Evidence-based Practice Center Systematic Review Protocol

Project Title: Systematic Review of Breastfeeding Programs and Policies, Breastfeeding Uptake, and Maternal Health Outcomes in Developed Countries

Initial publication date if applicable: 3/20/17

Amendment Date(s) if applicable: 9/12/17

(Amendments Details–see Section VII)

## I. Background and Objectives for the Systematic Review

Breast milk is the natural nutrition for all infants; evidence supports the association between breastfeeding and better health outcomes for both infants and mothers.[1-3] Multiple clinical guidelines and health-related organizations recommend exclusive breastfeeding up to (or around) 6 months, including the American Academy of Pediatrics,[4] the American Congress of Obstetrics and Gynecology,[5] the World Health Organization,[6, 7] and others.[8, 9] After 6 months, these organizations recommend continued breastfeeding through the first year of life and beyond.

A 2007 Agency for Healthcare Research and Quality (AHRQ) review by Ip and colleagues evaluated the evidence on the association between breastfeeding and infant and maternal health outcomes.[2] For maternal health outcomes, they concluded that a history of breastfeeding (compared with no breastfeeding or a shorter duration of breastfeeding) was associated with a reduced risk of type 2 diabetes and breast and ovarian cancer.[2] No benefit was found for risk of fracture; for other outcomes (e.g., postpartum depression) the relationship between breastfeeding and improved maternal health was unclear. Since 2007, several new studies have reported on outcomes not addressed in the 2007 AHRQ review, including hypertension, rates of myocardial infarction and other cardiovascular outcomes.[10-13]

Despite evidence supporting the association between breastfeeding and better health outcomes (for infants and mothers), 45 percent of U.S. women who initiate breastfeeding report early, undesired weaning.[14] The estimates for any breastfeeding for infants born in 2013 in the United States were 81.1 percent for initiation, 51.8 percent for infants breastfed at 6 months, and 30.7 percent for infants breastfed at 12 months.[15] Each decade, the US Department of Health and Human Services releases and monitors a list of "Healthy People" objectives to guide the nation's 10-year health promotion and disease prevention efforts; these objectives include several targets related to breastfeeding.[16] Healthy People 2020 targets for initiating breastfeeding, breastfeeding to 6 months, and breastfeeding to 12 months are 81.9 percent, 66.6 percent, and 34.1 percent, respectively.[17] There are racial and ethnic differences in breastfeeding initiation (starting) and duration (continuing) rates. From 2000–2013, the percentage of women who initiated breastfeeding went up from 47.4 percent to 66.3 percent for blacks, 71.8 percent to 84.3 percent for whites, and 77.6 percent to 83.0 percent for Hispanics.[18, 19] Sociodemographic factors associated with an increased likelihood of breastfeeding initiation and

continuation include older maternal age, being married, Asian or white race, Hispanic ethnicity, higher maternal education, and access to private insurance.[19-22]

Community, workplace and health care system-based programs and policies are seen as promising strategies to support initiation and increase duration breastfeeding. In addition to setting targets for breastfeeding initiation rates and duration of breastfeeding, other Healthy People 2020 objectives related to breastfeeding include increasing the proportion of employers that have worksite lactation support programs and increasing the proportion of live births that occur in facilities that provide recommended care for lactating mothers and their babies.[17]

Health care system-based interventions include implementation of the Baby-Friendly Hospital Initiative (BFHI). The BFHI is a global program sponsored by the World Health Organization and UNICEF to encourage and recognize hospitals and birth centers that create an environment that supports breastfeeding; the "10 Steps to Successful Breastfeeding for Hospitals" are listed in Table 1. For U.S. hospitals, Baby-Friendly accreditation is awarded to facilities that successfully implement the 10 steps and the International Code of Marketing of Breast-Milk Substitutes[7] and pass an intensive site visit.[23] Site visits and certification are adjudicated by Baby Friendly USA, a 501c3 non-profit organization.[24] In addition to certification by Baby Friendly USA, state departments of public health have encouraged implementation of the 10 Steps through local programs such as the Texas Ten Step Program,[25] the North Carolina Maternity Center Breastfeeding-Friendly Designation Program,[26] and others. On a national level, the Centers for Disease Control and Prevention has audited maternity care practices during the past 10 years with a biannual maternity practice survey, results of which are distributed to each maternity center.[27]

**Table 1. Baby-Friendly Hospital Initiative 10 Steps to Successful Breastfeeding[1]**

| |
|---|
| 1. Have a written breastfeeding policy that is routinely communicated to all health care staff. |
| 2. Train all health care staff in skills necessary to implement this policy. |
| 3. Inform all pregnant women about the benefits and management of breastfeeding. |
| 4. Help mothers initiate breastfeeding within 1 hour of birth. |
| 5. Show mothers how to breastfeed, and how to maintain lactation even if they should be separated from their infants. |
| 6. Give infants no food or drink other than breast milk, unless medically indicated. |
| 7. Practice rooming in—allow mothers and infants to remain together 24 hours a day. |
| 8. Encourage breastfeeding on demand. |
| 9. Give no pacifiers or artificial nipples to breastfeeding infants |
| 10. Foster the establishment of breastfeeding support groups and refer mothers to them on discharge from the hospital or birth center. |

[1] Baby Friendly USA *Ten Steps to Successful Breastfeeding*[28]

In terms of health care policy interventions beyond hospital policies, costs associated with breastfeeding support (e.g., comprehensive lactation support and counseling and breastfeeding equipment) are currently covered by health insurance marketplace plans and private nongrandfathered health plans under the 2010 Patient Protection and Affordable Care Act (ACA).[29] It is not clear whether certain lactation benefit packages (e.g., type of breastfeeding supplies offered, number of visits provided, or qualifications of intervention delivery personnel) are more or less effective in increasing breastfeeding initiation and duration.

Workplace interventions have been proposed as a way to increase duration and exclusivity of breastfeeding for mothers participating in paid work. If not supported by their employers, employed mothers may have difficulty expressing and storing milk and thus not be able to maintain breastfeeding. A prior systematic review in 2012 found no controlled trials evaluating the effectiveness of workplace programs.[30] The ACA included a provision aimed at workplace breastfeeding policies by amending section 7 of the Fair Labor Standards Act to require employers to provide reasonable break time and a private space (other than a bathroom) for breastfeeding women to express breast milk for at least 1 year after the child's birth.[31]

### Rationale

Programs and policies to support breastfeeding are quite diverse and often complex.[32-34] The purpose of this review is to conduct an evidence report that summarizes the effectiveness of community, workplace and health care system-based programs and policies aimed at supporting and promoting breastfeeding. This review will describe whether certain programs or policies are more or less effective than other approaches in supporting breastfeeding, and whether effectiveness varies for subgroups of women defined by important sociodemographic factors (e.g., maternal age, education, and income; family and social support). This review will not address the effectiveness of individual-level primary care interventions to support and promote breastfeeding; this evidence was recently summarized in a systematic review[35] to support the U.S. Preventive Services Task Force in updating its recommendation on counseling to promote and support breastfeeding.[36]

In addition, this review will also address the association between breastfeeding and maternal health. Substantial time has elapsed since the last AHRQ review on this topic in 2007, and the body of literature focused on the maternal health benefits of breastfeeding has grown.[1, 37-39] This review will conduct a partial update of the 2007 AHRQ review focused on the relationship of breastfeeding and various maternal health outcomes.

## II. The Key Questions

**Key Question (KQ) 1a**: What is the effectiveness and harms of programs and policies on initiation, duration, and exclusivity of breastfeeding?

**KQ 1b**: To what extent do the effectiveness and harms of programs and policies on initiation, duration, and exclusivity of breastfeeding differ for subpopulations of women defined by sociodemographic factors (e.g., age, race, ethnicity, socioeconomic status)?

**KQ 1c:** To what extent do intervention-related characteristics (e.g., type of breast pump provided—manual or electric; delivery personnel) influence the initiation, duration, and exclusivity of breast feeding?

**KQ 2a**: What are the comparative benefits and harms for maternal health outcomes among women who breastfeed for different intensities and durations?

**KQ 2b**: To what extent do benefits and harms for maternal health outcomes differ for subpopulations of women defined by age, race, ethnicity, and comorbidity?

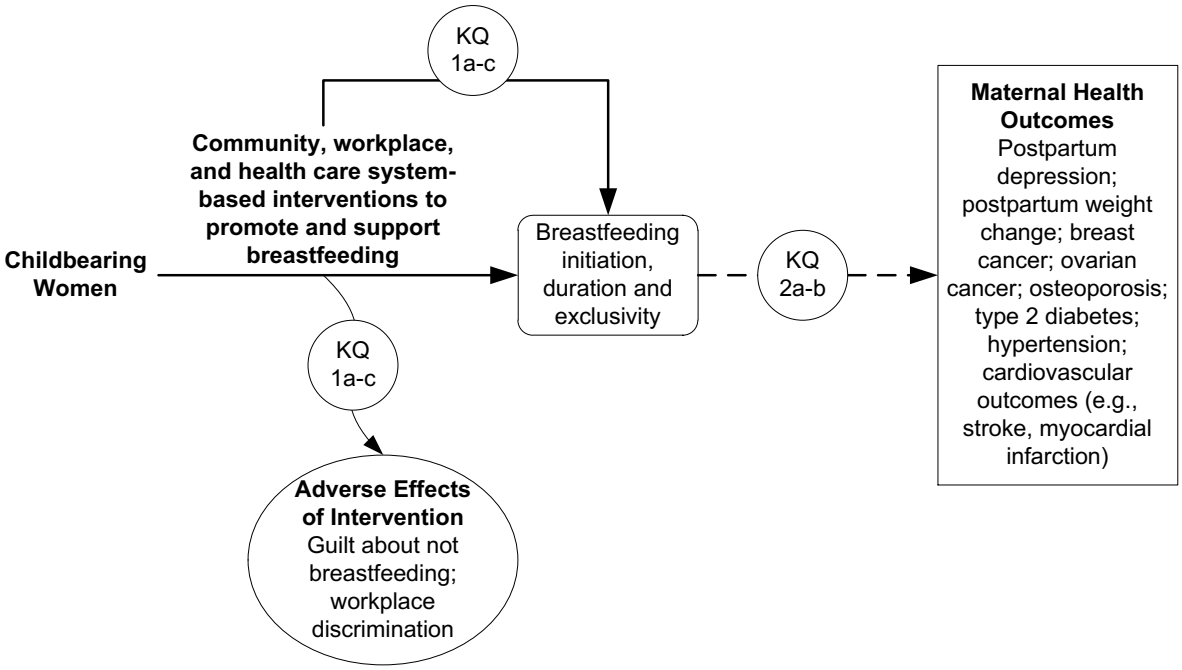
For the above KQs, the following population, intervention, comparator, outcomes, timing, setting (PICOTS) criteria apply:

- Population(s):
    - KQs 1, 2: Childbearing women and adolescents; we will also search for evidence on subgroups of women defined by age, race, ethnicity, comorbidity, and socioeconomic status (including insurance status and payer type).
- Interventions/Exposure
    - KQ 1: Community, workplace, and health care system-based interventions aimed at promoting and supporting breastfeeding, including the following: health plan benefits, state and federal policies or programs (e.g., WIC programs), hospital implementation of the BFHI, workplace or school-based programs, and others. For studies assessing the effectiveness of BFHI, we will include studies evaluating full and partial implementation (at least 3 steps) of the 10 steps (see Table 1).
    - KQ 2: Exposure to breastfeeding
- Comparators:
    - KQ 1: No intervention (or usual practice); comparisons of two interventions that differ in content or intensity.
    - KQ 2: No breastfeeding; shorter duration of breastfeeding (e.g., breastfeeding for 1 month vs. 12 months) and/or less intensive breastfeeding (e.g., exclusive breastfeeding vs. mixed feeding or formula feeding)
- Outcomes:
    - KQ 1: Rates of breastfeeding initiation; duration and exclusivity of breastfeeding, adverse effects of interventions (e.g., guilt about not breastfeeding, workplace discrimination, and other reported harms)
    - KQ 2: Postpartum depression, breast cancer, ovarian cancer, osteoporosis, cardiovascular outcomes (e.g., stroke, myocardial infarction), postpartum weight change, type 2 diabetes, hypertension
- Timing:
    - KQs 1, 2: We will have no minimum study duration or length of followup.
- Settings:
    - KQs 1, 2: Studies conducted in a developed country ["very high" (KQs 1, 2) and "high" (KQ 1) human development index per the United Nations Development Programme][40]
- **Study Design:**
    - KQ 1: Randomized and non-randomized controlled clinical trials; prospective cohort studies with concurrent control groups; systematic

reviews; for studies assessing policy or system-level interventions, we will also include pre-post studies with repeated outcome measures before and after the intervention

- KQ 2: Randomized and non-randomized controlled clinical trials; cohort studies; case-control studies; systematic reviews

## III. Analytic Framework




## IV. Methods

### Criteria for Inclusion/Exclusion of Studies in the Review

The criteria for inclusion and exclusion of studies are designed to identify studies that can answer the Key Questions (KQs) and are based on the population, intervention/exposure, comparator, outcomes, time frames, country settings, study design (PICOTs) are show in Table 2 and described in Section II above.

**Table 2. Eligibility Criteria**

| PICOTS | Inclusion | Exclusion |
|---|---|---|
| Population | KQs 1, 2: Childbearing women and adolescents[a]; we will also search for evidence on subgroups of women defined by age, race, ethnicity, comorbidity, and socioeconomic status (including insurance status and payer type). | KQs 1, 2: Men; nulliparous women; children |
| Intervention/ Exposure | KQ 1: Community, workplace, and health care system-based interventions aimed at promoting and supporting breastfeeding, including the following: health plan benefits; state and federal policies or programs (e.g., WIC programs); workplace and school-based programs; BFHI implementation, including full or partial implementation (defined as 3 or more steps).<br>KQ 2: Exposure to breastfeeding[b] | KQ 1: Interventions delivered in primary care settings as part of pre- or postnatal care KQ 2: All other exposures |
| Comparator | KQ 1: No intervention (or usual practice); comparisons of two interventions that differ in content or intensity<br>KQ 2: No breastfeeding; shorter duration (e.g., breastfeeding for 1 month vs. 12 months) and/or less intensive breastfeeding (e.g., exclusive breastfeeding vs. mixed feeding or formula feeding) | KQs 1, 2: All other comparisons; no comparisons |
| Outcomes | KQ 1: Rates of breastfeeding initiation, duration, and exclusivity of breastfeeding; harms of interventions (e.g., guilt about not breastfeeding, workplace discrimination, and other reported harms)<br>KQ 2: Postpartum depression, postpartum weight change, breast cancer, ovarian cancer, osteoporosis, type 2 diabetes, hypertension, cardiovascular outcomes (e.g., stroke, myocardial infarction) | KQ 1: Any other outcome not specified, including compliance with policies or practices and attitudes toward breastfeeding and complications of lactation<br>KQ 2: Any other outcome not specified, including complications of lactation (e.g., mastitis) |
| Country setting | KQs 1, 2: Studies conducted in a developed country ["very high" (KQs 1, 2)[c] and "high" (KQ 1) human development index per the United Nations Development Programme][40] | KQs 1, 2: Studies conducted in other countries |
| Study designs | KQ 1: RCTs; CCTs; prospective cohort studies with concurrent control groups; systematic reviews; for studies assessing policy or system-level interventions, pre-post studies with repeated outcome measures before and after the intervention are also eligible<br>KQ 2: RCTs; CCTs; cohort studies[d]; case-control studies; systematic reviews | KQs 1, 2: All other designs |
| Publication Language | KQs 1, 2: English | KQs 1, 2: Languages other than English |

BFHI = Baby-Friendly Hospital Initiative; CCT = controlled clinical trial; KQ = Key Question; PICOTS = population, intervention/exposure, comparator, outcomes, time frames, country settings, study design; RCT = randomized controlled trial; WIC = Special Supplemental Nutrition Program for Women, Infants, and Children.

[a] Childbearing women and adolescents are our population of interest; however, for KQ1, interventions may include or be targeted towards the woman's partner or family.

[b] This includes women who breastfeed their infant at the breast and/or express milk.

[c] The United Nations does not recognize Taiwan (i.e., Republic of China) as a sovereign state and does not include it in the 2015 Human Development Index report. However, Taiwan's government calculated its HDI to be 0.882, based on 2014 data and using the same methodology as the United Nations. This HDI value would place Taiwan among countries in the "very high" human development category and will be included in this report.[41]

[d] For all KQ 2 outcomes, we will include cohort studies that report on the incidence of eligible health outcomes prospectively regardless of whether or not women were classified into categories based on breastfeeding exposure prospectively (i.e., at study enrollment) or retrospectively. Additionally, for long-term outcomes for which no prospective studies of outcomes exist, we may include cohort studies that collect information on exposure and outcomes at a single time point (retrospectively). Such studies provide evidence on associations rather than on causal relationships.

## Searching for the Evidence: Literature Search Strategies for Identification of Relevant Studies to Answer the Key Questions

We will systematically search, review, and analyze the scientific evidence for each KQ. The steps that we will take to accomplish the literature review are described below.

To identify relevant published literature, we will search the following databases: PubMed/MEDLINE, the Cochrane Library, CINAHL and trial registries. We will conduct two separate search strategies, one for KQ1 and a second for KQ2. The preliminary search strategies formatted for MEDLINE are shown in the Appendix and are comprised of medical subject heading (MeSH) terms and natural language terms reflective of breastfeeding interventions and outcomes of interest. The search strategy will be adapted for the other databases as needed. An experienced librarian familiar with systematic reviews will design and conduct all searches in consultation with the review team. We will ask the Technical Expert Panel for feedback on the search terms and strategy.

For KQ 1, our literature searches will include articles published since 1980 to ensure that evidence is applicable to current breastfeeding policies and practices. For KQ 2, our literature searches will include articles published after November 1, 2005 (6 months prior to the date of the 2007 AHRQ review searches); we will also check reference lists of the included studies and systematic reviews to confirm that earlier studies were not missed. The literature search will be updated concurrent with the peer review process.

We will search the "gray literature" for unpublished studies relevant to this review and will include studies that meet all the inclusion criteria and contain enough methodological information to assess risk of bias. Gray literature sources will include ClinicalTrials.gov and any scientific information packages received from Federal register notices or informational requests.

## Data Abstraction and Data Management

To ensure accuracy, all titles and abstracts will be reviewed independently by two reviewers. We will retrieve the full text for all citations deemed appropriate for inclusion by at least one of the reviewers. Each full-text article, including any articles that peer reviewers suggest or that may arise from the public posting process, will be independently reviewed for eligibility by two team members. Any disagreements will be resolved by consensus. We will maintain a record of studies excluded at the full-text level with reasons for exclusion and will include this list in our final report.

After we select studies for inclusion, we will abstract data into categories that include (but are not limited to) the following: study design, year of publication, setting (including geographic location), sample size, eligibility criteria, population characteristics,

intervention characteristics, and outcomes relevant to each KQ as outlined in the previous PICOTs section. Relevant information that we will abstract for assessing applicability will include the characteristics of the population (e.g., demographic factors) and geographic setting. A second team member will verify abstracted study data for accuracy and completeness.

### Assessment of Methodological Risk of Bias of Individual Studies

To assess the risk of bias (i.e., internal validity) of studies, we will adapt existing tools (ROBIS-I[42] for observational studies, and the Cochrane tool[43] for trials) and use predefined criteria based on the AHRQ *Methods Guide for Comparative Effectiveness Reviews*. These include questions to assess selection bias, confounding, performance bias, detection bias, and attrition bias; concepts covered include those about adequacy of randomization, similarity of groups at baseline, masking, attrition, whether intention-to-treat analysis was used, method of handling dropouts and missing data, validity and reliability of outcome measures, and treatment fidelity).[44]

In general terms, results from a study assessed as having low risk of bias are considered to be valid. A study with moderate risk of bias is susceptible to some risk of bias but probably not enough to invalidate its results. A study assessed as high risk of bias has significant risk of bias (e.g., stemming from serious issues in design, conduct, or analysis) that may invalidate its results.

Two independent reviewers will assess risk of bias for each study. Disagreements between the two reviewers will be resolved by discussion and consensus or by consulting a third member of the team.

### Data Synthesis

We will summarize all included studies in narrative form and in summary tables that tabulate the important features of the study populations, design, intervention, outcomes, setting (including geographic location) and results.

For both KQs, we will capitalize on the availability of existing systematic reviews and meta-analyses; these will be captured in our database searches and identified during the literature review. KQ 2 is a partial update of the 2007 AHRQ review by Ip and colleagues; we plan to synthesize evidence from that review with newly identified evidence. For eligible outcomes that have previously been systematically reviewed, we will summarize the findings of recent (published within the past 5 years) relevant systematic reviews rated low or medium risk of bias using the ROBIS tool[45]; we will also summarize data from primary studies published after the latest search date of those reviews, Conclusions from systematic reviews rated as high risk of bias may not be valid due to bias stemming from uncertain study eligibility criteria, lack of dual-review during identification and selection of studies, and other factors. We may use reviews rated as high risk of bias to identify primary studies our database searches may have missed. For outcomes for which we do not identify previous systematic reviews, we will synthesize primary studies that meet our inclusion criteria published after the last search date of the 2007 review.

When recent, relevant existing systematic reviews are identified for a particular outcome, we will assess whether newly identified primary studies are likely to change judgments about conclusions made in existing reviews using a SOE framework (i.e., assessment of study limitations, consistency, precision, directness, and reporting bias). If the new studies are likely to change the conclusions, we will conduct a new quantitative synthesis if appropriate (i.e., if conclusions made in existing reviews are based on a pooled analysis of studies). If the new studies are consistent with prior syntheses and will not to change the conclusion of the review, we will present the results of the existing review along with an updated qualitative synthesis including the newly identified studies and an explanation of how they are consistent with the prior findings. In order to maintain a consistent approach, we will conduct a new SOE for each outcome and not use SOE grading from existing reviews.

We will consider performing meta-analyses where we have at least three unique studies of low or medium risk of bias that we deem to be sufficiently similar (in population, interventions, comparators, and outcomes). We are aware of the potential biases of meta-analyses that include a small number of studies;[46] before routinely calculating a pooled summary estimate in a meta-analysis, we will carefully consider the heterogeneity across studies. As described above, in cases where we identify a recent eligible meta-analysis for an eligible outcome, we will assess whether to update the analysis by considering how the results of recently published primary studies would change the conclusions of the meta-analyses using a SOE framework.

If meta-analysis seems appropriate in these circumstances, we will perform only random-effects model meta-analyses. We will look across trials to identify heterogeneity qualitatively any potential effect-modifying factors, such as age, race, setting (e.g., highly versus very highly developed countries), and components of the included intervention (for KQ 1). If clinical heterogeneity can be narrowed down to a small number of promising factors, we will consider these for subgroup analyses or meta-regression. For KQ 2, we expect to find heterogeneity in terms of the definition of "breastfeeding" and extent to which studies distinguish between exclusive and less intense breastfeeding (i.e., mixed feeding with breastmilk and formula supplementation). Similar to the 2007 review, we will accept all definitions of "exclusive breastfeeding" as provided by the different study authors, but will qualify our conclusions (and perform subgroups analyses if feasible) with respect to those specific definitions.

We plan to exclude studies deemed high risk of bias from our main data synthesis and main analyses; we will include them only in sensitivity analyses. We will show forest plots for all meta-analyses performed, either in the main report or in appendices.

### Grading the Strength of Evidence (SOE) for Major Comparisons and Outcomes

We will grade the strength of evidence based on the guidance established for the Evidence-based Practice Center Program. Developed to grade the overall strength of a body of evidence, this approach now incorporates five key domains: risk of bias (including study design and aggregate risk of bias), consistency, directness, and precision of the evidence, and reporting bias. It also considers other optional domains that may be relevant for some scenarios, such as plausible confounding that would decrease the

observed effect and strength of association (i.e., magnitude of effect) or factors that would increase the strength of association (i.e., dose-response effect).

Table 3 describes the grades of evidence that can be assigned. Grades reflect the strength of the body of evidence to answer the KQs on the comparative effectiveness, efficacy, and harms of the interventions in this review. Two reviewers will assess each domain for each key outcome, and differences will be resolved by consensus. We will grade the strength of evidence for all included outcomes.

**Table 3. Definitions of the Grades of Overall Strength of Evidence**

| Grade | Definition |
|---|---|
| High | We are very confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has few or no deficiencies. We believe that the findings are stable (i.e., another study would not change the conclusions). |
| Moderate | We are moderately confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has some deficiencies. We believe that the findings are likely to be stable, but some doubt remains. |
| Low | We have limited confidence that the estimate of effect lies close to the true effect for this outcome. The body of evidence has major or numerous deficiencies (or both). We believe that additional evidence is needed before concluding either that the findings are stable or that the estimate of effect is close to the true effect. |
| Insufficient | We have no evidence, we are unable to estimate an effect, or we have no confidence in the estimate of effect for this outcome. No evidence is available or the body of evidence has unacceptable deficiencies, precluding reaching a conclusion. |

Source: Berkman et al.[47]

## Assessing Applicability

We will assess the applicability of individual studies as well as the applicability of a body of evidence following guidance from the *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*.[48] For individual studies, we will examine conditions that may limit applicability based on the PICOTS structure. Some factors identified a priori that may limit the applicability of evidence include the following: race or ethnicity of enrolled populations, setting of enrolled populations, geographic setting, and availability of health insurance and other health-related employment benefits. We will pay close to attention to secular trends when interpreting the evidence. Such trends are of concern, in that breastfeeding rates in the United States have changed dramatically in the past 40 years, from a nadir of less than 25 percent in 1971[49] to more than 80 percent in 2013.[50] This is important because the time period between exposure to breastfeeding and some outcomes of interest (e.g., cancer, cardiovascular disease) may be decades, and secular trends in social determinants of infant feeding may confound observed associations. Findings linking breastfeeding to maternal health among women feeding their infants decades ago may not be generalizable to contemporary women.

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## VI. Definition of Terms

We will define important terms in the full report.

## VII. Summary of Protocol Amendments

**Table 4. Protocol Amendments**

| Date | Section | Original Protocol | Revised Protocol | Rationale |
|---|---|---|---|---|
| 9/12/17 | Section II. Key Questions and Table 2. Eligibility Criteria | KQ2 Outcomes: Postpartum depression, postpartum weight change, breast cancer, ovarian cancer, osteoporosis, type 2 diabetes, hypertension, cardiovascular outcomes (e.g., stroke, myocardial infarction) | Replaced "osteoporosis" with "fracture" | The evidence on osteoporosis and fracture risk has evolved since the original 2007 AHRQ report was published; the most clinically relevant outcome is fracture (given that many fractures occur in women with nonosteoporotic T-scores/ normal bone mass). There is evidence on incidence of fracture associated with breastfeeding exposure. For this reason, we will exclude outcomes reporting only on bone mineral density. |
| | Section II. Key Questions and Table 2. Eligibility Criteria | KQ 2 Outcomes: Postpartum depression, postpartum weight change, breast cancer, ovarian cancer, osteoporosis, type 2 diabetes, hypertension, cardiovascular outcomes (e.g., stroke, myocardial infarction) | Added mortality as an outcome | Mortality outcomes were not specifically included or excluded in the 2007 review. Some included studies report on condition-specific mortality rates and overall mortality. This is a relevant outcome of interest. |
| | Table 2. Eligibility Criteria | KQ 1 Intervention Exclusion: Interventions delivered in primary care settings as part of pre- or postnatal care<br>KQ 2: All other exposures | For KQ 1, added text after "postnatal care": and interventions targeted toward mothers of preterm infants or NICU settings | When the scope of work was developed, the idea was that the review be relevant to settings providing routine perinatal care, not to specialized setting such as Neonatal Intensive Care Units (NICUs). NICU-specific intervention to promote or support breastfeeding are excluded. |

## VIII. Technical Experts

Technical Experts constitute a multi-disciplinary group of clinical, content, and methodological experts who provide input in defining populations, interventions, comparisons, or outcomes and identify particular studies or databases to search. They are 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 results in a thoughtful, relevant systematic review. Therefore study questions, design, and methodological approaches do not necessarily represent the views of individual technical and content experts. Technical Experts provide information to the EPC to identify literature search strategies and suggest approaches to specific issues as requested by the EPC. Technical Experts do not do analysis of any kind nor do they contribute to the writing of the report. They have not reviewed the report, except as given the opportunity to do so through the peer or public review mechanism.

Technical Experts must disclose any financial conflicts of interest greater than $10,000 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. The AHRQ TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

## IX. 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.

## X. EPC Team Disclosures

No team members have financial conflicts of interest. Dr. Stuebe, as a practicing OBGYN and member of the ACOG, follows clinical practice guidelines in supporting breastfeeding. In the event that her published studies on the relationship between breastfeeding and outcomes are eligible for the review, Drs. Feltner and Viswanathan will review them for inclusion and exclusion, full-text, risk of bias, and any strength of evidence grading that arise from their inclusion. Dr. Stuebe will not be involved in any review activities related to her studies.

## XII. Role of the Funder

This project was funded under Contract No. HHSA290201500011I_HHSA29032008T from the Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services. The AHRQ Task Order Officer reviewed contract deliverables for adherence to contract requirements and quality. The authors of this report are 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.

## XIII. Registration

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

## APPENDIX

### KQ1 PubMed Search Strategy

| Search | PubMed Query |
|---|---|
| #1 | Search ((("Infant Nutritional Physiological Phenomena"[Mesh] OR "Milk, Human"[Mesh] OR "Breast Feeding"[Mesh] OR "breast feeding"[All Fields] OR "human milk"[All Fields] OR (human[tiab] AND milk[tiab]) OR "breast milk"[All Fields] OR breastmilk OR breastfeed* OR (breast[tiab] AND fed[tiab]) OR breastfed OR "Lactation"[Mesh] OR lactating OR lactation))) |
| #2 | Search ((Absenteeism[Mesh] OR "Affordable Care Act" OR ACA[tiab] OR "Baby friendly Hospital Initiative" OR BFHI OR (break*[tiab] AND (express* AND milk)) "Breast Milk Expression"[Mesh] OR "breast pump"[All Fields] OR "Child Day Care Centers"[Mesh] OR "Employment"[Mesh] OR (employ* AND (polic* OR program*)) OR "Health Knowledge, Attitudes, Practice"[Mesh] OR "Health Promotion"[Mesh] OR "Insurance Benefits"[Mesh] OR ("lactation consultant" OR "lactation consultants") OR "Maternal Health Services"[Mesh] OR "Mothers/psychology"[Majr] OR "Nurseries, Hospital"[Mesh] OR "Occupational Health Services"[Mesh] OR "Parental Leave"[Mesh] OR "Program Evaluation"[Mesh] OR "Salaries and Fringe Benefits"[Mesh] OR "Social Support"[Mesh] OR "Women, Working"[Mesh])) |
| #3 | Search (#1 and #2) |
| #4 | Search (("baby friendly"[All Fields] OR "hospital practices"[All Fields] OR "Ten Steps"[All Fields] OR Counseling[Mesh] OR WIC OR "Women, Infants, and Children Program" OR SNAP OR "Food Stamps"[All Field] OR "Food Assistance"[Mesh] OR "Food assistance"[All Fields] OR "Health Education"[Mesh] OR "House Calls"[Mesh] OR "Organizational Policy"[Mesh] OR "Patient Education as Topic"[Mesh] OR "Promotion of Breastfeeding Intervention Trial"[All Fields] OR PROBIT[All Fields] OR "Postnatal Care"[Mesh] OR "Social Support"[Mesh] OR 'Ten Steps to Successful Breastfeeding'[All Fields] OR "Workplace"[Mesh])) |
| #5 | Search (#1 and #4) |
| #6 | Search (#3 or #5) |
| #7 | Search ((((randomized[title/abstract] OR randomised[title/abstract]) AND controlled[title/abstract] AND trial[title/abstract]) OR (controlled[title/abstract] AND trial[title/abstract]) OR "controlled clinical trial"[publication type] OR "Randomized Controlled Trial"[Publication Type] OR "Single-Blind Method"[MeSH] OR "Double-Blind Method"[MeSH] OR "Random Allocation"[MeSH])) |
| #8 | Search (#6 and #7) |
| #9 | Search (("Cohort Studies"[Mesh] OR "Epidemiologic Studies"[Mesh] OR "Follow-up Studies"[Mesh] OR "prospective cohort" OR "prospective studies"[MeSH] OR (prospective*[All Fields] AND cohort[All Fields] AND (study[All Fields] OR studies[All Fields])))) |
| #10 | Search (#6 and #9) |
| #11 | Search (#8 or #10) |
| #12 | Search (#8 or #10) Filters: Publication date from 1980/01/01 to 2017/12/31 |
| #13 | Search (#8 or #10) Filters: Publication date from 1980/01/01 to 2017/12/31; Humans |
| #14 | Search (#8 or #10) Filters: Publication date from 1980/01/01 to 2017/12/31; Humans; English |
| #15 | Search (("systematic review"[ti] OR "meta-analysis"[pt] OR "meta-analysis"[ti] OR "systematic literature review"[ti] OR "this systematic review"[tw] OR ("systematic review"[tiab] AND review[pt]) OR meta synthesis[ti] OR "meta synthesis"[ti] OR "cochrane database syst rev"[ta])) Filters: Publication date from 1980/01/01 to 2017/12/31; Humans; English |
| #16 | Search (#6 and #15) Filters: Publication date from 1980/01/01 to 2017/12/31; Humans; English |

**KQ 2 PubMed Search Strategy**

| Search | Query |
|---|---|
| #1 | Search ("Infant Nutritional Physiological Phenomena"[Mesh] OR "Milk, Human"[Mesh] OR "Breast Feeding"[Mesh] OR “breast feeding”[All Fields] OR “human milk”[All Fields] OR (human[tiab] AND milk[tiab]) OR “breast milk”[All Fields] OR breastmilk OR breastfeed* OR (breast[tiab] AND fed[tiab]) OR breastfed OR "Lactation"[Mesh] OR lactating OR lactation) |
| #2 | Search ("HIV Infections"[Mesh] OR HIV OR "Fatty Acids"[Majr] OR "Amino Acids"[Majr]) |
| #3 | Search (#1 not #2) |
| #4 | Search ("Case-Control Studies"[MeSH] OR "Cohort Studies"[MeSH] OR "Epidemiologic Studies"[MeSH] OR "Cross-Sectional Studies"[MeSH] OR "Organizational Case Studies"[MeSH] OR "Cross-Over Studies"[MeSH] OR "Follow-Up Studies"[MeSH] OR "Seroepidemiologic Studies"[MeSH] OR "Evaluation Studies"[Publication Type] OR “observational study” OR “observational studies” OR "Comparative Study"[MeSH] OR “prospective studies”[MeSH] OR (prospective*[All Fields] AND cohort[All Fields] AND (study[All Fields] OR studies[All Fields]) OR “Longitudinal Studies” OR cohort*) |
| #5 | Search (#3 and #4) |
| #6 | Search (Addresses[pt] OR Autobiography[pt] OR Bibliography[pt] OR Biography[pt] OR "Case Reports"[pt] OR Congresses[pt] OR "Consensus Development Conference"[pt] OR "Consensus Development Conference, NIH"[pt] OR Dictionary[pt] OR Directory[pt] OR Editorial[pt] OR Festschrift[pt] OR "Government Publications"[pt] OR Interview[pt] OR Lectures[pt] OR "Legal Cases"[pt] OR Legislation[pt] OR Letter[pt] OR News[pt] OR "Newspaper Article"[pt] OR Overall[pt] OR "Patient Education Handout"[pt] OR "Periodical Index"[pt]) |
| #7 | Search (#5 not #6) |
| #8 | Search (#5 not #6) Filters: Publication date from 2005/01/11 to 2017/12/31 |
| #9 | Search (#5 not #6) Filters: Publication date from 2005/01/11 to 2017/12/31; Humans |
| #10 | Search (#5 not #6) Filters: Publication date from 2005/01/11 to 2017/12/31; Humans; English |
| #11 | Search ((“systematic review”[ti] OR “meta-analysis”[pt] OR “meta-analysis”[ti] OR “systematic literature review”[ti] OR “this systematic review”[tw] OR (“systematic review”[tiab] AND review[pt]) OR meta synthesis[ti] OR “meta synthesis”[ti] OR “cochrane database syst rev”[ta])))  Filters: Publication date from 2005/01/11 to 2017/12/31; Humans; English |
| #12 | #3 and #11 |