

# Kaiser Permanente Research Brief

## HIV/AIDS

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

Kaiser Permanente is the second largest provider of integrated human immunodeficiency virus (HIV) care in the United States (behind the Veterans Administration) and has cared for more than 60,000 HIV patients since the beginning of the epidemic in 1981. Over the years our research has advanced a greater understanding of the disease, informed policy and clinical practice, and more importantly, has helped more people live longer, healthier lives.

Our fully integrated care and coverage model has enabled research to be a foundational aspect of our HIV/AIDS care strategy. Because our member population is large and diverse, the research we conduct to understand HIV risk and risk reduction, improve patient outcomes, and translate research findings into policy and practice has been instrumental in shaping national guidelines, as well as providing tools for monitoring HIV care in the United States.

Kaiser Permanente scientists across the organization have used the rich, comprehensive, longitudinal data to conduct studies that have produced almost 500 peer reviewed papers over the past decade.<sup>[1]</sup> We are also actively engaged in clinical trials that contribute to the general knowledge base about effective treatments.

Because our research enterprise is embedded in the health system, our research scientists, clinicians, policy and health plan leaders collaborate to understand the breadth and depth of disease burden and inform policy and practice.

### Kaiser Permanente Publications Related to HIV/AIDS since 2007



Source: Kaiser Permanente Publications Library and PLUM metrics, as of 5 January 2018.

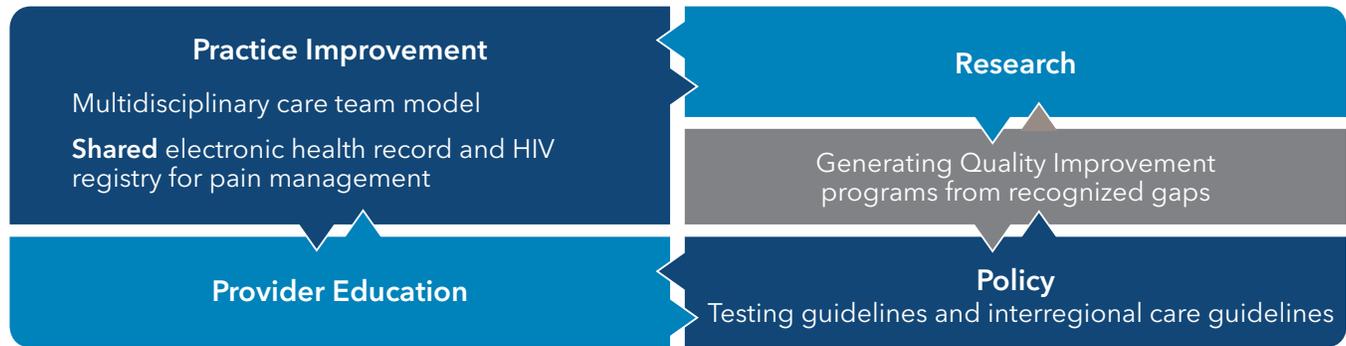
a Number of citing journal articles, according to Scopus.

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.

## KP HIV Overall Program Strategy: A Learning Organization



## Understanding Risk

### What advances have been made in preventing HIV infection?

Numerous advances to preventing HIV infection have been developed and studied over the years, including experimental products containing drugs that prevent vaginal and/or rectal transmission of HIV, vaccines and HIV Pre-Exposure Prophylaxis (PrEP).

Our researchers and clinicians are actively investigating the use of and effectiveness of PrEP, the most recently introduced HIV prevention technology. A study published in *Clinical Infectious Disease* showed that, since February 2015, there were no new cases of HIV infection in the Kaiser Permanente Northern California population despite high rates of sexually transmitted infections and decreased condom usage. This is significant because it was among the first to demonstrate the “real-world” effectiveness of this prevention strategy.<sup>[2]</sup>

A study in the *Journal of Acquired Immune Deficiency Syndrome* showed that PrEP adherence at Kaiser Permanente was 92 percent.<sup>[3]</sup> Although 15.5 percent experienced renal dysfunction, this rarely led to discontinuation.

In a study published in *Prevention Science*, researchers found that patients who initiated PrEP had other associated benefits, including reduced anxiety and feelings of stigma.<sup>[4]</sup>

### What are the risks associated with having HIV?

Using our HIV registry data, we reported in the *Journal of Acquired Immune Deficiency Syndromes* that having HIV was associated with an increased risk of both liver dysfunction and mortality related to liver dysfunction, particularly in patients with compromised immune systems and higher HIV viral loads, alcohol/drug use, diabetes, or co-infection with hepatitis B or C.<sup>[5]</sup> This has renewed attention for hepatitis B vaccination and aggressive screening for and treating of chronic hepatitis C among our HIV positive populations.

### What have we learned about aging with HIV?

For those living with HIV, the use of combination antiretroviral therapy (ART) has dramatically improved survival. It is estimated that approximately half of the HIV-positive population in the United States is now 50 years of age or older.<sup>[6]</sup> This milestone, reached several years ago in some of our regions, makes Kaiser Permanente an ideal setting to evaluate conditions associated with aging.<sup>[7]</sup>

Our research has demonstrated that, as this population lives longer, conditions associated with aging increasingly contribute to morbidity and mortality. For example, research from Kaiser

Permanente was among the first to document the high risk of several comorbidities compared with the general population, including heart attacks, strokes, and certain cancers, especially those with a known infectious cause.

### What is the link between cancer and HIV?

The link between cancer and HIV was established very early in the HIV epidemic as a rare cancer, Kaposi sarcoma (KS), was identified among otherwise healthy gay men in San Francisco and New York. Soon after, 2 additional cancers more commonly found in HIV patients were included in the definition of AIDS, specifically non-Hodgkin lymphoma and invasive cervical cancer.

Data from Kaiser Permanente was instrumental in expanding the list of cancers for which HIV patients are at increased risk. A retrospective cohort study in Kaiser Permanente evaluated the risk of cancers with and without a known infectious cause in more than 20,000 HIV-infected persons and 200,000 HIV-uninfected persons. Almost 70 percent of all cancers in HIV-infected persons had a known infectious cause, compared with only 12% in HIV-uninfected persons. While the AIDS-defining cancers were increased more than 37-fold in HIV-infected persons, other non-AIDS-defining cancers with a known infectious cause, particularly anal cancer and Hodgkin’s lymphoma, were increased by more than 9-fold. Other cancers without a known infectious cause had only a 30 percent increased risk in HIV-infected patients.<sup>[8]</sup>

The severity of HIV disease appears to play a role in this increased risk, with researchers demonstrating that HIV-infected patients with greater immunodeficiency are at particularly high risk of these aging-associated outcomes. These findings have confirmed the need for early and consistent treatment with ART to maintain immune function.

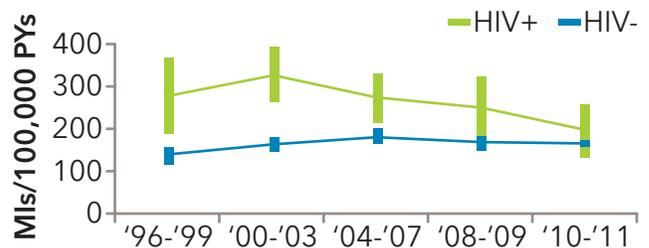
### What do we know about cardiovascular risk in those with HIV?

Cardiovascular disease, especially heart attacks emerged as a concern early in the ART era. In one of the first reports on this topic, Kaiser Permanente demonstrated an excess of risk in HIV patients.<sup>[9]</sup>

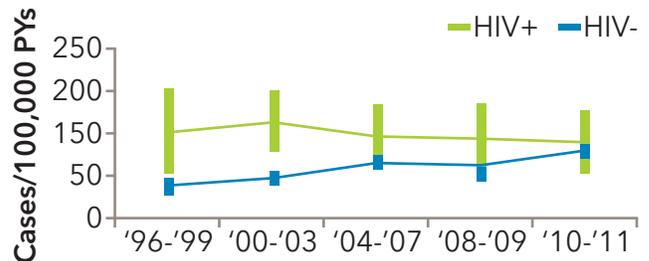
However, a more recent Kaiser Permanente study showed that, compared to a matched group of HIV-negative members in Northern and Southern California, the risk of heart attacks and strokes declined over time (see figure).<sup>[10,11]</sup>

Mitigation of clinical and behavioral risk factors and use of more lipid-friendly ART medications may also have an impact on other cardiovascular disease outcomes, such as heart failure, an understudied condition and currently under investigation at Kaiser Permanente.

Heart Attack Rates Over Time by HIV Status



Stroke Rates by HIV Status and Year



## How do mental health conditions impact HIV infected patients?

Kaiser Permanente has shown that mortality rates are higher in HIV-infected patients with substance abuse and/or psychiatric disease diagnoses even after controlling for ART and health status.<sup>[12, 13]</sup> We are now conducting research to understand why this is so and developing strategies to reduce the use of alcohol among HIV-infected patients. An ongoing randomized clinical trial is examining behavioral alcohol use interventions for hazardous-drinking HIV patients who are being seen in primary care clinic.

## Improving Patient Outcomes

### What strategies are effective in treating 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. In studies published in *AIDS Patient Care and STDs*, Kaiser Permanente performed favorably in the care of HIV patients with improvement over time on most performance measure.<sup>[14, 15]</sup>

Additional research published in *AIDS Patient Care Standards* has demonstrated the importance of office visits. In the study of nearly 3,000 members newly diagnosed with HIV, missing at least one office visit was associated with a 71percent increase in mortality over the study period, with each missed visit adding 12percent to mortality risk<sup>[16]</sup>. Kaiser Permanente research scientists have also demonstrated that multidisciplinary care – including patient engagement with a medical record system and the widespread use of clinical pharmacists – enhances the care coordination that supports adherence. Together, these studies demonstrate the importance of our multidisciplinary teams for keeping our patients with HIV engaged and retained in care, on ART, and achieving viral suppression.<sup>[17,18,19]</sup>

A new body of research 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.<sup>[20]</sup>

## 94 PERCENT TREATMENT ADHERENCE

among KP members in care and on ART



In research published in the *Journal of Acquired Immune Deficiency Syndromes*, patients with multidisciplinary care teams (instead of an infectious disease specialist alone), had significantly greater adherence to medication.



Also in research published in the same journal researchers found that patients who had a clinical pharmacist involved in their care had significantly fewer office visits.



Research published in *AIDS Behavior* showed that patients who enrolled in Kaiser Permanente's patient portal, which let them view information about their health care and engage in secure messaging with their clinicians, had better adherence to medications.

### How has Kaiser Permanente contributed to knowledge about medication efficacy and safety?

In a study published in the *Journal of Acquired Immune Deficiency Syndromes*, we found that a drug called etravirine, an ART agent used among patients with more advanced HIV

infection, improved viral load and immune system health for patients who had failed multiple prior antiretroviral therapy regimens.<sup>[21]</sup> Additional research has led to recognition of renal complications with tenofovir, a commonly used medication.<sup>[22]</sup>

## How are we working to reducing disparities?

In the more than 3 decades since AIDS was first reported, more than 150 people in the United States become infected with HIV each day. Racial and ethnic minorities among gay and bisexual men are disproportionately impacted by this epidemic in most parts of the nation and the world.

But things are different at Kaiser Permanente. In a retrospective study published in the *Journal of General Internal Medicine*, we reported no statistically significant differences in mortality or risk of progress to AIDS among black and Latino members with HIV compared to white members with HIV.<sup>[23]</sup>

## Translating Policy Into Practice

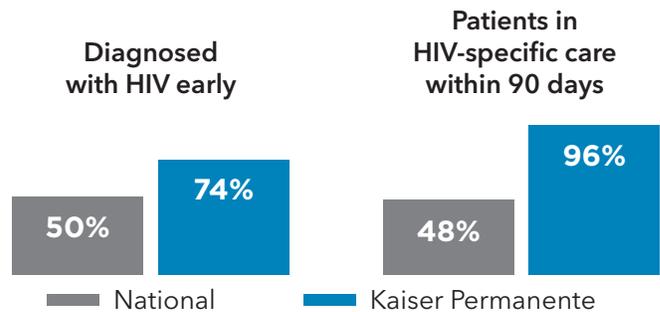
### How has Kaiser Permanente shared best practices?

In 2012, as part of Kaiser Permanente’s participation in the World AIDS Conference, we shared our toolkit of clinical best practices and challenged health care providers across the nation to improve the health equity for people living with HIV. We perform more than 300,000 screening HIV antibody tests annually to identify all of our members infected with HIV and move them into HIV multidisciplinary care, as well as help reduce risk among our HIV-negative members.

Our research scientists work closely with clinicians and leaders to generate quality improvement programs, inform practice improvement, as well as test guidelines that inform policy.

Kaiser Permanente clinician-researchers have made important contributions to the Infectious Disease Society of America and the HIV Medical Association Primary care guidelines and have held important leadership positions on HIV quality metrics panels convened by Centers for Medicare and Medicaid Services and American Health Insurance plans, as well as served on the Presidential Advisory Council on HIV/AIDS.<sup>[24-28]</sup>

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.



KP Research is committed to continuing to conduct research that improves the quality of life for patients with HIV / AIDS and to ensure that evidence-based advances in prevention and treatment are integrated into care delivery in our organization in a timely manner.

Kaiser Permanente’s nearly 170 research scientists and more than 1,600 support staff are based at eight regional research centers and one 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 eight states and the District of Columbia.

This brief was written by Maureen McInaney, Nicholas Emptage, Anna C Davis, and Elizabeth A McGlynn. It is available online from <https://share.kp.org/research/briefs>. The authors wish to thank the following researchers for their contributions to the development of this brief: Michael Horberg and Michael Silverberg.

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