

Web Material

A Population-Based Matched-Sibling Analysis Estimating the Associations Between First Interpregnancy Interval and Birth Outcomes

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Web Table 1. Odds of Preterm Birth in Secondborn Child as Estimated in an Unmatched Cohort Study, by Preterm Birth Category and Interpregnancy Interval between First and Second, Consecutive Live Births – Western Australia, 1980-2010 (N=192,041).

| Preterm Birth Category, by Interpregnancy Interval | Total | Secondborn with outcome | OR ^a | 95% CI ^a | adjusted | |
|--|--------|-------------------------------|-----------------|---------------------|-----------------|---------------------|
| | N | n (%) | | | OR ^b | 95% CI ^b |
| Iatrogenic preterm birth | | | | | | |
| <6 months | 5,486 | 131 (2.4) | 1.17 | 0.97, 1.41 | 1.20 | 0.99, 1.46 |
| 6–11 months | 28,071 | 521 (1.9) | 0.90 | 0.81, 1.01 | 0.92 | 0.82, 1.03 |
| 12–17 months | 41,454 | 726 (1.7) | 0.85 | 0.77, 0.95 | 0.86 | 0.77, 0.96 |
| 18–23 months | 33,427 | 686 (2.1) | 1.00 | Referent | 1.00 | Referent |
| 24–59 months | 62,849 | 1,508 (2.4) | 1.17 | 1.07, 1.29 | 1.15 | 1.05, 1.26 |
| ≥60 months | 14,321 | 525 (3.7) | 1.82 | 1.62, 2.04 | 1.66 | 1.48, 1.87 |
| Spontaneous preterm birth | | | | | | |
| <6 months | 5,740 | 385 (6.7) | 2.41 | 2.13, 2.72 | 1.92 | 1.70, 2.17 |
| 6–11 months | 28,637 | 1,087 (3.8) | 1.32 | 1.21, 1.44 | 1.22 | 1.11, 1.33 |
| 12–17 months | 42,030 | 1,302 (3.1) | 1.07 | 0.98, 1.16 | 1.04 | 0.96, 1.13 |
| 18–23 months | 33,719 | 978 (2.9) | 1.00 | Referent | 1.00 | Referent |
| 24–59 months | 63,418 | 2,077 (3.3) | 1.13 | 1.05, 1.23 | 1.13 | 1.05, 1.23 |
| ≥60 months | 14,400 | 604 (4.2) | 1.47 | 1.32, 1.63 | 1.56 | 1.41, 1.74 |
| Moderate preterm birth (32-36 weeks) | | | | | | |
| <6 months | 5,759 | 404 (7.0) | 1.74 | 1.55, 1.95 | 1.55 | 1.38, 1.74 |
| 6–11 months | 28,885 | 1,335 (4.6) | 1.11 | 1.03, 1.20 | 1.07 | 1.00, 1.16 |
| 12–17 months | 42,495 | 1,767 (4.2) | 1.00 | 0.93, 1.07 | 0.99 | 0.92, 1.06 |

| | | | | | | |
|--------------|--------|-------------|------|------------|------|------------|
| 18–23 months | 34,164 | 1,423 (4.2) | 1.00 | Referent | 1.00 | Referent |
| 24–59 months | 64,369 | 3,028 (4.7) | 1.14 | 1.07, 1.21 | 1.12 | 1.05, 1.20 |
| ≥60 months | 14,700 | 904 (6.1) | 1.51 | 1.38, 1.64 | 1.49 | 1.37, 1.63 |

Very preterm birth (28-31 weeks)

| | | | | | | |
|--------------|--------|-----------|------|------------|------|------------|
| <6 months | 5,441 | 86 (1.6) | 3.07 | 2.37, 3.99 | 2.54 | 1.95, 3.31 |
| 6–11 months | 27,739 | 189 (0.7) | 1.31 | 1.07, 1.62 | 1.22 | 0.99, 1.51 |
| 12–17 months | 40,916 | 188 (0.5) | 0.88 | 0.72, 1.09 | 0.86 | 0.70, 1.06 |
| 18–23 months | 32,912 | 171 (0.5) | 1.00 | Referent | 1.00 | Referent |
| 24–59 months | 61,743 | 402 (0.7) | 1.25 | 1.05, 1.50 | 1.27 | 1.06, 1.51 |
| ≥60 months | 13,960 | 164 (1.2) | 2.28 | 1.83, 2.82 | 2.46 | 1.97, 3.06 |

Extreme preterm birth (<28 weeks)

| | | | | | | |
|--------------|--------|-----------|------|------------|------|------------|
| <6 months | 5,381 | 26 (0.5) | 2.27 | 1.45, 3.57 | 1.81 | 1.15, 2.86 |
| 6–11 months | 27,634 | 84 (0.3) | 1.43 | 1.04, 1.96 | 1.32 | 0.96, 1.82 |
| 12–17 months | 40,801 | 73 (0.2) | 0.84 | 0.60, 1.16 | 0.82 | 0.59, 1.14 |
| 18–23 months | 32,811 | 70 (0.2) | 1.00 | Referent | 1.00 | Referent |
| 24–59 months | 61,496 | 155 (0.3) | 1.18 | 0.89, 1.57 | 1.15 | 0.87, 1.53 |
| ≥60 months | 13,857 | 61 (0.4) | 2.07 | 1.47, 2.92 | 2.06 | 1.45, 2.92 |

^a Odds ratio and corresponding 95% confidence interval based on logistic regression.

^b Adjusted for age, race, socioeconomic status, and calendar year of birth.

Web Table 2. Odds of Preterm Birth in Secondborn Child as Estimated by Matched Sibling-Pair Analysis, by Preterm Birth Category and Interpregnancy Interval between First and Second Consecutive, Live Births – Western Australia Between 1980 and 2010 (N=192,041).

| Preterm Birth Category, by Interpregnancy Interval | Total number of sibling pairs | Number of discordant pairs in analysis | Unadjusted interaction odds ratios | | Adjusted interaction odds ratios ^a | |
|--|--|---|--|------------|---|------------|
| | | | IOR | 95% CI | IOR | 95% CI |
| Iatrogenic preterm birth | | | | | | |
| <6 months | 5,486 | 239 | 0.88 | 0.60, 1.17 | 0.87 | 0.59, 1.16 |
| 6–11 months | 28,071 | 933 | 0.90 | 0.72, 1.07 | 0.89 | 0.71, 1.07 |
| 12–17 months | 41,454 | 1,253 | 1.02 | 0.86, 1.18 | 1.02 | 0.85, 1.18 |
| 18–23 months | 33,427 | 1,135 | 1.00 | Referent | 1.00 | Referent |
| 24–59 months | 62,849 | 2,416 | 1.11 | 0.96, 1.25 | 1.13 | 0.98, 1.27 |
| ≥60 months | 14,321 | 687 | 1.94 | 1.74, 2.13 | 2.11 | 1.85, 2.36 |
| Spontaneous preterm birth | | | | | | |
| <6 months | 5,740 | 560 | 1.47 | 1.28, 1.67 | 1.43 | 1.23, 1.62 |
| 6–11 months | 28,637 | 1,839 | 1.24 | 1.11, 1.37 | 1.21 | 1.07, 1.34 |
| 12–17 months | 42,030 | 2,273 | 1.17 | 1.04, 1.30 | 1.16 | 1.03, 1.29 |
| 18–23 months | 33,719 | 1,809 | 1.00 | Referent | 1.00 | Referent |
| 24–59 months | 63,418 | 3,702 | 1.04 | 0.93, 1.16 | 1.07 | 0.94, 1.18 |
| ≥60 months | 14,400 | 994 | 1.38 | 1.23, 1.54 | 1.52 | 1.32, 1.72 |
| Moderate preterm birth (33-36 weeks) | | | | | | |
| <6 months | 5,759 | 625 | 1.40 | 1.23, 1.58 | 1.37 | 1.19, 1.55 |
| 6–11 months | 28,885 | 2,352 | 1.11 | 1.00, 1.23 | 1.10 | 0.98, 1.21 |
| 12–17 months | 42,495 | 3,082 | 1.11 | 1.00, 1.22 | 1.11 | 1.00, 1.21 |

| | | | | | | |
|--------------|--------|-------|------|------------|------|------------|
| 18–23 months | 34,164 | 2,573 | 1.00 | Referent | 1.00 | Referent |
| 24–59 months | 64,369 | 5,195 | 1.11 | 1.01, 1.20 | 1.13 | 1.03, 1.23 |
| ≥60 months | 14,700 | 1,416 | 1.55 | 1.42, 1.68 | 1.71 | 1.54, 1.87 |

Very preterm birth (29-32 weeks)

| | | | | | | |
|--------------|--------|-----|------|------------|------|------------|
| <6 months | 5,441 | 112 | 1.10 | 0.65, 1.55 | 1.08 | 0.62, 1.53 |
| 6–11 months | 27,739 | 294 | 1.03 | 0.69, 1.37 | 1.05 | 0.71, 1.39 |
| 12–17 months | 40,916 | 337 | 1.11 | 0.78, 1.43 | 1.09 | 0.76, 1.42 |
| 18–23 months | 32,912 | 268 | 1.00 | Referent | 1.00 | Referent |
| 24–59 months | 61,743 | 708 | 0.83 | 0.55, 1.13 | 0.85 | 0.54, 1.15 |
| ≥60 months | 13,960 | 194 | 1.74 | 1.36, 2.11 | 1.76 | 1.28, 2.25 |

Extreme preterm birth (<28 weeks)

| | | | | | | |
|--------------|--------|-----|------|------------|------|------------|
| <6 months | 5,381 | 62 | 0.36 | 0.00, 1.07 | 0.36 | 0.00, 1.08 |
| 6–11 months | 27,634 | 126 | 0.98 | 0.45, 1.51 | 0.92 | 0.37, 1.47 |
| 12–17 months | 40,801 | 107 | 1.12 | 0.58, 1.67 | 1.07 | 0.50, 1.63 |
| 18–23 months | 32,811 | 103 | 1.00 | Referent | 1.00 | Referent |
| 24–59 months | 61,496 | 215 | 0.98 | 0.50, 1.45 | 0.94 | 0.45, 1.44 |
| ≥60 months | 13,857 | 71 | 1.98 | 1.36, 2.61 | 2.09 | 1.29, 2.89 |

^a Odds of secondborn being born with outcome under analysis compared with odds of firstborn being born with outcome; Interaction odds ratios (IOR) and corresponding 95% confidence interval adjusted by maternal age, socioeconomic status and calendar year of birth, where 18-23 month intervals is the reference category.

Web Table 3. Odds of Adverse Birth Outcomes in Secondborn Child as Estimated by an Unmatched Cohort Study Restricted to Discordant Sibling Pairs, by Interpregnancy Interval between First and Second Consecutive, Live Births – Western Australia, 1980-2010.

| Birth Outcome, by Interpregnancy Interval | Number of discordant sibling pairs | Secondborn with outcome | OR ^a | 95% CI ^a | adjusted | |
|--|--|-------------------------------|-----------------|---------------------|-----------------|---------------------|
| | N | n (%) | | | OR ^b | 95% CI ^b |
| Preterm birth | | | | | | |
| <6 months | 799 | 368 (46.1) | 1.26 | 1.07, 1.46 | 1.13 | 0.96, 1.32 |
| 6–11 months | 2,772 | 1,192 (43.0) | 1.10 | 0.99, 1.23 | 1.06 | 0.95, 1.17 |
| 12–17 months | 3,526 | 1,521 (43.1) | 1.11 | 1.00, 1.22 | 1.09 | 0.99, 1.21 |
| 18–23 months | 2,944 | 1,196 (40.6) | 1.00 | Referent | 1.00 | Referent |
| 24–59 months | 6,118 | 2,585 (42.3) | 1.07 | 0.98, 1.17 | 1.07 | 0.98, 1.17 |
| ≥60 months | 1,681 | 876 (52.1) | 1.59 | 1.41, 1.79 | 1.64 | 1.45, 1.85 |
| Small-for-gestational age | | | | | | |
| <6 months | 934 | 302 (32.3) | 0.99 | 0.85, 1.15 | 0.88 | 0.76, 1.03 |
| 6–11 months | 3,773 | 1,225 (32.5) | 0.99 | 0.90, 1.09 | 0.95 | 0.86, 1.04 |
| 12–17 months | 5,376 | 1,794 (33.4) | 1.03 | 0.95, 1.12 | 1.02 | 0.94, 1.11 |
| 18–23 months | 4,460 | 1,457 (32.7) | 1.00 | Referent | 1.00 | Referent |
| 24–59 months | 9,190 | 3,080 (33.5) | 1.04 | 0.96, 1.12 | 1.06 | 0.98, 1.14 |
| ≥60 months | 2,517 | 1,044 (41.5) | 1.46 | 1.32, 1.62 | 1.59 | 1.43, 1.76 |
| Low birthweight | | | | | | |
| <6 months | 599 | 214 (35.7) | 1.00 | 0.83, 1.21 | 0.89 | 0.74, 1.08 |
| 6–11 months | 1,971 | 749 (38.0) | 1.00 | 0.83, 1.21 | 1.05 | 0.92, 1.19 |
| 12–17 months | 2,471 | 914 (37.0) | 1.10 | 0.97, 1.25 | 1.03 | 0.91, 1.17 |

| | | | | | | |
|--------------|-------|--------------|------|------------|------|------------|
| 18–23 months | 2,019 | 721 (35.7) | 1.00 | Referent | 1.00 | Referent |
| 24–59 months | 4,653 | 1,680 (36.1) | 1.02 | 0.91, 1.13 | 1.03 | 0.92, 1.15 |
| ≥60 months | 1,334 | 631 (47.3) | 1.62 | 1.40, 1.86 | 1.71 | 1.48, 1.98 |

^a Odds ratio and corresponding 95% confidence interval based on logistic regression.

^b Adjusted for age, race, socioeconomic status, and calendar year of birth.

Web Table 4. Supplemental Analyses Estimating the Odds of Adverse Birth Outcomes in Secondborn Child as Estimated by Matched Sibling-Pair Analysis, by Interpregnancy Interval between First and Second Consecutive, Live Births – Western Australia Between 1996 and 2010 (N=87,100).

| Birth Outcome, by Interpregnancy Interval | Total number of sibling pairs | Number of discordant pairs in analysis | Unadjusted interaction odds ratios | | Adjusted interaction odds ratios ^a | |
|--|--|---|--|------------|---|------------|
| | | | IOR | 95% CI | IOR | 95% CI |
| Preterm Birth | | | | | | |
| <6 months | 2,769 | 377 | 1.21 | 0.98, 1.44 | 1.19 | 0.96, 1.42 |
| 6–11 months | 13,842 | 1,313 | 1.01 | 0.86, 1.17 | 1.00 | 0.84, 1.16 |
| 12–17 months | 19,974 | 1,651 | 1.11 | 0.92, 1.21 | 1.06 | 0.91, 1.21 |
| 18–23 months | 16,193 | 1,428 | 1.00 | Referent | 1.00 | Referent |
| 24–59 months | 29,146 | 2,799 | 1.06 | 0.93, 1.19 | 1.07 | 0.93, 1.20 |
| ≥60 months | 5,176 | 580 | 1.67 | 1.47, 1.86 | 1.72 | 1.48, 1.96 |
| Small-for-gestational age | | | | | | |
| <6 months | 2,769 | 423 | 1.19 | 0.97, 1.42 | 1.19 | 0.96, 1.41 |
| 6–11 months | 13,842 | 1,675 | 1.04 | 0.90, 1.18 | 1.05 | 0.90, 1.19 |
| 12–17 months | 19,974 | 2,387 | 1.05 | 0.92, 1.18 | 1.05 | 0.92, 1.18 |
| 18–23 months | 16,193 | 1,991 | 1.00 | Referent | 1.00 | Referent |
| 24–59 months | 29,146 | 3,955 | 1.16 | 1.04, 1.27 | 1.12 | 0.99, 1.24 |
| ≥60 months | 5,176 | 791 | 1.54 | 1.36, 1.71 | 1.37 | 1.16, 1.58 |
| Low birthweight | | | | | | |
| <6 months | 2,769 | 271 | 1.21 | 0.93, 1.49 | 1.19 | 0.91, 1.48 |
| 6–11 months | 13,842 | 912 | 1.06 | 0.87, 1.25 | 1.06 | 0.86, 1.25 |

| | | | | | | |
|--------------|--------|-------|------|------------|------|------------|
| 12–17 months | 19,974 | 1,068 | 0.99 | 0.81, 1.18 | 0.99 | 0.81, 1.18 |
| 18–23 months | 16,193 | 922 | 1.00 | Referent | 1.00 | Referent |
| 24–59 months | 29,146 | 2,039 | 1.01 | 0.85, 1.18 | 1.00 | 0.83, 1.17 |
| ≥60 months | 5,176 | 447 | 1.58 | 1.35, 1.81 | 1.57 | 1.29, 1.85 |

^a Odds of secondborn being born with outcome under analysis compared with odds of firstborn being born with same outcome; Interaction odds ratios (IOR) and corresponding 95% confidence interval adjusted by maternal age, socioeconomic status and calendar year of birth, where 18-23 month intervals is the reference category.

Web Appendix 1. Sample SAS Code for Running Unmatched and Matched Models

Estimating the Association between First Interpregnancy Interval and Birth Outcomes for the Second Infant.

*This example code summarizes models used to estimate associations for preterm birth. The code can be replicated to repeat analyses for other birth outcomes (i.e., SGA, low birthweight).

Required Variables:

Exposure

1. `intervall_gp6` = six-level categorical variable of interval between first birth and conception of second infant (1='<6 months, 2=6-11 months, 12-17 months, 18-23 months, 24-59 months, ≥60 months)

Outcomes

1. `preterm1` = preterm birth (gestational length <37 weeks) in first birth (1=yes, 0=no)
2. `preterm2` = preterm birth (gestational length <37 weeks) in second birth (1=yes, 0=no)

Covariates

3. `ses1` = Five-level categorical variable indicating the socioeconomic level of mother at first birth
4. `ses2` = Five-level categorical variable indicating the socioeconomic level of mother at second birth
5. `race` = Mother's race (1=Caucasian; 0=Non-Caucasian)
6. `agegp1` = Five-level categorical variable indicating mother's age at first birth (1=<20 years, 2=20-24 years, 3=25-29 years, 4=30-34 years, 5=≥35 years)
7. `agegp2` = Five-level categorical variable indicating mother's age at second birth (1=<20 years, 2=20-24 years, 3=25-29 years, 4=30-34 years, 5=≥35 years)
8. `year1` = Year of birth of first infant
9. `year2` = Year of birth of second infant

**Unmatched traditional cohort study analysis

*****;

**Perform unmatched analysis using unconditional logistic regression model;

```
proc logistic data=IPI;
```

```
class intervall_gp6(ref='18-23m') / param=ref;
```

```
model preterm2(event="1") = intervall_gp6 ;
```

```
run;
```

```
proc logistic data=IPI;
```

```
class intervall_gp6(ref='18-23m') agegp2(ref=first) ses2(ref=first)
```

```
race(ref=first) / param=ref;
```

```
model preterm2(event="1") = intervall_gp6 agegp2 ses2 year2 race;
```

```
run;
```

```

*****
**Matched sibling analysis
*****;

**Perform unmatched analysis using unconditional logistic regression model;

*Code used to create a dataset with one record for first birth and one
record for second birth for each sibling pair

New variables:

Exposure
  1. intervalgp = six-level categorical variable of interval between first
    birth and conception of second infant(1=<6 months, 2=6-11 months, 12-
    17 months, 18-23 months, 24-59 months, ≥60 months)

Outcome
  1. preterm = preterm birth (gestational length <37 weeks) in either
    first or second birth (1=yes, 0=no)

Matching variable
  1. MotherID = unique ID used to identify mother (and sibling pairs)

Covariates
  1. ses = Five-level socioeconomic level of mother at first or second
    birth
  2. age = Five-level categorical variables indicating mother's age at
    either first or second birth (1=<20 years, 2=20-24 years, 3=25-29
    years, 4=30-34 years, 5=≥35 years)
  3. year = Year of first or second birth

data preterm2; set IPI;
if preterm2=1 then preterm=1;
if preterm2=0 then preterm=0;
intervalgp = intervall_gp6;
age=agegp2;
ses=ses2;
year=year2;
birth=2;
keep birth year2 ses2 agegp2 intervall_gp6 preterm2 MotherID;
run;

data preterm1; set IPI;
if preterm1=1 then preterm=1;
if preterm1=0 then preterm=0;
intervalgp = intervall_gp6;
age=agegp1;
ses=ses1;
year=year1;
birth=1;
keep birth year1 ses1 agegp1 intervall_gp6 preterm1 MotherID;
run;

data matched_preterm;
set preterm1 preterm2;
run;

proc logistic data=matched_preterm;
strata MotherID;

```

```
class birth(ref='1') intervalgp (ref='18-23m')/ param=ref;
model preterm(event="1") = birth birth* intervalgp;
run;

proc logistic data=matched_preterm;
strata MotherID
class birth(ref='1') intervalgp (ref='18-23m') year(ref=last)
age(ref=last) ses(ref=first)/ param=ref;
model preterm(event="1") = birth year age ses birth*intervalgp;
run;

*END
*****;
```