Kaiser Permanente Research Brief

Diabetes

This brief summarizes the contributions of Kaiser Permanente Research on the topic of diabetes, including type 1, type 2, and gestational diabetes since 2007.

The Centers for Disease Control and Prevention estimate that 30.3 million people in the United States – more than 9 percent of the population – are living with diabetes, and an additional 34 percent of U.S. adults have prediabetes.[1] Prevalence of both diabetes (25 percent) and prediabetes (48 percent) is higher among adults age 65 or older than among those under age 65.

Diabetes is an active area of study for Kaiser Permanente Research. Scientists across the program have used our rich, comprehensive, longitudinal data to advance understanding of risk, improving patient outcomes, and translating research findings into policy and practice. We have published more than 840 articles related to diabetes over the past decade; together, they have been cited nearly 40,000 times.[2]

Kaiser Permanente Publications Related to Diabetes since 2007

Source: Kaiser Permanente Publications Library and PLUM metrics, as of 28 December 2017.
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.

These articles are the product of observational studies, randomized controlled trials, meta-analyses, and other studies led by Kaiser Permanente scientists. The unique environment – that includes our fully integrated care and coverage model – in which our research scientists, clinicians, medical groups and health plan leaders collaborate, enables us to contribute generalizable knowledge on diabetes and many other topics of research.

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.

Understanding Risk

Kaiser Permanente researchers have contributed to understanding the risk of developing diabetes, as well as the other risks that people with diabetes face.

Who is at risk for developing diabetes?

In adults, we have studied who is most at risk for developing type 2 diabetes. A selection of the risk factors for diabetes that Kaiser Permanente studies have assessed include fasting plasma glucose levels,[3] use of antidepressant medications,[4] and use of antihypertensive medication combination therapy.[5] Factors that reduce diabetes risk, such as weight loss,[6] have also been the subject of Kaiser Permanente research.

Gestational diabetes is an important health concern for pregnant women. One Kaiser Permanente study using data from 1999-2005 reported stable prevalence of gestational diabetes among our members, after adjusting for the increasing prevalence of pre-existing diabetes.[7] Factors that increase the risk of developing gestational diabetes[8-12] have been studied widely, as has risk of recurrence of gestational diabetes in subsequent pregnancies,[12] and the risk of sustained glycose dysregulation after pregnancy among women with a history of gestational diabetes.[13-17]

Among youth, Kaiser Permanente researchers have found significant increases over time in both incidence and prevalence of type 1 and type 2 diabetes,[18, 19] with minorities impacted more heavily. A substantial volume of work addresses diabetes risk factors among youth, including dietary, physical activity, and weight loss factors,[20, 21] and risk linked to maternal gestational diabetes status and other perinatal and neonatal factors.[22, 23]

What other health risks do people with diabetes face?

People with diabetes face added health risks, including risks related to the use of medications for treating diabetes. Kaiser Permanente research scientists have authored studies evaluating the risks of complications of diabetes and common comorbidities (for example, hypoglycemic episodes, neuropathy, retinopathy),[24-26] risk of developing various cancers[27-31] and risk of bone fractures.[32, 33] Studies have also demonstrated an increase in dementia risk for people with diabetes who have experienced hypoglycemic episodes and for those with comorbid depression.[34-36] Kaiser Permanente research has also investigated risks related to chronic conditions that are often comorbid with diabetes, such as pulmonary and cardiovascular diseases.[28, 37]

Diabetes Remission for Patients With Type 2 Diabetes Who Received Bariatric Surgery Versus Non-Surgical Approaches

Severely Obese Adults With Diabetes

1,395	63,322
BARIATRIC SURGERIES	NON-SURGICAL APPROACHES

Diabetes Remission at 2 years

73.7%	6.9%
95% CI: 70.7-76.5	95% CI: 6.9-7.1

Hazard Ratios for Secondary Outcomes

Relapse Lower for surgery group		**0.19** 95% CI:0.15-0.23
Death No difference between groups		**0.54** 95% CI: 0.22-1.30

Arterburn, D., et al., *Comparative effectiveness of bariatric surgery vs. nonsurgical treatment of type 2 diabetes among severely obese adults.* Obes Res Clin Pract, 2013. 7(4): p. e258-68

STUDY SPOTLIGHT

Effects of Intensive Glucose Lowering in Type 2 Diabetes.

Gerstein HC,
Miller ME, Byington RP, et al.

2008. N Engl J Med, 358(24): 2545-59

PMID: 18539917

4,438 Citations | 34 Clinical Citations

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The most-cited paper related to diabetes in the Kaiser Permanente Publications Library, this 2088 article has been widely cited in PubMed Clinical Guidelines related to diabetes, cardiovascular disease, stroke, kidney and liver transplantation, and other areas.

This study focused on patients with type 2 diabetes and either existing cardiovascular disease or heightened risk for it. The trial randomized over 10,000 patients to intensive glucose lowering therapy (HgA1c goal of 6.0) versus standard therapy (goal of 7.0-7.9), and followed them for nonfatal heart attack or stroke, and fatal cardiovascular events over an average of 3.5 years of follow-up.

The authors found that intensive glucose lowering was associated with increased mortality, and did not reduce the risk of nonfatal cardiovascular events. They concluded that this study uncovered a previously unrecognized harm associated with intensive glucose control for high-risk patients.

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One increasingly common risk-mitigation strategy for people with diabetes and obesity is bariatric surgery. Studies have shown that – particularly for people who are less severely obese – bariatric surgery can result in diabetes remission and a host of related benefits,[38-41] including improved life expectancy.[42] Even for people who experience a relapse of diabetes after a period of remission, the remission has been linked to longer-term health benefits, such as reduced risk of microvascular complications of diabetes.[38]

Also important are the risks for babies born to women who experience gestational diabetes. Among these risks are fetal and neonatal macrosomia,[43, 44] hypoglycemia and hyperbilirubinemia, childhood obesity, and development of autism.[45-50]

Improving Patient Outcomes

What strategies are effective in preventing diabetes?

For people at risk of type 2 diabetes, making a timely diagnosis of prediabetes creates an opportunity to encourage lifestyle changes that can reduce the risk of developing diabetes.[51, 52] Kaiser Permanente researchers have studied the performance of various approaches to detecting pre-diabetes,[53] and the rate of progression from first-recorded impaired fasting glucose (an intermediate state of hyperglycemia that is abnormal but does not meet the threshold for diabetes diagnosis) to diabetes.[54]

Approaches to prevention or risk reduction studied by Kaiser Permanente researchers include increasing knowledge about diabetes among youth,[20, 55] lifestyle interventions for high-risk adults [56], and personalized genetic-risk counseling.[57]

How does early identification of diabetes affect outcomes?

Early diagnosis of diabetes relies on screening of people at risk. Early recognition of type 1 and type 2 diabetes can confer substantial treatment and outcome benefits. For example, people who are diagnosed early can enter treatment before consequences of uncontrolled diabetes occur, such as diabetic ketoacidosis.[58]

What are the key factors in effective treatment of people with diabetes?

Glucose Control. For people with diabetes, glucose control – through self-management activities including lifestyle adaptations, self-monitoring of blood-glucose, and medication adherence – is essential to effective treatment. Diabetes-care guidelines suggest

an escalating medication treatment strategy for people with type 2 diabetes based on glucose control and responsiveness to medications. However, medications are not always escalated as recommended, even when glycemic control is inadequate,[59] in part because of barriers to insulin initiation.[60]

For most adults with diabetes, treatment is directed to maintain an HbA1c less than 7 percent. Kaiser Permanente studies have compared the effectiveness of alternative insulin regimens [61-64] and glucose control targets. [65] In particular, researchers have recently studied the appropriateness of low glycemic targets for older adults and concluded that relaxing glucose control targets (for example, up to HbA1c of 7.5 percent) for older adults can avoid hypoglycemic events and other adverse outcomes, and has few negative consequences.[66, 67] Such real-world studies in our large membership provide valuable insight that complement clinical trials,[68] which frequently exclude older adults and people with comorbidities.

Complications of Diabetes. Appropriate screening for serious complications of diabetes is an essential component of effective treatment. Recommended processes of care include eye exams, foot exams, and influenza immunizations. Kaiser Permanente studies have shown that documentation of these care processes is incomplete in administrative claims data[69] and have also measured the impact of insurance continuity or coverage type on receiving recommended preventive care.[70, 71] Even among insured people, gaps in recommended care processes are common for adults[72] but less problematic among youth.[73]

Comorbid Conditions. People with diabetes and multiple comorbid conditions face added challenges and risks. One of these is polypharmacy: the concurrent use of multiple prescription medications. Kaiser Permanente research has demonstrated that medication burden increases substantially for patients newly diagnosed with diabetes.[74] Polypharmacy is linked with decreased medication adherence[75] and increased medication interactions.[76]

Furthermore, polypharmacy has been associated with patient falls in studies focusing on adults with diabetes.[77]

In addition, chronic and acute conditions can be more difficult to treat in the context of diabetes than for people without diabetes. For example, surgical care of patients with diabetes and surgical treatment of diabetic foot infections is complicated by microvascular diseases that inhibit wound healing[78, 79]. Studies have also demonstrated that people with comorbid diabetes and hypertension, hyperlipidemia, and hyperglycemia often experience both treatment non-adherence and lack of appropriate treatment intensification for these comorbidities, leading to worse outcomes.[80]

Translating Into Policy & Practice

How has Kaiser Permanente research contributed to changes in policy and practice?

Kaiser Permanente is a learning health care system that works to systematically use research to inform and improve practice both within Kaiser Permanente and more broadly.

Within Kaiser Permanente, research, clinical, and operational partners have tested a range of interventions to prevent diabetes or improve diabetes outcomes. These have included strategies such as education, wellness, and behavior change programs focused on exercise, diet, and medication adherence,[81-83] workplace screening and wellness programs,[81, 84] and educational interventions specifically for women with gestational diabetes[85] and for youth.[55] Within Kaiser Permanente, studies have also evaluated the role of the electronic medical records (and other data assets) in promoting quality of diabetes care, identifying diabetes medication non-adherence, recognize prediabetes, and other outcomes.[86-90]

Disease management programs, often offered by third-party vendors, are increasingly popular in the United States, widely used by

state Medicaid programs and others. Our studies assessing online and telephonic disease management or coaching programs have found that they can be effective but are not uniformly so.[83, 91] Furthermore, these programs have been shown to face challenges related to low uptake among eligible individuals who might benefit[92] and suboptimal level of engagement with the platform over time.[93] Researchers have also found that linking these efforts back to primary care is challenging, even in an integrated care setting with an advanced electronic medical record system.[94, 95]

Kaiser Permanente research contributes not only to policy and practice change within our own delivery system, but has also advanced national understanding of diabetes. To date, Kaiser Permanente authors have been cited more than 220 times within recent consensus statements and clinical practice guidelines published by a wide range of entities, including the American Diabetes Association, American Heart Association, and the American Geriatrics Association, among others. In addition, Kaiser Permanente research and clinician scientists have directly contributed as authors of 7 practice guidelines, most recently the American Association of Clinical Endocrinologists and American College of Endocrinology's consensus statement on the type 2 diabetes management algorithm.[96]

Each of Kaiser Permanente's regional research centers participate in the Health Care Systems Research Network (HCSRN), a national research network that aims to improve individual and population health through research.[97] The SUPREME-DM study, focused on diabetes and led by a Kaiser Permanente researcher, is one of HCSRN's cornerstone projects. Kaiser Permanente researchers have led or collaborated on many more notable studies and trials related to diabetes epidemiology, prevention, risk factors, and treatment.

Notable Studies and Clinical Trials Focusing on Diabetes

STUDY	FUNDER
Diabetes and Aging	National Institute of Diabetes, Digestive and Kidney Diseases
TRIAD: Translating Research into Action for Diabetes	Centers for Disease Control and Prevention
ACCORD: Action to Control Cardiovascular Risk in Diabetes	National Heart, Lung, and Blood Institute
SUPREME-DM: SUveillance, PREvention, and ManagEment of Diabetes Mellitus	Agency for Healthcare Research and Quality
The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study and The HAPO Follow-Up Study	National Institute of Diabetes, Digestive, and Kidney Diseases and the National Institute of Child Health and Human Development
The SEARCH for Diabetes in Youth	Centers for Disease Control and Prevention and the National Institute of Diabetes, Digestive, and Kidney Diseases
NEXT-D: Natural Experiments in Diabetes Translation	Centers for Disease Control and Prevention

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 have published more than 12,000 articles in peer-reviewed journals. Kaiser Permanente currently serves more than 12 million members in eight states and the District of Columbia.

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