidelines (and updates thereafter) were, however, released after completion of data collection for all the studies included in this review.

The earliest HIV-related treatment guidelines did not address antiretroviral therapy but rather prophylaxis against *Pneumocystis carinii* pneumonia (PCP).^{24,25} Guidelines for prophylaxis against PCP and other opportunistic infections have been updated regularly.²⁶⁻³⁰ The 1995 U.S. Public Health Service/Infectious Disease Society of America guidelines for the prevention of opportunistic infections recommended trimethoprim-sulfamethoxazole as the preferred agent for primary prophylaxis of PCP, and dapsone plus pyrimethamine plus leucovorin as a second-line regimen.³¹ At this point, other regimens including clindamycin plus primaquine, atovaquone, aerosolized pentamidine, and intravenous trimetrexate were to be considered only in "unusual situations in which the recommended agents cannot be administered."³¹ Rifabutin was recommended for primary prophylaxis of *Mycobacterium avium* complex (MAC).³¹ In 1997, aerosolized pentamidine was recommended as a second-line agent for PCP prophylaxis.²⁹ The strength of the recommendation for MAC prophylaxis was upgraded, and the first-line agent recommendation was switched to clarithromycin or azithromycin.²⁹ In 1999, dapsone without pyrimethamine and atovaquone was added to the list of potential second-line agents for PCP prophylaxis.³⁰ The most significant change in these guidelines, however, was the discussion about preliminary evidence that suggested providers might wish to discontinue PCP prophylaxis in patients who had achieved sustained (3–6 months) CD4 count elevations >200 in response to HAART.³²

METHODS

We performed a detailed Web-based search of scientific publications for articles entered in the MEDLINE/HealthSTAR database of the University of California from January 1, 1985, through October 1, 2001. We set parameters of "English language" and "human subjects" and used the following standard subject (MeSH) headings, either alone or in selected combination: acquired immunodeficiency syndrome, HIV, HIV infections, anti-HIV agents, health services, health services accessibility, health services needs and demands, and health services research. We then expanded the

search process by identifying potential additional articles from references cited in articles obtained through our initial search.

We selected references for inclusion in this review on the basis of their ability to meet all of the following criteria: (a) published in peer-reviewed scientific journals; (b) presented and analyzed original data from U.S. populations; (c) included quantitative measures of outpatient use of antiretroviral medications (i.e., among non-institutionalized patients) and/or outpatient use of medications for prophylaxis against opportunistic infections as outcome variables; and (d) analyzed race/ethnicity as a potential predictor of outpatient antiretroviral or prophylactic medication use, and explicitly presented results of those analyses. We excluded references that reported only adherence to medications because the study populations were limited to patients who received prescriptions.

We found 28 references that met the above criteria.³²⁻⁵⁹ These references were published from 1991 to 2001, and presented data that were collected from 1984 to 1999.

RESULTS

Antiretroviral use

The reported overall range of use of antiretroviral agents ranged from 43% to 95% (with most rates clustering in the 50% to 75% range) across studies examined in this analysis. These studies included different populations, different medications (e.g., all antiretrovirals vs. classes of antiretrovirals vs. single agents), different study periods, and different time frames for medication use (e.g., ever used vs. using currently vs. used within a specified recent period of time). As would be expected, substantial changes have been observed in the reported rates of use of specific classes of agents and specific single agents over time, as newer agents have become available and treatment guidelines have changed.

In a study of 305 people with AIDS in Boston in 1990–1991, 95% of participants reported ever receiving zidovudine.³³ This high rate of reported use is reflective of the sample selected; all participants had an advanced disease stage (i.e., an AIDS diagnosis), and all were recruited from clinical care settings.³³ In the AIDS Cost and Service Utilization Survey (ACSUS) conducted in 1991, which included a larger sample with a broader spectrum of disease, use of zidovudine in the prior three months ranged from 59% among asymptomatic individuals to 67% among individuals with AIDS.³⁵ In an early analysis of 1,415 men at all sites of the Multicenter AIDS Cohort Study (MACS) in

1990–1992, recent use of zidovudine was reported by 68% to 77% of the cohorts.³⁸ In contrast, analysis of data for 1991–1996 found that among 307 men at the Baltimore MACS site, only 43% reported at their most recent study visit having used antiretroviral medications in the prior six months.⁴³ Another study in Baltimore found among 838 people who presented to the Johns Hopkins AIDS Service in 1990–1992 that 58% of African Americans and 63% of whites reported current antiretroviral use.³⁹

Somewhat later, in 1993–1995, 70% of 863 HIV-positive women enrolled in the HIV Epidemiology Research Study (HERS) reported ever having used antiretrovirals, but only 43% reported current use.⁴¹ HERS findings offered new insights because, unlike participants in the studies described above, HERS participants were not recruited exclusively from medical care settings. In 1996, a study of 224 people receiving HIV medical care in St. Louis found that 98% of clients reported having heard of AZT and 83% of these reported having taken the drug.⁴⁵ Among 1,034 adults recruited from a Los Angeles-area AIDS service organization, 66% reported taking a protease inhibitor in November 1996.⁴⁶ Among injection drug users with AIDS who were enrolled in New Jersey Medicaid in 1988–1996, 74% had a prescription filled for at least one antiretroviral medication.⁴² This database was later examined for use of newer antiretrovirals; among 2,089 adults with AIDS who received New Jersey Medicaid benefits in 1996–1998, 65% had received at least one prescription for a protease inhibitor or NNRTI.⁵⁵

The HIV Cost and Services Utilization Study (HCSUS) surveys a nationally representative probability sample of HIV-infected adults receiving regular medical care in the contiguous United States. In the HCSUS cohort, the cumulative proportion of patients who reported having ever received HAART increased from 37% in late 1996 to 71% in early 1998. Nevertheless, only 53% were “currently” using HAART at the time of this second follow-up interview.⁵⁴ In comparison, by 1998 fully 87% of the MACS participants reported having ever used antiretroviral therapy, 81% reported “current” use of any antiretrovirals, and only 63% reported “current” use of potent antiretroviral therapy (HAART).⁵² Among 764 Johns Hopkins AIDS Service patients (interviewed in 1998–1999) with a CD4 nadir <500 cells/mm³ and peak HIV RNA >30,000 copies/ml, 93% reported having ever used antiretrovirals, 76% reported having ever used HAART, and 48% reported current use of HAART.⁵⁶

Three additional studies provide information about unique subpopulations of HIV-infected people. Among 2,607 HIV-infected women who were receiving New

York Medicaid benefits and who had delivered a baby in 1993–1996, the proportion of women prescribed antiretrovirals during the second or third trimester of pregnancy increased from 12% in 1993 to 51% in 1996.⁴⁴ In a study examining the effect of housing status on health care utilization among New York Medicaid recipients in 1996–1997, 68% of homeless people reported current use of any antiretrovirals, compared with 78% of people in stable housing situations.⁵¹ Among 327 HIV-infected adolescents ages 12–18 years enrolled in the Reaching for Excellence in Adolescent Care and Health (REACH) study in 1996–1999, 25% had been prescribed HAART by the time of study enrollment.⁵⁷ Among those not on HAART by enrollment, 53% were prescribed HAART during their first two years in the study.⁵⁷

Associations between race/ethnicity and use of antiretroviral medications

Overall, 26 studies evaluated the effect of race and/or ethnicity on the use of antiretroviral medications.^{32–57} (See Table 1.) Overall, 15 studies had data collection periods that included 1996 or later,^{43–57} i.e., after FDA approval for use of the first protease inhibitor in late 1995. Ten of the these reports specifically measured the use of either protease inhibitors, NNRTIs, or HAART.^{45–48,50,53–57}

Overall, 14 studies found a negative association between non-white race and antiretroviral use in one or more multivariate analyses.^{32,36–39,45–48,52–55} Among these 14, eight studies found only a negative association across all outcomes assessed,^{32,36–39,45,55,56} and six studies found mixed results depending on the specific outcome measure.^{37,45,48,52–54} Three studies found a positive association with at least one antiretroviral use measure,^{40,44,48} two of which found either no association⁴⁴ or a negative association⁴⁸ across a different measure of antiretroviral use. Sixteen studies found no association between race/ethnicity and at least one measure of antiretroviral use,^{33–35,37,41–45,49–54,57} however, five of these also found a negative association on at least one antiretroviral use measure,^{37,45,52–54} and one also found a positive association.⁴⁴ In four of these studies an association between race/ethnicity and antiretroviral use explicitly noted in bivariate analyses lost statistical significance after adjustment for other covariates.^{49,50,53,54}

Negative association with use of antiretrovirals (n = 14 studies). In all 14 of these studies, people whose race/ethnicity was other than white had a lower likelihood than white study participants of receipt of antiretrovirals after adjustment for potential confounders (such as

Table 1. Summary of findings on race/ethnicity and antiretroviral (ARV) use

First author, year of publication (study period)	Design overview	Study population	Total N ^a (analysis N)	Race/ethnicity		ARV outcome definition AZT = zidovudine ddI = didanosine ddC = zalcitabine 3TC = lamivudine d4T = stavudine NRTI = nucleosides PI = protease inhibitors NNRTI=nonnucleosides HAART=highly active antiretroviral therapy and ARV use
				% white (W)	% black/African American (B) % Hispanic/Latino (H) % other (O)	
Stein 1991 ³² (1988–1989)	Cross-sectional survey	• RWJF AHSP^b • 9 cities • recruitment from hospital clinics and community-based organizations	880 (880)	68% W, 32% O		ever offered AZT ↓ ^c
Weissman 1994 ³³ (1990–1991)	Cross-sectional survey	• Boston Health Study • 3 clinical sites in Boston area	305 (249)	69% W, 31% O		starting AZT “late” or “never” ↔ ^d
Katz 1995 ³⁴ (1991)	Cross-sectional analysis of survey data	• San Francisco City Clinic Cohort • sexually transmitted disease clinic	178 (142)	94% W, 6% O		ever used AZT ↔
Hellinger 1993 ³⁵ (1991)	Cross-sectional analysis of survey data	• ACSUS^e • 10 cities • 26 clinical sites	1,949 (≤1,949)	42% W, 30% B, 28% O		used AZT in past 3 months ↔
McLaughlin 1999 ³⁶ (1989–1991)	Longitudinal analysis of claims data	Linked New Jersey AIDS Registry-Medicaid database	366 (≤366)	89% nonwhite		≥ claim for AZT during study period ↓
Crystal 1995 ³⁷ (1987–1992)	Longitudinal analysis of claims data	New Jersey Medicaid HIV/AIDS waiver program	1,306 (478) (828)	40% W, 4% B, 16% H, 40% O		ever used AZT cohort 1 ↓ ever used AZT cohort 2 ↔

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Table 1 (continued). Summary of findings on race/ethnicity and antiretroviral (ARV) use

First author, year of publication (study period)	Design overview	Study population	Total N ^a (analysis N)	Race/ethnicity % white (W) % black/African American (B) % Hispanic/Latino (H) % other (O)	ARV outcome definition AZT = zidovudine ddl = didanosine ddC = zalcitabine 3TC = lamivudine d4T = stavudine NRTI = nucleosides PI = protease inhibitors NNRTI=nonnucleosides HAART=highly active antiretroviral therapy and ARV use	
Graham 1994 ³⁸ (1990–1992)	Longitudinal analysis of survey data	MACS ⁱ	1,415 (1,415)	78% W, 15% B, 6% H	use of AZT, ddl, ddC during the study period	↓
Moore 1994 ³⁹ (1990–1992)	Cross-sectional analysis of survey data	Johns Hopkins Hospital AIDS Service	838 (586)	21% W, 78% B, <1% O	use of AZT, ddl or ddC at study enrollment	↓
Smith 1999 ⁴⁰ (1991–1992)	Longitudinal analysis of survey data	ACSUS	1,586 (1,586)	42% W, 29% B, 27% H	use of AZT, ddl or ddC during study period	↑ ^g
Solomon 1998 ⁴¹ (1993–1995)	Cross-sectional analysis of survey data	HERS ^h	863 (≤863)	23% W, 57% B, 16% H, 4% O	• ever • current ARV use	↔ ↔
Sambamoorthi 2000 ⁴¹ (1988–1995)	Longitudinal analysis of claims data	Linked New Jersey AIDS Registry-Medicaid database	2,600 (≤2,600)	20% W, 63% B, 17% H	≥ 1 claim for AZT, ddl, ddC, 3TC, or d4T	↔
Kass 1999 ⁴³ (1991–1996)	Cross-sectional analysis of survey data	MACS	307 (≤307)	78% W, 22% B	any ARV use during study period	↔

Table 1 (continued). Summary of findings on race/ethnicity and antiretroviral (ARV) use

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				% white (W) % black/African American (B) % Hispanic/Latino (H) % other (O)		
Turner 1999 ⁴⁴ (1993–1996)	Longitudinal analysis of claims data	New York State Medicaid database	2,607 (821 period 1) (504 period 2) (1,282 period 3)	10% W, 45% B, 45% L; period 1 13% W, 47% B, 40% L; period 2 34% W, 46% B, 20% H; period 3	ARV use in 2 nd or 3 rd trimester of pregnancy in 3 time periods ↔ period 1 ↔ period 2 ↑ period 3	
Jeffe 1998 ⁴⁵ (1996)	Cross- sectional survey	clinical sites in St. Louis area	224 (156–157 ever heard) (152 ever taken) (≤167 currently taken)	37% W, 63% B	• ever heard of, • ever taken, or • currently taking: AZT, ddl/ddC, d4T, 3TC, PI or NNRTI ↓ ever taken AZT ↔ currently taking	
Bing 1999 ⁴⁶ (1996)	Cross- sectional survey	HIV/AIDS community services organization in Los Angeles area	1,034 (881)	55% W, 14% B, 26% H, 5% O	current PI use ↓ current (non-English speakers)	
Andersen 2000 ⁴⁷ (1996)	Longitudinal analysis of survey data	HCSUS	2,864 (2,776)	49% W, 33% B, 14% H, 3% O	any HAART by 12/96 ↓	
Anderson 2000 ⁴⁸ (1993–1997)	Longitudinal analysis of claims data	Florida Medicaid claims database	24,646 (24,646)	42 % W, 49% B, 9% H	• any claim for 2 NRTI • any claim for a PI + 2 NRTI ↑ 2 NRTI ↓ PI + 2 NRTI	
Turner 2000 ⁴⁹ (1993–1997)	Longitudinal analysis of claims data	New York State Medicaid database	2,648 (≤2,648)	25% W, 43% B, 32% H	≥ 1 claim for any ARV during study period ↔	

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Table 1 (continued). Summary of findings on race/ethnicity and antiretroviral (ARV) use

First author, year of publication (study period)	Design overview	Study population	Total N ^a (analysis N)	Race/ethnicity % white (W) % black/African American (B) % Hispanic/Latino (H) % other (O)	ARV outcome definition AZT = zidovudine ddI = didanosine ddC = zalcitabine 3TC = lamivudine d4T = stavudine NRTI = nucleosides PI = protease inhibitors NNRTI = nonnucleosides HAART = highly active antiretroviral therapy and ARV use	
					ever prescribed PI	↔
Sorvillo 1999 ⁵⁰ (1996–1997)	Cross-sectional survey	Los Angeles County AIDS Surveillance Registry	339 (339)	27% W, 19% B, 47% H, 7% O	↔	↔
Smith 2000 ⁵¹ (1996–1997)	Cross-sectional analysis of survey data	• HIV/AIDS Client Cohort Study • New York State Medicaid recipients	1,445 (940)	17% W, 52% B, 29% H, 2% O	any ARV	↔
Jacobson 2001 ⁵² (1984–1998)	Longitudinal analysis of survey data	MACS	673 (≤388; CD4 < 500) (≤143; CD4 ≥ 500)	82% W, 11% B, 37% H, 1% O	• any ARV use if CD4 < 500 • any ARV use if CD4 ≥ 500	↔ if CD4 < 500 ↓ if CD4 ≥ 500
Shapiro 1999 ⁵³ (1996–1998)	Longitudinal analysis of survey data	HCSUS ⁱ	2864 (≤2,611)	49% W, 33% B, 15% H, 3% O	• ever PI or NNRTI by 12/96 • ever ARV	↓ ever PI or NNRTI ↔ ever ARV
Cunningham 2000 ⁵⁴ (1996–1998)	Longitudinal analysis of survey data	HCSUS	2,267 (2,263)	51% W, 31% B, 15% H, 3% O	current HAART	↓ in 2 models (fewer covariates) ↔ in 1 model (more covariates)
Sambamoorthi 2001 ⁵⁵ (1996–1998)	Longitudinal analysis of claims data	Linked New Jersey AIDS Registry-Medicaid databases	2,089 (≤2,089)	24 % W, 57% B, 19% H	any use of PI or NNRTI	↓

Table 1 (continued). Summary of findings on race/ethnicity and antiretroviral (ARV) use

First author, year of publication (study period)	Design overview	Study population	Total N ^a (analysis N)	Race/ethnicity		ARV outcome definition AZT = zidovudine ddl = didanosine ddC = zalcitabine 3TC = lamivudine d4T = stavudine NRTI = nucleosides PI = protease inhibitors NNRTI = nonnucleosides HAART = highly active antiretroviral therapy and ARV use
				% white (W)	% black/African American (B) % Hispanic/Latino (H) % other (O)	
Lucas 2001 ⁵⁶ (1998–1999)	Cross-sectional analysis	Johns Hopkins AIDS Service	764 (764)	80% B		ever used HAART ↓
Schwarz 2001 ⁵⁷ (1996–1999)	Longitudinal analysis of survey data and chart review	REACH ⁱ	327 (219)	18% W, 74 % B, 17% O		prescribed HAART ↔

^a Total N = total study sample size; analysis N = sample size for specific analysis presented in table. In instances where the authors did not specify the exact number of participants we used "≤" to denote the maximum sample size possible for that analysis.

ⁱRWJF AHSP = Robert Wood Johnson Foundation AIDS Health Services Program

↙ indicates nonwhite race/ethnicity is independently associated with a lower likelihood of taking the medication

↔ indicates no association between race/ethnicity and taking the medication

^{*}ACSUS = AIDS Cost and Services Utilization Study

ⁱMACS = Multicenter AIDS Cohort Study

^{§f} indicates nonwhite race/ethnicity is independently associated with a higher likelihood of taking the medication

^hHERS = HIV Epidemiologic Research Study

ⁱHCSUS = HIV Cost and Services Utilization Study

insurance status, income, and disease stage) in multivariate models. The earliest study was a cross-sectional survey of 880 adults with AIDS or symptomatic HIV recruited from community-based organizations and public hospital clinics across nine cities in the United States.²⁹ In a logistic regression model that adjusted for level of illness, injection drug use, gender, and insurance status, whites were more likely to report being offered AZT than non-whites (odds ratio [OR] = 1.73; 95% confidence interval [CI] 1.11, 2.69).³² McLaughlin et al. performed an analysis of data on 366 patients (age >12 years) with an index AIDS diagnosis in 1989–1991 (limited to AIDS patients who had continuous enrollment in New Jersey Medicaid before the AIDS diagnosis and who had not received any antiretrovirals or PCP prophylaxis during the year prior to an AIDS diagnosis).³⁷ After adjustment for age, injection drug use, gender, primary source of care, and year of AIDS diagnosis, non-whites were less likely to have had any Medicaid claim for AZT following the AIDS diagnosis than whites (OR = 0.76; 95% CI 0.5, 0.9).³⁷ Crystal et al. found that among 478 adults with AIDS or symptomatic HIV enrolled in the New Jersey Medicaid waiver program in 1987–1988, African Americans were almost half as likely (OR = 0.46; 95% CI 0.31, 0.69) to have ever used zidovudine (measured via claims data) as whites in analyses controlled for age, gender, injection drug use, and health status.³⁷ This racial disparity in zidovudine use was not statistically significant, however, among 828 Medicaid recipients who enrolled slightly later, in 1989–1990 (OR = 0.79; 95% CI 0.57, 1.08).³⁷ This suggests the possibility that racial disparities were eliminated quickly as zidovudine became a more widely accepted treatment. Results from other studies, however, suggest that non-whites remain less likely than whites to use zidovudine and other antiretrovirals. For example, data from 586 HIV-positive adults with a CD4 count ≤ 500 cells/mm³ from Johns Hopkins for 1990–1992 showed that African Americans were less likely than whites to be on antiretrovirals at presentation to the clinic (OR = 0.59; 95% CI 0.38, 0.93) after data were adjusted for age, gender, income, insurance, education, injection drug use, residence in East Baltimore, and duration of HIV infection.³⁹ During a similar time period, among 1,415 HIV-positive men without AIDS in the MACS cohort, whites were more likely to use antiretrovirals than non-whites (OR = 1.58; 95% CI 1.12, 2.07) after data were adjusted for age, income, education, CD4 cell count, symptoms, insurance status, hospitalization, and outpatient service use.³⁸ Mixed findings were noted in subsequent analyses of data on 673 men seen for a MACS study visit in 1998.⁵² Racial disparities appeared

to persist among men with a CD4 count >500 cells/mm³, with African American men being more likely to have never used antiretrovirals than white or Hispanic men (OR = 3.2; 95% CI given graphically from >1 to about 12),⁵² after adjustment for CD4 cell count, and number of outpatient visits. No association between race and “never use” was found when analyses were limited to men with a CD4 cell count of <500 cells/mm³.⁵² Among 152 HIV-infected patients with a CD4 count <500 cells/mm³ receiving care at a St. Louis clinic, African American patients were more likely to report having never taken AZT than white patients (OR = 3.139; 95% CI 1.084, 9.094), after adjustment for CD4 count.⁴⁵

Racial/ethnic disparities in use of newer antiretroviral medication regimens (e.g., protease inhibitors and NNRTIs) have also been documented.^{45–48,53–56} For example, Jeffe et al. found that African Americans were more likely to never have heard of protease inhibitors (OR = 7.62; 95% CI 3.02, 19.21) or NNRTIs (OR = 4.91; 95% CI 1.74, 13.85).⁴⁵ In a 1996 study conducted in the Los Angeles area among 881 HIV-positive clients of a large HIV/AIDS community services organization, non-English speakers had a greater likelihood of not taking a protease inhibitor (OR = 2.46; 95% CI 1.30, 4.64) than English speakers.⁴⁶ Data on 2,776 HIV-positive adults enrolled in the HCSUS showed that African Americans were significantly less likely to have received any HAART by December 1996 (OR = 0.44, $p \leq 0.001$), even after adjustment for predisposing variables, need variables, and enabling variables.⁴⁷ Another HCSUS publication reported antiretroviral use by December 1996 in a slightly different manner, specifically as lack of receipt of any protease inhibitor or NNRTI⁵³ rather than receipt of HAART.⁴⁷ Blacks (OR = 2.16; 95% CI 1.54, 3.05) and Latinos (OR = 1.48; 95% CI 1.10, 1.99) were more likely than whites to have not received protease inhibitors or NNRTIs after adjustment for age, gender, CD4 cell count, HIV exposure category, insurance status, education, and geographic region.⁵³ In a subsequent analysis covering HCSUS data for 1996–1998, black race was independently associated with lower use of HAART (OR = 0.68; 95% CI 0.43, 0.95) in models that included CD4 count and gender by exposure (e.g., female injection drug user); however, race lost statistical significance in a model that also included insurance status, education, and geographic region (OR = 0.74; 95% CI 0.51, 1.07).⁵⁴

The study with the largest sample size (using claims data for 24,646 HIV-positive adults enrolled in Florida Medicaid in 1993–1997) found divergent results depending on the outcome evaluated. After adjustment

for age, gender, income, health status measures, and other demographics in a marginal effects probit model, blacks had a 0.04 higher probability of receiving a regimen comprised of two nucleosides than whites ($p \leq 0.01$).⁴⁸ With respect to newer regimens containing a protease inhibitor plus two nucleosides, the reverse association was observed; blacks had a 0.01 ($p \leq 0.01$) lower probability of receiving this regimen.⁴⁸ Among 2,089 adults included in an analysis of linked New Jersey HIV/AIDS registry and New Jersey Medicaid data, the difference in use of protease inhibitors or NNRTIs narrowed from a 23.7 percentage point difference between African Americans and whites in 1996 to a 7.2 percentage point difference in 1998.⁵⁵ The difference between Hispanics and whites narrowed from 17.1 percentage points in 1996 to 10.1 in 1998.⁵⁵ In a multivariate model inclusive of all years (1996, 1997, 1998), both African Americans (OR = 0.58; 95% CI 0.45, 0.75) and Hispanics (OR = 0.65; 95% CI 0.47, 0.88) were less likely to have received a protease inhibitor or NNRTI than whites, after adjustment for age at diagnosis, gender, exposure category, year of diagnosis, insurance status, vital status, and county of residence.⁵⁵ In a study of 764 HIV-infected patients interviewed at the Johns Hopkins AIDS Service from late 1998 through late 1999, blacks were found to have a higher likelihood than whites of never having used HAART (OR = 1.8; 95% CI 1.1, 3.1) after adjustment for gender, CD4 cell count nadir, peak HIV RNA, prior opportunistic infection, and heroin/cocaine use.⁵⁶

Positive association with use of antiretrovirals ($n = 3$ studies). In an analysis of ACSUS data for 1991–1992, African Americans (OR = 1.30; 95% CI 1.04, 1.62) and Hispanics (OR = 1.38; 95% CI 1.11, 1.72) were more likely to be using antiretrovirals than whites, after adjustment for age, gender, injection drug use, insurance status, income, health service use measures, health status measures, and social support measures.⁴⁰ In an analysis of New York Medicaid claims from 1,282 women who delivered a baby in 1994–1996, and after publication of clinical trial results suggesting zidovudine reduces the risk of vertical transmission, Latinas were more likely (OR = 2.59; 95% CI 1.76, 3.80) to have been prescribed zidovudine during their second or third trimester of pregnancy.⁴¹ As mentioned above, Anderson et al. found blacks had a 0.04 higher probability of receiving a regimen comprised of 2 nucleosides than whites.⁴⁵

No association with use of antiretrovirals ($n = 16$). Overall, 16 studies did not find an association between race/ethnicity and at least one measure of antiretroviral

use.^{33–35,37,41–45,49–54,57} Among them, seven found a statistically significant association between race/ethnicity and one of the study's measures of antiretroviral use,^{37,44,45,52–54} and therefore were discussed in above sections.

Ten studies failed to find a significant association across any antiretroviral use outcome assessed by the authors.^{33–35,41–44,49–51,57} Among these ten, five reported on sample sizes of <350.^{30,31,40,47,54} Specifically, Weissman et al. measured AZT use among 249 patients with AIDS from the Boston Health Study;³³ Katz et al. evaluated use of AZT among 142 HIV-infected homosexual men with a CD4 cell count <500 cells/mm³ in San Francisco;³⁴ Kass et al. evaluated use of any antiretrovirals among 307 men enrolled in the Baltimore site of the MACS;⁴⁴ Sorvillo et al. evaluated protease inhibitor use among 339 people with AIDS in Los Angeles County;⁵⁰ and Schwarz et al. evaluated subsequent HAART use among 219 HIV-infected adolescents who were HAART-naïve at study enrollment.⁵⁷

The remaining five studies were not substantially different from the studies which found a negative association in terms of sample size, population selection, or overall methodology.^{35,41,42,49,51} Specifically, Hellinger et al. evaluated recent AZT use among 1,949 HIV-infected adults and adolescents in the ACSUS study;³⁵ Solomon et al. evaluated any antiretroviral use among 863 HIV-infected women enrolled in the HERS;⁴¹ Sambamoorthi et al. assessed prescription claims data (e.g. at least one antiretroviral prescription) among 2,600 injection drug users with AIDS captured in a merged New Jersey Medicaid–AIDS registry database;⁴² Turner et al. assessed prescription claims data for antiretroviral use during the first postpartum year among 2,648 HIV-infected postpartum women enrolled in New York State Medicaid;⁴⁹ and Smith et al. assessed antiretroviral use during the previous three months among 1,445 HIV-infected beneficiaries of New York Medicaid in 1996 and 1997.⁵¹

Associations between race and/or ethnicity and use of medications for PCP prophylaxis

Overall, 11 studies evaluated potential associations between race/ethnicity and use of medications for PCP prophylaxis (Table 2).^{33,36,38–41,45,51,53,58,59} Four studies found that subjects whose race/ethnicity was not white were less likely to use PCP prophylaxis,^{36,39,41,53} of which one study found a negative association between non-white race/ethnicity and one measure of PCP prophylaxis but no association for another measure.⁴¹ None of the studies found non-whites more likely to use PCP prophylaxis. Eight studies did not find any association,^{33,38,40,41,45,51,58,59} one of which (as mentioned

Table 2. Summary of findings on race/ethnicity and use of prophylaxis for *Pneumocystis carinii* pneumonia (PCP)

First author, year of publication (study period)	Design overview	Study population	N ^a (analysis N)	Race/ethnicity: % white (W) % black/African American (B) % Hispanic/Latino (H) % other (O)	PCP outcome definition PT = pentamidine TMP-S = trimethoprim-sulfamethoxazole DP = dapsone PYR = pyrimethamine ATQ = atovaquone	Association between non-white race/ethnicity and PCP prophylaxis
Katz 1995 ³⁴ (1991)	Cross-sectional analysis of survey data	- San Francisco City Clinic Cohort - sexually transmitted disease clinic	178 (60)	94% W, 6% O	ever PCP prophylaxis	↔ ^b
McLaughlin 1999 ³⁶ (1989–1991)	Longitudinal analysis of claims data	Linked New Jersey AIDS Registry-Medicaid database	366 (366)	89% nonwhite	use of PT, TMP-S, or DP during study period	↓
Graham 1994 ³⁸ (1990–1992)	Longitudinal analysis of survey data	MACS ^c	1,415 (1,415)	78% W, 15% B, 6% H	use of PT, TMP-S, or DP during study period	↔
Moore 1994 ³⁹ (1990–1992)	Cross-sectional analysis of survey data	Johns Hopkins Hospital AIDS Service	838 (283)	23% W, 75% B, 1% O	use of PT, TMP-S, or DP at study enrollment	↓ ^d
Smith 1999 ⁴⁰ (1991–1992)	Longitudinal analysis of survey data	ACSUS ^e	1,586 (1,586)	42% W, 29% B, 27% H	use of PT, TMP-S, DP or PYR during study period	↔
Solomon 1998 ⁴¹ (1993–1995)	Cross-sectional analysis of survey data	HERS ^f	863 (863)	23% W, 57% B, 16% H, 4% O	- ever use - current use of PCP prophylaxis	↓ ↔
Jeffe 1998 ⁴⁵ (1996)	Cross-sectional survey	clinical sites in St. Louis area	224 (224) (90) (87)	37% W, 63% B	- ever heard of, - ever taken, or - currently taking TMP, PT, DP	↔
Sackoff 1998 ⁴⁸ (1995–1997)	Longitudinal analysis of medical records data	New York City Adult/Adolescent Spectrum of Disease Study medical records review	149 ^g (149)	9% W, 48% B, 43% H ^g	use of PT, TMP-S, DP, PYR, or ATQ during the study period	↔

Table 2 (continued). Summary of findings on race/ethnicity and use of prophylaxis for *pneumocystis carinii* Pneumonia (PCP)

First author, year of publication (study period)	Design overview	Study population	N ^a (analysis N)	Race/ethnicity: % white (W) % black/African American (B) % Hispanic/Latino (H) % other (O)	PCP outcome definition	
					PT = pentamidine TMP-S = trimethoprim-sulfamethoxazole DP = dapsone PYR = pyrimethamine ATQ = atovaquone	Association between non-white race/ethnicity and PCP prophylaxis
Smith 2000 ⁵¹ (1996–1997)	Cross-sectional analysis of survey data	- HIV/AIDS Client Cohort Study - New York State Medicaid recipients	1,445 (940)	17% W, 52% B, 29% H, 2% O	use of PT, TMP-S, DP, ATQ, or other PCP prophylaxis during study period	↔
Murphy 2001 ⁵⁹ (1995–1998)	Cross-sectional analyses of enrollment study visits	Viral Activation Transfusion Study	531 (≤327)	52% W, 48% O	Use of PT, TMP-S, DP, ATQ, or clindamycin + primaquine during 30 days before study enrollment	↔
Shapiro 1999 ⁵³ (1996–1998)	Longitudinal analysis of survey data	HCSUS ^h	2,864 (≤1,515)	49% W, 33% B, 15% H, 3% O	TMP, DP, PT, ATQ, clindamycin plus primaquine within 6 months	↓

^aTotal N = total study sample size; analysis N = sample size for specific analysis presented in table. In instances where the authors did not specify the exact number of participants we used "≤" to denote the maximum sample size possible for that analysis.

^b↔ indicates no association between race/ethnicity and taking the medication

^cMACS = Multicenter AIDS Cohort Study

^d↓ indicates nonwhite race/ethnicity is independently associated with a lower likelihood of taking the medication

^eACSUS = AIDS Cost and Services Utilization Study

^fHERS = HIV Epidemiologic Research Study

^gThe cohort for PCP prophylaxis was different than the cohort for prophylaxis for other opportunistic infections (Table 3) in the Sackoff study³⁹

^hHCSUS = HIV Cost and Services Utilization Study

above) also found a negative association with one of two measures of PCP use.⁴¹

Negative association with PCP prophylaxis (n = 4 studies). Among 366 patients enrolled in New York Medicaid in 1989–1991, claims data revealed non-whites were less likely to have received PCP prophylaxis (OR = 0.57; 95% CI 0.4, 0.7) compared with whites, after adjustment for age, gender, injection drug use, year of AIDS diagnosis, and primary source of care.³⁵ Among 283 HIV-infected patients with CD4 counts ≤ 200 cells/mm³ presenting to the Johns Hopkins AIDS Service in 1990–1992, blacks were less likely to have used PCP prophylaxis at study entry compared with whites (OR = 0.27; 95% CI 0.13, 0.56) after adjustment for age, gender, injection drug use, insurance status, income, education, residence in East Baltimore, and duration of HIV infection.³⁹ Solomon et al. found that African Americans were less likely to have ever received PCP prophylaxis (OR = 0.34; 95% CI 0.13, 0.85) but just as likely to be currently receiving it (OR approximately 0.5, 95% CI approximately 0.2, 0.9, given graphically) among 863 HIV-infected women enrolled in HERS.⁴¹ In this study, Hispanic women were also less likely to have ever received PCP prophylaxis than whites (OR approximately 0.3; 95% CI approximately 0.1, 0.9, given graphically).⁴¹ Among approximately 1,500 HIV-infected patients with a CD4 count < 200 cells/mm³ in the HCSUS, blacks were more likely to report not having received PCP prophylaxis in the past six months (OR = 1.54; 95% CI 1.03, 2.29).⁵³

No association with PCP prophylaxis (n = 8 studies). Among these eight studies, only two have not been described in prior sections of this review.^{58,59} Sackoff abstracted medical records for 1995–1997 drawn from patients enrolled in the Adult/Adolescent Spectrum of Disease Study (ASD) to identify factors associated with prophylaxis for PCP ($N = 149$), *Mycobacterium avium* complex ($N = 130$), and *Toxoplasmosis gondii* ($N = 138$).⁵⁸ Murphy et al. measured prophylaxis use in the 30 days prior to enrollment among 327 patients eligible for primary or secondary PCP prophylaxis who enrolled in the Viral Activation Transfusion Study from 1995 to 1998.⁵⁹

Negative association with prophylaxis for other opportunistic infections (n = 3). Three studies also evaluated use of medications for prophylaxis of opportunistic infections other than PCP (Table 3).^{41,58,59} Two found non-whites were less likely to be using indicated medications,^{41,58} and one found no association.⁵⁹ Specifically, Solomon et al. found that African American women were less likely to report use of prophylaxis for non-PCP oppor-

tunistic infections than white women (OR = 0.50; 95% CI 0.30, 0.83), after adjustment for injection drug use, study site, and CD4 count.⁴¹ Similarly, Sackoff et al. found that prescription for MAC prophylaxis was less likely in blacks compared with whites (OR = 0.08; 95% CI 0.01, 0.52), after controlling for number of outpatient visits, clinic site, and eligible intervals for study observation.⁵⁸ Murphy et al. did not find an association between race/ethnicity and MAC prophylaxis.⁵⁹

DISCUSSION

African Americans and Latinos remain disproportionately affected by the HIV epidemic.⁶⁰ People of color have also historically had limited access to a variety of health care services,^{61,62} including HIV-related medical services. For example, previous studies among people with HIV infection have found that non-whites are less likely to have outpatient visits and more likely to have emergency room visits than whites.^{43,63,64} Among people with AIDS, non-whites are also more likely to have no insurance or public insurance.⁶⁵

The studies we identified in our literature review cover a 16-year period of data collection (1984–1999), during which HIV-related treatment guidelines were in rapid evolution. Furthermore, these studies used a variety of data sources (survey, claims data, chart review), measured race/ethnicity in a variety of ways (multiple categories vs. white/non-white), measured the outcomes in a variety of ways (both time period of medication use and coding of medications), and analyzed the data by a variety of methods (cross-sectional, longitudinal). These differences make it difficult to readily draw a simple conclusion from comparing the studies; nevertheless, careful evaluation of this body of literature as a whole does provide a different kind of insight than can be gleaned from any individual study.

A preliminary listing of articles measuring antiretroviral use reveals that 14 articles found a negative association between non-white race/ethnicity and antiretroviral use in at least one multivariate model,^{31,34–37,45–48,52–56} three articles found a positive association in at least one multivariate model,^{40,44,48} and 10 articles found no association in either bivariate or multivariate analyses for all the antiretroviral use outcomes assessed by the authors.^{33–35,41–43,49–51,57} A more detailed look at these studies yields patterns that help place these results in perspective. For example, among the 10 articles that failed to find any association across all outcomes examined, seven relied on cross-sectional survey data,^{33–35,41,43,50,51} and four had sample sizes less than 350.^{33,34,43,50} These two study characteristics may have limited the ability of the

Table 3. Summary of findings on race/ethnicity and use of prophylaxis for opportunistic infections (OI) other than *Pneumocystis carinii* pneumonia

First author, year of publication (study period)	Design overview	Study population	N ^a (analysis N)	Race/ethnicity: % white (W) % black/African American (B) % Hispanic/Latino (H) % other (O)		OI outcome definition	Association between non-white race/ethnicity and OI prophylaxis
Solomon 1998 ⁴¹ (1993–1995)	Cross-sectional analysis of survey data	HERS ^b	863 (≤863)	23% W, 57% B, 16% H, 4% O		OI prophylaxis	↓ ^c ever OI prophylaxis
Sackoff 1998 ⁵⁸ (1995–1997)	Longitudinal analysis of medical records data	New York City Adult/Adolescent Spectrum of Disease Study medical records review	130 ^d (≤130)	9% W, 55% B, 36% H ^d		Use of rifabutin, clarithromycin or azithromycin for MAC ^d prophylaxis	↓
Murphy 2001 ⁵⁹ (1995–1998)	Cross-sectional analyses of enrollment study visits	Viral Activation Transfusion Study	531 (≤415)	52% W, 48% O		Use clarithromycin, azithromycin, rifabutin, ethambutol, ciprofloxacin, clofazimine, rifampin, amikacin during 30 days before study enrollment	↔

^aTotal N = total study sample size; analysis N = sample size for specific analysis presented in table. In instances where the authors did not specify the exact number of participants we used "≤" to denote the maximum sample size possible for that analysis.

^bHERS = HIV Epidemiologic Research Study

^c↓ indicates nonwhite race/ethnicity is independently associated with a lower likelihood of taking the medication

^dThe cohort for OI prophylaxis was different from the cohort for PCP prophylaxis (Table 2) in the Sackoff study.³⁶

^eMAC = *Mycobacterium avium* complex

^fHCSUS = HIV Cost and Services Utilization Study

investigators to detect an effect, had such an effect truly existed. The possibility of this limitation is further supported by the fact that seven^{33–35,41,43,50,51} out of the 12 studies that performed cross-sectional analyses^{31–35,39,41,43,45,46,50,51,57} and five^{33,34,43,50,57} out of seven studies with analytic sample sizes less than 350^{33,34,43,45,52,57} found no association. In contrast, only three^{42,49,57} out of 14 studies that performed longitudinal analyses,^{36–38,40,42,44,47–49,52–55,57} and five^{35,41,42,49,51} out of 20 studies with analytic sample sizes greater than 350^{32,35–42,43,46–49,51–57} failed to find any association between race/ethnicity and antiretroviral use.

Among those studies that did identify an association between race/ethnicity and antiretroviral use, the overwhelming majority, 13 of 16, found a negative association,^{32,36–39,45–47,52–56} two found a positive association,^{40,44} and one found both negative and positive associations.⁴⁸ Given the general trend in ethnic/racial disparities across a variety of illnesses, the finding of greater use of antiretrovirals among people of non-white race/ethnicity is an unexpected one. In one of the studies, African Americans were more likely to be excluded from the analyses than were whites because of missing data; therefore, the authors concede that it is difficult to interpret this unexpected result.³⁷ One study differed systematically from all the other studies in that it focused only on zidovudine treatment during pregnancy.⁴⁴ As the main intent of this therapy was to reduce mother-to-child transmission rather than to treat the maternal infection, it is not inconceivable that the positive association between Latino ethnicity and receipt of zidovudine may reflect provider assumptions about the relative risk of mother-to-child HIV transmission and/or racial/ethnic differences in perceptions about potential risks and benefits of AZT to prevent transmission. In the study that found both a negative and a positive association, blacks were more likely to receive two nucleosides, and less likely to receive a protease inhibitor plus two nucleosides.⁴⁸ These findings suggest that the elevated probability of receiving two nucleosides may represent decreased access to newer, state-of-the-art regimens.

Based on all of these considerations, our summary interpretation of this literature is that there is a preponderance of evidence across time and across subpopulations that HIV-infected people of color in the United States have experienced a lower rate of utilization of antiretroviral medications than HIV-infected white people.

Interestingly, while there is some evidence to suggest non-whites are also at risk for a lower rate of use of prophylaxis against opportunistic infections, the strength of the evidence is not as strong as it was for

antiretroviral use. Only four^{36,39,41,53} out of 11 studies^{34,36,38–41,45,51,53,58,59} found a negative association between non-white race/ethnicity and use of PCP prophylaxis. One might speculate that there was greater penetration of PCP prophylaxis because PCP prophylaxis was available and recommended before antiretroviral use, and because PCP prophylaxis regimens have been much more stable over time than recommended antiretroviral regimens. While this may in part be true, the recent HCSUS finding that blacks are less likely to have received PCP prophylaxis in the past six months indicate that the picture may be more complex.⁵³

With the advent of new and more efficacious antiretroviral therapies, access to and utilization of antiretrovirals has emerged as an important determinant of health outcomes. Thus, the substantial scientific evidence that racial and/or ethnic minorities are at risk for a lower rate of use of HIV-related medications, even after adjustment for important covariates such as health status and health insurance status, has particularly troubling implications for the future health outcomes of at-risk populations. Our challenge now is to shift the focus from documenting differences to aggressively developing, implementing, and evaluating strategies to eliminate these disparities.

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