Evidence Gaps Research Taxonomy Table
Research to Address Evidence Gaps in Preventive Services for the USPSTF
Topic: Screening and Supplementation for Iron Deficiency and Iron Deficiency Anemia During Pregnancy

To fulfill its mission to improve health by making evidence-based recommendations for preventive services, the USPSTF routinely highlights the most critical evidence gaps for making actionable preventive services recommendations. As summarized in Table 2 in the recommendation statement, the USPSTF often needs additional evidence to create the strongest recommendations for everyone and especially for persons with the greatest burden of disease.

In this table, the USPSTF summarizes key bodies of evidence needed to make recommendations for screening and supplementation for iron deficiency and iron deficiency anemia during pregnancy. For each of the evidence gaps listed below, the USPSTF provides guidance to researchers and funders on the types of studies needed to expand the evidence and enable the USPSTF to make evidence-based recommendations in primary care settings and be inclusive of populations with an increased prevalence of iron deficiency and iron deficiency anemia.

The research taxonomy is intended to provide general guidance to investigators. Investigators are encouraged to develop research designs that are responsive to the research taxonomy outlined in the table, in collaboration with their research teams and areas of expertise and experience. The research developed will be reviewed according to standard USPSTF criteria for inclusion in its evidence report; inclusion criteria are summarized in the final Research Plan (https://www.uspreventiveservicestaskforce.org/uspstf/document/final-research-plan/iron-deficiency-anemia-during-pregnancy-screening-supplementation) and Procedure Manual (https://www.uspreventiveservicestaskforce.org/uspstf/about-uspstf/methods-and-processes/procedure-manual).

Research Gap	Key Questions* or Contextual Questions	Direct/ Indirect Pathway†	Type of Gap‡	Study Characteristics	Population	Intervention/ Comparison	Outcomes/ Timing	Setting
Research is needed in pregnant persons with iron deficiency and iron deficiency anemia to assess whether changes in maternal iron status (e.g., because of supplementation or treatment for screen-detected populations) improves maternal and infant health outcomes in settings relevant to U.S. primary care clinical practice.	KQ3 (supplementation) KQ5 (screening)	Indirect	Grade assignment, health equity	Observational studies, including those embedded within clinical trials (sufficiently powered to include subpopulation analysis)	Asymptomatic adults (age ≥18 years) and adolescents (ages 13 to <18 years), regardless of iron status, who are pregnant and their infants (supplementation), including in populations§ disproportionately affected by iron deficiency/iron deficiency anemia during pregnancy Asymptomatic adults (age ≥18	Improved maternal iron status (maternal iron deficiency status, iron deficiency anemia status, or both)	**Maternal health outcomes:** Examples include mortality; health-related quality of life; hypertensive disorders of pregnancy; postpartum hemorrhage; blood transfusion; postpartum depression **Infant health outcomes:** Examples include perinatal mortality, respiratory distress, and NICU admission	Settings relevant to U.S. primary care clinical practice

Research Gap	Key Questions* or Contextual Questions	Direct/ Indirect Pathway†	Type of Gap‡	Study Characteristics	Population	Intervention/ Comparison	Outcomes/ Timing	Setting
					years) and adolescents (ages 13 to <18 years) with iron deficiency or iron deficiency anemia who are pregnant and their infants (screening)			
Research is needed to assess the benefits and harms of screening (e.g., with hemoglobin, hematocrit, or ferritin values) for iron deficiency and iron deficiency anemia during pregnancy on maternal (e.g., quality of life or need for transfusion) and infant (e.g., low birth weight or preterm birth) health outcomes.	KQ1, KQ2 (screening)	Direct	Grade assignment, health equity	Randomized, controlled trials; controlled cohort studies; nonrandomized studies of interventions with contemporaneous control groups (sufficiently powered to include subpopulation analysis)	Pregnant adolescents (ages 13 to <18 years) and adults (age ≥18 years) and their infants who are asymptomatic for iron deficiency or iron deficiency anemia, including in populations disproportionately affected by iron deficiency/iron deficiency anemia during pregnancy	Screen for iron deficiency anemia (e.g., with hemoglobin, hematocrit, or ferritin values) vs. no screening comparison	**KQ1: Maternal health outcomes:** Examples include mortality; health-related quality of life; hypertensive disorders of pregnancy; postpartum hemorrhage; blood transfusion; postpartum depression, anxiety (preferred) **Infant health outcomes:** Examples include perinatal mortality, morbidity (NICU admission, respiratory distress) **If studies measure intermediate outcomes, additional evidence would be needed to link intermediate outcomes to health outcomes**	Relevant to U.S. primary care clinical practice

Research Gap	Key Questions* or Contextual Questions	Direct/ Indirect Pathway†	Type of Gap‡	Study Characteristics	Population	Intervention/ Comparison	Outcomes/ Timing	Setting
							Maternal intermediate outcomes: Examples include incidence of iron deficiency anemia; incidence of iron deficiency; hematologic indices and ferritin levels;¶ cesarean delivery rates** **Infant intermediate outcomes:** Examples include hematologic indices and ferritin levels; low birth weight, small for gestational age, and preterm delivery **KQ2:** Examples include overdiagnosis, anxiety, and labeling	
Research is needed to assess the benefits and harms of treatment (e.g., oral or intravenous iron) in asymptomatic, screen-detected populations with iron deficiency and iron deficiency anemia during pregnancy on maternal and infant health outcomes in settings relevant to U.S. primary care clinical practice.	KQ3, KQ4, KQ5 (screening)	Indirect	Grade assignment, health equity	**KQ3:** Randomized, controlled trials; controlled cohort studies; nonrandomized studies of interventions with contemporaneous control groups **KQ4:** Studies from KQ3 and large	**KQs 3,4:** Pregnant adolescents (ages 13 to <18 years) and adults (age ≥18 years) with iron deficiency anemia and their infants, including in populations disproportionately affected by iron deficiency/iron	**KQs 3,4:** Oral or intravenous iron supplementation, iron-fortified foods vs. no treatment comparator†† **KQ5:** Improvement in maternal iron status (deficiency status, iron deficiency anemia status, or both)	**KQs 3,5: Maternal health outcomes:** Examples include mortality; health-related quality of life; hypertensive disorders of pregnancy; blood transfusion; postpartum	Relevant to U.S. primary care clinical practice

Research Gap	Key Questions* or Contextual Questions	Direct/ Indirect Pathway†	Type of Gap‡	Study Characteristics	Population	Intervention/ Comparison	Outcomes/ Timing	Setting
				observational studies **KQ5:** Association studies of intermediate outcomes/health outcomes link (observational studies, including those embedded within clinical trials). Evidence should be sufficiently powered to include subpopulation analysis	deficiency anemia during pregnancy **KQ 5:** Pregnant adolescents (ages 13 to <18 years) and adults (age ≥18 years) with iron deficiency, with or without anemia, and their infants, including in populations disproportionately affected by iron deficiency/iron deficiency anemia during pregnancy		depression, anxiety (preferred) **Infant health outcomes:** Examples include perinatal mortality, morbidity (NICU admission, respiratory distress) **If studies measure intermediate outcomes, additional evidence would be needed to link intermediate outcomes to health outcomes** **Maternal intermediate outcomes:** Examples include incidence of iron deficiency anemia; incidence of iron deficiency; hematologic indices and ferritin levels;¶ cesarean delivery rates** **Infant intermediate outcomes:** Examples include hematologic indices and ferritin levels; low birth weight, small for gestational	

Research Gap	Key Questions* or Contextual Questions	Direct/ Indirect Pathway†	Type of Gap‡	Study Characteristics	Population	Intervention/ Comparison	Outcomes/ Timing	Setting
							age, and preterm delivery **KQ4:** **Harms outcomes:** Serious harms; harms leading to discontinuation; overtreatment	
Research is needed to assess the benefits and harms of routine iron supplementation in asymptomatic pregnant persons without known iron deficiency or iron deficiency anemia on maternal and infant health outcomes.	KQ1, KQ2, KQ3 (supplementation)	Direct and Indirect	Grade assignment, health equity	**KQ1:** Randomized, controlled trials; controlled cohort studies; other controlled observational studies **KQ2:** Studies from KQ1 and large uncontrolled observational studies **KQ3:** Association studies of intermediate outcomes/health outcomes link (observational studies, including those embedded within clinical trials) Evidence should be sufficiently powered to include subpopulation analysis	Asymptomatic adults (age ≥18 years) and adolescents (ages 13 to <18 years), regardless of iron status, who are pregnant and their infants, including in populations disproportionately affected by iron deficiency/iron deficiency anemia during pregnancy	**KQs 1,2:** Intervention: oral iron supplementation, iron-fortified foods vs. no supplementation comparator†† **KQ3:** A change in maternal iron deficiency status, iron deficiency anemia status, or both	**KQs 1,3:** **Maternal health outcomes:** Examples include mortality; health-related quality of life; hypertensive disorders of pregnancy); postpartum hemorrhage; blood transfusion; postpartum depression, anxiety (preferred) **Infant health outcomes:** Examples include perinatal mortality, morbidity (NICU admission, respiratory distress) **If studies measure intermediate outcomes, additional evidence would be needed to link intermediate outcomes to health outcomes**	Relevant to U.S. primary care clinical practice

Research Gap	Key Questions* or Contextual Questions	Direct/ Indirect Pathway†	Type of Gap‡	Study Characteristics	Population	Intervention/ Comparison	Outcomes/ Timing	Setting
							Maternal intermediate outcomes: Examples include incidence of iron deficiency anemia; incidence of iron deficiency; hematologic indices and ferritin levels;¶ cesarean delivery rates** **Infant intermediate outcomes:** Examples include hematologic indices and ferritin levels; low birth weight, small for gestational age, and preterm delivery **KQ2:** More serious harms; harms leading to discontinuation; accidental overdose	

* Key questions are an integral part of the approach to conducting systematic reviews that the USPSTF uses in its recommendation process. Along with the analytic framework, these questions specify the logic and scope of the topic, and are critical to guiding the literature searches, data abstraction, and analysis processes. Analytic frameworks can evolve with time and may appropriately differ when recommendations are updated because of changes in clinical questions or important uncertainties about the evidence. (https://www.uspreventiveservicestaskforce.org/uspstf/about-uspstf/methods-and-processes/procedure-manual)

† The direct pathway is typically derived from RCTs of the targeted screening or preventive intervention that adequately measure the desired health outcomes in the population(s) of interest. If certainty for net benefit cannot be derived from the direct pathway, then the USPSTF determines if the evidence is sufficient across the key questions and linkages in the indirect pathway to determine overall certainty.

‡ Types of gaps may include: grade assignment (moving from an I statement to a letter grade), change in letter grade (e.g., from a C to B or C to D), health equity (e.g., populations with a disproportionate burden of the condition), combined (e.g., grade assignment and health equity), and general gap (e.g., uptake of a clinical preventive service).

§ Social risk factors could include populations with inadequate access to nutritional resources, screening services, and access to prenatal care and timely health care.

¶ Variation in ferritin thresholds to define iron deficiency in pregnancy makes interpretation challenging; studies should report ferritin thresholds for defining iron deficiency.

** Studies should report indications (e.g., emergency, nonelective) for cesarean delivery.

†† Given the backdrop of evolving clinical standards, it may not be possible to use placebo-controlled groups; thus, usual care control groups may be considered.

Abbreviations: KQ=key question; NICU=neonatal intensive care unit; RCT=randomized, controlled trial; USPSTF=U.S. Preventive Services Task Force.