

## Kaiser Permanente Research Brief

# HIV and 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 and 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.<sup>1</sup> Nevertheless, according to 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.<sup>2,3</sup> 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.<sup>3</sup> Moreover, despite representing just 30% of the U.S. population, nearly 2 out of 3 new HIV infections occur in Black and Latino Americans.<sup>3</sup>

Because of treatment advances and improved survival that began in the late 1990s, the number of Americans living with HIV has increased substantially.<sup>1</sup> By the end of 2015, an estimated 1.1 million adolescents and adults were living with HIV.<sup>2</sup> Among those living with HIV, nearly two-thirds were receiving treatment for the disease, and approximately half had achieved viral suppression.<sup>4</sup> 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, or PrEP, which is a prescription of HIV antiviral drugs that helps prevent infection in people without HIV.

HIV and AIDS is an active area of study for Kaiser Permanente Research. Scientists across the organization 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

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



Source: Kaiser Permanente Publications Library and PlumX metrics, as of October 19, 2020.

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 8 regions and was supported by a wide range of funding sources including internal research support as well as both governmental and nongovernmental extramural funding.

practice. We have published nearly 750 articles related to HIV and AIDS since 2007, which have been cited more than 40,000 times.<sup>5</sup> These articles are the product of observational 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 groups, and health plan leaders collaborate – lets us contribute generalizable knowledge on HIV and AIDS, and many other topics of research.

## Understanding Risk

### Who is at risk for the development or progression of HIV and 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.<sup>6-9</sup> Our researchers have studied disparities in HIV risk, and have found elevated risks among men who have sex with men, as well as Latinos and transgender patients.<sup>10-12</sup>

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.<sup>13</sup> Furthermore, while timely initiation of antiretroviral therapy has increased with time, many patients with known HIV are unable to access the care they need.<sup>14,15</sup> Our research has found that the immune status of patients making their first contact for HIV care has not improved over time,<sup>13</sup> and that this effect is particularly pronounced among older patients.<sup>16</sup> 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.<sup>17-20</sup>

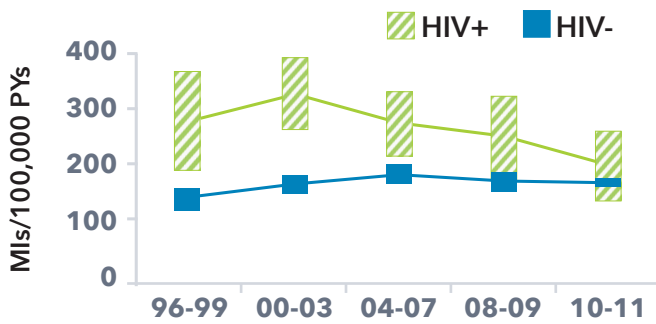
### What health risks do people with HIV and AIDS face?

In the early years of the HIV and AIDS epidemic, death from AIDS-related illnesses was the primary health risk in this group of patients. In 2021, with effective treatments being widely available, this is no longer the case.<sup>21-23</sup> Rather, with HIV-positive people living as long as those without HIV infection,<sup>24</sup> conditions associated with aging,<sup>25,26</sup> such as non-AIDS-defining cancers,<sup>25,27-32</sup> cardiovascular disease,<sup>33,34</sup> chronic respiratory illness,<sup>35</sup> and neurocognitive degeneration,<sup>36</sup> 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.<sup>37,38</sup>

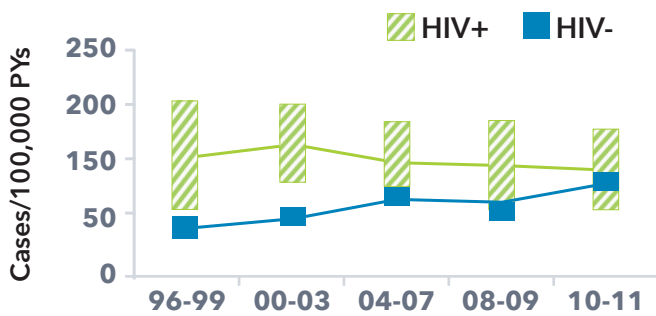
More generally, data from Kaiser Permanente have been instrumental in enriching our understanding of those cancers for which HIV patients are at increased risk. Large studies conducted in Kaiser Permanente members have found significantly higher risks for several forms of cancer among people with HIV,<sup>39-45</sup> 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.<sup>28,46,47</sup> 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.<sup>48</sup> Finally, compared to those without HIV, patients with HIV have lower 5-year survival rates for some forms of cancer,<sup>49</sup> and higher rates of cancer-attributable mortality.<sup>50</sup>

Our scientists were among the first to demonstrate an excess risk of cardiovascular diseases, including heart attacks, in HIV patients.<sup>33,34,45,51</sup> Moreover, the use of antiretroviral therapy, known as ART, has greatly complicated the treatment of elevated blood cholesterol.<sup>52-55</sup> However, a more recent study conducted in Kai-

## Heart Attack Rates Over Time by HIV Status<sup>56</sup>



## Stroke Rates by HIV Status and Year<sup>57</sup>



ser Permanente members found that the risk of heart attacks and strokes has declined in recent years.<sup>45,56,57</sup> Increased attention to clinical and behavioral cardiovascular risk factors, and increased use of lipid-friendly ART medications,<sup>58</sup> 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 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.<sup>59,60</sup> This has renewed attention to hepatitis B vaccination and aggressive screening for and treatment of chronic hepatitis C among HIV-positive populations.<sup>61-63</sup> 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,<sup>64</sup> these risks remain high,<sup>45</sup> particularly in African American patients,<sup>65</sup> and moderate kidney dysfunction in patients with HIV remains a problem.<sup>66</sup>

Research conducted at Kaiser Permanente has also shown that mortality rates, rates of comorbid 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.<sup>67-72</sup> 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.<sup>22</sup> Alcohol use disorders are common, and often undertreated, among patients with HIV,<sup>73,74</sup> and increases in alcohol use are associated with higher rates of sexually transmitted infections and poorer control of HIV disease.<sup>75,76</sup> 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.<sup>77-82</sup>

## Improving Patient Outcomes

### What strategies are effective in preventing HIV and AIDS?

Screening of people whose HIV status is unknown is effective in preventing transmission of the virus.<sup>83</sup> Our research has explored factors associated with screening rates, including addressing concerns about the cost of implementing screening<sup>84</sup> and improving levels of HIV knowledge at the community level.<sup>11,85</sup> Kaiser Permanente scientists have explored numerous interventions for improving HIV screening,<sup>7,86-88</sup> including the implementation of electronic health record alerts for screening pregnant women<sup>8</sup> and high-risk populations.<sup>89</sup> 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.<sup>90</sup> 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.<sup>83,91-94</sup> 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.<sup>83,91</sup> Work by Kaiser Permanente researchers has demonstrated that, as treatment within a community lowers its total



**Kaiser Permanente's San Francisco Medical Center cares for over 170,000 adult members.**



**From July 2012 through February 2015, 657 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 period.<sup>88</sup>**

viral load, transmission of the virus is reduced, and total mortality declines as a result.<sup>23,95</sup>

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, or 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;<sup>96</sup> PrEP adherence in this study was 92%.<sup>97</sup> A more recent study found that an alternative PrEP regimen was similarly effective among Kaiser Permanente members in San Francisco.<sup>98</sup> Other benefits of PrEP may include reduced anxiety and feelings of stigma.<sup>99</sup> Despite these promising results, awareness and uptake of PrEP in high-risk populations and compliance with recommended dosing are continuing challenges.<sup>100-103</sup> Recent research has suggested that younger age, cannabis use, presence of a sexually transmitted infection, and fewer sexual partners may be risk factors for PrEP discontinuation.<sup>104</sup>

## How does early identification of HIV affect outcomes?

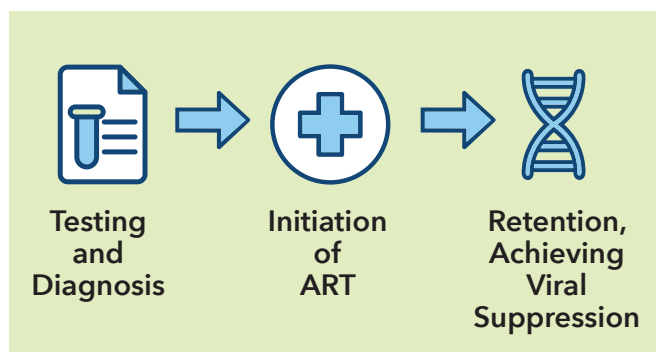
Large numbers of people with HIV are not aware that they have contracted the virus, and remain at risk for both disease transmission and progression of HIV.<sup>13</sup> Screening efforts are critical for the long-term health of these patients and those who may be vulnerable to HIV transmission,<sup>83</sup> and early identification and treatment may prevent comorbid cancer, cardiovascular disease, and other illnesses that occur frequently in people with HIV.<sup>29,41,56,57,105,106</sup>

## What are the key factors in effective treatment of people with HIV and 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.<sup>17,20,107</sup> Kaiser Permanente scientists have identified subgroups of patients with HIV who may require additional outreach to foster their engagement with these care processes.<sup>108</sup> 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%.<sup>109</sup>

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.<sup>110</sup> Further, our scientists and HIV care leaders have broadened

## Effective care for patients with HIV requires engagement throughout the continuum of care<sup>83</sup>



the definition of quality care for HIV to include reduced hospitalizations and prevention of other health conditions, and have investigated opportunities for providing such care at Kaiser Permanente.<sup>111,112</sup>

Our scientists are also involved in studies of antiretroviral therapy, or ART, medication effectiveness and safety.<sup>58,113-119</sup> 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.<sup>120,121</sup> 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.<sup>122</sup> Other research has led to the recognition of renal complications with tenofovir, a commonly used medication.<sup>123</sup> Our scientists have also contributed to research on the weight gains associated with various ART regimens.<sup>124</sup>

HIV disproportionately affects people who are Black and Latino, as well as those from the LGBTQ community.<sup>11,21,61,125,126</sup> These disparities are of great concern to Kaiser Permanente, given our long-standing commitment to eliminating them.<sup>127</sup> 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.<sup>128</sup> 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.<sup>129</sup>

## Translating Research Into Policy and Practice

### How has Kaiser Permanente research on HIV and 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 risks of HIV and AIDS and improve outcomes for patients with HIV and 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 and AIDS.<sup>86,130</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. More recently, our scientists participated in a randomized study that demonstrated the effectiveness of a pharmacist-led intervention to reduce inappropriate medication prescribing among patients with HIV.<sup>131</sup>

Kaiser Permanente research contributes not only to policy and practice changes within our own delivery system, but also to advancing national understanding of HIV and AIDS. Our research on HIV and AIDS since 2007 has been cited more than 260 times in recent consensus statements, clinical practice guidelines, and point-of-care decision aid tools, including guidelines issued by the U.S. Public Health Service<sup>132</sup> and the World Health Organization.<sup>133</sup> 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 Diseases Society of America<sup>134</sup> and the HIV Medical Association<sup>135,136</sup> guidelines,<sup>137</sup> and have led systematic reviews for the U.S. Preventive Services Task Force.<sup>94,138</sup> Our scientists were also co-authors of a position statement on stewardship of antiretroviral medications from the Infectious Diseases Society of America, the HIV Medicine Association, and the American Academy of HIV Medicine.<sup>139</sup>

Kaiser Permanente is also an established national and international leader in the field of HIV and 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 health equity for people living with HIV.<sup>140</sup> Our research groups lead numerous large trials evaluating new antiretroviral therapy treatments,<sup>58,120</sup> 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 185 research scientists and more than 1,530 support staff are based at 9 research centers. There are currently more than 2,355 studies underway, including clinical trials. Since 2007 our research scientists have published nearly 19,000 articles in peer-reviewed journals. Kaiser Permanente currently serves more than 12.4 million members in 8 states and the District of Columbia.

This brief was written by Nicholas P. Emptage, Anna C. Davis, and Elizabeth A. McGlynn. It is available online at [about.kaiserpermanente.org/our-story/health-research/research-briefs](http://about.kaiserpermanente.org/our-story/health-research/research-briefs). The authors wish to thank the following researchers for their contributions to the development of this brief: Michael J. Silverberg and Michael A. Horberg.

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