Reducing Risk for Mother-to-Infant Transmission of Hepatitis C Virus: A Systematic Review for the U.S. Preventive Services Task Force

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Background: Mother-to-infant transmission is the leading cause of childhood hepatitis C virus (HCV) infection, with up to 4000 new cases each year in the United States.

Purpose: To evaluate effects of mode of delivery, labor management strategies, and breastfeeding practices on risk for mother-to-infant transmission of HCV.

Data Sources: MEDLINE (1947 to May 2012), the Cochrane Library Database, clinical trial registries, and reference lists.

Study Selection: Randomized trials and observational studies on mode of delivery, labor management strategies, and breastfeeding practices and risk for mother-to-infant transmission of HCV.

Data Extraction: Investigators abstracted and reviewed study details and quality using predefined criteria.

Data Synthesis: Eighteen observational studies evaluated the association between mode of delivery, labor management strategies, or breastfeeding practices and risk for mother-to-infant HCV transmission. Fourteen studies (2 good-quality, 4 fair-quality, and 8 poor-quality studies) found no clear association between mode of delivery (vaginal versus cesarean delivery) and risk for transmission. Two studies (1 good-quality and 1 poor-quality study) reported an association between prolonged duration of ruptured membranes and increased risk for transmission. Fourteen studies (2 good-quality, 2 fair-quality, and 10 poor-quality studies) found no association between breastfeeding and risk for transmission.

Limitations: Only English-language articles were included. Studies were observational, and most had important methodological shortcomings, including failure to adjust for potential confounders and small sample sizes.

Conclusion: No intervention has been clearly demonstrated to reduce the risk for mother-to-infant HCV transmission. Avoidance of breastfeeding does not seem to be indicated for reducing transmission risk.

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An estimated 40,000 children are born to hepatitis C virus (HCV)–positive women each year (1). Mother-to-infant (vertical) transmission is the main route of childhood HCV infection (2). Estimates for the rate of vertical transmission range from 3% to 10% (2–5). Risk for transmission is highest among women with a high viral load at delivery (2–6) and those co-infected with HIV (5, 7). Although antiviral therapies are contraindicated in pregnancy because of teratogenic risks, prenatal HCV screening to identify HCV-infected women unaware of their status might lead to other interventions during labor and delivery or in the perinatal period that reduce risk for mother-to-infant transmission (8).

The purpose of this review was to synthesize the evidence on the effects of mode of delivery, labor management strategies, and breastfeeding practices on risk for mother-to-infant transmission. This review was performed as part of a larger report on HCV screening (9) and will be used by the U.S. Preventive Services Task Force (USPSTF) to inform its prenatal HCV screening recommendations.

Methods

Scope

We developed a review protocol by using a standardized process with input from experts and the public to address the following key question: “What is the effect of mode of delivery, labor management strategy, or breastfeeding on risk for mother-to-infant transmission of HCV?” Detailed methods and data for the review, including the full USPSTF analytic framework on screening, search strategies, detailed abstraction tables, and quality ratings of individual studies, are available in the full report (9).

Data Sources and Searches

A research librarian searched Ovid MEDLINE (1947 to May 2012), EMBASE, the Cochrane Library Database, Scopus, PsycINFO, clinical trial registries (including clinicaltrials.gov), and grants databases. We supplemented electronic searches by reviewing reference lists of retrieved articles. Searches were peer reviewed by a second librarian.

Study Selection

At least 2 reviewers independently evaluated each study to determine inclusion eligibility. We selected for full-review randomized trials, cohort studies, and case–control studies that evaluated the association between mode of delivery (cesarean versus vaginal delivery), labor management strategies (use of internal fetal monitoring or management of premature rupture of membranes), or breastfeeding on risk for mother-to-infant transmission. We restricted inclusion to English-language articles and...
excluded studies published only as abstracts. Women co-infected with HIV are advised to avoid breastfeeding and deliver by elective cesarean if they are viremic in order to reduce risk for HIV transmission (10). Therefore, we excluded studies of HIV co-infected women, unless results for women not co-infected with HIV were reported separately or co-infected women made up less than 10% of the study sample.

**Data Extraction and Quality Rating**

One investigator abstracted details about the study design, patient population, setting, interventions, analysis, follow-up, and results. A second investigator reviewed data for accuracy. Two investigators independently applied predefined criteria to assess the quality of each study as good, fair, or poor (11–13). Discrepancies were resolved through a consensus process.

**Data Synthesis**

We assessed the overall strength of each body of evidence as “high,” “moderate,” “low,” or “insufficient” in accordance with the AHRQ “Methods Guide for Comparative Effectiveness Reviews” (14), based on the quality of studies, consistency between studies, precision of estimates, and directness of evidence.

**Role of the Funding Source**

This research was funded by AHRQ’s Effective Health Care Program. Investigators worked with AHRQ staff to develop and refine the scope, analytic framework, and key questions. AHRQ staff had no role in study selection, quality assessment, synthesis, or development of conclusions. AHRQ staff provided project oversight, distributed the draft report for peer review, and reviewed the draft report and manuscript. The investigators are solely responsible for the content of the manuscript and the decision to submit for publication.

**RESULTS**

The search and selection of articles are summarized in the study flow diagram (Appendix Figure, available at www.annals.org). Of 2580 potentially relevant citations, 444 articles were selected for full-text review and 18 met inclusion criteria.

**Mode of Delivery**

Fourteen observational studies reported in 16 publications (sample sizes of 56 to 1034 mother–infant pairs) evaluated the association between mode of delivery and vertical transmission of HCV (Appendix Table, available at www.annals.org) (4, 5, 15–28). Nine studies were conducted in Europe (4, 15–17, 19–21, 23, 25, 27, 28), 2 in Australia (18, 24), 2 in Japan (22, 26), and 1 in the United States (5). Two studies were rated as good quality (5, 15, 16), 4 fair quality (4, 19, 21, 23), and the remainder poor quality. Two reports from the European Pediatric Hepatitis C Network evaluated overlapping populations (15, 16), and 2 studies evaluated nonoverlapping (different periods of enrollment) populations in Dublin, Ireland (19, 21). Only 4 studies adjusted for potential confounders in analyses (4, 5, 15, 16, 19); no study reported baseline characteristics according to mode of delivery or matched women on key potential confounders.

Four studies (5, 15, 19, 21) totaling 2080 mother–infant pairs (2 good-quality [5, 15] and 2 fair-quality [19, 21] studies) compared risk for transmission after elective cesarean delivery before the onset of labor versus vaginal or emergency (after onset of labor) cesarean delivery (Appendix Figure, available at www.annals.org). Three of these studies (5, 19, 21) reported higher transmission risk after vaginal or emergent cesarean delivery, but the difference was statistically significant in only 1 fair-quality study (19). That study (n = 424) reported no cases of transmission after elective cesarean delivery, compared with 7.4% after vaginal or emergency cesarean delivery (adjusted odds ratio, 0.0 [95% CI, 0.0 to 0.87]) (19). The 2 good-quality studies reported conflicting results. One (n = 181) reported a direction of effect that was not statistically significant but was similar to that of the fair-quality study, with a vertical transmission rate of 4.1% (7 of 169) after vaginal or emergent cesarean delivery compared with no cases after 12 elective cesarean births (relative risk, 1.1 [CI, 0.07 to 19]) (5). The other, larger (n = 1034) good-quality study found elective cesarean to be associated with increased risk for vertical transmission compared with vaginal or emergency cesarean delivery (adjusted odds ratio, 1.6 [CI, 0.88 to 2.9]) (15).

Eleven studies (total of 2308 mother–infant pairs) compared the risk for vertical transmission after vaginal versus cesarean delivery, without specifying whether the cesarean delivery was elective or emergent (Appendix Figure) (4, 16–18, 20, 22–28). Ten of the 11 studies (1 good-quality [16], 2 fair-quality [4, 23], and 8 poor-quality [17, 18, 20, 22, 24–28] studies) found no association between mode of delivery and risk for HCV transmission (4, 16–18, 20, 23–28). The exception was 1 small (n = 59), poor-quality Japanese prospective cohort study that reported a statistically significant increase in risk with vaginal delivery in a subgroup of women with high viral load (≥2.5 × 10^6 RNA copies/mL) (22).

**Labor Management**

**Internal Fetal Monitoring**

Three studies (2 good-quality [5, 16] studies and 1 fair-quality [21] study) reported conflicting findings on the relationship between use of internal fetal monitoring and risk for vertical transmission (Appendix Figure). One good-quality study (n = 181) (5) found internal fetal monitoring versus no monitoring was associated with increased risk (adjusted odds ratio, 6.7 [CI, 1.1 to 36]), but another, larger good-quality study (n = 724) found no association (relative risk, 1.2 [CI, 0.70 to 2.2]) (16).
Duration of Rupture of Membranes

One good-quality study (5) and 1 poor-quality study (24) (total of 245 mother–infant pairs) found an association between longer duration of rupture of membranes and increased risk for transmission (Appendix Figure). The good-quality study reported greater risk for vertical transmission in women with membrane rupture longer than 6 hours (odds ratio, 9.3 [CI, 1.5 to 180]) (5). The poor-quality study reported longer average duration of membrane rupture in women who transmitted virus to their infant than in those who did not transmit virus (28 versus 16 hours; \( P = 0.03 \)) (24).

Breastfeeding

Fourteen cohort studies (total of 2971 mother–infant pairs) found no association between breastfeeding by women infected with HCV and risk for transmission to infants (Appendix Figure) (5, 15, 17, 19, 20, 23–32). Most studies prospectively followed infants for at least 1 year. Sample sizes ranged from fewer than 50 (29, 31, 32) to more than 1000 (15). Two studies were rated good quality (5, 15), 2 fair quality (19, 23), and 10 poor quality (17, 20, 24–32). Methodologic shortcomings in the poor-quality studies included failure to perform statistical adjustment on potential confounders and insufficient information to determine comparability of groups at baseline stratified by breastfeeding status.

**DISCUSSION**

Vertical transmission is the leading cause of childhood HCV infection, and identification of effective management strategies to reduce risk for transmission is an important clinical and public health concern. However, the primary finding of this review as summarized in the Table is that no perinatal management strategy has clearly been shown to reduce risk for HCV transmission. Observational studies consistently found no evidence of an association between breastfeeding and risk for vertical transmission, consistent

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### Table. Summary of Evidence: Effect of Mode of Delivery, Labor Management Strategies, or Breastfeeding Practices on Risk for Mother-to-Child Transmission of HCV*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall Strength of Evidence</th>
<th>Studies Identified, n Participants, n</th>
<th>Overall Quality (High, Moderate, Low)</th>
<th>Consistency (High, Moderate, Low)</th>
<th>Directness (Direct or Indirect)</th>
<th>Precision (High, Moderate, Low)</th>
<th>Summary of Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mode of delivery</td>
<td>Low</td>
<td>4 cohort studies 2080</td>
<td>Fair</td>
<td>Moderate</td>
<td>Direct</td>
<td>Low</td>
<td>The 2 good-quality studies found no statistically significant difference in risk for transmission with elective cesarean versus vaginal delivery, with trends in opposite directions</td>
</tr>
<tr>
<td>Any cesarean versus vaginal delivery</td>
<td>Moderate</td>
<td>11 cohort studies 2308</td>
<td>Fair</td>
<td>High</td>
<td>Direct</td>
<td>Low</td>
<td>Ten of 11 studies (1 good-quality) found no statistically significant difference in risk for transmission with cesarean (not specified whether elective or emergent) versus vaginal delivery</td>
</tr>
<tr>
<td>Labor management</td>
<td>Insufficient</td>
<td>3 cohort studies 928</td>
<td>Fair</td>
<td>Moderate</td>
<td>Direct</td>
<td>Low</td>
<td>Three studies (2 good-quality) found inconsistent evidence on the risk for transmission with fetal monitoring, with no association in 2 studies and increased risk for transmission in 1 of the good-quality studies (adjusted OR, 6.7 [95% CI, 1.1–36])</td>
</tr>
<tr>
<td>Internal fetal monitoring versus no internal fetal monitoring</td>
<td>Low</td>
<td>2 cohort studies 245</td>
<td>Fair</td>
<td>High</td>
<td>Direct</td>
<td>Low</td>
<td>Two studies (1 good-quality, 1 poor-quality) found an association between longer duration of rupture of membranes and risk for transmission, with the good-quality study reporting higher risk for transmission with membrane rupture &gt;6 hours (adjusted OR, 9.3 [CI, 1.5–180])</td>
</tr>
<tr>
<td>Breastfeeding</td>
<td>Moderate</td>
<td>14 cohort studies 2971</td>
<td>Fair</td>
<td>High</td>
<td>Direct</td>
<td>High</td>
<td>Fourteen studies found no significant association between breastfeeding and risk for transmission</td>
</tr>
</tbody>
</table>

HCV = hepatitis C virus; OR = odds ratio.

* The full report is available on the Agency for Healthcare Research and Quality Web site at www.effectivehealthcare.ahrq.gov (9).
with data suggesting that transmission typically occurs in utero (23, 33). Evidence on the effects of labor management strategies and mode of delivery on risk for transmission was somewhat conflicting. Two studies (5, 24) reported increased risk for HCV transmission with more prolonged duration of ruptured membranes, similar to findings for other infectious agents transmitted vertically (such as group B streptococcus and HIV). However, other studies did not find vaginal delivery associated with increased risk for vertical transmission versus cesarean delivery, and the largest single study (15) reported a non-statistically significant trend toward decreased risk, even though vaginal delivery is associated with longer duration of ruptured membranes. Possible explanations for the failure to find an association between vaginal delivery and increased risk for transmission could include threshold or modifying effects related to the duration of rupture, viral load, or other factors. Cohort studies that focus on women with longer rupture of membranes or high viral load and perform statistical adjustment on other potential confounding factors could help clarify the effects of mode of delivery on transmission risk. Randomized trials are less susceptible to confounding but would involve potential challenges related to the acceptability of randomly assigning HCV-infected women to elective cesarean delivery versus planned vaginal birth.

Other reviews and reports were consistent with our findings. A review of cesarean delivery versus vaginal delivery for preventing mother-to-infant HCV transmission found no randomized trials and concluded that a systematic review of observational studies is needed (34). A 2007 American College of Obstetricians and Gynecologists report identified a possible association between prolonged rupture of membranes after labor and increased risk for vertical transmission but concluded that no preventive measures have been proven effective for reducing the risk for mother-to-infant transmission (35).

Our review has limitations. Evidence on the effects of interventions to prevent mother-to-infant transmission was restricted to observational studies, most with methodological shortcomings (including failure to adjust for confounders) and small sample sizes. If practices that are more effective at reducing transmission are preferentially used in women at higher risk, this could have biased results toward null findings. We excluded non–English-language articles, which could result in language bias. We were also unable to formally assess publication bias due to small numbers of studies and methodological shortcomings in the studies.

This review was conducted as part of a larger review on HCV screening (9). For prenatal screening to be effective, there must be an effective intervention. Our findings indicate that avoidance of breastfeeding is not warranted to reduce risk for vertical transmission. Given limited evidence of an association between prolonged rupture of membranes and increased transmission risk, clinicians may consider avoiding prolonged rupture of membranes in HCV-infected women until more definitive data are available.

From Oregon Health & Science University, Portland, Oregon.

Disclaimer: The findings and conclusions in this document are those of the authors, who are responsible for its content, and do not necessarily represent the views of AHRQ. No statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

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Current author addresses and author contributions are available at www.annals.org.

References


10. Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce


Annals of Internal Medicine

**Current Author Addresses:** Drs. Cottrell, Chou, Wasson, Rahman, and Guise: 3181 SW Sam Jackson Park Road, Mail Code BICC, Portland, OR 97239.


**Appendix Figure. Summary of evidence search and selection.**

Records identified through database searching and other sources* ($n = 2580$)

Records after duplicates removed ($n = 2499$)

Records screened ($n = 2499$)

Records excluded ($n = 2055$)

Full-text articles assessed for eligibility ($n = 444$)

Full-text articles excluded ($n = 426$)

Studies included in synthesis ($n = 18$)†

The flow diagram summarizes the search and selection of articles addressing the effect of mode of delivery, labor management strategies, or breastfeeding practices on risk for mother-to-infant transmission of hepatitis C virus. Reproduced from reference 9.

* Includes hand searches and gray literature searches.
† One study resulted in 2 publications.
### Appendix Table. Studies on Mode of Delivery, Labor Management Strategies, and Breastfeeding Practices and Mother-to-Infant Transmission of HCV

<table>
<thead>
<tr>
<th>Study, Year; Country (Reference)</th>
<th>Quality</th>
<th>Participants, n</th>
<th>Age, y</th>
<th>Nonwhite Participants, %</th>
<th>HIV-Positive Participants, %</th>
<th>HCV Viral Load, RNA copies ×10^6/L</th>
<th>Results* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mode of delivery</strong></td>
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<tr>
<td>Elective cesarean versus vaginal delivery/emergent cesarean</td>
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<tr>
<td>EPHN (Tovo), 2005; Italy, Spain, Germany, Ireland, Scotland, Belgium, Sweden (15)</td>
<td>Good</td>
<td>1034</td>
<td>Mean (SD), 31.7 (5.17)</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>Rates NR, OR, 1.57 (0.88–2.83); P = 0.13; unadjusted OR, 1.59 (0.88–2.86); P = 0.13; adjusted for sex, mode of delivery, prematurity, and breastfeeding</td>
</tr>
<tr>
<td>Gibb et al, 2000; Ireland, United Kingdom (19)</td>
<td>Fair</td>
<td>424</td>
<td>Mean (SD), 27 (6)</td>
<td>5</td>
<td>NR</td>
<td>NR</td>
<td>0/31 (0%) versus 29/393 (7.4%); OR, 0 (0–0.87); P = 0.04; adjusted for HIV status and breastfeeding</td>
</tr>
<tr>
<td>Mast et al, 2005; United States (5)</td>
<td>Good</td>
<td>181</td>
<td>&lt;20 y: 7 (2.9%); 20–29 y: 103 (42.9%); 30–39 y: 120 (49.6%); ≥40 y: 12 (4.9%)</td>
<td>0/31 (0%) versus 29/393 (7.4%); Mean HCV RNA level at delivery: 2.38</td>
<td>RR, 1.1 (0.07–19)</td>
<td>0/12 (0%) versus 7/169 (4.1%); adjusted for breastfeeding, maternal age at delivery, center category</td>
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<tr>
<td>McMenamin et al, 2008; Ireland (21)</td>
<td>Fair</td>
<td>441</td>
<td>Median (range), 26 (16–44)</td>
<td>5.9</td>
<td>NR</td>
<td>1/33 (3%) versus 17/408 (4.2%); RR, 0.73 (0.09–5.30)</td>
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<tr>
<td><strong>Total</strong></td>
<td></td>
<td>2080</td>
<td></td>
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<tr>
<td><strong>Any cesarean (elective or emergent) versus vaginal delivery</strong></td>
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<td></td>
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<tr>
<td>EPHN (Pembrey), 2001; Italy, Spain, Germany, Ireland, Scotland, Belgium, Sweden (16)</td>
<td>Good</td>
<td>884</td>
<td>&lt;20 y: 219 (17%); 20–25 y: 563 (43%); 30–39 y: 495 (38%); ≥40 y: 34 (3%)</td>
<td>0</td>
<td>NR</td>
<td>15/218 (6.9%) versus 39/666 (5.9%); OR, 1.17 (0.59–2.31); adjusted for breastfeeding, maternal age at delivery, center category</td>
<td></td>
</tr>
<tr>
<td>Ceci et al, 2001; Italy (4)</td>
<td>Fair</td>
<td>78</td>
<td>Median (range), 30 (21–42)</td>
<td>0/2: 9 (15%); &gt;0.2: 51 (85%)</td>
<td>NR</td>
<td>1/106 (0.9%) versus 7/259 (2.7%); RR, 0.35 (0.04–2.80)</td>
<td>No association (data not reported)</td>
</tr>
<tr>
<td>Conte et al, 2000; Italy (17)</td>
<td>Poor</td>
<td>365</td>
<td>Mean (SD), 30.9 (5.2)</td>
<td>4%</td>
<td>NR</td>
<td>0/22 (0%) versus 3/61 (4.9%); RR not calculated</td>
<td></td>
</tr>
<tr>
<td>Garland et al, 1998; Australia (18)</td>
<td>Poor</td>
<td>83</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>0/14 (7.1%) versus 1/66 (1.5%); RR, 4.71 (0.31–70.94)</td>
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<tr>
<td>La Torre et al, 1998; Italy (20)</td>
<td>Poor</td>
<td>80</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>0/18 (0%) versus 7/41 (14%); RR not calculated (P = 0.045)</td>
<td></td>
</tr>
<tr>
<td>Okamoto et al, 1999; Japan (22)</td>
<td>Poor</td>
<td>59</td>
<td>NR</td>
<td>0/2: 5.2; 21 (25%)</td>
<td>NR</td>
<td>0/18 (0%) versus 7/41 (14%); RR not calculated (P = 0.045)</td>
<td></td>
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<tr>
<td>Resti et al, 1998; Italy (23)</td>
<td>Fair</td>
<td>275</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>4/62 (6.5%) versus 9/213 (4.2%); RR, 1.53 (0.48–4.79)</td>
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<tr>
<td>Spencer et al, 1997; Australia (24)</td>
<td>Poor</td>
<td>63</td>
<td>Mean: 30</td>
<td>0</td>
<td>NR</td>
<td>0/17 (14%) versus 5/55 (9.1%); RR, 1.57 (0.21–11.6)</td>
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<tr>
<td>Syriopoulou et al, 2005; Greece (25)</td>
<td>Poor</td>
<td>56</td>
<td>Mean (SD), 29.6 (3)</td>
<td>2</td>
<td>NR</td>
<td>0/17 (0%) versus 2/39 (5.1%); RR not calculated (P = 0.34)</td>
<td></td>
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<tr>
<td>Tajiri et al, 2001; Japan (26)</td>
<td>Poor</td>
<td>114</td>
<td>NR</td>
<td>0/2: High: 46 (40%); Low: 27 (24%); NR: 41 (36%)</td>
<td>RR</td>
<td>1/24 (4.2%) versus 8/90 (8.8%); RR, 0.46 (0.61–3.53)</td>
<td></td>
</tr>
<tr>
<td>Zanetti et al, 1998, (28) and 1999 (27); Italy</td>
<td>Poor</td>
<td>251</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>1/58 (1.7%) versus 7/193 (3.6%); RR, 0.48 (0.06–3.79)</td>
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<tr>
<td><strong>Total</strong></td>
<td></td>
<td>2308</td>
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<tr>
<td><strong>Labor management</strong></td>
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<tr>
<td>Internal fetal monitoring versus no internal fetal monitoring</td>
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</tr>
<tr>
<td>EPHN (Pembrey), 2001; Italy, Spain, Germany, Ireland, Scotland, Belgium, Sweden (16)</td>
<td>Good</td>
<td>724</td>
<td>&lt;20 y: 219 (17%); 20–25 y: 563 (43%); 30–39 y: 495 (38%); ≥40 y: 34 (3%)</td>
<td>0</td>
<td>NR</td>
<td>11/93 (11.8%) versus 58/631 (9.2%); RR, 1.24 (0.70–2.2)</td>
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### Appendix Table—Continued

<table>
<thead>
<tr>
<th>Study, Year; Country</th>
<th>Quality</th>
<th>Participants, n</th>
<th>Age, y Participants, %</th>
<th>HIV-Positive Participants, %</th>
<th>HCV Viral Load, RNA copies &lt;10^6/L</th>
<th>Results* (95% CI)</th>
</tr>
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<tr>
<td><strong>Breastfeeding versus no breastfeeding</strong></td>
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<tr>
<td>Mast et al, 2005; United States (5)</td>
<td>Good</td>
<td>182</td>
<td>&lt;20 y: 7 (2.9%)&lt;br&gt;20–29 y: 103 (42.9%)&lt;br&gt;30–39 y: 120 (49.6%)&lt;br&gt;≥40 y: 12 (4.9%)&lt;br&gt;67.4</td>
<td>0</td>
<td>Mean HCV RNA level at delivery: 2.38</td>
<td>3/16 (18.8%) versus 4/165 (2.4%); RR, 7.7 (1.9–31.6); P = 0.02; unadjusted for maternal demographic characteristics, HCV RNA level, history of intravenous drug use, and cigarette smoking during pregnancy</td>
</tr>
<tr>
<td>McMenamin et al, 2008; Ireland (21)</td>
<td>Fair</td>
<td>23</td>
<td>Median (range), 26 (16–44) NR</td>
<td>5.9</td>
<td>NR</td>
<td>Infant HCV RNA-positive: 0/11 (0%); Infant not tested for HCV: 12</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>928</td>
<td></td>
<td></td>
<td></td>
<td>Mean duration (SD), transmitted versus not transmitted: 28 (10) h versus 16 (4) h (P = 0.03)</td>
</tr>
<tr>
<td><strong>Prolonged rupture of membranes versus less prolonged rupture of membranes</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Mast et al, 2005; United States (5)</td>
<td>Good</td>
<td>182</td>
<td>&lt;20 y: 7 (2.9%)&lt;br&gt;20–29 y: 103 (42.9%)&lt;br&gt;30–39 y: 120 (49.6%)&lt;br&gt;≥40 y: 12 (4.9%)&lt;br&gt;67.4</td>
<td>0</td>
<td>Mean HCV RNA level at delivery: 2.38</td>
<td>&lt;1 versus 1–5 versus 6–12 versus ≥13 h: 0/53 versus 1/59 (1.7%) versus 4/40 (10%) versus 2/30 (6.7%); P = 0.02; Membrane rupture &gt;6 h: OR, 9.3 (1.5–179.7); adjusted for maternal demographic characteristics, HCV RNA level, fetal monitoring, history of intravenous drug use, and cigarette smoking during pregnancy</td>
</tr>
<tr>
<td>Spencer et al, 1997; Australia (24)</td>
<td>Poor</td>
<td>63</td>
<td>Mean: 30 NR</td>
<td>0</td>
<td>NR</td>
<td>Mean duration (SD), transmitted versus not transmitted: 28 (10) h versus 16 (4) h (P = 0.03)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>245</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**EPHN = European Paediatric Hepatitis C Virus Network; HCV = hepatitis C virus; NR = not reported; OR = odds ratio; RR = relative risk.**<br>* Unadjusted unless otherwise indicated.