

Kaiser Permanente Research Brief

HIV/AIDS

This brief summarizes the contributions of Kaiser Permanente Research since 2007 on the topic of HIV and AIDS.

Since the height of the HIV/AIDS epidemic in the mid-1980s, the number of new HIV infections occurring each year in the United States has fallen by more than two-thirds.¹ Nevertheless, according to the Centers for Disease Control and Prevention (CDC), approximately 40,000 new cases of HIV are diagnosed each year in the United States, and just over 18,000 people received a diagnosis of AIDS in 2016.^{2,3} Further, the CDC estimates that 13% of people living with HIV are unaware of their infection. Two-thirds of new HIV diagnoses occur in men who have sex with men.³ Moreover, despite representing just 30% of the U.S. population, nearly 2 out of 3 new HIV infections occur in African Americans and Latino Americans.³

Because of treatment advances and improved survival that began in the late 1990s, the number of Americans living with HIV has increased substantially.¹ By the end of 2015, an estimated 1.1 million adolescents and adults were living with HIV.² Among those living with HIV, nearly two-thirds were receiving treatment for the disease, and approximately half had achieved viral suppression.⁴ People who sustain viral suppression can remain healthy and have almost no risk of sexually transmitting HIV to uninfected partners. The risk of transmission has been further reduced through interventions such as pre-exposure prophylaxis (PrEP), which is a prescription of HIV antiviral drugs that helps prevent infection in those without HIV.

HIV/AIDS is an active area of study for Kaiser Permanente Research. Scientists across the program have used our rich and comprehensive longitudinal data to advance knowledge in the areas of understanding risk, improving patient outcomes, and translating research findings into policy and practice. We have published more than 650 articles related to HIV and AIDS since 2007, which have been cited nearly 45,000 times.⁵ These articles are the product of observational studies, randomized controlled trials, meta-analyses, and other studies

Kaiser Permanente Publications Related to HIV/AIDS since 2007



Source: Kaiser Permanente Publications Library and PLUM metrics, as of July 24, 2019.

- a Number of citing journal articles, according to Scopus.
- b Number of references in PubMed guidelines.
- c Citations in DynaMed Plus, a point-of-care clinical reference tool.

This brief summarizes a selection of the publications contained within the Kaiser Permanente Publications Library, which indexes journal articles and other publications authored by individuals affiliated with Kaiser Permanente. The work described in this brief originated from across Kaiser Permanente's eight regions and was supported by a wide range of funding sources including internal research support as well as both governmental and non-governmental extramural funding.

led by Kaiser Permanente scientists. Our unique environment – a fully integrated care and coverage model in which our research scientists, clinicians, medical groups, and health plan leaders collaborate – lets us contribute generalizable knowledge on HIV/AIDS, and many other topics of research.

Understanding Risk

Who is at risk for development or progression of HIV/AIDS?

The work of Kaiser Permanente's scientists has contributed to a richer understanding of risk factors for transmission of HIV. In addition to well-established risk factors for HIV infection, such as high-risk sexual behavior or use of injected drugs, maternal-fetal transmission remains a risk, although it has been mitigated by improvements in screening and prevention practices.⁶⁻⁹ Our researchers have studied disparities in HIV risk, and have found elevated risks among men who have sex with men, as well as members of minorities defined by ethnicity or sexual orientation.¹⁰⁻¹²

Our research has also informed the question of disease progression in patients with HIV infection. Many people with HIV are unaware that they have contracted the virus, and as such, do not receive appropriate treatment.¹³ Furthermore, while timely initiation of antiretroviral therapy has increased with time, many patients with known HIV are unable to access the care they need.^{14,15} Our research has found that the immune status of patients making their first contact for HIV care has not improved over time,¹³ and that this effect is particularly pronounced among older patients.¹⁶ Our scientists have also explored instances of poor adherence to and refusal of anti-HIV treatment, with the goal of developing interventions to address the objections and concerns of these patients.¹⁷⁻²⁰

What health risks do people with HIV/AIDS face?

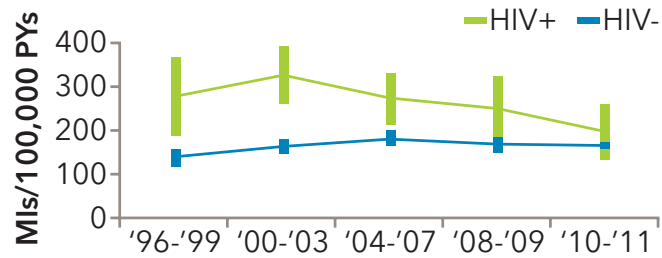
In the early years of the HIV/AIDS epidemic, death from AIDS-related illnesses was the primary health risk in this group of patients. In 2019, with effective treatments being widely available, this is no longer the case.²¹⁻²³ Rather, with HIV-positive people living as long as those without HIV infection, conditions associated with aging,^{24,25} such as non-AIDS-defining cancers,^{24,26-30} cardiovascular disease,^{31,32} chronic respiratory illness,³³ and neurocognitive degeneration,³⁴ have increasingly contributed to morbidity and mortality. Given these trends, our researchers have studied the delivery of screening and other forms of preventive care to patients with HIV.^{35,36}

More generally, data from Kaiser Permanente have been instrumental in enriching our understanding of those cancers for which HIV patients are at increased risk. Large studies conducted in Kaiser Permanente members have found significantly higher risks for several forms of cancer among people with HIV,³⁷⁻⁴³ and other work has suggested that risk factors for cancer (for example, smoking and infection with oncogenic viruses such as human papillomavirus) are very common among these patients.^{27,44,45} Another study in more than 200,000 of our members found that almost 70% of cancers in HIV-infected patients had a known infectious cause, compared with only 12% in people not infected with HIV. While the prevalence of AIDS-defining cancers was more than 37 times higher in HIV-infected people in this study, the prevalence of other non-AIDS defining cancers with a known infectious cause, particularly anal cancer and Hodgkin's lymphoma, was more than 9 times higher.⁴⁶ Finally, compared to those without HIV, patients with HIV have lower 5-year

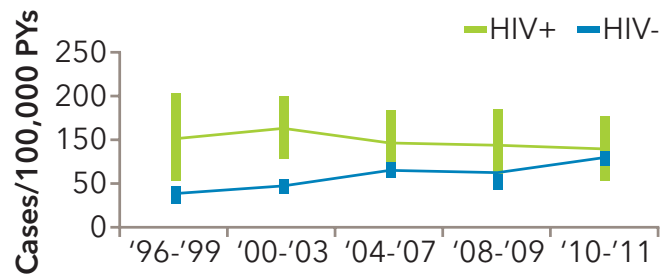
survival rates for some forms of cancer,⁴⁷ and higher rates of cancer-attributable mortality.⁴⁸

Our scientists were among the first to demonstrate an excess risk of cardiovascular diseases, including heart attacks, in HIV patients.^{31,32,43,49} Moreover, the use of antiretroviral therapy (ART) has greatly complicated the treatment of elevated blood cholesterol.⁵⁰⁻⁵³ However, a more recent study conducted in Kaiser Permanente members found that the risk of heart attacks and strokes has declined in recent years.^{43,54,55} Increased attention to clinical and behavioral cardiovascular risk factors, and increased use of lipid-friendly ART medications,⁵⁶ may also have an effect on cardiovascular outcomes such as heart failure, a historically understudied condition currently being investigated actively within Kaiser Permanente.

Heart Attack Rates Over Time by HIV Status⁵⁴



Stroke Rates by HIV Status and Year⁵⁵



HIV has also been associated with an increased risk of both liver dysfunction and related mortality, particularly in patients with compromised immune systems and higher HIV viral loads, alcohol use, drug use, diabetes, or co-infection with hepatitis B or C.^{57,58} This has renewed attention to hepatitis B vaccination and aggressive screening for and treatment of chronic hepatitis C among HIV-positive populations.⁵⁹⁻⁶¹ Finally, although the risks of chronic kidney disease and end-stage renal disease in patients with HIV are declining with the availability of improved treatments,⁶² these risks remain high,⁴³ particularly in African American patients,⁶³ and moderate kidney dysfunction in patients with HIV remains a problem.⁶⁴

Research conducted at Kaiser Permanente has also shown that mortality rates, rates of co-morbid illness, and other outcomes are poorer in HIV-infected patients with substance abuse and/or psychiatric disease diagnoses, even after controlling for ART and health status.⁶⁵⁻⁷⁰ Our scientists have found that the gap in life expectancies between HIV-infected and HIV-uninfected Kaiser Permanente members is narrower in patients with no history of drug or alcohol use,²² and that increases in alcohol use are associated with poorer control of HIV disease.⁷¹ Research is underway to learn more about co-occurring behavioral health conditions in HIV-positive patients and to evaluate strategies for reducing the use of alcohol among these patients.⁷²⁻⁷⁵

Improving Patient Outcomes




What strategies are effective in preventing HIV/AIDS?

Screening of people whose HIV status is unknown is effective in preventing transmission of the virus.⁷⁶ Our research has explored factors associated with screening rates, including addressing concerns about the cost of implementing screening⁷⁷ and

improving levels of HIV knowledge at the community level.^{11,78} Kaiser Permanente scientists have explored numerous interventions for improving HIV screening,^{7,79,80} including the implementation of electronic health record alerts for screening in pregnant women⁸ and high-risk populations.⁸¹ Our researchers have also explored the use of artificial intelligence techniques for identifying individuals at high risk of HIV infection using electronic health record information.⁸² In patients with HIV infection identified through screening tests, counseling regarding sexual behaviors and use of injected drugs may be critical in preventing HIV transmission.^{76,83-86} In addition, treatment of HIV infection may be viewed more broadly as a component of prevention, insofar as viral suppression in treated individuals reduces the risk of transmission to their contacts.^{76,83} Work by Kaiser Permanente researchers has demonstrated that, as treatment within a community lowers its total viral load, transmission of the virus is reduced, and total mortality declines as a result.^{23,87}

More recently, vaccines and other experimental products containing drugs that prevent vaginal or rectal transmission of HIV are being developed and studied within Kaiser Permanente. Our researchers and clinicians also are actively investigating the use of and effectiveness of HIV pre-exposure prophylaxis (PrEP). One study in

our Northern California population found no new cases of HIV infection from 2012 through early 2015 among members enrolled in a PrEP protocol, despite high rates of sexually transmitted infections and decreased condom usage;⁸⁸ PrEP adherence in this study was 92%.⁸⁹ Other benefits of PrEP may include reduced anxiety and feelings of stigma.⁹⁰ Despite these promising results, uptake of PrEP in high-risk populations and compliance with recommended dosing are continuing challenges.^{91,92}

	Kaiser Permanente's San Francisco Medical Center (KP SF) cares for over 170,000 adult members
	From July 2012 through February 2015, 657 KP SF members initiated pre-exposure prophylaxis for HIV
	Despite little change in behaviors related to HIV transmission risk, there were no new cases of HIV diagnosed during this period⁸⁸

How does early identification of HIV affect outcomes?

Large numbers of people with HIV are not aware that they have contracted the virus, and remain at risk for both disease transmission and progression of HIV.¹³ Screening efforts are critical for the long-term health of these patients and those who may be vulnerable to HIV transmission,⁷⁶ and early identification and treatment may prevent co-morbid cancer, cardiovascular disease, and other illnesses that occur frequently in those with HIV.^{28,39,54,55,93,94}

What are the key factors in effective treatment of people with HIV/AIDS?

Research at Kaiser Permanente has emphasized the importance of multidisciplinary care that addresses the behavioral, financial, and health concerns common to patients with HIV. Multidisciplinary care elements, including patient engagement with a medical record system and the use of clinical pharmacists, have been shown to enhance the care coordination that supports adherence and the achievement of viral suppression.^{17,20,95} Our research has also underscored the role of a continuum of HIV care, in

which linkages between timely diagnosis, use of antiretroviral therapy, and retention in care are carefully maintained. Recent research from Kaiser Permanente scientists has demonstrated the importance of office visits. Although the causality of the association is unclear, a study of nearly 3,000 members with HIV found that missing at least 1 office visit was associated with a 71% increase in mortality over the study period, and that each missed visit increased the patient's risk of dying by 12%.⁹⁶

More recent work is evaluating what types of health care visits lead to higher rates of viral suppression. For example, researchers have established that a single annual visit supplemented by email (with or without telephone visit) may lead to the same viral suppression achieved by 2 traditional in-person visits.⁹⁷

Our scientists are also involved in studies of antiretroviral therapy (ART) medication effectiveness and safety.^{56,98-103} For example, 2 studies of etravirine, an ART agent used among patients with more advanced HIV infection, have found that this drug improved viral load and immune system health for patients who had failed multiple prior antiretroviral therapy regimens.^{104,105} With respect to safety, most modern ART agents are much safer than older drugs and drug regimens. An observational study conducted in Kaiser Permanente members linked ritonavir-boosted atazanavir with greater virologic control and immune response in patients with no prior ART but suggested a possible risk of liver dysfunction.¹⁰⁶ Other research has led to the recognition of renal complications with tenofovir, a commonly used medication.¹⁰⁷

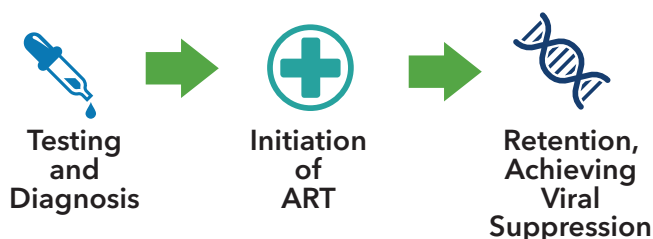
Minority groups – whether defined by race, ethnicity, or sexual orientation – are disproportionately affected by HIV in most parts of the nation and the world.^{11,21,59,108,109} These disparities are of great concern to Kaiser Permanente, given our long-standing commitment to eliminating them.¹¹⁰ A retrospective study conducted among our members with HIV reported no statistically significant differences in mortality or risk of disease progression among black and Latino members compared to white members.¹¹¹ More recent research also failed to find significant disparities in access to recommended treatments or viral load among Kaiser Permanente members with HIV and hepatitis C co-infection.¹¹²

Translating Research Into Policy and Practice

How has Kaiser Permanente research on HIV/AIDS contributed to changes in policy and practice?

Kaiser Permanente is a learning health care organization that works to systematically use research to inform policy and improve practice. Research, clinical, and operational partners within Kaiser Permanente have tested a range of interventions to reduce

Effective care for patients with HIV requires engagement throughout the continuum of care⁷⁶



the risk of HIV/AIDS and improve outcomes for patients with HIV/AIDS. Kaiser Permanente's HIV Care Cascade and quality metrics have contributed to the national conversation by demonstrating that medication regimens with high rates of adherence are critical to the successful treatment of HIV/

AIDS.^{79,113} The Kaiser Permanente hepatitis task force and HIV Interregional Initiative provide ongoing quality measurement and guide improvements in patient care and outcomes, with continued focus on improving HIV prevention, linkage and retention in care, tolerability of antiretroviral therapy, and outcomes. More recently, our scientists participated in a randomized study which demonstrated the effectiveness of a pharmacist-led intervention to reduce inappropriate medication prescribing among patients with HIV.¹¹⁴

Kaiser Permanente research contributes not only to policy and practice changes within our own delivery system, but also to advancing national understanding of HIV/AIDS. Our research on HIV/AIDS since 2007 has been cited nearly 300 times in recent consensus statements, clinical practice guidelines, and point-of-care decision aid tools, including guidelines issued by the U.S. Public Health Service¹¹⁵ and the World Health Organization.¹¹⁶ Kaiser Permanente researchers and clinicians have also directly contributed to many consensus statements and practice guidelines. Kaiser Permanente clinician-researchers have made important contributions to the Infectious Disease Society of America¹¹⁷ and the HIV Medical Association^{118,119} guidelines, and have led numerous systematic reviews for the U.S. Preventive Services Task Force.

Kaiser Permanente is also an established national and international leader in the field of HIV/AIDS research. In 2012, as part of our participation in the International AIDS Conference, we shared our toolkit of clinical best practices and challenged clinicians across the nation to improve the health equity for people living with HIV.¹²⁰ Our research groups lead numerous large trials evaluating new antiretroviral therapy treatments,^{56,104} and our scientists hold key leadership positions in important collaborative research efforts such as the Antiretroviral Therapy Cohort Collaboration, The District of Columbia HIV Cohort, and the North American AIDS Cohort Collaboration on Research and Design, all funded by the National Institutes of Health.

Kaiser Permanente researchers also hold leadership roles in organizations such as the HIV Medical Association and the American Academy of HIV Medicine. Our scientists have provided support to federal government decision-makers at the Health Resources and Services Administration and the Department of Health and Human Services, including our work on the HIV quality metrics panels convened by the Centers for Medicare and Medicaid Services and America's Health Insurance Plans.

Kaiser Permanente's nearly 170 research scientists and more than 1,600 support staff are based at 8 regional research centers and 1 national center. There are currently more than 2,400 studies underway, including clinical trials. Since 2007, our research scientists and clinicians have published more than 12,000 articles. Kaiser Permanente currently serves more than 12 million members in 8 states and the District of Columbia.

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References

1. Centers for Disease Control and Prevention. *CDC Fact Sheet: Today's HIV/AIDS Epidemic*. Atlanta, GA: Author;2016.
2. Centers for Disease Control and Prevention. *Estimated HIV incidence and prevalence in the United States, 2010-2015. HIV Surveillance Supplemental Report 2018*. Atlanta, GA: Author;2018.
3. Centers for Disease Control and Prevention. *HIV Surveillance Report, 2016*. Atlanta, GA: Author;2017.
4. Centers for Disease Control and Prevention. *Monitoring selected national HIV prevention and care objectives by using HIV surveillance data—United States and 6 dependent areas, 2015. HIV Surveillance Supplemental Report 2017*. Atlanta, GA: Author;2017.
5. KPPL Search, conducted on July 24, 2019: (dc.title:HIV OR dc.title:" human immunodeficiency virus" OR dc.title:AIDS OR dc.subject.mesh:" Acquired Immunodeficiency Syndrome" OR dc.subject.mesh:"Acquired Immunodeficiency Syndrome/*" OR dc.subject.mesh:"HIV-1" OR dc.subject.mesh:"HIV-1/*" OR dc.subject.mesh:"Sarcoma, Kaposi " OR dc.subject.mesh:" Anti-HIV Agents " OR dc.subject.mesh:" Anti-HIV Agents/*" OR dc.subject.mesh:"HIV Infections" OR dc.subject.mesh:" CD4 Lymphocyte Count" OR dc.subject.mesh:HIV OR dc.subject.mesh:"aids-related opportunistic infections") AND dc.type:"Journal Article" AND dc.date.issued:[2007 2019].
6. Coonrod DV, Jack BW, Stubblefield PG, et al. The clinical content of preconception care: infectious diseases in preconception care. *Am J Obstet Gynecol*. 2008;199(6 Suppl 2):S296-309.
7. Lawrence JM, Liu IL, Towner WJ. Trends and correlates of HIV testing during pregnancy in racially/ethnically diverse insured population, 1997-2006. *Matern Child Health J*. 2009;13(5):633-640.
8. McLean TA, Lewkowitz AK, Test E, Zlatnik MG. Does an Electronic Health Record Improve Completeness of Prenatal Studies? *Appl Clin Inform*. 2015;6(4):669-676.
9. Dionne-Odom J, Khan MJ, Jauk VC, et al. HIV Status and Other Risk Factors for Prevalent and Incident Sexually Transmitted Infection during Pregnancy (2000-2014). *Infect Dis Obstet Gynecol*. 2019;2019:6584101.
10. Vega WA, Rodriguez MA, Gruskin E. Health disparities in the Latino population. *Epidemiol Rev*. 2009;31:99-112.
11. Rios-Ellis B, Becker D, Espinoza L, et al. Evaluation of a Community Health Worker Intervention to Reduce HIV/AIDS Stigma and Increase HIV Testing Among Underserved Latinos in the Southwestern U.S. *Public Health Rep*. 2015;130(5):458-467.
12. Smith LR, Yore J, Triplett DP, et al. Impact of Sexual Violence Across the Lifespan on HIV Risk Behaviors Among Transgender Women and Cisgender People Living With HIV. *J Acquir Immune Defic Syndr*. 2017;75(4):408-416.
13. Althoff KN, Gange SJ, Klein MB, et al. Late presentation for human immunodeficiency virus care in the United States and Canada. *Clin Infect Dis*. 2010;50(11):1512-1520.
14. Hanna DB, Buchacz K, Gebo KA, et al. Trends and disparities in antiretroviral therapy initiation and virologic suppression among newly treatment-eligible HIV-infected individuals in North America, 2001-2009. *Clin Infect Dis*. 2013;56(8):1174-1182.
15. Hanna DB, Buchacz K, Gebo KA, et al. Association between U.S. State AIDS Drug Assistance Program (ADAP) Features and HIV Antiretroviral Therapy Initiation, 2001-2009. *PLoS ONE*. 2013;8(11):e78952.
16. Althoff KN, Gebo KA, Gange SJ, et al. CD4 count at presentation for HIV care in the United States and Canada: Are those over 50 years more likely to have a delayed presentation? *AIDS Res Ther*. 2010;7:45.
17. Horberg MA, Hurley LB, Silverberg MJ, et al. Effect of clinical pharmacists on utilization of and clinical response to antiretroviral therapy. *J Acquir Immune Defic Syndr*. 2007;44(5):531-539.
18. Horberg M, Silverberg M, Hurley L, et al. Influence of prior antiretroviral experience on adherence and responses to new highly active antiretroviral therapy regimens. *AIDS Patient Care STDS*. 2008;22(4):301-312.
19. Ralston JD, Silverberg MJ, Grothaus L, et al. Use of web-based shared medical records among patients with HIV. *Am J Manag Care*. 2013;19(4):e114-124.
20. Saberi P, Catz SL, Leyden WA, et al. Antiretroviral Therapy Adherence and Use of an Electronic Shared Medical Record Among People Living with HIV. *AIDS Behav*. 2015;19 Suppl 2:177-185.
21. Samji H, Cescon A, Hogg RS, et al. Closing the Gap: Increases in Life Expectancy among Treated HIV-Positive Individuals in the United States and Canada. *PLoS ONE*. 2013;8(12):e81355.
22. Marcus JL, Chao CR, Leyden WA, et al. Narrowing the gap in life expectancy between HIV-infected and HIV-uninfected individuals with access to care. *J Acquir Immune Defic Syndr*. 2016;73(1):39-46.

23. Althoff KN, Buchacz K, Hall HI, et al. U.S. Trends in Antiretroviral Therapy Use, HIV RNA Plasma Viral Loads, and CD4 T-Lymphocyte Cell Counts Among HIV-Infected Persons, 2000 to 2008. *Ann Intern Med.* 2012;157(5):325-335.
24. John MD, Greene M, Hessel NA, et al. Geriatric Assessments And Association With VACS Index Among HIV-Infected Older Adults In San Francisco. *J Acquir Immune Defic Syndr.* 2016;72(5):534-541.
25. Wong C, Gange SJ, Moore RD, et al. Multimorbidity Among Persons Living with Human Immunodeficiency Virus in the U.S. *Clin Infect Dis.* 2018;66(8):1230-1238.
26. Wang CC, Silverberg MJ, Abrams DI. Non-AIDS-Defining Malignancies in the HIV-Infected Population. *Curr Infect Dis Rep.* 2014;16(6):406.
27. Silverberg MJ, Abrams DI. AIDS-defining and non-AIDS-defining malignancies: cancer occurrence in the antiretroviral therapy era. *Curr Opin Oncol.* 2007;19(5):446-451.
28. Dubrow R, Silverberg MJ, Park LS, et al. HIV infection, aging, and immune function: implications for cancer risk and prevention. *Curr Opin Oncol.* 2012;24(5):506-516.
29. Shiels MS, Althoff KN, Pfeiffer RM, et al. HIV Infection, Immune Suppression and Age at Diagnosis of Non-AIDS-Defining Cancers. *Clin Infect Dis.* 2017;64(4):468-475.
30. Burger EA, Dyer MA, Sy S, et al. Development and Calibration of a Mathematical Model of Anal Carcinogenesis for High-Risk HIV-Infected Men. *J Acquir Immune Defic Syndr.* 2018;79(1):10-19.
31. Silverberg MJ, Leyden WA, Xu L, et al. Immunodeficiency and Risk of Myocardial Infarction Among HIV-Positive Individuals With Access to Care. *J Acquir Immune Defic Syndr.* 2014;65(2):160-166.
32. Drozd DR, Kitahata MM, Althoff KN, et al. Increased Risk of Myocardial Infarction in HIV-Infected Individuals in North America Compared to the General Population. *J Acquir Immune Defic Syndr.* 2017;75(5):568-576.
33. Crothers K, Rodriguez CV, Nance RM, et al. Accuracy of electronic health record data for the diagnosis of chronic obstructive pulmonary disease in persons living with HIV and uninfected persons. *Pharmacoepidemiol Drug Saf.* 2019;28(2):140-147.
34. Valcour V, Watters MR, Williams AE, et al. Aging exacerbates extrapyramidal motor signs in the era of highly active antiretroviral therapy. *J Neurovirol.* 2008;14(5):362-367.
35. Lam JO, Hurley LB, Udaltsova N, et al. Colorectal Cancer Screening in People With and Without HIV in an Integrated Health Care Setting. *J Acquir Immune Defic Syndr.* 2019;81(3):284-291.
36. Barnell GM, Merchant M, Lam JO, Silverberg MJ. Early Outcomes of a High-Resolution Anoscopy-Based Anal Cancer Screening Program Among People With HIV Enrolled in an Integrated Health Care System. *J Acquir Immune Defic Syndr.* 2019;81(3):292-299.
37. Silverberg MJ, Leyden W, Warton EM, et al. HIV Infection Status, Immunodeficiency, and the Incidence of Non-Melanoma Skin Cancer. *J Natl Cancer Inst.* 2013;105(5):350-360.
38. Silverberg MJ, Chao C, Leyden WA, et al. HIV Infection, Immunodeficiency, Viral Replication, and the Risk of Cancer. *Cancer Epidemiol Biomarkers Prev.* 2011;20(12):2551-2559.
39. Silverberg MJ, Lau B, Justice AC, et al. Risk of Anal Cancer in HIV-Infected and HIV-Uninfected Individuals in North America. *Clin Infect Dis.* 2012;54(7):1026-1034.
40. Abraham AG, D'Souza G, Jing Y, et al. Invasive cervical cancer risk among HIV-infected women: A North American multi-cohort collaboration prospective study. *J Acquir Immune Defic Syndr.* 2013;62(4):405-413.
41. Beachler DC, Abraham AG, Silverberg MJ, et al. Incidence and risk factors of HPV-related and HPV-unrelated Head and Neck Squamous Cell Carcinoma in HIV-infected individuals. *Oral Oncol.* 2014;50(12):1169-1176.
42. Asgari MM, Ray GT, Quesenberry CP, et al. Association of Multiple Primary Skin Cancers With Human Immunodeficiency Virus Infection, CD4 Count, and Viral Load. *JAMA Dermatol.* 2017;153(9):892-896.
43. Mayer KH, Loo S, Crawford PM, et al. Excess Clinical Comorbidity Among HIV-Infected Patients Accessing Primary Care in US Community Health Centers. *Public Health Rep.* 2018;133(1):109-118.
44. Park LS, Hernández-Ramírez RU, Silverberg MJ, et al. Prevalence of non-HIV cancer risk factors in persons living with HIV/AIDS: a meta-analysis. *AIDS.* 2016;30(2):273-291.
45. Schwartz LM, Castle PE, Follansbee S, et al. Risk factors for anal HPV infection and anal precancer in HIV-infected men who have sex with men. *J Infect Dis.* 2013;208(11):1768-1775.
46. Silverberg MJ, Chao C, Leyden WA, et al. HIV infection and the risk of cancers with and without a known infectious cause. *AIDS.* 2009;23(17):2337-2345.

47. Marcus JL, Chao C, Leyden WA, et al. Survival Among HIV-Infected and HIV-Uninfected Individuals with Common Non-AIDS-Defining Cancers. *Cancer Epidemiol Biomarkers Prev.* 2015;24(8):1167-1173.
48. Engels EA, Yanik EL, Wheeler W, et al. Cancer-Attributable Mortality Among People With Treated Human Immunodeficiency Virus Infection in North America. *Clin Infect Dis.* 2017;65(4):636-643.
49. Marcus JL, Neugebauer RS, Leyden WA, et al. Use of abacavir and risk of cardiovascular disease among HIV-infected individuals. *J Acquir Immune Defic Syndr.* 2016;71(4):413-419.
50. Falutz J, Allas S, Blot K, et al. Metabolic effects of a growth hormone-releasing factor in patients with HIV. *N Engl J Med.* 2007;357(23):2359-2370.
51. Silverberg MJ, Leyden W, Horberg MA, et al. Older age and the response to and tolerability of antiretroviral therapy. *Arch Intern Med.* 2007;167(7):684-691.
52. Wohl D, Scherzer R, Heymsfield S, et al. The associations of regional adipose tissue with lipid and lipoprotein levels in HIV-infected men. *J Acquir Immune Defic Syndr.* 2008;48(1):44-52.
53. Wiggins BS, Lamprecht DG, Page RL, Saseen JJ. Recommendations for Managing Drug-Drug Interactions with Statins and HIV Medications. *Am J Cardiovasc Drugs.* 2017;17(5):375-389.
54. Klein DB, Leyden WA, Xu L, et al. Declining Relative Risk for Myocardial Infarction Among HIV-Positive Compared With HIV-Negative Individuals With Access to Care. *Clin Infect Dis.* 2015;60(8):1278-1280.
55. Marcus JL, Leyden WA, Chao CR, et al. HIV infection and incidence of ischemic stroke. *AIDS.* 2014;28(13):1911-1919.
56. Palella FJ, Fisher M, Tebas P, et al. Simplification to rilpivirine/emtricitabine/tenofovir disoproxil fumarate from ritonavir-boosted protease inhibitor antiretroviral therapy in a randomized trial of HIV-1 RNA-suppressed participants. *AIDS.* 2014;28(3):335-344.
57. Towner WJ, Xu L, Leyden WA, et al. The Effect of HIV Infection, Immunodeficiency and Antiretroviral Therapy on the Risk of Hepatic Dysfunction. *J Acquir Immune Defic Syndr.* 2012;60(3):321-327.
58. Klein MB, Althoff KN, Jing Y, et al. Risk of End-Stage Liver Disease in HIV-Viral Hepatitis Coinfected Persons in North America From the Early to Modern Antiretroviral Therapy Eras. *Clin Infect Dis.* 2016;63(9):1160-1167.
59. Hoover KW, Butler M, Workowski KA, et al. Low Rates of Hepatitis Screening and Vaccination of HIV-Infected MSM in HIV Clinics. *Sex Transm Dis.* 2012;39(5):349-353.
60. Marcus JL, Leyden WA, Chao CR, et al. Differences in Response to Antiretroviral Therapy by Sex and Hepatitis C Infection Status. *AIDS Patient Care STDS.* 2015;29(7):370-378.
61. Adams LM, Balderson B, Packett BJ, 2nd. Meeting the Challenge: Hepatitis C Virus and HIV Care Experiences Among HIV Specialty Providers. *AIDS Patient Care STDS.* 2018;32(8):314-320.
62. Muzaale AD, Althoff KN, Sperati CJ, et al. Risk of End-Stage Renal Disease in HIV-Positive Potential Live Kidney Donors. *Am J Transplant.* 2017;17(7):1823-1832.
63. Abraham AG, Althoff KN, Jing Y, et al. End Stage Renal Disease Among HIV-Infected Adults in North America. *Clin Infect Dis.* 2015;60(6):941-949.
64. Odden MC, Scherzer R, Bacchetti P, et al. Cystatin C level as a marker of kidney function in human immunodeficiency virus infection: the FRAM study. *Arch Intern Med.* 2007;167(20):2213-2219.
65. Satre DD, DeLorenze GN, Quesenberry CP, et al. Factors Associated With Treatment Initiation for Psychiatric and Substance Use Disorders Among Persons With HIV. *Psychiatr Serv.* 2013;64(8):745-753.
66. DeLorenze GN, Weisner C, Tsai AL, et al. Excess mortality among HIV-infected patients diagnosed with substance use dependence or abuse receiving care in a fully integrated medical care program. *Alcohol Clin Exp Res.* 2011;35(2):203-210.
67. Chao C, Jacobson LP, Tashkin D, et al. Recreational amphetamine use and risk of HIV-related non-Hodgkin lymphoma. *Cancer Causes Control.* 2009;20(5):509-516.
68. Horberg MA, Silverberg MJ, Hurley LB, et al. Effects of depression and selective serotonin reuptake inhibitor use on adherence to highly active antiretroviral therapy and on clinical outcomes in HIV-infected patients. *J Acquir Immune Defic Syndr.* 2008;47(3):384-390.
69. DeLorenze GN, Satre DD, Tsai AL, et al. Mortality after diagnosis of psychiatric disorders and co-occurring substance use disorders among HIV-infected patients. *AIDS Patient Care STDS.* 2010;24(11):705-712.
70. Cofrancesco J, Jr., Scherzer R, Tien PC, et al. Illicit drug use and HIV treatment outcomes in a US cohort. *AIDS.* 2008;22(3):357-365.

71. Williams EC, McGinnis KA, Bobb JF, et al. Changes in alcohol use associated with changes in HIV disease severity over time: A national longitudinal study in the Veterans Aging Cohort. *Drug Alcohol Depend.* 2018;189:21-29.
72. Silverberg MJ, Leyden WA, Leibowitz A, et al. Factors associated with hazardous alcohol use and motivation to reduce drinking among HIV primary care patients: Baseline findings from the Health & Motivation study. *Addict Behav.* 2018;84:110-117.
73. Williams EC, Lapham GT, Bobb JF, et al. Documented brief intervention not associated with resolution of unhealthy alcohol use one year later among VA patients living with HIV. *J Subst Abuse Treat.* 2017;78:8-14.
74. Williams EC, Lapham GT, Shortreed SM, et al. Among patients with unhealthy alcohol use, those with HIV are less likely than those without to receive evidence-based alcohol-related care: A national VA study. *Drug Alcohol Depend.* 2017;174:113-120.
75. Satre DD, Leibowitz AS, Leyden W, et al. Interventions to Reduce Unhealthy Alcohol Use among Primary Care Patients with HIV: the Health and Motivation Randomized Clinical Trial. *J Gen Intern Med.* 2019.
76. Cheever LW, Lubinski C, Horberg M, Steinberg JL. Ensuring access to treatment for HIV infection. *Clin Infect Dis.* 2007;45 Suppl 4:S266-274.
77. Berg LJ, Delgado MK, Ginde AA, et al. Characteristics of U.S. Emergency Departments That Offer Routine Human Immunodeficiency Virus Screening. *Acad Emerg Med.* 2012;19(8):894-900.
78. Hoehn EF, FitzGerald MR, Bhatt SR, et al. Do Adolescents With Higher Knowledge of HIV Have Lower Sexual Risk Behaviors? *Pediatr Emerg Care.* 2016;32(12):846-850.
79. Horberg M, Hurley L, Towner W, et al. HIV quality performance measures in a large integrated health care system. *AIDS Patient Care STDS.* 2011;25(1):21-28.
80. Rodriguez CV, Horberg MA. HIV Testing, Staging, and Evaluation. *Infect Dis Clin North Am.* 2014;28(3):339-353.
81. Hechter RC, Bider-Canfield Z, Towner W. Effect of an Electronic Alert on Targeted HIV Testing Among High-Risk Populations. *Perm J.* 2018;22:18-015.
82. Marcus JL, Hurley LB, Krakower DS, et al. Use of electronic health record data and machine learning to identify candidates for HIV pre-exposure prophylaxis: a modelling study. *Lancet HIV.* 2019.
83. Gardner EM, McLees MP, Steiner JF, et al. The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. *Clin Infect Dis.* 2011;52(6):793-800.
84. Edelman EJ, Moore BA, Caffrey S, et al. HIV Testing and Sexual Risk Reduction Counseling in Office-Based Buprenorphine/Naloxone Treatment. *J Addict Med.* 2013;7(6):410-416.
85. O'Connor E, Lin JS, Burda BU, et al. U.S. Preventive Services Task Force Evidence Syntheses, formerly Systematic Evidence Reviews. *Behavioral Sexual Risk Reduction Counseling in Primary Care to Prevent Sexually Transmitted Infections: An Updated Systematic Evidence Review for the U.S. Preventive Services Task Force.* Rockville (MD): Agency for Healthcare Research and Quality (US); 2014.
86. Lin JS, Whitlock E, O'Connor E, Bauer V. Behavioral counseling to prevent sexually transmitted infections: a systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med.* 2008;149(7):497-508.
87. Gonsalves GS, Paltiel AD, Cleary PD, et al. A Flow-Based Model of the HIV Care Continuum in the United States. *J Acquir Immune Defic Syndr.* 2017;75(5):548-553.
88. Volk JE, Marcus JL, Phengrasamy T, et al. No New HIV Infections with Increasing Use of HIV Preexposure Prophylaxis in a Clinical Practice Setting. *Clin Infect Dis.* 2015;61(10):1601-1603.
89. Marcus JL, Hurley LB, Hare CB, et al. Preexposure Prophylaxis for HIV Prevention in a Large Integrated Health Care System: Adherence, Renal Safety, and Discontinuation. *J Acquir Immune Defic Syndr.* 2016;73(5):540-546.
90. Storholm ED, Volk JE, Marcus JL, et al. Risk Perception, Sexual Behaviors, and PrEP Adherence Among Substance-Using Men Who Have Sex with Men: a Qualitative Study. *Prev Sci.* 2017;18(6):737-747.
91. Rolle CP, Rosenberg ES, Siegler AJ, et al. Challenges in Translating PrEP Interest into Uptake in an Observational Study of Young Black MSM. *J Acquir Immune Defic Syndr.* 2017;76(3):250-258.
92. Volk JE, Nguyen DP, Hare CB, Marcus JL. HIV Infection and Drug Resistance with Unsupervised Use of HIV Preexposure Prophylaxis. *AIDS Res Hum Retroviruses.* 2018;34(4):329-330.
93. Silverberg MJ, Lau B, Achenbach CJ, et al. Cumulative Incidence of Cancer Among Persons With HIV in North America: A Cohort Study. *Ann Intern Med.* 2015;163(7):507-518.
94. Borges AH, Dubrow R, Silverberg MJ. Factors contributing to risk for cancer among HIV-infected individuals, and evidence that earlier combination antiretroviral therapy will alter this risk. *Curr Opin HIV AIDS.* 2014;9(1):34-40.

95. Horberg MA, Bartemeier Hurley L, James Towner W, et al. Determination of Optimized Multidisciplinary Care Team for Maximal Antiretroviral Therapy Adherence. *J Acquir Immune Defic Syndr*. 2012;60(2):183-190.
96. Horberg MA, Hurley LB, Silverberg MJ, et al. Missed Office Visits and Risk of Mortality Among HIV-Infected Subjects in a Large Healthcare System in the United States. *AIDS Patient Care STDS*. 2013;27(8):442-449.
97. Horberg MA, Blank JG, Rubenstein KB, et al. Impact of Alternative Encounter Types on HIV Viral Suppression Rates in an Integrated Health System. *AIDS Patient Care STDS*. 2018;32(11):425-431.
98. Mills A, Crofoot G, McDonald C, et al. Tenofovir Alafenamide vs. Tenofovir Disoproxil Fumarate in the First Protease Inhibitor-based Single Tablet Regimen for Initial HIV-1 Therapy: A Randomized Phase 2 Study. *J Acquir Immune Defic Syndr*. 2015;69(4):439-445.
99. Towner W, Klein D, Kerrigan HL, et al. Virologic outcomes of changing enfuvirtide to raltegravir in HIV-1 patients well controlled on an enfuvirtide based regimen: 24-week results of the CHEER study. *J Acquir Immune Defic Syndr*. 2009;51(4):367-373.
100. Elion R, Dejesus E, Sension M, et al. Once-daily abacavir/lamivudine and ritonavir-boosted atazanavir for the treatment of HIV-1 infection in antiretroviral-naive patients: a 48-week pilot study. *HIV Clin Trials*. 2008;9(3):152-163.
101. Grinsztejn B, Di Perri G, Towner W, et al. A review of the safety and tolerability profile of the next-generation NNR-TI etravirine. *AIDS Res Hum Retroviruses*. 2010;26(7):725-733.
102. Horberg MA, Oakes AH, Hurley LB, et al. Association of raltegravir use with long-term health outcomes in HIV-infected patients: an observational post-licensure safety study in a large integrated healthcare system. *HIV Clin Trials*. 2018;19(5):177-187.
103. Chen R, Scherzer R, Hsue PY, et al. Association of Tenofovir Use With Risk of Incident Heart Failure in HIV-Infected Patients. *J Am Heart Assoc*. 2017;6(4).
104. Towner W, Lalezari J, Sension MG, et al. Efficacy, safety, and tolerability of etravirine with and without darunavir/ritonavir or raltegravir in treatment-experienced patients: analysis of the etravirine early access program in the United States. *J Acquir Immune Defic Syndr*. 2010;53(5):614-618.
105. Katlama C, Clotet B, Mills A, et al. Efficacy and safety of etravirine at week 96 in treatment-experienced HIV type-1-infected patients in the DUET-1 and DUET-2 trials. *Antivir Ther*. 2010;15(7):1045-1052.
106. Horberg M, Klein D, Hurley L, et al. Efficacy and safety of ritonavir-boosted and unboosted atazanavir among antiretroviral-naive patients. *HIV Clin Trials*. 2008;9(6):367-374.
107. Horberg M, Tang B, Towner W, et al. Impact of tenofovir on renal function in HIV-infected, antiretroviral-naive patients. *J Acquir Immune Defic Syndr*. 2010;53(1):62-69.
108. Wong C, Gange SJ, Buchacz K, et al. First Occurrence of Diabetes, Chronic Kidney Disease, and Hypertension Among North American HIV-Infected Adults, 2000-2013. *Clin Infect Dis*. 2017;64(4):459-467.
109. Desir FA, Lesko CR, Moore RD, et al. One Size Fits (n)One: The Influence of Sex, Age, and Sexual Human Immunodeficiency Virus (HIV) Acquisition Risk on Racial/Ethnic Disparities in the HIV Care Continuum in the United States. *Clin Infect Dis*. 2019;68(5):795-802.
110. Kaiser Permanente Statement on Our Commitment to Diversity and Inclusion [press release]. 2017.
111. Silverberg MJ, Leyden W, Quesenberry CP, Jr., Horberg MA. Race/ethnicity and risk of AIDS and death among HIV-infected patients with access to care. *J Gen Intern Med*. 2009;24(9):1065-1072.
112. Lam JO, Hurley LB, Chamberland S, et al. Hepatitis C treatment uptake and response among human immunodeficiency virus/hepatitis C virus-coinfected patients in a large integrated healthcare system. *Int J STD AIDS*. 2019;30(7):689-695.
113. Horberg MA, Hurley LB, Klein DB, et al. The HIV Care Cascade Measured Over Time and by Age, Sex, and Race in a Large National Integrated Care System. *AIDS Patient Care STDS*. 2015;29(11):582-590.
114. McNicholl IR, Gandhi M, Hare CB, et al. A Pharmacist-Led Program to Evaluate and Reduce Polypharmacy and Potentially Inappropriate Prescribing in Older, HIV-Positive Patients. *Pharmacotherapy*. 2017;37(12):1498-1506.
115. Centers for Disease Control and Prevention: U.S. Public Health Service. *Preexposure prophylaxis for the prevention of HIV infection in the United States—2017 Update: a clinical practice guideline*. 2018.
116. World Health Organization. *Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV*. 2015.
117. Gallant JE, Adimora AA, Carmichael JK, et al. Essential components of effective HIV care: a policy paper of the HIV Medicine Association of the Infectious Diseases Society of America and the Ryan White Medical Providers Coalition. *Clin Infect Dis*. 2011;53(11):1043-1050.

118. Aberg JA, Gallant JE, Ghanem KG, et al. Primary Care Guidelines for the Management of Persons Infected With HIV: 2013 Update by the HIV Medicine Association of the Infectious Diseases Society of America. *Clin Infect Dis*. 2014;58(1):e1-34.
119. Aberg JA, Gallant JE, Ghanem KG, et al. Executive Summary: Primary Care Guidelines for the Management of Persons Infected With HIV: 2013 Update by the HIV Medicine Association of the Infectious Diseases Society of America. *Clin Infect Dis*. 2014;58(1):1-10.
120. AIDS 2012 Conference [press release]. 2012.