2020 Dietary Guidelines Advisory Committee: Pregnancy and Lactation Subcommittee

Subcommittee Chair: Sharon Donovan
    Kathryn Dewey
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    Jamie Stang
    Elsie Taveras

Vice Chair Rep: Ron Kleinman
Overview of Subcommittee Status

• Assigned questions in three general categories
  • **Nutrients from Supplements and Fortified Foods**
    • Before and during pregnancy and lactation
    • **6 Nutrients**: B\textsubscript{12}, Folate, Iron, Iodine, Vit D, omega-3 fatty acids
    • **5 Outcomes**: human milk composition, gestational diabetes, hypertensive disorders, neurocognitive development, micronutrient status
  
  • **Dietary Patterns**
    • **During pregnancy – 5 outcomes**: gestational diabetes, hypertensive disorders, micronutrient status, gestational weight gain, gestational age at birth, infant birthweight
    • **During lactation – 3 outcomes**: human milk composition and quantity, infant neurocognitive development, postpartum weight loss

• **Maternal diet and food allergies and atopic diseases**

Protocols for questions discussed in this presentation are available at DietaryGuidelines.gov
• NESR staff has been screening articles and preparing the evidence portfolios
  • ~21,500 articles have been screened thus far and additional searches are underway
  • Extracted data and assessed risk of bias for 42 articles and additional extraction is underway
### Nutrients from Supplements and Fortified Foods

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Outcomes</th>
<th>Status</th>
</tr>
</thead>
</table>
| Folate   | • Human milk composition  
          • Gestational diabetes | Meeting 3 (Oct 2019) – evidence & draft conclusions |
| Folate   | • Hypertension disorders  
          • Neurocognitive development  
          • Micronutrient status | Meeting 4 (Jan 2020) – evidence & draft conclusions |
| Omega-3  | • Human milk composition  
          • Gestational diabetes  
          • Hypertension disorders  
          • Neurocognitive development  
          • Micronutrient status | Refining/prioritizing nutrients and outcomes |

Protocols for questions discussed in this presentation are available at DietaryGuidelines.gov
## Subcommittee Status:
Dietary Patterns & Food allergies/atopic diseases

### Dietary Patterns

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Status</th>
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</thead>
<tbody>
<tr>
<td>Human milk composition</td>
<td>Meeting 4 (Jan 2020) – evidence &amp; draft conclusions</td>
</tr>
<tr>
<td>Risk of hypertensive disorders</td>
<td>Meeting 4 (Jan 2020) – conclusions from P/B24 existing reviews</td>
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<tr>
<td>Risk of gestational diabetes</td>
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<tr>
<td>Gestational age at birth</td>
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<tr>
<td>Birth weight</td>
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<tr>
<td>Gestational weight gain</td>
<td>Meeting 5 (March 2020)</td>
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<tr>
<td>Postpartum weight loss</td>
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<tr>
<td>Micronutrient status</td>
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<tr>
<td>Neurocognitive development</td>
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</tbody>
</table>

### Maternal diet and food allergies and atopic diseases

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Food allergies and atopic diseases</em></td>
<td>Meeting 5 (March 2020)</td>
</tr>
</tbody>
</table>

Protocols for questions discussed in this presentation are available at DietaryGuidelines.gov
Implementing the plan: Question

What is the relationship between folic acid from supplements and/or fortified foods consumed before and during pregnancy and risk of hypertensive disorders?

Approach to Answer Question: NESR Systematic Review
Supplements & Fortified foods: Key Definitions

• **Dietary Supplement** -- a product (other than tobacco) that: is intended to supplement the diet; contains one or more dietary ingredients (including vitamins; minerals; herbs or other botanicals; amino acids; and other substances) or their constituents; is intended to be taken by mouth as a pill, capsule, tablet, or liquid; and is labeled on the front panel as being a dietary supplement. *(ODS; Dietary Supplement Health and Education Act, 1994)*

• **Fortification** -- the deliberate addition of one or more essential nutrients to a food, whether or not it is normally contained in the food. *(FDA)*

All protocols discussed in this presentation are available at DietaryGuidelines.gov
**Systematic review question:** What is the relationship between *folic acid* from supplements and/or fortified foods consumed before and during pregnancy and risk of hypertensive disorders during pregnancy?

<table>
<thead>
<tr>
<th>Intervention/exposure</th>
<th>vs</th>
<th>Comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure to, including intake of, <em>Folic acid</em> from:</td>
<td>Different level of exposure to, including intake of, <em>Folic acid</em> from:</td>
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<tr>
<td>Dietary supplements (including multiple-nutrient supplements)</td>
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<tr>
<td>Dietary supplements + fortified foods</td>
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</table>

**Population:** Women before and during pregnancy; healthy and/or at risk for chronic disease

**Intermediate outcomes:**
- Blood pressure (systolic and diastolic)
- Protein in the urine (proteinuria)

**Population:** Women during pregnancy

**Health outcomes:**
Hypertensive disorders during pregnancy, including:
- Eclampsia
- Preeclampsia
- Gestational hypertension

**Legend:**
- The relationship of interest in the systematic review
- Factors that may impact the relationship of interest in the systematic review

**Key Confounders:** Age, Race/ethnicity, Socioeconomic status, Anthropometry (pre-pregnancy BMI and gestational weight gain (during pregnancy) or Obesity status (before pregnancy)), Smoking, History/diagnosis of hypertension or CVD, Parity

**Other factors to be considered:** Physical activity, substance use (alcohol, drug use), gestational age
Literature Search and Screening Results

- **Electronic databases searched**: PubMed, Cochrane, Embase, CINAHL
  - N=829 (N=622 after duplicates removed)

- **Manual search**: References of included articles and existing systematic reviews

- **Titles screened**: N=622
  - Articles excluded: N=411

- **Abstracts screened**: N=211
  - Articles excluded: N=135

- **Full-texts screened**: N=76
  - Articles excluded: N=68

- **Articles from electronic database search**: N=8
  - Articles from manual search: N=0

- **Articles included in the systematic review**: N=1 (GDM); N=8 (HTN)

8 Included articles:
- 3 RCT
- 2 NRCT
- 3 PCS

All 4 studies addressed the question - what is the relationship between **folic acid from supplements consumed before and during pregnancy and risk of hypertensive disorders**?
Description of the Evidence: 3 RCTs

• **Sample characteristics**
  - n=123-450/group (Baseline n=246-900/study)
  - All studies conducted in Iran
  - ~25y, pre-pregnancy BMI ~25kg/m²
  - Race/ethnicity and SES not reported

• **Interventions varied by dose**
  - Dose: 0.5 or 1 mg/d FA, 5 mg/d FA
  - Initiation: 1st trimester
  - Duration: through delivery

• **Outcomes:** all reported preeclampsia & blood pressure
  - Other outcomes: proteinuria (2 studies); eclampsia, gestational hypertension (1 study)
Description of the Evidence: 2 NRCTs

• **Sample characteristics**
  - n=146-4884/group (n=303-7812/study)
  - Italy, China
  - ~31y; ~20-40y
  - Caucasian (Italy) or race/ethnicity NR* (China); SES NR
  - Preeclampsia in preceding pregnancy (Italy)

• **Interventions varied by dose and initiation**
  - Dose: 0 mg/d vs 15mg /d 5-MTHF; No supplement vs Individualized FA supplement
  - Initiation: <14 GW; 3mo before pregnancy
  - Duration: through delivery

• **Outcome:** Preeclampsia (Italy); Gestational Hypertension (China)

* NR = not reported
Description of the Evidence: 3 PCS

• **Sample characteristics**
  • n=404-2468/group (n=2261-10,050/study)
  • Australia, Canada, Denmark
  • ~20-30y
  • Australian Aboriginal or Torres Straight Islander; Caucasian; Danish or from another Nordic country
  • Low to high SES

• **Exposure**
  • Dose: no supplement or Folate/Folic acid alone
  • Initiation/Duration: 1\(^{st}\) - 3\(^{rd}\) trimesters
    12-20 GW - delivery
    4 wk before – 14 wk after LMP

• **Outcome:** Preeclampsia

Folic acid and hypertensive disorders
2020 Dietary Guidelines Advisory Committee: *Meeting 4*
None of the RCTs found an association between folic acid supplementation and the incidence of hypertensive disorders of pregnancy, including:

- Gestational hypertension
- Preeclampsia
- Eclampsia

None of the studies compared folic acid supplementation to a control group that had no supplementation.
Summary of the Evidence Synthesis: NRCTs

• Both NRCTs found a significant association between folic acid supplementation from early pregnancy through delivery and reduced risk of preeclampsia or gestational hypertension compared to controls (with no folic acid supplementation).
  • Preeclampsia - Control vs Intervention:
    High risk: 39.7% vs 21.7%, P=0.019
    Lower risk: 39.3% vs 20.2%, P<0.05
  • Gestational hypertension - Control vs Intervention:
    0.98% vs ~0.00%, P<0.05
• One NRCT was among a high-risk population in which women had been diagnosed with preeclampsia in their preceding pregnancy.
Summary of the Evidence Synthesis: PCS

• The results of the three PCS were mixed.
  • One study found an association between folic acid use in the first trimester and lower incidence of preeclampsia in the full sample, and specifically for those with a BMI ≥25 kg/m².
  • Another found a significant association between folic acid use at 12 to 20 weeks gestation and incidence of preeclampsia among high-risk women.
  • The third found no association.
Limited evidence suggests that folic acid supplementation during early pregnancy, may have a beneficial effect on reducing the risk of hypertensive disorders during pregnancy among women at high-risk (e.g. history or preeclampsia or pre-pregnancy BMI ≥25 kg/m²) compared to no folic acid supplementation.

Assessment of the evidence:
- Conclusion statement supported by 2 NRCT and 3 PCS
- Studies were direct
- Results were consistent for high risk women
- There were concerns regarding risk of bias, precision and generalizability
Moderate evidence suggests that higher levels of folic acid supplementation during pregnancy compared to lower levels (including no folic acid supplementation) does not affect the risk of hypertensive disorders during pregnancy among women at low-risk.

Assessment of the evidence:
- Conclusion statement supported by 3 RCTs and 3 PCSs
- Studies were direct
- Results were consistent for low risk women
- There were concerns regarding risk of bias, precision and generalizability
• **No evidence** is available to draw a conclusion about the relationship between folic acid from *fortified foods* consumed *before and/or during pregnancy* and risk of hypertensive disorders during pregnancy. (Grade not assignable)
What is the relationship between folic acid from supplements and/or fortified foods consumed before and during pregnancy and lactation and developmental milestones, including neurocognitive development?

Approach to Answer Question: NESR Systematic Review
Analytic Framework (folic acid & developmental milestones)

**Systematic review question:** What is the relationship between folic acid from supplements and/or fortified foods consumed before and during pregnancy and lactation and developmental milestones, including neurocognitive development?

<table>
<thead>
<tr>
<th>Intervention/ exposure</th>
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<th>Comparator</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure to, including intake of, Folic acid from:</td>
<td>Different level of exposure to, including intake of, Folic acid from:</td>
<td></td>
<td>• Developmental domains, examined via milestone achievement and/or scales/indices, including:</td>
</tr>
<tr>
<td>• Dietary supplements (including multiple-nutrient supplements)</td>
<td>• Dietary supplements (including multiple-nutrient supplements)</td>
<td>• Cognitive,</td>
<td>• Academic performance</td>
</tr>
<tr>
<td>• Fortified foods</td>
<td>• Fortified foods</td>
<td>• Language/communication,</td>
<td>• Attention deficit disorder (ADD) or attention-deficit/hyperactivity disorder (ADHD)</td>
</tr>
<tr>
<td>• Dietary supplements + fortified foods</td>
<td>• Dietary supplements + fortified foods</td>
<td>• Movement/physical,</td>
<td>• Anxiety</td>
</tr>
<tr>
<td><strong>Population:</strong> Women before and during pregnancy and/or during lactation; healthy and/or at risk for chronic disease</td>
<td><strong>Population:</strong> Infants and toddlers (birth to 24 months), children and adolescents (ages 2-18 years)</td>
<td>• Social-emotional</td>
<td>• Depression</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Autism spectrum disorder (ASD)</td>
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</tbody>
</table>

**Key Confounders:** Age, Race/ethnicity, Socioeconomic status, Anthropometry (pre-pregnancy BMI and gestational weight gain (during pregnancy) or Obesity status (before pregnancy and lactation)), Smoking, Parity, Child sex, Gestational age, Breastfeeding practices (intensity, duration). Other factors to be considered: Maternal substance use (alcohol, drug use), Family history/diagnosis of neurocognitive disorders, complementary feeding
Literature Search and Screening Results (folic acid & developmental milestones)

4 studies (6 Included articles):
- 2 RCTs (3 articles)
- 1 PCS (2 articles)
- 1 Nested case-control

All 6 articles addressed the question - what is the relationship between folic acid from supplements consumed during pregnancy and developmental milestones, including neurocognitive development?
Description of the Evidence: 2 RCTs

- **Sample characteristics**
  - n=39 to 130/study; children n=17 to 37/group
  - UK, Germany/Hungary/Spain
  - Maternal: ~28-31y, mostly white, high SES
  - Children: 6.5, 7, and 8.5 years

- **Interventions varied by dose**
  - Dose: 400 µg/d FA; 400 µg/d 5-MTHF (with or without fish oil)
  - Initiation: 14wk or 20wk gestation
  - Duration: through delivery

- **Outcomes:**
  - Cognitive development, Language/communication development, Social-emotional development, and Autism Spectrum Disorder
Description of the Evidence: 1 PCS

• **Sample characteristics**
  - n=16,179 to 45,266; 16,157 to 51,747 children
  - Norway
  - Maternal: ~25-35y, high SES
  - Children: assessed at 3y

• **Intervention**
  - Dose: FA supplementation (questionnaire)
  - Initiation: Early and late pregnancy
    - (4w before conception – 8 GW or 9-29GW)
  - Duration: Assessed 9 or 3 intervals

• **Outcome:** Language competence (1 article); language delay (1 article)
• **Sample characteristics**
  - n=45,300
  - Israel
  - Maternal: <35y, 60% low SES
  - Children: assessed at 8-12y

• **Intervention**
  - Dose: FA Prescription (Rx register)
  - Initiation: Before and/or during pregnancy
  - Duration: Assessed before or during pregnancy or both

• **Outcome:** ASD Diagnosis
Summary of the Evidence Synthesis

• Generally, folic acid supplementation before or during pregnancy was either **not associated with** or had a **beneficial association** with the included outcomes

  • *Language development*: 2 articles from 1 PCS. Results showed a lower risk of severe language delay in 3 year-old children whose mothers consumed folic acid supplements during early pregnancy

  • *ASD*: 1 nested case-control found a significant association between folic acid supplementation before and during pregnancy and lower risk of ASD in 8-12 year old children
Summary of the Evidence Synthesis, continued

- **Cognitive development**: findings were inconsistent; no conclusion could be drawn
- **Social-emotional development**: included 1 study with concerns; no conclusion could be drawn
- **Movement/physical development, academic performance, attention deficit disorder (ADD) or attention-deficit/hyperactivity disorder (ADHD), anxiety, or depression**: no evidence on supplementation before and/or during pregnancy
- **Developmental milestones/neurocognitive development**: no evidence on supplementation during lactation or on intake of folic acid from fortified foods consumed before/during pregnancy or lactation
• **Limited** evidence suggests folic acid *supplementation during early pregnancy*, may be associated with lower risk of delayed *language development* in the child.

• **Assessment of the evidence:**
  - Conclusion based on two studies from one PCS
  - Studies were direct
  - Consistency could not be assigned
  - There were some concerns regarding risk of bias, precision and generalizability
• **Limited** evidence suggests folic acid *supplementation before and/or during pregnancy*, may be associated with lower risk of *autism spectrum disorder* in the child.

• **Assessment of the evidence:**
  • Conclusion based on 1 nested case-control study
  • Study was direct
  • Consistency could not be assigned
  • There were some concerns regarding risk of bias, precision and generalizability

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Folic acid and developmental milestones
2020 Dietary Guidelines Advisory Committee: *Meeting 4*
• **Insufficient** evidence is available to determine the relationship between folic acid from *supplements and/or fortified foods* consumed *before and during pregnancy* and
  • cognitive development in the child.
  • social emotional development in the child.
• **No evidence** is available to determine the relationship between folic acid from supplements and/or fortified foods consumed before and during pregnancy and lactation and movement/physical development in the child.

• **No evidence** is available to determine the relationship between folic acid from supplements and/or fortified foods consumed before and during pregnancy and lactation and academic performance in the child.

• **No evidence** is available to determine the relationship between folic acid from supplements and/or fortified foods consumed before and during pregnancy and lactation and attention-deficit disorder (ADD) or attention-deficit/hyperactivity disorder (ADHD) in the child.

**All (Grade not assignable)**
• **No evidence** is available to determine the relationship between folic acid from *supplements and/or fortified foods* consumed *before and during pregnancy and lactation* and *anxiety* in the child.

• **No evidence** is available to determine the relationship between folic acid from *supplements and/or fortified foods* consumed *before and during pregnancy and lactation* and *depression* in the child.

• All *(Grade not assignable)*
• **No evidence** is available to determine the relationship between folic acid from supplements consumed during lactation and developmental milestones, including neurobehavioral development in the child.

  (Grade not assignable)

• **No evidence** is available to determine the relationship between folic acid from fortified foods consumed before and during pregnancy and lactation and developmental milestones, including neurobehavioral development in the child.

  (Grade not assignable)
Question
(folic acid and micronutrient status)

What is the relationship between folic acid from supplements and/or fortified foods consumed before and during pregnancy and lactation and micronutrient status?

Approach to Answer Question: NESR Systematic Review
## Analytic Framework
(folic acid & micronutrient status)

**Systematic review question:** What is the relationship between folic acid from supplements and/or fortified foods consumed before and during pregnancy and lactation and micronutrient status?

<table>
<thead>
<tr>
<th>Intervention/exposure</th>
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<th>Comparator</th>
<th>Health outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure to, including intake of, <strong>Folic acid</strong> from:</td>
<td>Different levels of exposure to, including intake of, <strong>Folic acid</strong> from:</td>
<td>Micronutrient status:</td>
<td>Population: Women during pregnancy and/or lactation</td>
</tr>
</tbody>
</table>
| • Dietary supplements (including multiple-nutrient supplements)  
• Fortified foods  
• Dietary supplements + fortified foods | • Dietary supplements (including multiple-nutrient supplements)  
• Fortified foods  
• Dietary supplements + fortified foods | • Folate  
• Vitamin B12  
• Hemoglobin  
• Mean Corpuscular Volume (MCV)  
• Red Blood Cell Distribution Width (RDW) | |

**Population:** Women before and during pregnancy and/or during lactation; healthy and/or at risk for chronic disease

**Key Confounders:** Age, Race/ethnicity, Socioeconomic status, Anthropometry (pre-pregnancy BMI and gestational weight gain (during pregnancy) or Obesity status (before pregnancy and lactation)), Smoking, Parity  **Other factors to be considered:** Substance use (alcohol, drug use), gestational age
Literature Search and Screening Results
(folic acid & micronutrient status)

Electronic databases searched
PubMed, Cochrane, Embase, CINAHL
N= 7817 (N= 4512 after duplicates removed via Endnote and Distiller)

Manual search
References of included articles and existing systematic reviews

14 Included articles:
• 9 RCTs
• 3 PCS
• 1 RCS
• 1 Uncontrolled before-and-after study

All studies addressed the question - what is the relationship between folic acid from supplements consumed before and/or during pregnancy or during lactation and micronutrient status?

N= 15 (Human milk composition: N= 4, Micronutrient status: N= 14)
Description of the Evidence: 9 RCTs

• **Sample characteristics**
  - n=6 to 189/group (n=12 to 267/study)
  - Canada (3), US (2), Iran, UK, Mexico, France
  - ~26-34y, mostly white, high SES; 1 study ~17y, low SES
  - One study: 100% iron deficient anemic women

• **Interventions varied by**
  - Dose/form: 300 µg/d – 5 mg/d FA
    - 400 µg/d, 1mg/d 5-MTHF
    - 0.37 mg folinic acid
  - Initiation: Preconception, during pregnancy, postpartum
  - Duration: 1-12 months

• **Outcomes**: Most included serum, plasma or RBC folate
  - Other outcomes included: serum vitamin B12 (2), hemoglobin (4) or mean corpuscular volume (3)
Description of the Evidence - 3 PCS

• **Sample characteristics**
  - n=10 to 91/group (n=101 to 109/study)
  - Ireland, Germany, Canada
  - Maternal: ~29-30y, Race/ethnicity and SES not reported

• **Intervention**
  - Dose: FA supplementation (questionnaire) vs none
  - Timing: 1 to 16 GW; 12 to 25 GW; 9-12 to 25-38 GW

• **Outcome**: all reported plasma folate
  - 2 reported RBC folate
  - One study also included incidence of folate deficiency
Description of the Evidence:
1 Retrospective cohort study

- **Sample characteristics**
  - n=397; n=103, 294/group
  - Turkey
  - Maternal: ~26y, Race/ethnicity and SES not reported

- **Intervention**
  - Dose: 0 vs 400 µg/d FA
  - Initiation: Preconception
  - Duration: Time of assessment varied by participant

- **Outcome:** serum folate, hemoglobin, incidence of folate deficiency

Folic acid and micronutrient status
2020 Dietary Guidelines Advisory Committee: Meeting 4
Description of the Evidence: 1 uncontrolled before-and-after study

• **Sample characteristics**
  - n=16 (1 group)
  - Japan
  - Only participant characteristic reported: women in study from “same SES group”

• **Intervention**
  - Dose: 1.0 mg/d FA
  - Initiation: 3 to 25 weeks postpartum
  - Duration: 4 weeks

• **Outcome**: Plasma folate, RBC folate
Summary of the Evidence

• All but one study found a significant association between folic acid supplementation and at least one outcome measure.
  • 9 of 13 studies found a positive association between folic acid supplementation and plasma or serum folate.
  • 9 of 10 studies reported a positive association between folic acid supplementation and RBC folate.
  • 2 of 5 studies reported a positive association between folic acid supplementation and hemoglobin.

• No association found between folic acid supplementation and
  • MCV (3 studies), vitamin B12 (2 studies), prevalence of folate deficiency (2 studies)
• **Strong** evidence suggests that folic acid *supplementation before and/or during pregnancy* is positively associated with *folate status (serum, plasma, and/or RBC folate)*.

• **Assessment of the evidence:**
  • Studies were direct and precise
  • Results were consistent
  • There were some concerns regarding generalizability
• **Moderate** evidence suggests that folic acid *supplementation during lactation* is positively associated with RBC folate, and may be positively associated with *serum/plasma folate*.

• **Assessment of the evidence:**
  • Studies were direct
  • Results were consistent
  • There were some concerns regarding risk of bias, precision, and generalizability
• **Insufficient** evidence is available to determine the relationship between folic acid from *supplements consumed before and/or during pregnancy, or during lactation* and
  • hemoglobin
  • mean corpuscular volume (MCV)
  • vitamin B12
  *(Grade not assignable)*

• **No evidence** is available to determine the relationship between folic acid from *supplements consumed before and/or during pregnancy, or during lactation* and red cell distribution width (RDW).
  *(Grade not assignable)*
• **No evidence** is available to determine the relationship between folic acid from *fortified foods consumed before and/or during pregnancy, or during lactation* and folate status. *(Grade not assignable)*
Question:
dietary patterns & human milk

What is the relationship between dietary patterns consumed during lactation and human milk composition and quantity?

Approach to Answer Question: NESR Systematic Review
Key Definitions

- **Dietary Patterns** – the quantities, proportions, variety, or combination of different foods, drinks, and nutrients (when available) in diets, and the frequency with which they are habitually consumed.
What is the relationship between dietary patterns consumed during lactation and human milk composition and quantity?

**Analytic framework**

<table>
<thead>
<tr>
<th>Intervention/exposure</th>
<th>vs</th>
<th>Comparator</th>
</tr>
</thead>
</table>
| Consumption of and/or adherence to a dietary pattern | • Consumption of and/or adherence to a different dietary pattern  
• Different levels of consumption of and/or adherence to a dietary pattern |  |

**Population:** Human milk composition: Women during lactation; healthy and/or at risk for chronic disease  
Human milk quantity: Exclusively or predominantly breastfeeding women; healthy and/or at risk for chronic disease

**Outcomes**

**Human milk composition** assessed in milk collected ≥ 14 days postpartum  
• Macronutrients: Fatty acids, total protein  
• Water soluble vitamins: B, C and choline  
• Fat soluble vitamins: A, D, E, and K  
• Minerals: Iodine and Selenium  
• Human milk oligosaccharides  
• Bioactive proteins (alpha-lactalbumin, lactoferrin, casein, alpha (1) antitrypsin, osteopontin, slgA, lysozyme)

**Human milk quantity** assessed in milk collected ≥14 days postpartum

**Population:** Human milk composition: Women during lactation; healthy and/or at risk for chronic disease  
**Human milk quantity:** Exclusively or predominantly breastfeeding women; healthy and/or at risk for chronic disease

**Legend**

- The relationship of interest in the systematic review
- Factors that may impact the relationship of interest in the systematic review

**Key Confounders:** Age, Race/ethnicity, Socioeconomic status, Anthropometry (obesity status during lactation and gestational weight gain), Smoking, Parity, Gestational age, Supplement intake during lactation
7 Included articles:
• 3 RCTs (4 articles)
• 2 Cross-sectional studies (3 articles)

All 7 studies addressed the question - what is the relationship between dietary pattern consumed during lactation and human milk composition and quantity?
Description of the Evidence: 3 RCTs (4 articles)

• **Sample characteristics**
  - n=7-15/study
  - US, Canada
  - ~29y, SES NR, Race/ethnicity: NR (2 studies)

• **Interventions**
  - Initiation: 6 wk to 6 mo postpartum
  - Duration: 4 to 14 d
  - Varied patterns
    - CHO <45% & FAT >35% vs. consumption within acceptable macronutrient distribution range (AMDR)
    - FAT >35% vs. CHO >65% & FAT <20%
    - FAT >35% vs. consumption within AMDR

• **Outcomes:**
  - Human milk composition: Fatty acids (total fat, SFA, MUFA, & PUFA), total protein, vitamin B12
  - Human milk quantity

Dietary pattern and human milk
2020 Dietary Guidelines Advisory Committee: *Meeting 4*
Description of the Evidence: 2 cross-sectional studies (3 articles)

• **Sample characteristics**
  • n=22 to 73/group, 74 to 274/study
  • US, China
  • ~30.8y
  • SES: High educated (US), Med-high income (China)
  • Race/ethnicity: Mostly white

• **Interventions**
  • Initiation: 22d to 6mo, 9.5mo postpartum
  • Varied patterns
    • Vegan vs Vegetarian vs Non-vegetarian (US)
    • Mushrooms, meat, seafood; Soy, nuts, dairy; Fruits, vegetables; and Grains/potato, beans, eggs (China)

• **Outcomes:**
  • Fatty acids, Vitamin B12 (US)
Summary of the Evidence
dietary patterns & total fat

• 1 cross-sectional study assessed the relationship between maternal dietary patterns and total fat levels in human milk
  • No association

• 3 RCTs assessed the relationship between maternal diet, based on macronutrient proportions, and total fat levels in human milk
  • 2 studies found a positive relationship between >35% energy from fat and total fat in human milk, while 1 study found no association between macronutrient proportions in maternal diet and total fat in human milk
Fatty acids – Total fats

• **Insufficient evidence** is available to determine the relationship between *dietary patterns* consumed during lactation and total fat in human milk.

  *(Grade not assignable)*

• **Limited** evidence suggests that *maternal consumption of diets higher in fat (>35% fat)* during lactation is related to higher total fat in human milk in the short-term

  *(Limited)*

**Assessment of evidence:** Studies were consistent, but there were concerns about precision, generalizability and consistency
Summary of the Evidence
dietary patterns, macronutrient proportions & fatty acids

• 2 cross-sectional studies and 3 RCTs assessed the relationship between maternal dietary patterns, including diets based on macronutrient proportions, and levels of saturated fat, MUFAs, and PUFAs in human milk
  • Mixed results
Fatty acids – Saturated fats, MUFA, PUFA

**Limited** evidence suggests that maternal dietary patterns during lactation, including diets based on macronutrient distributions, are related to the relative proportions of saturated fat, MUFAs and PUFAs in human milk.

*(Limited)*

**Assessment of evidence:**

- Some concerns about risk of bias
- Limited precision and generalizability
Summary of the Evidence Synthesis
human milk quantity, protein, and vitamin B12

- 1 RCT assessed the relationship between maternal diet, based on macronutrient proportions, and human milk quantity
  - No association

- 1 RCT assessed the relationship between maternal diet, based on macronutrient proportions, and total protein levels in human milk
  - No association

- 1 cross-sectional study assessed the relationship between maternal dietary patterns and vitamin B$_{12}$ levels in human milk
  - No association
Human milk quantity

No evidence is available to determine the relationship between maternal dietary patterns during lactation and human milk quantity

Grade not assignable

Insufficient evidence is available to determine the relationship between maternal diets differing in macronutrient distributions during lactation and human milk quantity

Grade not assignable
Total protein in human milk

No evidence is available to determine the relationship between maternal dietary patterns during lactation and total protein concentration in human milk. **Grade not assignable**

Insufficient evidence is available to determine the relationship between maternal diets differing in macronutrient distribution during lactation and total protein concentration in human milk. **Grade not assignable**
Vitamin B12 in human milk

• **Insufficient evidence** is available to determine the relationship between maternal dietary patterns during lactation and vitamin B12 concentration in human milk

*Grade not assignable*
Summary of the Evidence
dietary patterns & other components of human milk

- No studies were found that assessed the relationship between maternal dietary patterns and human milk levels of:
  - water soluble vitamins B (other than vitamin B12), C, and choline
  - fat soluble vitamins A, D, E and K
  - iodine and selenium
  - human milk oligosaccharides
  - bioactive proteins
No evidence is available to determine the relationship between maternal dietary patterns during lactation and vitamins B (other than vitamin B12), C, and choline in human milk.

No evidence is available to determine the relationship between maternal dietary patterns during lactation and vitamins A, D, E and K in human milk.

No evidence is available to determine the relationship between maternal dietary patterns during lactation and iodine and selenium in human milk.

No evidence is available to determine the relationship between maternal dietary patterns during lactation and human milk oligosaccharides.

No evidence is available to determine the relationship between maternal dietary patterns during lactation and bioactive proteins including alpha-lactalbumin, lactoferrin, casein, alpha (1) antitrypsin, osteopontin, sIgA, lysozyme in human milk.

All Grade not assignable.
Questions

What is the relationship between **dietary patterns during pregnancy** and

- risk of hypertensive disorders during pregnancy?
- risk of gestational diabetes?

- gestational age at birth?
- birth weight standardized by gestational age and sex?

Approach to Answer Question: **Existing NESR Systematic Review**

New protocol posted at DietaryGuidelines.gov
Approach to Answer Question

• The Committee will be answering these questions using four existing NESR systematic review(s) completed as part of the Pregnancy and Birth to 24 Months project by the Pregnancy Technical Expert Collaborative.

• Complete documentation is available at:
  • Links also provided in question protocol at DietaryGuidelines.gov
## Members of the Pregnancy Technical Expert Collaborative

### Technical Expert Collaborative

- **Barbara Abrams**, DrPH, RD  
  University of California, Berkeley
- **Anne Bartholomew**, MS, RD  
  USDA Food and Nutrition Service
- **Lisa M. Bodnar**, PhD, MPH, RD  
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- **Alison D. Gernand**, PhD, MPH, RD  
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- **Kathleen Rasmussen**, ScD, RD  
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- **Anna Maria Siega-Riz**, PhD  
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- **Jamie S. Stang**, PhD, MPH, RDN  
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### NESR Analysts

- **Kripa Raghavan**, DrPH, MPH, MSc  
  Carol Dreibelbis, MPH
- **Brittany L. Kingshripp**, PhD

### Librarian

- **Yat Ping Wong**, MLS, MPH

### Project Leads

- **Kellie O. Casavale**, PhD, RD  
  Joanne M. Spahn, MS, RDN, FADA
- **Eve E. Stoody**, PhD
Approach to Answer Questions

• These 4 SR were also published as 2 manuscripts in the *American Journal of Clinical Nutrition* in 2019

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Dietary patterns before and during pregnancy and maternal outcomes: a systematic review

Ramkripa Raghavan,¹ Carol Dreibelbis,¹ Brittany L Kingship,¹ Yat Ping Wong,² Barbara Abrams,³ Alison D Gernand,⁴ Kathleen M Rasmussen,⁵ Anna Maria Siega-Riz,⁶ Jamie Stang,⁷ Kellie O Casavale,⁸ Joanne M Spahn,² and Eve E Stoody²

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Dietary patterns before and during pregnancy and birth outcomes: a systematic review

Ramkripa Raghavan,¹ Carol Dreibelbis,¹ Brittany L Kingship,¹ Yat Ping Wong,² Barbara Abrams,³ Alison D Gernand,⁴ Kathleen M Rasmussen,⁵ Anna Maria Siega-Riz,⁶ Jamie Stang,⁷ Kellie O Casavale,⁸ Joanne M Spahn,² and Eve E Stoody²
What is the relationship between dietary patterns during pregnancy and risk of hypertensive disorders during pregnancy?

- This systematic review included 8 studies from 4 cohorts and 1 RCT
- Search date range: Jan 1980 – Jan 2017
What is the relationship between **dietary patterns during pregnancy** and risk of hypertensive disorders during pregnancy?

- **Limited** evidence in healthy Caucasian women with access to health care suggests that **dietary patterns** before and during pregnancy higher in vegetables, fruits, whole grains, nuts, legumes, fish, and vegetable oils and lower in meat and refined grains are **associated with a reduced risk of hypertensive disorders of pregnancy**, including preeclampsia and gestational hypertension. Not all components of the assessed dietary patterns were associated with all hypertensive disorders.

  **Grade: Limited**

- **Evidence is insufficient** to estimate the association between **dietary patterns** before and during pregnancy and risk of hypertensive disorders of pregnancy in **minority women and those of lower socioeconomic status**.

  **Grade: Grade not assignable**
What is the relationship between dietary patterns during pregnancy and risk of gestational diabetes?

- This systematic review included 10 prospective cohort studies and 1 pilot RCT
- Search range: Jan 1980 – Jan 2017
Conclusion Statement and Grade (1, 2) from Existing NESR Systematic Review

What is the relationship between dietary patterns during pregnancy and risk of gestational diabetes?

Limited but consistent evidence suggests that certain dietary patterns before pregnancy are associated with a reduced risk of gestational diabetes mellitus. These protective dietary patterns are:

• higher in vegetables, fruits, whole grains, nuts, legumes, and fish, and
• lower in red and processed meats.

Most of the research was conducted in healthy, Caucasian women with access to health care.

Grade: Limited

Evidence is insufficient to estimate the association between dietary patterns during pregnancy and risk of gestational diabetes mellitus.

Grade: Grade not assignable

Question as shown on tracker

2020 Dietary Guidelines Advisory Committee: Meeting 4
What is the relationship between **dietary patterns during pregnancy** and **gestational age at birth**?

- This systematic review included 10 prospective cohort studies and 1 RCT
- Search range: Jan 1980 – Jan 2017
What is the relationship between dietary patterns during pregnancy and gestational age at birth?

**Limited** but consistent evidence suggests that certain dietary patterns during pregnancy are associated with a lower risk of preterm birth and spontaneous preterm birth. These protective dietary patterns are:

- higher in vegetables; fruits; whole grains; nuts, legumes and seeds; and seafood (preterm birth, only), and
- lower in red and processed meats and fried foods.

Most of the research was conducted in healthy, Caucasian women with access to health care.

**Grade: Limited**

**Evidence is insufficient** to estimate the association between dietary patterns before pregnancy and gestational age at birth as well as the risk of preterm birth.

Grade: Grade not assignable
What is the relationship between **dietary patterns during pregnancy** and **birth weight standardized by gestational age and sex**?

- This systematic review included 18 prospective cohorts, 1 retrospective cohort and 2 randomized control trials.
- Search range: Jan 1980 – Jan 2017
What is the relationship between dietary patterns during pregnancy and birth weight standardized by gestational age and sex?

**No conclusion can be drawn** on the association between dietary patterns during pregnancy and birth weight outcomes. Although research is available, the ability to draw a conclusion is restricted by

- inconsistency in study findings,
- inadequate adjustment of birth weight for gestational age and sex, and
- variation in study design, dietary assessment methodology, and adjustment of key confounding factors.

**Grade: Grade not assignable**

**Insufficient evidence exists** to estimate the association between dietary patterns before pregnancy and birth weight outcomes. There are not enough studies available to answer this question.

**Grade: Grade not assignable**
Refining and Prioritizing Remaining Work

• Dietary patterns during pregnancy and micronutrient status

• Dietary patterns during lactation and developmental milestones, including neurocognitive development

• Dietary supplements and fortified foods for omega-3 fatty acids, iron, vitamin D, vitamin $B_{12}$, and iodine
Next Steps

• Review the evidence, grade and draft conclusion statements for the following questions
  • Dietary patterns during pregnancy and gestational weight gain
  • Dietary patterns during lactation and postpartum weight loss
  • Maternal diet during pregnancy and lactation and risk of child food allergies and atopic allergic diseases
Pregnancy and Lactation Subcommittee: Members and Staff

Subcommittee members:
Sharon Donovan (SC chair)
Kathryn Dewey
Rachel Novotny

Jamie Stang
Elsie Taveras
Ron Kleinman (Chair rep)

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