Cerebral Palsy Among Term and Postterm Births

JAMA. 2010; 304(9):976-982

UAB Dept OB/Gyn Journal Club 10/7/10
Context

• Cerebral Palsy (CP) known complication of preterm delivery.

• \( \frac{3}{4} \) of patients with CP born after 36wks

• Little info on relation of CP risk to gestational age when term and postterm.
Population

• Birth and linked registries of Norway
  – 1967-2001 Births
  – Singleton Live Births
  – EGA 37-44wks by LMP
  – Exclusion
    • BW + > 3 SD of mean for GA
    • Anomalies
    • Baby died < 4yo
    • Missing GA information

• 2,024,215 → 1,682,441
1. State study objective before this slide
2. Specify exposure as GA categorized in completed weeks from 37 to 44
3. Specify study outcome as CP

Alan Thevenet N. Tita, 10/7/2010
Stats

• RR (95% CI) of CP using log-binomial regression

• Adjustments
  – Year of birth
  – Baby’s Sex
  – Maternal Age
  – Maternal and Paternal Education Level
  – Maternal Marital Status
  – Immigrant Status of parents

• All tests 2-sided with 5% significance level
Results

• Highest prevalence CP @ 37wks and >42 wks
• Lowest prevalence CP @ 40wks

• RR CP at respective EGA
  – 37wks RR compared to 40wks = 1.9
  – >42wks RR compared to 40wks = 1.5
Results

• Children with CP more likely to...
  – single mothers (P=.03)
  – lower maternal education (P<.001)
  – complications of labor (p<.001)
  – lower mean BW (p<.001)
  – smaller head circumference (p<.001)

• Adjustments provided identical RR by EGA.
Results

• U/S vs LMP
  – 139,976 w/ US dating (1998-2001)
  – CP risk with EGA stronger with U/S dating
    • 37wks RR compared to 40wks = 3.7
    • >42wks RR compared to 40wks = 2.4

• Comparing time intervals
  – Prevalence decreased
  – Association with EGA consistent
Conclusions

• Risk of CP lowest at 40wks and highest at 37wks and ≥42wks

• U-shaped risk stronger among U/S dating than LMP dating

• Adjustment for parental characteristics had no influence on results

• No adjustment for circumstances of labor and delivery or neonatal period because may be part of causal pathway or early expression CP.
Implications

• Is this question important?
• Will it change my practice?
Purpose

• Do the authors provide a clear and specific question and hypothesis?
• Is the research objective clear and unambiguous?
Methodology

• Is the study design appropriate for the research question?

• Advantages & disadvantages of chosen methodology:
  – Level of evidence?
  – Confounding, bias, & validity
Study Population

- Is the study population appropriate?
- Characteristics of the “sample”
- Is the population similar to my patients?
- Specific inclusion & exclusion criteria
  - Are these appropriate? Any missing?
  - Selection bias?
Measurement Issues & Bias

- How are the variables measured?
- Bias?
- Confounding?
- Masking or blinding?
Statistical Analysis

• How were the data analyzed?
  – What tests were used?
  – Multivariable methods?
Sample Size and Power

• Was sample size calculation done beforehand?
• Did the investigators specify a clinically important difference they would like to detect?
  – Was this necessary?
• Potential for Type I or Type II error?
Results

• Are the results clearly presented and understandable?

• How were the results interpreted?
  – Are the interpretations appropriate?

• Threats to validity
  – Loss to follow-up
  – Missing information
  – Control of confounding
  – Issues of bias
Discussion

• Are the conclusions supported by the data?
• Relate findings to other studies in the medical literature. Are these findings consistent?
• Do the authors “stretch” too far?
• What are the strengths of this study?
• What are the weaknesses or flaws?
  – Do the authors recognize them?
Conclusions

• Do the findings contribute to our knowledge of the subject?
• What additional questions does this study raise?

• Will this study change how we practice?
• Will it change how we counsel patients?
Cohort Studies

Objectives

• Definitions
• Study populations
• Benefits & Limitations of this design
• Types of cohort studies, advantages and disadvantages of each
• Basic Analytical Approach
• Loss to follow-up & biased relative risk
Cohort Study

• Cohort = Any defined group of people who are followed over a given time period

• Cohort study = Group (cohort) identified and followed to ascertain the occurrence of health-related events

• Purpose: To investigate whether incidence of an event is related to a suspected exposure
Types of Cohorts: Study Populations

- Geographical
  - Norway
- Occupational
  - Coal workers
- High risk of particular disease
  - Homosexual men
- Convenience (willingness or ease of follow-up)
  - Nurses Health Study
<table>
<thead>
<tr>
<th>Benefits</th>
<th>Limitations</th>
</tr>
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<tbody>
<tr>
<td>• Establish sequence of events (temporal relationship)</td>
<td>• Large sample size</td>
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<tr>
<td>• Can study several outcomes</td>
<td>• Long duration/follow-up</td>
</tr>
<tr>
<td>• Number of events increases with time (dose response)</td>
<td>• Problematic for rare disease</td>
</tr>
<tr>
<td>• Yields incidence, relative risk</td>
<td>• Cost</td>
</tr>
<tr>
<td>• Good for rare exposure</td>
<td>• Selection bias (selection of unexposed)</td>
</tr>
<tr>
<td>• Control of subject selection &amp; measurements (if prospective)</td>
<td>• Observer bias</td>
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<tr>
<td></td>
<td>• Detailed records needed (if retrospective)</td>
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</tbody>
</table>
Types of Cohort Studies

• Prospective (*Concurrent*)
  – Cohort is assembled at present time & followed up toward the future

• Retrospective or Historical (*Nonconcurrent*)
  – Cohort is assembled in the past and “followed” to present time

• Mixed/Ambidirectional
## Advantages & Disadvantages

<table>
<thead>
<tr>
<th>Prospective Cohort</th>
<th>Retrospective Cohort</th>
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<tbody>
<tr>
<td>Details are planned &amp; implemented for purposes of the study</td>
<td>Obligatory reliance on available information</td>
</tr>
<tr>
<td>Quality control as needed</td>
<td>Quality of data sometimes less than ideal</td>
</tr>
<tr>
<td>Take longer to complete</td>
<td>More expeditious</td>
</tr>
<tr>
<td>More expensive</td>
<td>Less expensive</td>
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</tbody>
</table>
Basic Analytical Approach

- Subjects are classified according to exposure status
- Incidence of disease ascertained for each
  Incidence = occurrence of NEW disease
- Comparison between exposed & unexposed

Relative risk: is disease more common in those exposed?

\[
\frac{\text{incidence for exposed}}{\text{incidence for unexposed}} = \frac{A/(A+B)}{C/(C+D)}
\]

<table>
<thead>
<tr>
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<tr>
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<td>A</td>
<td>B</td>
</tr>
<tr>
<td>Unexposed</td>
<td>C</td>
<td>D</td>
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What about loss to follow-up?

- Designated as *censored observations* or *withdrawals*
- Must be taken into account for calculation of incidence

**Important assumption:** Those lost to follow-up are similar to those remaining in the study

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Biased Relative Risk

• If losses are similar in exposed & unexposed, relative risks will cancel out, BUT...
• A biased relative risk occurs when losses are different in exposed & unexposed subjects (if losses are affected by both exposure & disease status)