EFFECTS OF BIRTH SPACING ON MATERNAL, PERINATAL, INFANT, AND CHILD HEALTH: A SYSTEMATIC REVIEW OF CAUSAL MECHANISMS

Agustin Conde-Agudelo*
Anyeli Rosas-Bermudez
Fabio Castaño
May Post
Linda Casey
Maureen H. Norton*

Extending Service Delivery (ESD) Project . Washington D.C.
**BACKGROUND**

**Conclusions**  Interpregnancy intervals shorter than 18 months and longer than 59 months are significantly associated with increased risk of adverse perinatal outcomes. These data suggest that spacing pregnancies appropriately could help prevent such adverse perinatal outcomes.


Long interpregnancy intervals, possibly longer than 5 years, are independently associated with an increased risk of preeclampsia. There is emerging evidence that women with long interpregnancy intervals are at increased risk for labor dystocia and that short intervals are associated with increased risks of uterine rupture in women attempting a vaginal birth after previous cesarean delivery and uteroplacental bleeding disorders (placental abruption and placenta previa).


Preceding interpregnancy intervals shorter than 36 months are significantly associated with a greater risk of child and under five years mortality whereas intervals shorter than 24 months increase significantly the risk of early neonatal, neonatal, and infant mortality.

OBJECTIVES

- To identify causal mechanisms for explaining the effects of both short and long intervals between pregnancies on maternal, perinatal, infant, and child health.

- To critically examine the scientific support for each causal mechanism identified by using formal methods for systematic reviews of observational studies.
METHODS

- **Identification of studies**: databases, key/text words, bibliography of the retrieved articles, proceedings of meetings, reviews. No language restrictions.

- **Inclusion criteria**: observational studies dealing with causal mechanisms or hypotheses with adjustment of results for at least maternal age or parity and socioeconomic status.

- **Exclusion criteria**: studies that did not adjust for at least maternal age or parity and socioeconomic status or if they did not provide data.
Study selection and data extraction: review of studies to determine inclusion and data extraction were performed independently by two authors.

Assessment of study quality: study design, measure of spacing used, selection of participants, assessment of exposure/outcomes, blinding, loss to follow-up or exclusions and/or period of time for recruitment, control for confounding factors, report of a dose-response gradient, and biologic or behavioral plausibility of causal mechanisms.

Data analysis: meta-analysis not feasible. Narrative synthesis.
RESULTS

198 studies potentially relevant

58 studies included in systematic review
- 41 → causal mechanisms or hypotheses
- 17 → maternal folate levels

141 excluded
- Lack of data/adjustment

- 62% of studies → Developing countries
- 46% → High methodological quality
- 9 hypothetical causal mechanisms for explaining association between short intervals and adverse outcomes
- 1 hypothetical causal mechanism for explaining association between long intervals and adverse outcomes
1. INCOMPLETE HEALING OF THE UTERINE SCAR FROM THE PREVIOUS C/S

- 3 studies:
  1→ultrasonographic evaluation of uterine scar
  1→MRI evaluation of uterine scar healing
  1→hysteroscopic evaluation of uterine scar

- Growing evidence supports this hypothesis

2. ABNORMAL PROCESS OF REMODELING OF ENDOMETRIAL BLOOD VESSELS

- No studies evaluated this hypothesis
3. MATERNAL NUTRITIONAL DEPLETION

- 15 studies provided data
- 9 studies evaluated maternal anthropometric status (4 → positive association; 5 → mixed or conflicting results)
- 7 studies evaluated maternal anemia (2 → significant association; 5 → no association)
- 1 study evaluated serum micronutrients → no association
- No clear evidence to support this hypothesis
4. FOLATE DEPLETION

- 20 studies provided data
- 17 studies examined maternal folate levels during postpartum period (14 → low folate levels 4 weeks-12 months; 3 studies → no association)
- 2 studies evaluated folate levels according to IPI (1 → significant association; 1 → no association)
- 1 study → dose-dependent mitigating effect of folic acid supplementation on unfavorable effects of short intervals on birth weight and SGA
- Growing evidence supports this hypothesis
5. CERVICAL INSUFFICIENCY

- 1 study provided data → Cervical collagen concentration was not normalized until 12 months after spontaneous delivery.
- Scarce evidence supports this hypothesis.

6. VERTICAL TRANSMISSION OF INFECTIONS

- 2 studies provided data → BI <2 yrs and <12 months increased risks of congenital CMV infection and recurrent GBS colonization, respectively.
- Emerging evidence supports this hypothesis.
7. SIBLING COMPETITION

- 20 studies provided data
- Effects of short intervals on neonatal and infant mortality: stronger when the preceding sibling dies than when it survives → does not favor hypothesis
- Effects of short intervals on post-neonatal mortality: stronger when the preceding sibling survives than when it dies → favors hypothesis.
- Effects of short intervals on child and <5 years mortality according to survival status: inconclusive
2 studies provided data

1 study → birth intervals <24 months were associated with an increased risk of diarrhea

1 study → children born within 4 years after the older sibling were 4 times (95% CI, 2.0-8.6) more likely to be infected by Helicobacter pylori than children born ≥10 years. The infection was transmitted most frequently from older siblings to younger ones.

Some evidence supports this hypothesis
9. SUBOPTIMAL LACTATION RELATED TO BREASTFEEDING-PREGNANCY OVERLAP

- No studies evaluated this hypothesis. Two studies evaluated effects of B-PO on neonatal outcomes: one found lower intakes per feed among infants whose mothers breastfeed during last trimester of pregnancy. Other found a change in breast milk composition that affects the immunity properties of breast milk.

- Some evidence supports this hypothesis.

10. WOMAN’S PHYSIOLOGICAL REGRESSION

- No studies evaluated this hypothesis.
LONG INTERVALS CONCEPTUAL FRAMEWORK

LONG INTERVAL BETWEEN PREGNANCIES

Woman's physiological regression

ADVERSE MATERNAL OUTCOMES
- Preeclampsia
- Labor dystocia

ADVERSE HEALTH OUTCOME

ADVERSE PERINATAL OUTCOMES
- Preterm birth
- Low birth weight
- Small for gestational age

CAUSAL MECHANISMS HYPOTHEZIZED