



## **Evidence-based Practice Center Systematic Review Protocol**

### **Project Title: *Schedule of Visits and Use of Telemedicine for Routine Antenatal Care: A Systematic Review***

## **I. Background and Purpose of the Systematic Review**

### **Background**

Antenatal care is one of the most common preventive health services in the United States, accessed by 4 million women annually. Antenatal care aims to improve the health and wellbeing of pregnant patients and their babies through 1) medical screening and treatment; 2) anticipatory guidance; and 3) psychosocial support.<sup>1, 2</sup> The World Health Organization's definition of antenatal care includes the patient-centered goal of a "positive pregnancy experience".<sup>2</sup> However, the way routine antenatal care has been delivered has remained largely unchanged since the 1930s.<sup>3-5</sup> Clinical practice guidelines (CPG) for antenatal care delivery (including visit frequency, timing, and use of telemedicine) are based largely on expert opinion.<sup>1, 6</sup>

Studies have established the benefit to maternal and neonate outcomes of several evidence-based practices (screenings, counseling, and interventions) delivered during antenatal care visits.<sup>7-9</sup> However, the evidence on specific aspects of delivering antenatal care related to frequency and cadence [timing] of visits, and to telemedicine for women with uncomplicated pregnancies is less clear. In the U.S., current recommendations include 12 to 14 office-based visits for low-risk pregnant patients, in addition to laboratory testing and ultrasounds.<sup>1</sup> Notably, the overall number and cadence of visits has remained unchanged since the schedule was first published by the Children's Bureau in 1930: monthly visits until 28 weeks, every 2 weeks until 36 weeks, and weekly until delivery.<sup>10</sup> The American College of Obstetricians and Gynecologists (ACOG) has instituted a set of recommended services for pregnant individuals to receive during the course of their antenatal care.<sup>11</sup> These include first trimester laboratory tests (complete blood count, blood type and screen, urinalysis, and testing for HIV, hepatitis B, syphilis, chlamydia, and rubella immunity), first and second trimester ultrasounds (for dating and viability and to evaluate anatomy, respectively), a diabetes screen between 24 and 28 weeks, and, in the third trimester, a repeat complete blood count, Tdap vaccination, testing for group B strep, and an assessment for fetal presentation. In addition, it is recommended to discuss risk counseling, psychosocial issues including mental health screening, and expectations about the course of pregnancy during the course of antenatal care.

Since 1989, several US-based and international CPGs have recommended fewer antenatal visits (6 to 9),<sup>2, 6, 12, 13</sup> but most of U.S. practice has not changed. Telemedicine is a relatively new approach to routine antenatal care. As for most healthcare, telemedicine for routine visits became ubiquitous during the COVID-19 pandemic. The potential benefits and harms or concerns related to telemedicine, as opposed to in-person care, have yet to be elucidated for routine antenatal care.

Several health systems in the U. S. and abroad have implemented alternative antenatal care schedules for uncomplicated pregnancies.<sup>14</sup> Although there is evidence that too few contacts ( $\leq 4$ ) may result in poorer health outcomes,<sup>15</sup> these data are highly confounded by other psychosocial risk factors that might limit access to care. On the flip side, more care may also not be better, with at least some evidence that more frequent visits ( $>10$ ) may be associated with higher risk for induction and cesarean delivery without improvement in maternal or perinatal outcomes.<sup>16</sup> However, determination of the true association between number of visits and outcomes is complicated. In particular, there is substantial potential for reverse causality or confounding, in which an individual's personal characteristics or medical considerations dictate the number of prenatal care visits amassed as well as maternal and child outcomes. For example, socioeconomic risk factors (e.g., low-income teenage pregnancy) may lead to both few antenatal visits (that may also be initiated later in pregnancy) and to poor maternal and child outcomes. But an increased number of visits may be an indication of clinician or patient concerns about the pregnancy and an increased likelihood of poor outcomes. Furthermore, women who deliver prior to full term do not have the opportunity to accumulate as many prenatal visits as persons who deliver full term or later. Yet a lack of prenatal care leading to preterm delivery may be implicated in only a fraction of these situations.

The COVID-19 pandemic increased the urgency of determining the ideal timing and frequency of prenatal care. It also further highlighted the need to understand which visits are acceptable to be carried out via telemedicine, with a particular focus on maternal and child outcomes and maternal preferences. Telemedicine is one component of telehealth and is the practice of medicine using technology to deliver care at a distance. In particular, telemedicine refers to clinician-patient interactions and discussions that occur remotely, by phone, video calls, text messaging, and other formats.

Because in-person care during the pandemic was suddenly unavailable or potentially unsafe for both clinicians and patients, alternate models of care were implemented. These included hybrid models with reduced in-person visit schedules for care that could not be delivered remotely, and telemedicine visits to maintain contact between visits. Such approaches grew at a more accelerated pace than before the pandemic as promising strategies to reduce a patient's risk of contracting COVID-19 while continuing to deliver consistent and necessary care.<sup>17</sup> These included using videoconferences to replace in-person visits, implementing at-home monitoring of measures historically surveyed only in the setting of prenatal office visits, and enabling consultation with remote specialists. More frequent measurements through telemedicine platforms may allow for less frequent antenatal visits while also improving health outcomes. Current evaluations of these prenatal care delivery models are limited and focus mainly on patient and provider experience,<sup>18</sup> but warrant further investigation to understand their impact on health and patient centered outcomes.

Clinical guidance that, at least in part, focuses on the volume of antenatal care (frequency, cadence, etc.) and modern modes of delivery (i.e., telemedicine), and that is explicitly evidence-based is needed to inform and enable the best care for pregnant patients and their babies without overburdening the healthcare system, pregnant patients, or their families. Advances in, and new evidence about, telemedicine—particularly during the COVID-19 pandemic—offer a potential opportunity to improve care with reduced resources, time, and costs.

## **Purpose of the Review**

ACOG and the Society for Maternal-Fetal Medicine (SMFM) nominated the topic of antenatal care to the Agency for Healthcare Research and Quality for systematic review. ACOG and SMFM develop clinical practice guidelines and consensus statements both individually and jointly based on the needs of its members who are clinicians that provide gynecologic, obstetric, and high-risk pregnancy care. The scope of the current systematic review was developed to support ACOG and SMFM in their effort to create a new joint consensus statement that will be based on evidence and address the preferred frequency, timing, and cadence of routine antenatal care visits. It will also address the use of telemedicine for routine antenatal care.

Specifically, the systematic review will summarize (1) the findings from studies of the effectiveness of antenatal care schedules that vary by number and timing of visits for uncomplicated pregnancies, including studies comparing group and individual visits; (2) studies of the effectiveness of telemedicine modalities for providing antenatal care for uncomplicated pregnancies; and (3) qualitative evidence of the patient and provider perspectives, preferences, and perceptions related to the frequency and timing of antenatal care visits and telemedicine approaches to prenatal care.

The intended audience includes guideline developers, clinicians and other providers of antenatal care, healthcare policy makers, and patients.

## **II. Key Questions and Eligibility Criteria**

### **Key Questions**

**KQ 1:** What are the benefits and harms of different antenatal care schedules that vary by number or timing of visits for pregnancies requiring routine care and monitoring?

**KQ 2:** What are the benefits and harms of telemedicine for providing routine antenatal care during pregnancy?

**KQ 3:** What are patient, partner/family, and provider perspectives, preferences, and experiences related to antenatal care visit schedules and use of telemedicine for routine antenatal care?

# Study Eligibility Criteria

## Key Question 1

### Population

- Pregnant individuals receiving routine / standard / basic / traditional antenatal care
- Allow studies of pregnant individuals at increased risk of poor outcomes (e.g., with gestational diabetes, gestational hypertension, fetal growth restriction, those receiving part of their antenatal care by maternal-fetal medicine [MFM] or other specialists), as long as the study pertains to their routine antenatal care (i.e., not specifically to their enhanced care for their high-risk condition)

#### Exclude:

- *Non-routine care provided by MFM or other specialists*
- *Care specific to high-risk conditions (e.g., home glucose or blood pressure monitoring)*

Modifiers/Subgroups of interest:

- Age groups
- Race/ethnicity or different cultural groups
- Location (rural, urban, etc.)
- Socioeconomic status
- Disparities, incl. socioeconomic, healthcare, other
- Other social determinants of health
- Different providers
- Baseline pregnancy risk of complications, poor outcomes etc. (within the context of routine care)
- Nulliparous vs. multiparous
- Different levels of social support
- Different pregnancy education needs (e.g., because of health literacy differences, education, adolescent vs. adult)
- Different psychosocial factors
- Other modifiers/subgroups analyzed in studies

### Interventions

- Defined routine antenatal care schedules with focus on:
  - Total number of planned visits
  - Overall schedule (timing, frequency, cadence)
  - Number of planned in-person visits
- Providers of routine antenatal visits include
  - Obstetricians/gynecologists, nurse practitioners, nurse midwives, nurses, physician assistants, family medicine clinicians

#### Exclude

- *Doulas, social workers, counselors, dieticians, non-licensed or non-medical personnel*
- Include interventions designed to evaluate different types of providers (e.g., a nurse instead of a doctor) if there is a concomitant comparison of different schedule of planned visits
- Include interventions designed to evaluate group visits if the group visits replace individual visits and there is a concomitant comparison of different schedule of planned visits
- Include interventions designed to evaluate home visits if the home visits replace in-clinic visits and there is a concomitant comparison of different schedule of planned visits

#### Exclude

- *Interventions where the different provider visits, group visits, or home visits are simply added on to the standard of care visits (with no change made to the scheduled standard visits).*

Exclude:

- *Observational studies of realized visits (as opposed to scheduled or planned visits)*
- *Events that occur separately from/outside of routine visits (that do not occur during the visit)*
- *Interventions conducted during specific visits or their timing (unrelated to frequency of use of interventions) e.g. ultrasound (U/S) at the week 18 vs. week 22 visit*
- *Addition of interventions conducted during antenatal care for specific evaluation (e.g., U/S screening for intrauterine growth retardation or cervical length)*
- *Novel (nonstandard) clinical interventions conducted during visits, (e.g., electrocardiography at every visit)*
- *Evaluations of behavioral interventions (e.g., smoking cessation, exercise) or screening during antenatal care (e.g. substance use, domestic violence)*
- *Interventions outside of the scope of typical antenatal care, (e.g., teeth cleaning at antenatal care visit, psychiatric care)*
- *Specialist visits*
- *Unplanned office or emergency department visits, other ancillary or risk/complaint-driven care visits*
- *Preconception care*
- *Care for a pregnant person who is in labor*
- *Postpartum care*
- *Interventions spanning pregnancy and periods before or after pregnancy*

## Comparators

- Standard, routine, or alternative antenatal care schedule (as defined by the study)

## Outcomes (prioritized outcomes have an asterisk)

- Pregnancy complications:
  - Maternal mortality
  - Antenatal pregnancy complications
    - Gestational diabetes
    - Gestational hypertension
    - Pre-eclampsia
    - Intrauterine growth restriction (IUGR)
    - Anemia
    - Urinary tract infections
  - Delivery-related complications
    - Lacerations
    - Hemorrhage
    - Transfusion need
- Other maternal health outcomes:
  - Delivery outcomes
    - Cesarean delivery—must be adjusted to account for provider/patient preferences
    - Induction of labor
    - Operative vaginal delivery
  - Inappropriate weight gain
  - Postpartum contraception—must be adjusted to account for patient preferences
- Maternal psychosocial, preferences, and related outcomes:
  - Quality of life measures\*
  - Psychosocial measures
  - Mental health measures or diagnosis (e.g., anxiety, depression)\*
  - Patient satisfaction with antenatal care\*
  - Patient preferences
  - Resources
    - Patient financial costs
    - Patient travel (e.g., driving miles or costs)

- Lost work time (including used vacation/health days)\*
- Fetal/neonatal/infant outcomes:
  - Delivery timing
    - Preterm birth\*
    - Full-term delivery\*
    - Post-term delivery
    - Gestational age at birth\*
  - Mortality
  - Perinatal morbidity (e.g., birth trauma)
  - Small for gestational age (e.g., birth weight <10% for similar age neonates)\*, low birth weight (e.g., <2.5 kg [5 lb, 8 oz])\*
  - Abnormal Apgar score (threshold, e.g. <7)\*
  - Breastfeeding\*—must be adjusted to account for patient preferences
  - Need for social services
- Care utilization:
  - Attendance at planned antenatal visits (adherence/compliance)
  - Completion of ACOG recommended services\*
  - Number of unplanned visits\*
  - Number of referrals to other providers
  - Unplanned hospital admissions
  - Emergency room/triage visits
  - Neonatal intensive care unit [NICU] admissions\* / length of stay
  - Number of unplanned contacts (e.g., portal/phone messages)
- Provider outcomes:
  - Provider satisfaction with antenatal care
- Harms:
  - Overdiagnosis (“unnecessary” negative workups or misdiagnoses)
  - Delayed diagnoses (e.g., gestational diabetes)\*
  - Harms to marginalized groups / equity outcomes

\* Prioritized outcomes

## Study Design

- Comparative studies (comparisons of different interventions), including parallel design, pre-post studies, and other comparisons
  - Randomized or observational (nonrandomized)
  - Prospective or retrospective
- Surveys that compare interventions (specifically for patient preferences and satisfaction)
- Registry (e.g., PRAMS [Pregnancy Risk Assessment Monitoring System], National family study) and other retrospective data sources may be eligible, but only if the comparison is between different numbers of *planned or scheduled visits*
- Single group studies (no direct comparison of interventions)
  - Preference and satisfaction outcomes only
- N ≥10 per intervention group
- (Existing systematic reviews and guidelines will be used as sources of otherwise missed eligible studies)

### Exclude

- *Retrospective studies comparing number of realized visits (i.e., where differences in care were not planned)*
- *Single group studies (no direct comparison of interventions) except for preference and satisfaction outcomes*

## Timing

- Interventions: During antenatal period (excluding labor and delivery)
- Followup/Outcomes: Any (antenatal, peripartum, postpartum, or later)

## Setting

- High income countries based on World Bank classifications
- Outpatient care

## Key Question 2

### Population

- Same as Key Question 1

### Interventions

- Antenatal care programs using telemedicine, including remote synchronous (real-time visits such as video calls) and asynchronous interactions (e.g., portal email discussions)
  - Allow inclusion of devices designed to transmit information *only if* use of the devices are part of telemedicine interactions between patients and providers

#### Exclude:

- *Exclusions listed for KQ 1*
- *Telemedicine monitoring specifically for gestational diabetes, gestational hypertension, fetal growth restriction (<10% normal), or other high-risk pregnancies*
- *Communications that do not provide opportunity for two-way discussion, that include only a single round of communication (e.g., an email asking a question and an email response to that question), that are based on forms to be completed, or that include one-direction information (e.g., educational materials from the provider, bot messages such as appointment reminders)*
- *Devices or interactions that do not employ contemporary internet connectivity (or human interaction by phone), e.g., mail, fax, patient-completed charts brought to office visits for review*
- *Mobile health (mHealth) applications that are not part of clinical care delivery (clinic does not communicate through the app)*
- *Social media or peer groups*
- *Non-routine antenatal care provided by MFM specialists*
- *Teleconsultations between clinicians (e.g., remote U/S or telerobotics)*
- *Evaluation of remote device accuracy (e.g., of home blood pressure monitor) or comparison of specific devices (e.g., different monitors)*
- *Proof of concept or development studies of new medical technologies or apps*

### Comparators

- All in-person care, alternative telemedicine/remote care
- No (explicit) comparator

### Outcomes

- Same as KQ 1
- Access to telemedicine, equipment (e.g., home blood pressure cuff, phone, internet)

### Study Design

- Comparative studies (comparisons of different interventions), including parallel design, pre-post studies, and other comparisons
  - Randomized or observational (nonrandomized)
  - Prospective or retrospective
- Single group studies (no comparator)

- Surveys (specifically for patient preferences and satisfaction)
- Registry (e.g., PRAMS, National family study) and other retrospective data sources may be eligible, but only if there is a specific evaluation of telemedicine
- N ≥10 per intervention group
- (Existing systematic reviews and guidelines will be used as sources of otherwise missed eligible studies)

## Timing

- Same as Key Question 1

## Setting

- Same as Key Question 1

## Key Question 3

### Population

- Pregnant individuals
- Postpartum individuals
- Individuals considering or planning pregnancy
- Partners/family
- Providers of antenatal care (any profession or licensure)
- Allow studies that include high-risk patients, as long as the interventions being assessed pertain to routine care

### Interventions

- Routine antenatal care, specific to interventions covered in KQ 1 and 2

### Comparators

- Not applicable

### Outcomes

- Perspectives and preferences related to interventions covered by KQ 1 and KQ 2
- Barriers and facilitators related to interventions covered by KQ 1 and KQ 2

#### Exclude:

- *Perspectives on high-risk antenatal care, such as provided by MFM clinicians*

### Study Design

- Qualitative studies
  - Interviews
  - Focus groups
  - Ethnographic studies
  - Surveys with open-ended questions amenable to qualitative analysis
- Any size

#### Exclude

- Surveys with closed-ended questions with only quantitative analyses
- (Although, these might be relevant for Key Questions 1 or 2)



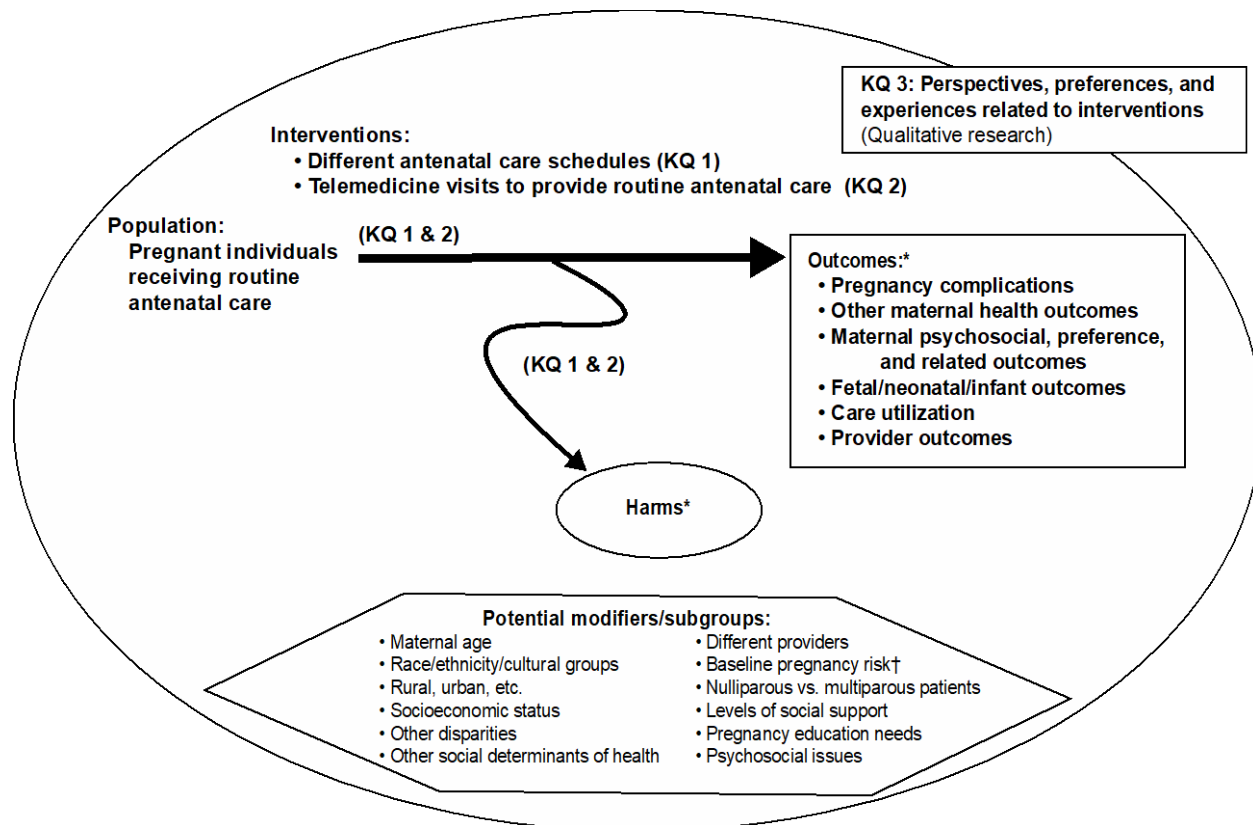
## Timing

- Any (as long as interventions of interest occurred during antenatal period)

## Setting

- Same as Key Question 1

## III. Analytic Framework



Abbreviations: KQ = Key Question, QoL = quality of life.

\* Pregnancy complications: maternal mortality, antenatal pregnancy complications (gestational diabetes, gestational hypertension, pre-eclampsia, intrauterine growth restriction, anemia, urinary tract infections), delivery related complications (lacerations, hemorrhage, transfusion need); Other maternal health outcomes: delivery outcomes (cesarean delivery, induction of labor, operative vaginal delivery), inappropriate weight gain, postpartum contraception. Maternal psychosocial, preferences, and related outcomes: quality of life measures, psychosocial measures, mental health measures or diagnosis (e.g., anxiety, depression), patient satisfaction with antenatal care, patient preferences, resources (patient financial costs, patient travel, lost work time). Fetal/neonatal/infant outcomes: delivery timing (preterm birth, full-term delivery, post-term delivery, gestational age at birth), mortality, perinatal morbidity (e.g. birth trauma), abnormal Apgar score, breastfeeding, need for social services. Care utilization: attendance at planned antenatal visits (adherence), completion of ACOG recommended services, number of unplanned visits, number of referrals, unplanned hospital admissions, emergency room/triage visits, NICU admissions and length of stay, number of unplanned contacts (e.g., portal/phone messages). Provider outcomes: provider satisfaction with antenatal care. Harms: overdiagnosis, delayed diagnoses, harms to marginalized groups/equity outcomes.

† Within the context of standard antenatal care.

## IV. Methods

The systematic review for KQs 1 and 2 will follow the Evidence-based Practice Center Program methodology, as laid out in its Methods Guide, particularly as it pertains to reviews of comparative effectiveness.<sup>19</sup> In the absence of a formal Evidence-based Practice Center Program Methods Guide for the qualitative synthesis for KQ3, we will follow methods outlined by the Cochrane Collaboration and ongoing Evidence-based Practice Center Program qualitative training.<sup>20-26</sup>

**Criteria for Inclusion/Exclusion of Studies in the Review:** See detailed eligibility criteria in Section II.

In brief, for Key Question 1, we will include comparative studies that compare different numbers, timing, frequency, and cadence of routine antenatal care visits. We will focus on routine care for “low risk” pregnant individuals. In other words, we will focus on the care received that is usual or standard pregnancy care, regardless of whether the individual patient is at increased risk of poor outcomes. We will exclude evaluations of realized visits (i.e., people who received more versus fewer visits for reasons other than planned scheduling). As feasible, we will evaluate different providers, group versus individual visits, and home versus clinic visits, but only within the context of number and timing of routine antenatal care visits; we will not evaluate these interventions as simple add-ons to standard care. Routine antenatal care must be provided by obstetricians/gynecologists, nurse midwives, family medicine clinicians, nurses, or other licensed personnel who provide full antenatal care services. We will evaluate outcomes as listed in the *Study Eligibility Criteria* Table. We will include only studies from high-income countries since the context of routine antenatal care in low and middle income countries is unlikely to pertain to the U.S. healthcare system.

For Key Question 2, we will include comparative and single group studies of telemedicine interventions for pregnant individuals receiving routine antenatal care. The population and outcomes of interest will be the same as for Key Question 1. Regarding the intervention, we start with the Health Resources and Services Administration (HRSA) definition of telehealth, that “is defined as the use of electronic information and telecommunication technologies to support long-distance clinical health care, patient and professional health-related education, public health, and health administration. Technologies include video conferencing, the internet, store-and-forward imaging, streaming media, and terrestrial and wireless communications.”<sup>27</sup> However, we restrict to telemedicine, referring specifically to remote clinical services between provider and patient. We will include telemedicine visits that, at least to some extent, approximate in-person visits and that include direct two-way communication between the patients and their providers. The communication may be synchronous (e.g., patient and provider virtual/video or phone conversation) or asynchronous (e.g., text messages or email discussions). However, the mode of communication must allow for two-way discussion and must not be limited to simple single questions and answers (e.g., patient questions transmitted via a portal with an answer to just that question or electronic forms). The telemedicine interventions may include home monitoring but must incorporate patient-clinician interactions (e.g., blood pressure is collected by patient, reviewed by provider, and discussed together). We will exclude apps and other forms of remote healthcare that do not include interactions with providers (e.g., self-measured blood pressure monitors, fitness apps, social media) or that do not directly include patients (e.g., remote readings of ultrasounds).

For Key Questions 1 and 2, we will prioritize the following list of outcomes. As described below, we will evaluate the strength of evidence (SoE) for these outcomes. We may also evaluate SoE for other included outcomes. The prioritized outcomes include:

- Quality of life (maternal)
- Patient satisfaction with antenatal care
- Lost work time
- Preterm birth
- Full-term delivery
- Gestational age at birth
- Small for gestational age / Low birth weight
- Abnormal Apgar score
- Completion of ACOG recommended services
- Number of unplanned visits
- NICU admissions
- Delayed diagnoses

For Key Question 3, we will conduct a qualitative evidence synthesis of studies involving focus groups, interviews, and other published qualitative studies of any group of individuals addressing the topics covered by Key Questions 1 or 2. We will summarize information related to patient/pregnant individual's preferences regarding the interventions and the outcomes they deem important as well as related themes that emerge from the studies.

### **Literature Search Strategies To Identify Relevant Studies to Answer the Key Questions:**

#### **Quantitative studies (KQ 1 & 2)**

We will search for studies and existing systematic reviews in MEDLINE (via PubMed), The Cochrane Register of Clinical Trials, The Cochrane Database of Systematic Reviews, Embase, and CINAHL. Duplicate citations will be removed prior to screening. There will be no language restriction, but we will exclude studies tagged as being from low- or middle-income countries (per the World Bank classification). Search strategies include filters to remove nonhuman studies and articles that are not primary studies, systematic reviews, or clinical practice guidelines.

The searches include MeSH or Emtree terms, along with free-text words, related to antenatal care, prenatal care, obstetric care, and pregnancy care; telemedicine, and telemedicine; and office visits, care schedules, and appointments. Searches will be independently peer reviewed by a librarian at another Evidence-based Practice Center. The planned search strategies are included in Appendix A; the strategies for other databases will be adapted from this strategy.

Additional searches will be conducted in the ClinicalTrials.gov registry for unpublished study protocols, unpublished study results, and ongoing studies. The reference lists of relevant existing systematic reviews will be screened for additional eligible studies.

#### **Qualitative studies (KQ 3)**

We will search for qualitative studies as part of the overall search described for the quantitative studies. However, to capture qualitative studies that may not be indexed in medical databases, we will extend our database searches to also include PsycINFO and SocINDEX using the same set of concepts included in the search for quantitative studies. No study type filters are used in any search query, so all study types will be retrieved, including those likely to include qualitative data. If it appears a particular aspect of the qualitative review is not well developed,

further targeted searches will be developed iteratively. We will also perform citation tracing and other snowballing techniques based on all relevant studies to identify studies that may have been missed in the database searches.<sup>21</sup>

Based on screening of the literature during the Topic Refinement period, there appears to be a large number of focus group and other qualitative studies that use appropriate methods to determine themes across participants. Therefore, the literature search will not be extended into the grey literature (evidence from sources not identified using standard methods, as described above).

### All Key Questions

A Supplemental Evidence And Data for Systematic review (SEADS) portal will be available for this review. Additional articles suggested to us from any source, including peer and public review, will be screened applying identical eligibility criteria.

Non-English language articles will be screened and data extracted either by readers of the relevant languages or after translation via Google Translate (<https://translate.google.com/>), if possible.

Searches will be updated during the public posting period.

During Topic Refinement, we conducted a highly focused search in MEDLINE yielding approximately 600 citations. These were entered into Abstrackr software (<http://abstrackr.cebm.brown.edu/>) to enable abstract screening. All 600 citations were screened by all team members and all conflicts were resolved in conference. Citations found by the full literature searches will be added to the already-screened citations in Abstrackr. We will then continue abstract screening in duplicate. The Abstrackr software has machine learning capabilities that predict the likelihood of relevance of each citation. Daily, the list of unscreened abstracts will be sorted so that the most potentially relevant articles are presented first. This process will make screening more efficient and will enable us to capture the large majority of relevant articles relatively early in the abstract screening process.

As has become standard for our Center, we will take advantage of the machine learning capacities of Abstrackr to limit resources spent on abstract screening. We will stop double screening when the predicted likelihood of the remaining unscreened papers being relevant is very low. We will use a threshold for the prediction score of the unscreened citations of 0.40. (This threshold is based on experience with several dozen screening projects and an analysis in preparation for publication.) To confirm that the selected prediction score threshold is appropriate for this literature base, when the maximum prediction score is <0.40, we will screen approximately 400 additional consecutive citations. (This sample size chosen because the upper 97.5% confidence interval bound for a proportion of 0/400 is less than 1%). If any of the 400 citations are screened in (at the abstract level) we will repeat the process until we have rejected at least 400 consecutive citations.

Potentially relevant citations will be retrieved in full text. These articles will be retrieved and rescreened in duplicate.

### **Data Extraction and Data Management:**

#### Quantitative studies (KQ 1 & 2)

Data from eligible quantitative studies will be extracted into the Systematic Review Data Repository-Plus (SRDR+) software. Each article will be extracted by one researcher and entered data will be confirmed by a second researcher. Individual studies with multiple publications will

be extracted as a single study (with a single entry in SRDR+). Articles that report multiple studies will be entered into SRDR+ separately for each study.

For each study, we will extract publication data, study design features, population characteristics, intervention and comparator names and descriptions, relevant outcomes and their definitions, and funding source. All subgroup analyses or other evaluations of heterogeneity of treatment effect will be extracted.

### Qualitative studies (KQ 3)

Eligible qualitative studies will be extracted in Google sheets (to allow team editing). For each study, we will extract publication data, study setting, and study design features (e.g., recruitment methods, qualitative data collection and analysis methods, theoretical models used to interpret or contextualize the data). We will extract the qualitative findings (i.e., perspectives, preferences, and experiences) separately for routine antenatal care schedules and telemedicine for antenatal care, and within topics, separately for different stakeholders (pregnant people, partners/family, providers). Specific qualitative findings to extract may take the form of exemplar quotations from participants or themes identified by the study's authors (or other related exemplar primary data or interpretation from the study's author). We will use the Theoretical Domains Framework (TDF) as a structure to guide our extraction of reported themes and supporting text for themes.<sup>28, 29</sup> The TDF was developed to assist in identifying the cognitive, affective, social and environmental factors that may influence an individual's performance of a health behavior. Behavioral determinants are categorized into one or more of 14 domains: knowledge; skills; social/professional role and identity; belief about capabilities; optimism; beliefs about consequences; reinforcement; intention; goals; memory, attention, and decision processes; environmental context and resources; social influences; emotion; and behavioral regulation. We will use a Best Fit Framework approach in the application of the TDF; we will attempt to extract qualitative study findings into the 14 TDF domains as appropriate.<sup>30</sup> We will also extract and map findings that do not fit within the framework to interrogate further.

Congruent with qualitative methods for individual studies, qualitative data extraction and synthesis will be conducted in tandem. Two researchers will extract the first few studies in duplicate to ensure reliability and agreement, particularly in the coding of TDF themes. Subsequent studies will be extracted by one person and confirmed by a second senior researcher. We will conduct extractions iteratively, meeting frequently to discuss and interrogate choices in coding themes within TDF domains and additional domains as identified. We will note decisions in coding interpretation in a coding manual, as needed. We will stop searching for, and including, new studies when we reach saturation (i.e., no new themes are identified).

**Assessment of Quality and/or Methodological Risk of Bias of Individual Studies:** We will evaluate each study for risk of bias and methodological quality.

### Quantitative studies (KQ 1 & 2)

For randomized controlled trials (RCTs), including cluster randomized trials, we will complete the revised Cochrane Risk of Bias tool (ROB 2),<sup>31</sup> which addresses issues related to randomization and allocation concealment; blinding; deviations from intended intervention; missing data; outcome measurement; and reporting biases. We will also evaluate the adequacy of descriptions of study participants, interventions, outcomes, and study designs. In addition, we will assess the adequacy of analyses. Questions related to outcome assessor blinding, missing

data, outcome measurement reporting adequacy, and analytic adequacy will be assessed for each outcome.

For nonrandomized comparative studies, we will add assessments of specific elements from ROBINS-I,<sup>32</sup> in particular related to selection bias (comparability of groups) and relevant concepts addressed for RCTs (i.e., related to missing data, outcome measurement, analysis plan). The questions will be assessed for each outcome (e.g., whether each outcome was adjusted for potential confounders).

For single group studies, we will primarily assess specific elements from ROBINS-I,<sup>32</sup> in particular related to selection bias (appropriateness of included participants) and completeness of outcome (primarily harms) reporting (for each outcome separately).

### Qualitative studies (KQ 3)

For qualitative studies, we will assess risk to rigor using the Critical Appraisal Skills Programme (CASP) appraisal tool for qualitative studies, which addresses issues related to clear qualitative research aims; congruence between the research aims and methodological approach; sampling and data collection; appropriate application of methods; richness/conceptual depth of findings; appropriate interrogation of findings; reflexivity of the researchers.<sup>22, 26, 33</sup>

## **Data Synthesis:**

### Quantitative studies (KQ 1 & 2)

We will summarize the evidence both narratively and, when feasible, quantitatively. Each study will be described in summary and evidence tables presenting study design features, study participant characteristics, descriptions of interventions, outcome results, and risk of bias/methodological quality.

We do not expect to be able to conduct statistical analyses on these evaluations (i.e., meta-analysis, meta-regression) because we expect that studies will differ sufficiently by specific comparison made and/or outcomes reported that data will be too sparse for pooling. However, where feasible, we will conduct restricted maximum likelihood (REML) random effects model meta-analyses of effect sizes (e.g., odds ratio) or proportions. For meta-analyses of proportions, we will use Freeman-Tukey double arcsine transformations to account for non-normal distributions.

For KQ 1 and much of KQ 2, we will summarize comparative differences between interventions. Most of these analyses will be for odds ratios for categorical outcomes and net differences (difference-in-difference) for continuous outcomes. We will preferentially summarize adjusted analyses. From single group studies evaluated for KQ 2 we will summarize event rates (percent) for categorical outcomes and average (mean or median) values for continuous outcomes. Conclusions from single group studies (of telemedicine interventions) will not include implied differences with in-person visits (derived from other sources).

As feasible, we will describe reporting of differences in effects and harms by different factors, subgroups, or predictors. We expect to primarily rely on reported within-study differences in effects (or harms). However, we will look for opportunities to qualitatively and/or quantitatively summarize and/or compare results across studies.

### Qualitative studies (KQ 3)

We will synthesize qualitative evidence using a Framework synthesis which is useful in qualitative syntheses of complex interventions. We will use the TDF to characterize themes within qualitative studies and note domains that emerge, or do not emerge, as important to participants' perceptions about antenatal care schedules and telemedicine interventions.<sup>28, 29</sup>

**Grading the Strength of Evidence for Prioritized Outcomes:** Following AHRQ Methods guidance,<sup>19</sup> we will evaluate the strength of evidence (SoE) addressing each prioritized outcome for Key Questions 1 and 2, as listed above. We will assess the SoE for the qualitative studies using the GRADE-CERQual tool.<sup>22, 34</sup>

**Assessing Applicability:** For each Key Question (or specific subquestion), we will describe the applicability of the included studies primarily based on the studies' eligibility criteria and their included participants. We will describe the populations to which the evidence may be most applicable and will highlight populations for whom the evidence may be less applicable. In particular, we will assess such factors as prior history, age and race/ethnicity. Other factors may include the age and geographic location of the study.

**Integrating Quantitative and Qualitative Evidence:** The review is being conceived with two parallel approaches, in which the quantitative (KQ 1 and 2) and qualitative (KQ 3) reviews are completed independently but given opportunities to "speak" to each other (e.g., by altering the prioritization of outcomes).<sup>24</sup> While we do not plan a formal integration of results (i.e., a third synthesis of the first two syntheses), we will consider findings from KQ 3 in interpretation and contextualization of KQ 1 and 2 (e.g., ordering of outcomes by importance, opportunities for future research) and vice versa.

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## VI. Definition of Terms and Abbreviations

ACOG	American College of Obstetricians and Gynecologists
AHRQ	Agency for Healthcare Research and Quality
CPG	Clinical practice guidelines
KQ	Key Question
MeSH	Medical Subject Heading
MFM	Maternal-fetal medicine: medical field comprised of obstetricians with specialized training caring for pregnant persons with high-risk pregnancies and complications during pregnancy
mHealth	Mobile health: the provision of healthcare delivery, support, or interventions using mobile technologies such as phones, tablets, or wearable devices
PICOTS	Population, intervention, comparator, outcome, time, and setting details for systematic review search
PRAMS	Pregnancy Risk Assessment Monitoring System: population-based surveillance survey about pregnancy and the first several months after birth managed by the Centers for Disease Control and Prevention in partnership with state and local health departments
SEADS	Supplemental Evidence And Data for Systematic Review
SMFM	Society for Maternal-Fetal Medicine
SoE	Strength of Evidence
SR	Systematic review
SRDR+	Systematic Review Data Repository Plus
TEP	Technical expert panel
U/S	Ultrasound
WHO	World Health Organization

## VII. Summary of Protocol Amendments

If we need to amend this protocol, we will give the date of each amendment, describe each change and give the rationale in this section.

## VIII. Review of Key Questions

The Agency for Healthcare Research and Quality (AHRQ) posted the Key Questions on the AHRQ Effective Health Care Website for public comment. The Evidence-based Practice Center (EPC) refined and finalized them after reviewing the public comments and seeking input from Key Informants (KIs).

## IX. Key Informants (KIs)

KIs are end users of research, including patients and caregivers, practicing clinicians, relevant professional and consumer organizations, purchasers of health care, and others with a role in making health care decisions. Within the EPC program, the KIs' role is to provide input into refining the Key Questions for research that will inform healthcare decisions. The EPC solicits input from KIs when refining questions for systematic review. KIs are not involved in analyzing the evidence or writing the report and have not reviewed the report, except as given the opportunity to do so through the peer or public review mechanism.

KIs must disclose any financial conflicts of interest greater than \$10,000 and any other relevant business or professional conflicts of interest. Drawing upon their roles as end-users, diverse individuals are invited to serve as KIs. Those who present with potential conflicts can be retained although the TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

## **X. Technical Expert Panel (TEP)**

Technical Experts constitute a multi-disciplinary group of clinical, content, and methodological experts who provide input in defining populations, interventions, comparisons, or outcomes. The Technical Expert Panel is selected to provide broad expertise and perspectives specific to the topic under development. Divergent and conflicting opinions are common and perceived as healthy scientific discourse that fosters the completion of a thoughtful, relevant systematic review. As such, study questions, design, and methodological approaches do not necessarily represent the views of individual technical and content experts.

Technical Experts provide further input to finalize the KQs, study eligibility criteria, and analysis plans. The Technical Experts provide feedback on the full protocol. They provide information to the EPC to identify literature search strategies and suggest approaches to specific issues as requested by the EPC. They may help to identify particular studies or databases to search for studies to be included in the review. Technical Experts do not do analysis of any kind; neither do they contribute to the writing of the report. They do not review the report, except as given the opportunity to do so through the peer or public review mechanism.

Members of the TEP must disclose any financial conflicts of interest greater than \$5,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals are invited to serve as Technical Experts and those who present with potential conflicts may be retained although the AHRQ TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

## **XI. Peer Reviewers**

Peer reviewers are invited to provide written comments on the draft report based on their clinical, content, or methodological expertise. The EPC considers all peer review comments on the draft report in preparation of the final report. Peer reviewers do not participate in writing or editing of the final report or other products. The final report does not necessarily represent the views of individual reviewers. The EPC will complete a disposition of all peer review comments. The disposition of comments for systematic reviews and technical briefs will be published three months after the publication of the evidence report.

Potential Peer Reviewers must disclose any financial conflicts of interest greater than \$10,000 and any other relevant business or professional conflicts of interest. Invited Peer Reviewers may not have any financial conflict of interest greater than \$10,000. Peer reviewers who disclose potential business or professional conflicts of interest may submit comments on draft reports through the public comment mechanism.

## **XII. EPC Team Disclosures**

EPC core team members must disclose any financial conflicts of interest greater than \$1,000 and any other relevant business or professional conflicts of interest. Related financial conflicts of

interest that cumulatively total greater than \$1,000 will usually disqualify EPC core team investigators from participation in the review.

### **XIII. Role of the Funder**

This project was funded under Contract No. 75Q80120D00001 from the Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services. The TOO will review contract deliverables for adherence to contract requirements and quality. The authors of this report will be responsible for its content. Statements in the report should not be construed as endorsement by the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

### **XIV. Registration**

This protocol will be registered in the international prospective register of systematic reviews (PROSPERO).