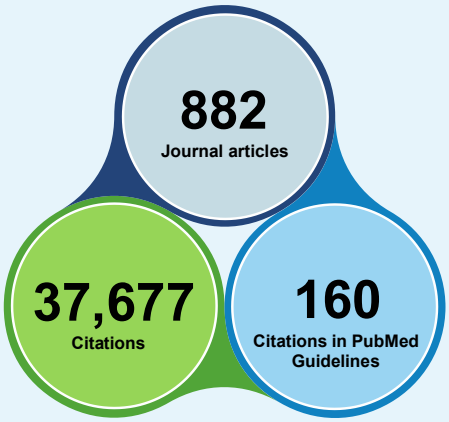
Kaiser Permanente Research Brief

Vaccines

This brief summarizes the contributions of Kaiser Permanente Research since 2012 on the topic of vaccines. This includes vaccinations delivered in early childhood as well as those delivered to adolescents and adults.

Although the development of vaccinations against communicable diseases dates back to the 18th century, the creation of modern vaccines and their widespread use in the United States began in the 20th century.[1] Today, the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention provides national recommendations for vaccines, including pertussis (whooping cough) shots for pregnant women and numerous vaccinations delivered to children, adolescents, and adults.[2] Although vaccination has largely eliminated diseases such as measles and rubella in the United States,[1] these and other diseases are still found frequently in countries with lower rates of vaccine coverage,[3] and the ease of global travel has led to cases in which unvaccinated people from well-vaccinated nations have contracted these infections.[4] Moreover, diseases such as pertussis,[1] varicella (chicken pox),[5] and human papillomavirus (HPV)[6] still occur frequently in the United States.

Kaiser Permanente publications related to vaccines since 2012



Source: Kaiser Permanente Publications Library and Scite metrics, as of June 18, 2024.

In addition to the direct effect of immunizing patients against dangerous diseases, vaccination also benefits society more broadly through so-called “herd immunity” effects. Through herd immunity, higher rates of effective vaccination for a given illness at a population level confer protection to unvaccinated individuals by making encounters with infected individuals increasingly rare. For example, increased uptake of the pediatric pneumococcal vaccine has been associated with decreased rates of the disease among adults, many of whom have not, until recently, received this vaccine.[7; 8] The level of vaccination coverage required to create herd immunity for a given disease depends on both the vaccine’s effectiveness and how easily the disease is transmitted between unvaccinated people.

Vaccination is an active area of study for Kaiser Permanente Research. Scientists across the organization have used our rich, 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 880 articles related to vaccines since 2012.[9] Together, these articles have been cited nearly 38,000 times. These articles are the product of observational studies, randomized controlled trials, meta-analyses, and other studies led by Kaiser Permanente scientists. Our unique environment, which includes our fully integrated care and coverage model, lets our research scientists, clinicians, medical

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.

groups, and health plan leaders collaborate to contribute generalizable knowledge on vaccines, and many other research topics.

Understanding risk

Who is at risk of acquiring vaccine-preventable communicable diseases?

Any person who has not been vaccinated against a particular disease and encounters a person infected with that disease is at risk of infection. Additionally, no vaccine is 100% effective in preventing disease transmission, so vaccinated people may continue to be at risk.[10; 11] In children, undervaccination (either delaying or not receiving vaccines) appears to be increasingly common.[12; 13] Parental refusal of vaccines has been associated with outbreaks of measles, pertussis, varicella, Haemophilus influenzae type b (Hib), and pneumococcal disease,[14] and our recent studies have linked parental hesitancy with significantly higher rates of pertussis, varicella, and pneumococcal disease.[15] Another study conducted by our scientists found lower rates of vaccination in children diagnosed with autism spectrum disorder, as well as their younger siblings.[16] Our researchers also have found higher rates of infection in children who failed to complete all courses of multicourse vaccines.[17] In some instances, delaying vaccinations can increase the risk of side effects. For example, delayed receipt of measles-mumps-rubella (MMR) or measles-mumps-rubella-varicella (MMRV) vaccine has been associated with a higher risk of febrile seizures.[18] Other research has shown that neonatal intensive care unit-treated infants may not receive all appropriate vaccines.[19]

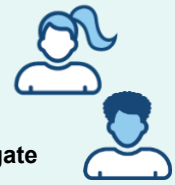
In adults, our research has found higher risks of herpes zoster[20] and influenza[21] among the unvaccinated, and cervical cancer may be more common among women who do not receive HPV vaccination during adolescence.[22] Individuals with weakened immune systems also are at higher risk of acquiring vaccine-preventable diseases. For example, reactivation of latent herpes zoster infection is more likely to occur in patients using immunosuppressive drugs.[23]

The CDC's Advisory Committee on Immunization Practices sets national guidelines for recommended vaccines.

Childhood
(Birth to 10 years)

- **Pertussis** (during pregnancy)
- **Diphtheria, tetanus, and pertussis**
- **Hepatitis A, hepatitis B**
- **Polio**
- **Pneumococcal disease**
- **Haemophilus influenza, type B** (Hib)
- **Measles, mumps, rubella, and varicella**
- **Rotavirus**
- **Annual flu** (beginning at 6 months and older)
- **COVID-19** (6 months and older)

Adolescence
(11 to 18 years)



- **Human papillomavirus (HPV)**
- **Meningococcal conjugate**
- **Tetanus, diphtheria, and pertussis**
- **Annual flu**
- **COVID-19**

Adulthood
(19+ years)

- **Annual flu**
- **Tetanus and diphtheria** (with/without pertussis)
- **COVID-19**
- **Hepatitis B** (ages 19-59)
- **Herpes zoster** (at age 50)
- **Pneumococcal** (at age 65)

How safe are vaccines?

Because vaccines are, by definition, delivered to large numbers of healthy individuals, they are judged by very strict standards of safety, and regulatory approval is only granted to vaccines with extremely low observed risks. Kaiser Permanente researchers have been involved in studying the safety of COVID-19, meningococcal,[24-30] pneumococcal,[31-35] HPV,[36-42] MMR,[43] MMRV,[44; 45] tetanus-diphtheria-pertussis (Tdap),[46-50] diphtheria-tetanus-pertussis (DTaP)-polio,[51] flu,[52-64] shingles,[65; 66] pertussis,[67] hepatitis A[68], and hepatitis B[69; 70]

vaccines, among others.[71-76] The rarity of problems with vaccine safety makes the prediction of risks challenging, and requires considerable research expertise[77-80] and ongoing surveillance.[54; 81-85]

Swelling or soreness at the vaccination site[86-88] and complications such as febrile seizures[89; 90] or fevers[91; 92] are known side effects of vaccines, though these are rarely associated with long-term health problems.[93] Our scientists have led studies linking febrile seizure risks to specific vaccines, including the MMRV[94; 95] and influenza[96] vaccines. Elderly patients have also experienced higher rates of adverse effects from the shingles[86] and tetanus-diphtheria-pertussis (Tdap)[97] vaccines, although these risks are arguably outweighed by the benefits of these vaccines, such as prevention of neuralgic pain and tetanus or diphtheria infection. Kaiser Permanente scientists are also involved in studies of safety concerns associated with COVID-19 vaccines,[81; 98] including myocarditis and pericarditis,[81; 99-105] Guillain-Barre syndrome,[106] post-surgical risks,[107] adverse birth outcomes,[108-110] hypersensitivity reactions,[111-115] adverse outcomes associated with simultaneous administration with other vaccines,[116] and other adverse events.[81; 117-122]

Improving Patient Outcomes

What strategies are effective in increasing vaccination rates?

Kaiser Permanente scientists have developed and tested programs that address parental concerns about vaccinating their young children.

Beginning during pregnancy and continuing through infancy, physicians should provide information about vaccines and work actively to build trust with hesitant parents.

A website featuring vaccine information and social sharing capabilities that allows parents to communicate and share information is associated with improved vaccination rates.

Despite the importance of routine vaccination, compliance with many recommendations is inconsistent, and research conducted by our scientists has demonstrated racial and socioeconomic disparities in receipt of early childhood,[123; 124] flu,[125] and COVID-19[126-129] vaccines, as well as suboptimal rates of flu vaccination among pregnant women.[130] In addition, our research has highlighted the challenges of completing recommended vaccinations during the COVID-19 pandemic, in light of disrupted access to medical care.[131-134] Kaiser Permanente researchers have explored a variety of approaches for increasing vaccination rates. In general, the approaches used for early-childhood vaccination are very different from those used for other types of vaccines. Successful interventions for increasing vaccine uptake in young children include physician-oriented approaches to address parental hesitancy[135-142] and financial barriers to vaccination,[143] tailored messages delivered via social and other media,[144-151] automated reminders,[152] school-based vaccination,[153-156] and community-based education (for example, public service announcements).[148; 157] In contrast, outreach approaches that have been shown to increase adolescent and adult uptake of vaccines include workplace vaccination programs,[158] reminders placed in the electronic health records of patients or parents,[159-161] mailed or electronic reminders,[162-164] and use of vaccine series requiring fewer doses for completion.[70; 165; 166] Kaiser Permanente scientists have also conducted extensive research on public perceptions and hesitancy regarding COVID-19 vaccination in a variety of populations, including young adults,[167] immunocompromised patients,[168] pregnant women,[169; 170] parents,[171-173] essential workers,[174] health care workers,[127; 175] members of ethnic minorities,[176] and homeless people.[177]

How effective is vaccination in preventing the transmission of communicable diseases?

Kaiser Permanente researchers have been actively involved in research on vaccine effectiveness, including herd immunity effects[178-180] and protection of vulnerable populations, including the elderly,[181-191] infants,[192-199] young children,[200; 201] people with suppressed immune systems,[23; 202] and people with certain chronic diseases.[203; 204] Our scientists participate in clinical trials and evaluations of the real-world effectiveness of influenza and COVID-19 vaccines,[205-241] including studies of booster dose effectiveness,[242-254] studies exploring the waning effects of these vaccines over time,[255-260] evaluations of the transmission of vaccine-associated immunity from mothers to newborn children,[241] and evaluations of the risk of postvaccination breakthrough infections among immunocompromised patients.[261-263] Recent work by our scientists has explored the mechanisms by which zoster and pneumococcal vaccination in older adults appears to protect against other infectious illnesses,[264; 265] as well as evaluating the prevention of gonorrhea infections through meningococcal vaccination.[266] Other Kaiser Permanente research has identified shortcomings in vaccine effectiveness. Numerous studies of annual flu vaccinations have identified waning effects over time,[267-269] differences in effectiveness between vaccine types,[237; 270-272] and variable effectiveness from year to year.[21; 273] More recently, we have repeatedly found evidence of the waning effectiveness of the pertussis[274-279] and herpes zoster[188; 189; 280; 281] vaccines. This work contributed directly to changes in the ACIP's recommendations regarding immunization for these conditions. Finally, our scientists are actively involved in randomized trials evaluating the effectiveness of simultaneous administration of multiple vaccines to adolescents[74] and adults.[76]

How does vaccination affect a person's health?

Vaccine-preventable diseases carry serious and well-known health risks, including cervical cancer from HPV, liver failure from hepatitis, meningitis from Hib, and death from illnesses such as influenza, pertussis, or hepatitis.[282; 283] Vaccination affects health in numerous ways beyond the transmission of communicable diseases. For example, vaccination in pregnant women has been shown to transmit immunity to their children,[284; 285] and annual flu vaccinations appear to have small but statistically significant effects on hospitalization rates[236; 239; 286] and numbers of outpatient visits.[287]

Translating Research Findings Into Policy and Practice

As part of a learning health care organization that uses research to inform and improve practice, our research, clinical, and operational partners have tested a range of interventions to increase uptake of recommended vaccines. Pediatricians in Kaiser Permanente have worked to address parental vaccine hesitancy,[136; 288; 289] leading to the development and evaluation of messaging interventions.[137; 145] This work was subsequently expanded to flu and HPV vaccination. Reminders placed in Kaiser Permanente's electronic health record system have been used to inform changes in vaccination policies,[290-292] including a change in herpes zoster vaccines. Our scientists have also explored multicomponent programs for increasing rates of HPV vaccination.[293]

Collectively, research from Kaiser Permanente authors has been cited 160 times in recent practice guidelines, including the vaccination guidelines for influenza,[294] HPV,[295] herpes zoster,[296] and Tdap[297] published by the CDC's Morbidity and Mortality Weekly Report. More recently, our scientists have contributed to COVID-19 and other vaccine recommendations published by the CDC's Advisory Committee on Immunization Practices,[298-310] as well as COVID-19 recommendations and guidance on vaccination in patients with rheumatic and musculoskeletal diseases from the American College of Rheumatology,[311-316] and a guideline for vaccination of patients with cancer from the American Society of Clinical Oncology.[317] Our

research has also directly influenced national vaccine policies. Work questioning the durability of the pertussis vaccine delivered to children[275; 279] led to increased emphasis on prenatal vaccination,[284] and other work[280] prompted uptake of a newer zoster vaccine.[281]

Kaiser Permanente has also shown considerable leadership in the field of vaccine research. Our researchers are leaders in the CDC's Vaccine Safety Datalink, or VSD, an ongoing effort to use data from large health care organizations to evaluate vaccine safety.[318-322] In the VSD, which began in 1990, 6 of our regions contribute electronic patient data that are used to study rare but serious adverse reactions, the safety of new vaccines, and changes in vaccine recommendations. Vaccine safety in pregnancy is an emphasis of VSD research, along with the development of new research methods and rapid cycle analysis techniques for promptly notifying the public of possible risks.[83; 323-326] We are also involved in the U.S. Flu Vaccine Effectiveness Network, which provides interim and annual estimates of the effectiveness of each year's flu vaccine by studying individuals entering health care facilities during flu season.[327-342] Our researchers continue to be involved in early-stage vaccine development through the large, long-standing vaccine clinical trials program in the Northern California Vaccine Study Center, and through the National Institutes of Health's Vaccine and Treatment Evaluation Units (VTEU) network.[343; 344] The VTEU, based in Kaiser Permanente's Washington Region, is the only such unit in the country housed in an integrated health organization. Our researchers have also participated in a recent workshop on pertussis vaccine waning, organized by the National Institute of Allergy and Infectious Diseases,[345] as well as a Brighton Collaboration effort aimed at standardizing the case definition of multisystem inflammatory syndrome.[346] Finally, our scientists are part of ongoing research efforts to develop vaccines in response to COVID-19.[347] The VTEU was the lead site for the first-ever trial of a COVID-19 vaccine, evaluating the vaccine developed by Moderna Therapeutics and the National Institute of Allergy and Infectious Diseases.[348; 349] Our researchers have been involved in several late-phase efficacy trials, including trials of the vaccines developed by Pfizer and BioNTech, Moderna and NIAID, and Johnson & Johnson.[350] Kaiser Permanente scientists have also participated in the ACIP Vaccine Safety Technical (VaST) Work Group, an expert panel convened to improve the monitoring of COVID-19 vaccine safety,[351] as well as the National Vaccine Advisory Committee's Vaccine Safety Subcommittee and the Western States COVID-19 Scientific Safety Review Workgroup. One of our researchers also served on a National Academy of Medicine committee that recently completed a report on the safety of COVID-19 vaccines.[352]

Highlights of the Vaccine Safety Datalink (VSD) Project

COVID-19

- Vaccine coverage in 2021
- Risks of mortality and myocarditis
- Safety in pregnant women

Influenza

- Seasonal effectiveness
- Risk of venous thromboembolism
- Safety in pregnant women

Childhood vaccines

- Overall effectiveness
- Risk of mortality and adverse events
- Safety of specific vaccines

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