

## Kaiser Permanente Research Brief

# HIV and AIDS

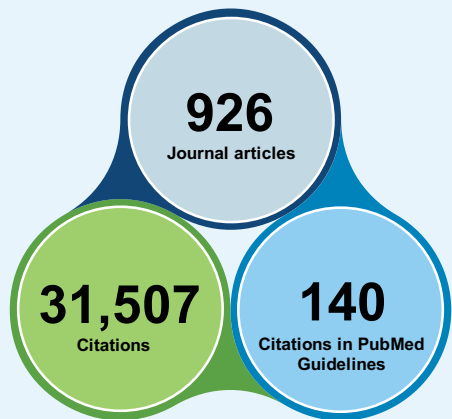
This brief summarizes the contributions of Kaiser Permanente Research since 2012 on the topic of HIV and AIDS.

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 36,000 new cases of HIV were diagnosed in the United States in 2021.<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, more than 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 2021, an estimated 1.1 million adolescents and adults were living with HIV.<sup>2</sup> Among those living with HIV, approximately 80% were receiving treatment for the disease, and nearly 70% of those being treated 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 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 practice. We have published more than 900 articles related to HIV and AIDS since 2012, which have been cited approximately 31,500 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 research topics.

### Kaiser Permanente publications related to HIV and AIDS since 2012



Source: Kaiser Permanente Publications Library and Scite metrics, as of November 9, 2023.

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.

## Understanding risk

### Who is at risk for the development and 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; 7</sup> Our researchers have studied disparities in HIV risk, and have found elevated risks among men who have sex with men, Latinos, and transgender patients.<sup>8; 9</sup>

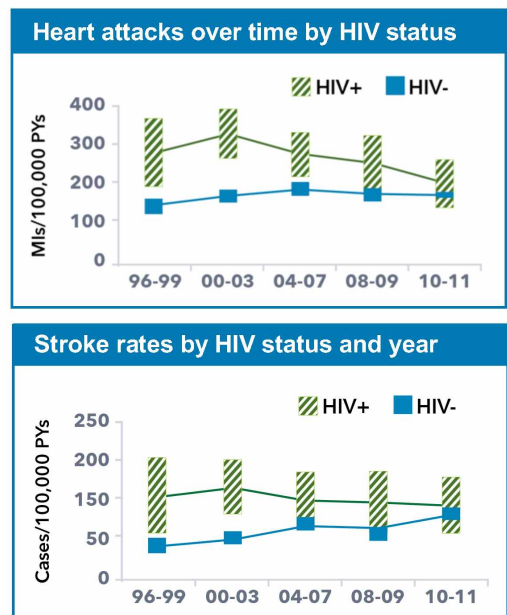
Our research has also informed the question of disease progression in patients with HIV infection. Many people with HIV are unaware that they have contracted the virus, and as such, do not receive appropriate treatment.<sup>10</sup> Furthermore, while timely initiation of antiretroviral therapy has increased with time, many patients with known HIV are unable to access the care they need.<sup>11; 12</sup> Our research has found that the immune status of patients making their first contact for HIV care has not improved over time.<sup>10</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>13; 14</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 2023, with effective treatments being widely available, this is no longer the case.<sup>15-21</sup> While people with HIV are now living as long as people without HIV infection, evidence suggests that patients with HIV remain at higher risk of comorbid conditions, and that the onset of these conditions occurs earlier, relative to the onset in people without HIV.<sup>22</sup> As such, conditions associated with aging,<sup>23-26</sup> such as non-AIDS-defining cancers,<sup>23; 27-33</sup> cardiovascular disease,<sup>34; 35</sup> chronic respiratory illness,<sup>36</sup> dementia,<sup>37; 38</sup> and other forms of neurocognitive degeneration,<sup>23</sup> have increasingly contributed to morbidity and mortality among patients with HIV. Given these trends, our researchers have studied the delivery of screening and other forms of preventive care to these patients.<sup>39; 40</sup>

Data from Kaiser Permanente have been instrumental in enriching our understanding of those cancers for which patients with HIV 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>41-46</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>47-49</sup> Compared to those without HIV, patients with HIV have lower 5-year survival rates for some forms of cancer,<sup>50</sup> and higher rates of cancer-attributable mortality.<sup>51</sup> Recent research, however, suggests that earlier initiation of antiretroviral therapy may reduce the risk of virus-related cancers.<sup>52</sup>

Our scientists were among the first to demonstrate an excess risk of cardiovascular diseases, including heart attacks, in patients with HIV.<sup>34; 35; 46; 53; 54</sup> Moreover, the use of antiretroviral therapy, known as ART, has greatly complicated the treatment of elevated blood



cholesterol,<sup>55-57</sup> and our research has demonstrated that many statin-eligible patients with HIV do not receive these medications.<sup>58</sup> However, a more recent study conducted in Kaiser Permanente members found that the risk of heart attacks and strokes has declined in recent years.<sup>46; 59; 60</sup> Increased attention to clinical and behavioral cardiovascular risk factors, and increased use of lipid-friendly ART medications,<sup>61</sup> may also have an effect on cardiovascular outcomes such as heart failure, a historically understudied condition currently being investigated actively within Kaiser Permanente.<sup>54; 62-64</sup>

HIV has also been associated with an increased risk of liver dysfunction, liver cancer, and related mortality, particularly in patients with compromised immune systems and higher HIV viral loads, alcohol use, drug use, diabetes, or coinfection with hepatitis B or C.<sup>65-68</sup> This has renewed attention to hepatitis B vaccination and aggressive screening for and treatment of chronic hepatitis C among populations with HIV.<sup>69-71</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>72</sup> these risks remain high,<sup>46</sup> particularly in Black patients.<sup>73</sup>

Research conducted at Kaiser Permanente has also shown that mortality rates, rates of comorbid illness, and other outcomes are poorer in patients with HIV and concurrent substance use and/or psychiatric disorders, even after controlling for ART and health status.<sup>74-80</sup> Our scientists have found that the gap in life expectancies between Kaiser Permanente members with and without HIV is narrower in patients with no history of drug or alcohol use.<sup>16</sup> Smoking and alcohol use disorders are common, and often undertreated, among patients with HIV,<sup>81-83</sup> and increases in alcohol use are associated with higher rates of sexually transmitted infections and poorer control of HIV disease.<sup>80; 84</sup> Research is underway to learn more about co-occurring behavioral health conditions in patients with HIV and to evaluate strategies for reducing the use of alcohol among these patients.<sup>76; 77; 85-88</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, and Kaiser Permanente continues to develop and refine innovative approaches to screening for HIV and other sexually transmitted diseases.<sup>89</sup> Our research has explored factors associated with screening rates, including addressing concerns about the cost of implementing screening<sup>90</sup> and improving levels of HIV knowledge at the community level.<sup>8; 91</sup> Kaiser Permanente scientists have explored numerous interventions

**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>100</sup>**



for improving HIV screening,<sup>10; 92</sup> including report cards<sup>93</sup> and the implementation of electronic health record alerts for screening pregnant women<sup>6</sup> and other patients at high risk.<sup>94</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>95</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>94; 96; 97</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>94</sup> 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.<sup>17; 98</sup>

Kaiser Permanente researchers and clinicians also are actively investigating the use and effectiveness of HIV pre-exposure prophylaxis, or PrEP. Research in our Northern California population among members enrolled in a PrEP protocol found high rates of PrEP adherence<sup>99</sup> and no new cases of HIV infection despite high rates of sexually transmitted infections and decreased condom usage.<sup>100; 101</sup> Other benefits of PrEP may include reduced feelings of anxiety and stigma.<sup>102</sup> Despite these promising results, awareness and uptake of PrEP in patients at high risk, and compliance with recommended dosing, are continuing challenges.<sup>103-109</sup> Kaiser Permanente scientists in Southern California have studied the implementation of a primary care screening program that has significantly increased identification and enrollment of eligible patients into PrEP efforts.<sup>110</sup> Nevertheless, barriers to PrEP initiation and adherence, including clinician identification of eligible patients, remain common.<sup>111; 112</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>113</sup> Moreover, high rates of sexually transmitted infections among PrEP users have emphasized the need for ongoing testing and programs to mitigate these risks.<sup>114; 115</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 virus transmission and progression of HIV.<sup>10</sup> Screening efforts are critical for the long-term health of these patients and those who may be vulnerable to HIV transmission,<sup>92; 94; 116</sup> and early identification and prompt initiation of antiretroviral treatment may prevent comorbid cancer, cardiovascular disease, and other illnesses that occur frequently in people with HIV.<sup>28; 41; 59; 60; 117-119</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>14; 120</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>121-123</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, and has worked to identify subgroups of patients whose linkage with this continuum is suboptimal.<sup>79</sup> 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>124</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>125</sup> Further, our scientists and HIV care leaders have broadened 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>126; 127</sup>

Our scientists are also involved in studies of antiretroviral therapy, or ART, medication effectiveness, acceptability, and safety.<sup>61; 128-133</sup> Recent studies comparing the efficacy and safety of non-nucleoside reverse transcriptase inhibitors (NNRTIs) and integrase-strand transfer inhibitors (INSTIs) has found that

drug resistance is more common in patients using NNRTIs,<sup>134</sup> and that the risk of virologic failure is lower in resistant patients switched to INSTIs.<sup>135</sup> However, while most modern ART agents are much safer than older drugs and drug regimens, there are substantial risks associated with INSTIs,<sup>131</sup> including weight gain<sup>136; 137</sup> and an elevated risk of diabetes.<sup>136; 138</sup> Other research has suggested that some protease inhibitor ART agents may be associated with higher rates of liver complications.<sup>139</sup> Our scientists have contributed to research on the weight gains associated with various ART regimens,<sup>137; 140; 141</sup> and have identified clinic factors, including regular medication dispensing reviews and enhanced adherence services, associated with higher rates of ART initiation and viral suppression.<sup>142</sup>

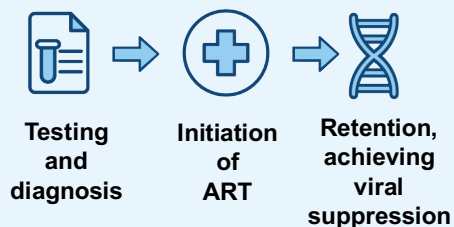
HIV disproportionately affects people who are Black and Latino, as well as people from the LGBTQ community.<sup>8; 15; 69; 143-145</sup> These disparities are of great concern to Kaiser Permanente, given our long-standing commitment to eliminating them.<sup>146</sup> Although racial disparities in access to recommended treatments persist at a national level,<sup>147</sup> recent research has failed to find significant disparities in treatment access or viral load among Kaiser Permanente members with HIV and hepatitis C coinfection.<sup>148</sup>

Researchers at Kaiser Permanente have also been involved in numerous studies illustrating the challenges of caring for patients with HIV during the COVID-19 pandemic. Our scientists found evidence that adherence to composite medications for HIV declined during the acute phase of the pandemic,<sup>123</sup> though other data suggested that the use of tenofovir, either for the prevention or treatment of HIV infection, was protective against poor COVID-19 outcomes.<sup>149</sup> Other research found that the risk of post-vaccination breakthrough COVID-19 infection was higher among patients with HIV, suggesting that these patients may derive greater benefit from booster doses of these vaccines.<sup>150</sup>

## Translating Research Findings Into 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 to improve outcomes for patients with HIV. 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

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



of HIV.<sup>151</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>152</sup> Another recent randomized trial tested the use of an HIV risk score, developed using electronic health record data, to identify patients who may benefit from HIV pre-exposure prophylaxis.<sup>95</sup>

Kaiser Permanente research contributes not only to policy and practice changes within our own care delivery system, but also to the advancement of national understanding of HIV and AIDS. Our research on HIV and AIDS since 2012 has been cited 140 times in recent consensus statements and clinical practice guidelines, including guidelines issued by the U.S. Public Health Service<sup>153</sup> and the World Health Organization.<sup>154</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 and the HIV Medicine Association guidelines,<sup>155-159</sup> and have led systematic reviews for the U.S. Preventive Services Task Force.<sup>160</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>161</sup>

Kaiser Permanente is also an established national and international leader in the field of HIV 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>162</sup> Our research groups lead numerous large trials evaluating new antiretroviral therapy treatments<sup>61</sup> and our scientists hold key leadership positions in important collaborative research efforts such as the Antiretroviral Therapy Cohort Collaboration,<sup>21; 163; 164</sup> The District of Columbia HIV Cohort,<sup>20; 165</sup> and the North American AIDS Cohort Collaboration on Research and Design,<sup>58; 133; 166; 167</sup> all funded by the National Institutes of Health.

Kaiser Permanente researchers also hold leadership roles in organizations such as the HIV Medicine 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 & Medicaid Services and America's Health Insurance Plans.

This brief was written by Nicholas P. Emptage, Anna C. Davis, and Elizabeth A. McGlynn. It is available online from [about.kaiserpermanente.org/our-story/health-research/research-briefs](https://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. Learn more about Kaiser Permanente Research at [about.kaiserpermanente.org/health-and-wellness/health-research](https://about.kaiserpermanente.org/health-and-wellness/health-research).

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