

# Maternal and Child Health

This brief summarizes the contributions of Kaiser Permanente Research since 2007 on the topic of maternal and child health, including pre-pregnancy risk factors and a variety of risks and outcomes occurring both during and following childbirth.

According to the Centers for Disease Control and Prevention, approximately 4 million babies are born in the United States each year.<sup>1</sup> Although most babies are healthy and born without complications, pregnancy carries risks for both mothers and infants, and high-quality care during the prenatal period is essential for ensuring positive perinatal and postnatal health outcomes. Many women have underlying health problems that may present challenges during pregnancy. Approximately half of women who become pregnant are overweight or obese,<sup>2</sup> and conditions such as diabetes and chronic hypertension are present in 1% to 2% of women at the time of conception.<sup>3</sup> Moreover, recent data suggest that approximately 7% of pregnant women smoke,<sup>1</sup> and more than 10% consume alcohol.<sup>4</sup> In addition, 8.5% of pregnant women report recent use of illicit drugs, with increasingly common use of marijuana and opioids in particular.<sup>5</sup> During pregnancy, approximately 2% to 10% of pregnant women experience gestational diabetes,<sup>6,7</sup> and rates of both postpartum hemorrhage and hypertension have increased dramatically in recent years.<sup>8</sup> Finally, about 10% of births in the U.S. are preterm, and over 8% are low-birthweight babies. Preterm and low-weight births are each associated with serious long-term health consequences, including developmental delay, breathing problems, and infant mortality.

Maternal and child health 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 nearly 1,000 articles related to maternal and child health since 2007;<sup>9</sup> together, these articles have been cited almost 30,000

## Kaiser Permanente Publications Related to Maternal and Child Health since 2007



Source: Kaiser Permanente Publications Library and PLUM metrics, as of June 24, 2019.

- 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.

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 – 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 maternal and child health, and many other topics of research.

## Understanding Risk

### For which health problems are mothers and newborn children at increased risk?

Mothers and newborns may experience a variety of unique health issues, and Kaiser Permanente researchers have studied potential risk factors associated with these conditions. Research conducted at Kaiser Permanente has linked pre-pregnancy obesity,<sup>10,11</sup> hypertension<sup>12</sup> and prediabetes<sup>13</sup> with the risk of gestational diabetes mellitus (GDM), which is, in turn, associated with risks to the child,<sup>14,15</sup> including high birth weight,<sup>16,17</sup> neonatal hypoglycemia, and elevated bilirubin.<sup>15,17</sup> Maternal hypertension may increase the risk of congenital defects,<sup>18</sup> and women with higher pre-pregnancy cardiovascular risks are more likely to be diagnosed with preeclampsia.<sup>19,20</sup> Pre-pregnancy obesity may also be linked to infants being born large for their gestational age.<sup>21</sup> Our scientists have also found that a variety of pregnancy complications, including preterm delivery and macrosomia, are associated with gestational weight gain that is greater than recommended.<sup>22-25</sup>



**Kaiser Permanente research is helping to address the lack of research on the safety of common medications in pregnancy.**

In over 375,000 pregnancies, maternal use of the beta-blockers metoprolol and propranolol was not associated with higher risks of infants being born small for gestational age.<sup>41</sup>



A study of angiotensin-converting enzyme inhibitor (ACEI) safety in over 460,000 pregnancies found that the risk of congenital malformations arises from underlying hypertension rather than the use of ACEIs.<sup>18</sup>



In an analysis involving 1.2 million pregnancies, the use of sulfonamide antibiotics was not associated with the risk of congenital malformations.<sup>42</sup>



Kaiser Permanente scientists have also explored the role of behavioral health conditions on pregnancy outcomes. Women who develop symptoms of depression early in their pregnancies may gain more weight,<sup>26</sup> and the risk of preterm delivery is significantly higher in women with depression.<sup>27</sup> Preterm delivery and low birth weight have also been linked to use of benzodiazepines during pregnancy,<sup>28</sup> and alcohol use during pregnancy has been associated with the risk of miscarriage.<sup>29</sup> Although the risks associated with cannabis use during pregnancy are unclear, pregnant women appear to be increasing their use of cannabis.<sup>30,31</sup>

Scientists at Kaiser Permanente have also studied the risks associated with induced or cesarean deliveries. Use of cesarean delivery has increased over time,<sup>32</sup> and these procedures are not without postpartum risks for the mother.<sup>33</sup> Studies conducted by our scientists have also found that infants born via cesarean took longer to regain their birth weight during the first month of life.<sup>34</sup> Of particular concern is evidence that the decision to use cesarean delivery is sometimes driven by non-medical factors rather than medical necessity.<sup>35</sup> Elective induction of labor may be associated with a lower odds of cesarean delivery,<sup>36</sup> although its safety remains to be clearly established.<sup>36-39</sup>

## **What issues arise with respect to the safety of routine care for pregnant women?**

As an integrated system, Kaiser Permanente actively works to ensure that routine medical care is maintained throughout a woman's pregnancy. While many elements of routine care can be maintained safely during pregnancy, basic data regarding the safety of medications during pregnancy are often lacking.<sup>40</sup> Our scientists have been involved in research examining the safety of medications in wide use among pregnant women, such as beta-blockers,<sup>41</sup> ACE inhibitors,<sup>18</sup> and sulfonamide antibiotics.<sup>42</sup> Kaiser Permanente has also been involved in numerous studies of the prevalence of medication use during pregnancy. Two of these studies showed rapid increases in the use of atypical antipsychotics and antiepileptic drugs among pregnant women in recent years, despite limited information on the safety of these medications.<sup>43,44</sup> Studies such as this can lead to future research with the potential to improve the safety of medications prescribed during pregnancy. Researchers at Kaiser Permanente have also studied the safety of vaccines in pregnant women.<sup>45</sup> A series of studies conducted through the Vaccine Safety Datalink project found no increased risk of adverse birth outcomes in women receiving immunizations for flu,<sup>46-48</sup> tetanus-diphtheria-pertussis (Tdap),<sup>49-51</sup> pertussis alone,<sup>52</sup> hepatitis B,<sup>53</sup> or human papillomavirus (HPV).<sup>54,55</sup>

## **Are there subgroups of mothers and/or newborn children who are at particularly high risk for health problems?**

Our scientists have studied subpopulations of mothers and newborns for whom health risks are heightened. Women with ongoing comorbid conditions may experience adverse outcomes if these conditions are not managed effectively during pregnancy.<sup>56</sup> Complications such as gestational diabetes mellitus or preeclampsia that occur during one pregnancy are likely to recur in future pregnancies,<sup>57,58</sup> and weight gain between pregnancies may increase the risk of GDM<sup>59</sup> and preeclampsia<sup>60</sup> in the subsequent pregnancy. Our research has also found that a stillbirth may increase the risks of future adverse outcomes, including infant mortality.<sup>61</sup>

Racial, ethnic, socioeconomic and social factors<sup>62</sup> are also associated with increased risk for health problems during and after pregnancy. Our scientists have identified elevated risks of gestational diabetes in Asian American<sup>63-65</sup> and African American<sup>64,66</sup> women, and infertility,<sup>67</sup> diabetes,<sup>68</sup> and higher-weight infants<sup>69,70</sup> have been found to be more common in African American women. Our research has also confirmed that poor nutrition during pregnancy – common among people of lower socioeconomic status – is associated with poor birth outcomes<sup>71,72</sup> and ongoing health problems including insulin resistance<sup>73</sup> and weight gain.<sup>74</sup> Finally, a study conducted among Kaiser Permanente members found that higher psychosocial stress was associated with greater gestational weight gain,<sup>75</sup> and women with greater levels of conflict with their partners may be at greater risk of postpartum depression.<sup>76</sup>

## What are the health consequences of the risks that mothers and newborn children face?

Kaiser Permanente scientists have studied a variety of factors associated with the significant health risks that may be associated with pregnancy. Health conditions that mothers experience during pregnancy may also increase their risks for longer-term chronic diseases, including obesity,<sup>77,78</sup> diabetes,<sup>79-81</sup> hypertension,<sup>82-84</sup> cardiovascular disease,<sup>85</sup> non-alcoholic liver disease,<sup>86</sup> and even ophthalmic disorders.<sup>87</sup> In particular, health issues requiring treatment and monitoring, such as depression, gestational diabetes, or hypertension, may go untreated if the mother's primary care physician is not involved in her post-delivery care,<sup>88,89</sup> or if she is not referred for needed mental health services.<sup>90-92</sup> One recent study found that self-harming behaviors may be a significant contributor to maternal mortality.<sup>93</sup>

Maternal diabetes has been linked to neonatal deaths,<sup>94</sup> and children born to mothers with pre-pregnancy obesity, greater gestational weight gain, or GDM may also experience longer-term health problems including obesity<sup>14,95-104</sup> and asthma.<sup>105</sup> Additional long-term risks to newborns that may arise from conditions in pregnancy include metabolic illnesses,<sup>106,107</sup> childhood asthma,<sup>108</sup> autism,<sup>109-111</sup> attention-deficit/hyperactivity disorders,<sup>112,113</sup> developmental delay,<sup>110</sup> cerebral palsy, and other congenital defects.<sup>114-116</sup> Our scientists have studied a variety of factors associated with greater risk of autism,<sup>109</sup> including toxic exposures,<sup>117</sup> inflammatory conditions,<sup>118-120</sup> maternal fever<sup>121</sup> or infection,<sup>122</sup> gestational weight gain,<sup>110</sup> gestational diabetes,<sup>123</sup> and preterm birth.<sup>124</sup> Use of opioids during pregnancy has been shown to increase the risk of neurodevelopmental problems, including autism spectrum disorder and developmental delay,<sup>125</sup> and fetal alcohol syndrome<sup>126</sup> and autism spectrum disorder<sup>127</sup> are among the risks of drinking alcohol while pregnant. Preterm delivery,<sup>116</sup> maternal fever,<sup>121</sup> and pre-pregnancy obesity<sup>110</sup> have also been linked by Kaiser Permanente research to the risk of developmental delay. One study of preterm and very low birth weight infants found that they often experience significantly reduced quality of life in young adulthood,<sup>128</sup> and preterm birth is also associated with increased social isolation and financial stress on the part of the child's family.<sup>129</sup>

## Improving Patient Outcomes








### What prevention or early intervention strategies can mitigate the health risks faced by mothers and newborn children?

Prevention and other early intervention strategies are critical components of Kaiser Permanente's work to improve pregnancy outcomes. Engaging women in birth planning<sup>130,131</sup> and early prenatal care<sup>131-134</sup> have been shown to contribute to superior outcomes. Other programs evaluated in Kaiser Permanente encourage natural vaginal delivery as a way of preventing unnecessary cesarean births,<sup>135,136</sup> as natural delivery is associated with fewer risks and shorter recovery times.<sup>34,137</sup> Our research has consistently suggested that breastfeeding may reduce the risk of childhood obesity,<sup>99,138-140</sup> and we have evaluated a variety of programs for encouraging breastfeeding among new mothers.<sup>141,142</sup>

Screening programs are an integral piece of our organization's approach to preventive health, and our researchers have studied efforts to screen pregnant women for peripartum and postpartum depression,<sup>143-145</sup> preeclampsia,<sup>146,147</sup> and gestational

diabetes.<sup>148-150</sup> Our scientists have conducted comparisons of the 1-step GDM screening protocol recommended by the International Association of Diabetes and Pregnancy Study Groups versus standard 2-step screening, and have found that 1-step screening does not lead to improved maternal or neonatal outcomes.<sup>151,152</sup> Our scientists have also studied postpartum screening efforts to identify diabetes following pregnancies affected by GDM.<sup>153,154</sup> Other strategies that contribute to improved outcomes for mothers and babies include management of weight<sup>155-159</sup> and nutrition<sup>71,72,160,161</sup> and provision of specialized care and outreach for high-risk pregnancies.<sup>145,162,163</sup> In addition, our scientists have studied screening and brief intervention efforts for alcohol use during pregnancy,<sup>164-167</sup> as well as counseling and other programs aimed at promoting cessation of tobacco<sup>168</sup> and alcohol<sup>169</sup> use in pregnant women.

**Kaiser Permanente has studied the effectiveness of early intervention efforts to improve pregnancy outcomes**

	<b>Birth Planning</b> <sup>130,131</sup>
	<b>Early Prenatal Care</b> <sup>131-134</sup>
	<b>Weight Management</b> <sup>155-159</sup>
	<b>Nutrition</b> <sup>71,72,160,161</sup>
	<b>Specialized Care for High-Risk Pregnancies</b> <sup>145,162,163</sup>
	<b>Postpartum Depression Prevention</b> <sup>171</sup>
	<b>Screening for:</b> <ul style="list-style-type: none"> <li>• <b>Preeclampsia</b><sup>146,147</sup></li> <li>• <b>Gestational Diabetes</b><sup>148-150</sup></li> <li>• <b>Postpartum Depression</b><sup>143-145</sup></li> </ul>

Strategies to prevent and mitigate postpartum risks are also a focus of Kaiser Permanente’s research. In light of evidence that care for postpartum depression has not improved despite provisions of the Affordable Care Act,<sup>170</sup> we have studied various prevention strategies, including mindfulness-based cognitive behavioral therapy,<sup>171</sup> as well as behavioral activation<sup>172</sup> and collaborative care<sup>173</sup> for depression during pregnancy. In a randomized trial comparing various programs for postpartum weight control, a lifestyle intervention based on the Diabetes Prevention Program improved physical activity and weight maintenance.<sup>157,174</sup> Finally, our scientists have studied a variety of interventions to address new parents’ hesitancy regarding vaccinations for newborns.<sup>175-180</sup>

**What are the key components of approaches to reduce disparities in care and outcomes experienced by mothers and newborn children?**

As part of Kaiser Permanente’s commitment to reducing disparities in access to care and clinical outcomes, we have also studied the experiences of women and newborn children at increased risk of poor outcomes. Our research has found that cesarean deliveries are more common in African American women,<sup>32</sup> and access to

recommended care for postpartum depression among Medicaid enrollees in New Jersey was lower for African American and Latina women than for white women.<sup>181</sup> Moreover, infants with similar respiratory symptoms may receive different treatments depending on their race/ethnicity.<sup>182</sup> As part of a strategy to address these and other disparities, researchers at Kaiser Permanente have studied interventions to increase the cultural competence of care provided during and after pregnancy.<sup>183</sup>

## Translating Research Findings into Policy and Practice

### How has Kaiser Permanente research on maternal and child health 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. Research, clinical, and operational partners within Kaiser Permanente have tested a range of interventions to reduce the risk of poor maternal and child outcomes, both during and following pregnancy. Our scientists are involved in a perinatal care center managed by nurse-midwives, in which cesarean section is used in just 10% of deliveries, and nearly all mothers are engaged in breastfeeding.<sup>184</sup> Kaiser Permanente clinicians returned to a 2-step strategy for GDM screening after experimenting with a 1-step strategy, after two studies conducted by our researchers found that 1-step screening was associated with increased rates of GDM diagnoses without improved outcomes.<sup>151,152</sup> Based on research demonstrating that the 1979 National Diabetes Data Group glucose threshold for diagnosing GDM was associated with greater newborn health risks than the lower American Diabetes Association (ADA) threshold published in 2000, Kaiser Permanente implemented the ADA threshold throughout our system.<sup>15</sup> Finally, based on randomized trials conducted by our scientists, we have successfully translated

**Two studies conducted in Kaiser Permanente members found that 1-step screening for gestational diabetes was associated with more GDM diagnoses, but not better outcomes<sup>151,152</sup>**

SOUTHERN CALIFORNIA		WASHINGTON STATE	
1-Step	2-Step	1-Step	2-Step
<b>PREGNANCIES</b>			
<b>3,094</b> 2011-2013	<b>2,972</b> 2010-2011	<b>6,337</b> 2012-2014	<b>4,977</b> 2009-2011
<b>GDM DIAGNOSES</b>			
<b>27%</b>	<b>17%</b>	<b>11%</b>	<b>7%</b>
<b>LARGE FOR GESTATIONAL AGE BIRTHS</b>			
<b>9%</b>	<b>10%</b>	<b>10%</b>	<b>10%</b>
<b>NEONATAL MACROSOMIA</b>			
<b>7%</b>	<b>8%</b>	<b>2%</b>	<b>3%</b>



interventions into practice for preventing postpartum depression,<sup>171</sup> improving gestational weight gain,<sup>185</sup> and increasing vaccine uptake.<sup>175,177</sup>

Kaiser Permanente research contributes not only to policy and practice change within our own delivery system, but has also advanced national understanding of maternal and child health. To date, Kaiser Permanente's research on maternal and child health since 2007 has been cited nearly 270 times within recent consensus statements and clinical practice guidelines published by a wide range of entities, including the CDC's Advisory Committee on Immunization Practices,<sup>186,187</sup> the American Academy of Pediatrics,<sup>188</sup> and the American College of Obstetrics and Gynecology.<sup>189</sup> In addition, Kaiser Permanente researchers and clinician-scientists have directly contributed as authors of guidelines and policy statements for the Society for Obstetric Anesthesia and Perinatology<sup>190</sup> and the U.S. Preventive Services Task Force.<sup>142,146,147,149,168,191-193</sup> Our scientists have also contributed to a consensus bundle developed for the National Partnership for Maternal Safety, which addresses recommended clinical practices for recognizing and responding to venous thromboembolisms in obstetric patients.<sup>194</sup>

Finally, Kaiser Permanente has shown leadership in the broader field of maternal and child health research. Our scientists are leaders in a number of prominent studies in this field, including the Medication Exposure in Pregnancy Risk Evaluation Program (MEPREP) study, an effort to explore the *in utero* safety of medications delivered to pregnant women.<sup>40,195</sup> We are also involved in ongoing efforts to study the effectiveness and safety of vaccines delivered to mothers and infants as part of our involvement in the Vaccine Safety Datalink, a nationwide project sponsored by the CDC.<sup>196</sup>

Kaiser Permanente's nearly 170 research scientists and more than 1,600 support staff are based at 8 regional research centers and one national center. There are currently more than 2,400 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 12.3 million members in 8 states and the District of Columbia.

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ject:“Diagnostic Techniques, Obstetrical and Gynecological” OR subject:“Prenatal Exposure Delayed Effects” OR subject:“Prenatal Injuries” OR subject:“Maternal Exposure” OR ((subject:“infant, newborn” OR subject:infant) NOT (subject:child OR subject:adolescent)) OR (title:newborn\* OR (title: fetus OR foetus) OR Title:Periconceptional OR (title: “maternal exposure”~6 ) OR (title: “In-utero exposure”~6 ) OR (title: “Birth Weight”~6 ) OR Title: “Premature birth” OR Title: “Preterm birth” OR Title:“Early development” OR Title: Prepregnant OR Title:Birthweight OR Title: Gestation OR Title: Breastfeeding OR Title:“breast milk” OR title:pregnan\*) AND type:“journal article” AND datelsued:[2007 2019].

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