

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 CDC (the Centers for Disease Control and Prevention), 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 percent 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 percent 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 diagnosed or undiagnosed 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 PrEP, or pre-exposure prophylaxis, 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 600 articles related to HIV and AIDS since 2007, which have been cited approximately 38,000 times. These articles are the product of observational

Kaiser Permanente Publications Related to HIV/AIDS since 2007



Source: Kaiser Permanente Publications Library and PLUM metrics, as of 11 September 2018.

- 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.

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

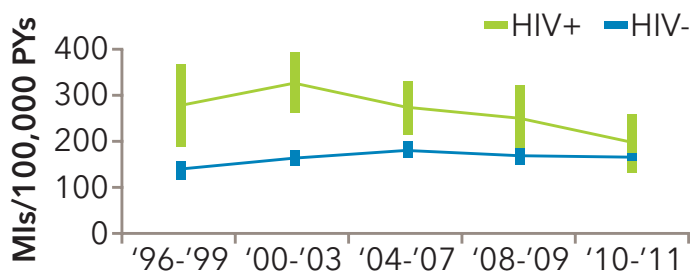
Understanding Risk

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

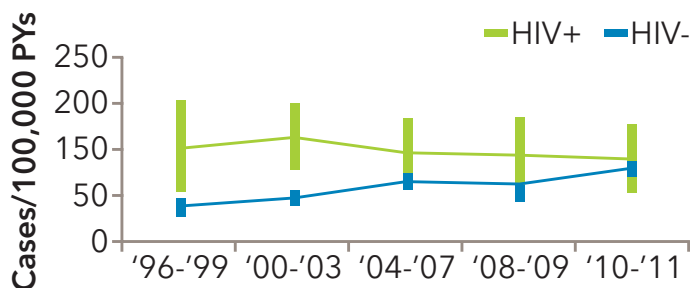
The work of Kaiser Permanente’s scientists has contributed to a richer understanding of risk factors for transmission of HIV. In addition to well-established risk factors for HIV infection, such as high-risk sexual behavior or use of injected drugs, maternal-fetal transmission remains a risk, although it has been mitigated by improvements in screening and prevention practices.⁵⁻⁷ 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 ethnic minorities.^{8,9}

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.¹⁰ Furthermore, while timely initiation of antiretroviral therapy has increased with time, many patients in the United States with known HIV can’t access the care they need.^{11,12} Our research has found

Heart Attack Rates Over Time by HIV Status³⁷



Stroke Rates by HIV Status and Year³⁸



that the immune status of patients making their first contact for HIV care has not improved over time,¹⁰ and that this effect is particularly pronounced among older patients.¹³ 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.¹⁴⁻¹⁷

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 2018, with effective treatments being widely available, this is no longer the case.¹⁸⁻²⁰ Rather, with HIV-positive people living as long as those without HIV infection, conditions associated with aging,^{21,22} such as non-AIDS-defining cancers,^{21,23-25} cardiovascular disease,^{26,27} and neurocognitive degeneration,²⁸ have increasingly contributed to morbidity and mortality.

More generally, data from Kaiser Permanente were instrumental in enriching our understanding of those cancers for which HIV patients are at increased risk. Large studies conducted in Kaiser Permanente members found significantly higher risks for several forms of cancer among people with HIV,²⁹⁻³⁵ 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.^{24,36,37} Another study in more than 200,000 of our members found that almost 70 percent of cancers in HIV-infected patients had a known infectious cause, compared with only 12 percent 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.³⁸ Finally, compared to those without HIV, patients with HIV have lower 5-year survival rates for some forms of cancer,³⁹ and higher rates of cancer-attributable mortality.⁴⁰

Our scientists were among the first to demonstrate an excess risk of cardiovascular diseases, including heart attacks, in HIV patients.^{26,27,35,41} Moreover, the use of antiretroviral therapy (ART) has greatly complicated the treatment of elevated blood cholesterol.⁴²⁻⁴⁴ However, a more recent study conducted in Kaiser Permanente members found that the risk of heart attacks and strokes has declined in recent years.^{35,45,46} Increased attention to clinical and behavioral cardiovascular risk factors, and increased use of lipid-friendly ART medications,⁴⁷ may also have an effect on cardiovascular outcomes such as heart failure, a historically understudied condition currently being investigated actively within Kaiser Permanente.

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.^{48,49} This has renewed attention to hepatitis B vaccination and aggressive screening for and treatment of chronic hepatitis C among HIV-positive populations.⁵⁰⁻⁵² 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,⁵³ these risks remain high,³⁵ particularly in African-American patients,⁵⁴ and moderate kidney dysfunction in patients with HIV remains a problem.⁵⁵

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.⁵⁶⁻⁶¹ For example, a study comparing life expectancies in HIV-infected and HIV-uninfected Kaiser Permanente members suggested that the gap in survival was narrower in patients with no history of drug or alcohol use.¹⁹ 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.⁶²⁻⁶⁴

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.⁶⁵ Our research has explored factors associated with screening rates, including addressing concerns about the cost of implementing screening⁶⁶ and im-

proving levels of HIV knowledge at the community level.^{9,67} Kaiser Permanente scientists have explored numerous interventions for improving HIV screening,^{6,68,69} including the implementation of an electronic health record alert for prenatal screening.⁷ 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.^{65,70-73} 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.^{65,70} 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.^{20,74}




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 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;⁷⁵ PrEP adherence in this study was 92 percent.⁷⁶ Other benefits of PrEP may include reduced anxiety and feelings of stigma.⁷⁷ Despite these promising results, uptake of PrEP in high-risk populations and compliance with recommended dosing are continuing challenges.^{78,79}

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.¹⁰ Screening efforts are critical for the long-term health of these patients and those who may be vulnerable to HIV transmission,⁶⁵ and early identification and treatment may prevent co-morbid cancer, cardiovascular disease, and other illnesses that occur frequently in those with HIV.^{25,31,45,46,80,81}

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.^{14,17,82} 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 associ-

	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 period⁶⁶

ation is unclear, a study of nearly 3,000 members with HIV found that missing at least one office visit was associated with a 71 percent increase in mortality over the study period, and that each missed visit added 12 percent to the patient’s risk of dying.⁸³

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 contact) may lead to the same viral suppression achieved by 2 traditional in-person visits.⁸⁴

Our scientists are also involved in studies of antiretroviral therapy (ART) medication effectiveness and safety.^{47,85-89} 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.^{90,91} 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.⁹² Other research has led to recognition of renal complications with tenofovir, a commonly used medication.⁹³

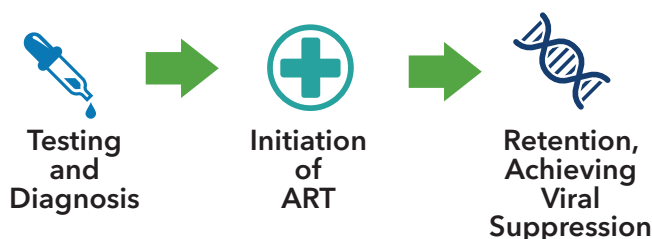
Minority groups – whether defined by race, ethnicity, or sexual orientation – are disproportionately affected by HIV in most parts of the nation and the world.^{9,18,50,94} These disparities are of great concern to Kaiser Permanente, given our long-standing commitment to eliminating them.⁹⁵ A retrospective 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.⁹⁶

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 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.^{68,97} 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

Effective care for patients with HIV requires engagement throughout the continuum of care⁶⁵



on improving HIV prevention, linkage and retention in care, tolerability of antiretroviral therapy, and outcomes.

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 more than 250 times in recent consensus statements, clinical practice guidelines, and point-of-care decision aid tools, including guidelines issued by the U.S. Public Health Service⁹⁸ and the World Health Organization.⁹⁹ 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 America¹⁰⁰ and the HIV Medical Association^{101,102} 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.¹⁰³ Our research groups lead numerous large trials evaluating new antiretroviral therapy treatments,^{47,90} and our scientists hold key leadership positions in important collaborative research efforts such as the Antiretroviral Therapy Cohort Collaboration and the North American AIDS Cohort Collaboration on Research and Design.

Kaiser Permanente researchers also hold leadership roles in organizations such as the Presidential Advisory Council on HIV/AIDS, 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 2,500 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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