Evidence Table 10: Key Question 7. Pregnancy Intervention Observational Studies

| **Author, yearCountryStudy NameOverall Quality** | **Study Type** | **Definition of mother-to-child transmission** | **Confounders assessed in analysis** | **Duration of followup** | **Eligibility**  | **Exclusion**  | **Number screened/ eligible/ enrolled/ analyzed** | **Demographic characteristics of study population**  | **HCV genotypeHCV viral loadHIV infectionIV drug use** | **Overall transmission**  | **Transmission by labor mgmt:Intra-uterine pressure catheter (IUPC)** |
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| Ceci, 2001156ItalyFair | Prospective cohort study | Presence of anti-HCV antibodies beyond 18 months or HCV-positive on two separate tests | HCV maternal risk factors (exposure to blood products and IVDU), HCV viral load, HCV genotype, gestational age, mode of delivery, birth weight | 24 months | HCV-positive, HIV-negative women | HIV-positive | 2447/78/78/78 | **Maternal age (n=78)**Median (range): 30 (21-42)**\*Characteristics of HCV-RNA positive mothers (n=60)HCV risk factors**Absent: 25 (42%)Blood transfusion: 14 (23%)IVDU: 20 (33%)Blood transfusion and IVDU: 1 (2%)**Mode of delivery**Vaginal: 43 (72%)Cesarean: 17 (28%)**Gestational age**<36 weeks: 9 (15%)>=36 weeks: 51 (85%)**Birth weight**<2500g: 14 (23%)>=2500g: 46 (77%) | **Maternal HCV-RNA status (n=78)**Positive: 60 (77%)Negative: 18 (23%)**\*Characteristics of HCV-RNA positive mothers (n=60)genotype**1a: 9 (15%)1b: 25 (42%)2a: 20 (33%)3: 6 (10%)**Viral load**<0.2X106: 9 (15%)>0.2X106: 51 (85%) | **Overall transmission (n=78)**2 consecutive positive tests: 8 (10%)24 month followup: 2 (3%)\*not adjusted | Not reported |
| Conte, 2000157ItalyPoor | Prospective cohort study | Newborns of anti-HCV positive mothers were tested at birth (on cord blood samples) and infants underwent determination of AST, ALT, anti-HCV and HCV/RNA after 4, 8, 12, and 18 months  | Not Reported | First month of pregnancy through 18 months after birth | Anti-HCV positive pregnant women between 1/95 and 12/98 attending Ob/Gyn unit of local Ospedale Maggiore (living in area of about 20 km around Bergamo in northern Italy) | Not Reported | 15,250/370/370/370 | **Maternal age (n=370) mean (SD):** 30.9 (± 5.2)**Mode of delivery (n=370)**Vaginal: 259 (71%)Cesarean: 106 (29%) | **Maternal HCV/RNA status (n=370)**Positive: 266 (72%)Negative: 104 (28%)**Maternal genotype (n=370):**1a: 51 (19%)1b: 82 (31%)2: 64 (24%)3a: 53 (20%)4: 5 (2%)Indeterminate: 11 (4%)**Maternal HIV infection (n=370)**Yes**:** 15 (4%)No: 355 (96%)**Past or current IVDU (heroin only) (n=370)** 118 (32%)**Past blood transfusions (n=370)**68 (18.4%) | **HCV/RNA+** at birth (n=366): 18 (4.9%)4 months (n=167): 8 (4.8%)8 months (n=161): 8 (5%)12 months (n=155): 8 (5.1%)  | Not Reported |
| European Pediatric Hepatitis C Virus Network, 2001158 (Pembrey)Italy, Spain, Germany, Ireland, Scotland, Belgium, SwedenGood | Multicenter prospective cohort study | Infected: antibody positive beyond 18 months and/or had at least two positive PCR tests (on 2 separate occasions)Indeterminate: born more than 18 months before data collection, antibody positive before 18 months of age, and either 1) no PCR performed, 2) no positive PCR result, or 3) only a single PCR result | Mode of delivery, breastfeeding, HIV status, maternal age at delivery | At least until 18 months of age | Mother HCV positive at or before delivery or baby identified as HCV positive within 1 month of delivery & maternal infection confirmedChildren born on or after Jan 1 1992 (when 2nd generation tests widely used) and at least 18 months at last laboratory assessment (or born more than 18 months before data collection and no longer in followup) | Children with a history of blood transfusion | 1655 mother-child pairs/1474 children/1474/1474 (916 HIV-) | **Maternal age (n=1311)**<20: 219 (17%) 20-25: 563 (43%)30-39: 495 (38%)>=40: 34 (3%)**Gestational age (n=1248)**<36 weeks: 105 (8%)>=36 weeks: 1143 (92%)**Low birth weight (<2500g) (n=1362)**Yes: 523 (38%)No: 839 (62%)**Fetal scalp monitors (n=724)**Yes: 93 (13%)No: 631 (87%)**Mode of delivery (n=1400)**Cesarean: 382 (27%)Vaginal: 1018 (73%)**Breastfeeding (n=1424)**Breastfed: 351 (25%)Not breastfed: 1073 (75%)**Other infections in pregnancy (n=996)**Yes: 90 (9%)No: 906 (91%) | **Maternal HIV infection (n=1419)**Yes: 503 (35%)No: 916 (65%)**Maternal IV drug use (n=1384)**During this pregnancy: 362 (26%)Yes, but not during pregnancy: 455 (33%)Never: 567 (41%)**Maternal history of hepatitis (n=1038)**Yes: 421 (41%)No: 617 (59%) | **Overall transmission (n=1474)**136 (9.2%)\*not adjusted | Not Reported |
| European Pediatric Hep C Virus Network, 2005159 (Tovo)Italy, Spain, Germany, Ireland, UK, Norway, SwedenGood | Multicenter prospective cohort study | Children considered infected if they had >=2 positive HCV RNA PCR test results and/or were anti-HCV antibody positive after 18 months. Children considered uninfected if they had <2 positive HCV RNA PCR test results and <=2 negative HCV RNA PCR rest results and/or were anti-HCV antibody negative after 18 months.  | To account for differences between centers in the HCV RNA PCR assays used to determine infection, and to allow for center-associated unobserved differences in background characteristics, the authors incorporated a random effect in the multivariable models at the center level | Children received clinical examinations at birth, 6 weeks, and 3, 6, 9, 12, 18, and 24 months; and thereafter every 6 months if infected or every year if uninfected  | HCV infected mothers and their singleton infants or first-born infants from multiple pregnancies with confirmed HCV infection status. | Second-born twins and second- and third-born triplets were excluded. Mother-infant pairs with infants of indeterminate infection status were excluded. | 1787/1479/1479/1220 (1034 HIV-) | **Maternal age (n=1205)**Mean (SD): 31.7 (5.17)Median (range): 32 (17.1-45.1)**Mode of delivery (n=1455)**Vaginal: 764 (52.5%)Emergency CS: 160 (11%)Elective CS: 480 (33%)CS (unspecified): 51 (3.5%)**Infant feeding type (n=1357)**Breast-fed: 452 (32.7%)Formula fed: 930 (67.3%)**Sex of child (n=1470)**Male: 802 (54.6%)Female: 668 (45.4%)**Gestational age (n=1382)**<=34 weeks: 97 (7%)35-36 weeks: 122 (8.8%)>=37 weeks: 1163 (84.2%) | **Maternal HIV infection (n=1391)**Yes: 208 (15%)No: 1183 (85%)**Child HIV infection (n=1435)**Yes: 10 (0.7%)No: 1397 (97.4%)Indeterminate: 28 (1.9%)**Maternal IV drug use (n=1162)**History: 448 (38.6%)No history: 714 (61.4%) |   |   |
| Garland, 1998160AustraliaPoor | Prospective cohort study | Infants tested at 3, 6 and 12 months for HCV antibodies. Testing included detection of antibody to HCV, and genotyping for presence of 1a, 2a, 2b, 3 a, 4 & 6 HCV genotypes.  | NR/Unclear: Collected data on age, parity, type of delivery, time of rupture, drug use, scalp electrodes and breastfeeding but did not indicate if adjustment for confounding was analyzed. | Three years; followup included seropositive women, their newborns & siblings of the newborns.  | Women with a history of illicit IV drug use, seen in the Chemical Dependency Unit (CDU) of the Royal Women's Hospital and subject to routine screening for HCV. Women with positive anti-HCV test results.  | Not Reported | Not Reported/84/83/83 women, 91 newborns & 16 siblings of newborns  | **Mode of delivery (n=83)** Vaginal: 61 (74%) | **Maternal HIV infection (n=83)**Yes: 0 (100%) **Maternal IV drug use** (n=83) Yes: 83(100%)  | 3/91 (3%) | Not Reported |
| Gibb, 2000161Ireland, UKFair | Prospective cohort study | Positive result for HCV antibody within 90 days of birth | adjusted for HIV status, breastfeeding, and mode of delivery  | 24 months | Mother known to be HCV infected during pregnancy or if child had positive result for HCV antibody within 90 days of birth | UK children born before 1996 | 499/441/441/441 | **Maternal age (n=441)** Mean (SD): 27 (6)**Race (n=441)**White: 413 (94%)Non-white: 28 (6%)**Breastfeeding (n=414)**Yes: 59 (14%)No: 355 (86%)**Mode of delivery (n=424)**Vaginal: 339 (80%)Emergency cesarean: 54 (13%) Elective cesarean: 31 (7%) | **Maternal HIV infection (n=441)**Yes: 22 (5%)No: 328 (74%)Unknown: 91 (21%)**Maternal IV drug use (n=441)**History: 343 (78%) No history: 98 (22%) | **Overall (n=441)**6.7% (4.1-10.2)unadjusted | Not Reported |
| LaTorre, 1998162ItalyPoor  | Prospective cohort study | Babies were tested for ALT levels, anti-HCV antibodies by ELISA III and RIBA II and HCV-RNA by RT-PCR. Babies who retained anti-HCV antibodies through 12 months were considered infected | none | Blood test and clinical evaluation of infants within days after birth and then every 4 months for 2 years | Mothers who tested anti-HCV positive before delivery and were HIV negative | Mothers who tested negative for HCV or positive for HIV | 5025/5000/80/80 | **Mode of delivery (n=80)**Vaginal: 66 (82.5%)\*52/66 were HCV-RNA positivecesarean: 14 (17.5%)**Breastfeeding (n=80)**yes: 24 (30%)\*Including 10 HCV-RNA positive and 14 HCV-RNA negative women | **Maternal HCV-RNA status (n=80)**Positive: 56 (70%)Negative: 24 (30%)**HCV viral load (n=19)**ALT increase>40 U/L: 18 (32.5%)**Maternal IV drug use (n=80)**Yes:34 (43%)**Blood transfusion (n=80)**10 (12%) | **Overall transmission (n=80)**2/80 (2.5%) | Not Reported |
| Lin, 1995163Republic of ChinaPoor | Prospective cohort study  | Detection of HCV antibodies (serum); detection of HCV RNA in infants tested at 1, 3, 6, 9 or 12 months of age | Not Reported | Up to 12 months | HCV infected mothers | NR | Not Reported/40/15/+3 healthy controls15 | Not Reported | **HCV viral load**(n=15) RNA titers 102 to 2.5 x 108copies/mL **HIV infection** None | 0/15 (0%) | Not Reported |
| Mast, 2005164US (Houston & Honolulu)Good | Prospective cohort study | Infant serum collected at birth and 8 well-child visits. Testing included detection of antibody to HCV, detection of HCV RNA (qualitative and quantitative), and genotyping.  | Variables with p<.1 from the univariate analysis and maternal demographic characteristics included in multivariate analysis | Infants born to HCV+ mothers followed from birth to >=12 months, HCV-infected infants followed annually until age 5 | Women presenting for prenatal care (and in Houston, those who didn't receive prenatal care who presented for delivery at 2 county hospitals) were offered testing. Women with positive anti-HCV test results were invited to enroll (those with indeterminate status were invited to enroll until HCV status was confirmed).  | Mothers with serum testing as RIBA indeterminate and HCV RNA negative were excluded from the analysis.  | 75,909/567/332/242 women & 244 infants | **Age (n=242)**<20: 7 (2.9%)20-29: 103 (42.6%)30-39: 120 (49.6%)>=40: 12 (4.9%)**Race (n=242)**White: 79 (32.6%)Black: 77 (31.8%)Hispanic: 49 (20.3%) | **Mother HCV RNA+ (n=242)**At enrollment or delivery: 194 (79.5%)Both: 179 (77.2%)Delivery: 5 (2.2%) Enrollment: 4 (1.7%)**Maternal HIV infection (n=242):** Yes: 11 (4.5%)**HIV and HCV RNA+ (n=242)**7 (2.9%)**Maternal** **IVDU (n=242)**126 (52.3%) **Geometric mean HCV RNA level at delivery (n=194)**HIV-: 2.38\*106**Maternal HCV genotype (n=116)**Genotype 1a: 76 (66%)Genotype 1b: 16 (14%)Genotype 2b: 10 (9%)Genotype 3a: 13 (11%)Genotype 4a: 1 (.01%) | 9/244(3.7%) | Not Reported |
| McMenamin, 2008165 Ireland Fair | Retrospective cohort study | Positive neonatal results for HCV antibody after 1 month of age | None | Infant HCV RNA samples tested at median of 6 weeks after delivery, mean 12.5 weeks (range 4-166 weeks) | Mothers who tested positive for HCV antibody antenatally and delivered a liveborn infant, HCV positive mothers identified through the National Virus Reference Laboratory | Mothers who tested negative for HCV antenatally or mothers who tested positive for HCV antenatally and miscarried or had a stillbirth | 26,390/559/559/441 | **Maternal age (n=559)**Median (range): 26 (16-44)**Mode of delivery (n=559)**Vaginal delivery: 443 (79%) Emergency cesarean: 72 (13%)Planned pre labor cesarean: 44 (8%)**Gestation (n=559)**Median (range): 39 (28-42)**Intrapartum procedures (n=559)**Intrapartum fetal blood sample: 1 (.002%)Fetal scalp electrode: 23 (4%) | **Maternal HIV infection (n=559)**Yes: 18 (3%)**Maternal HBV status (n=559)**Positive: 3 (0.5%)**Maternal HCV RNA status (n=559)**Positive: 295 (53%)Negative: 166 (30%)Missing: 98 (17%) | **Overall transmission (n=441)** 18/441 (4.1%) | Not Reported |
| Moriya, 1995166 JapanPoor | 2 prospective cohort studies, additional pediatric chart review | Infants testing positive for antibody to HCV | Not Reported | 12 months, up to 24 months | Infants born to mothers who were HCV RNA positive | Not Reported | 16714/163/100 mothers/ 84 mothers, 87 infants | Not Reported | **Maternal HIV infection** None(n=84) **Maternal genotype (n=4)**Type 111/2a: n=2Type 11/1b: n=2 | 2/87 (2.3%) ("during followup period") | Not Reported |
| Okamoto et al, 2000167Japan (Tottori University & Medical Center)Poor | Prospective cohort study | Positive test for HCV RNA by RT-PCR analysis with high titers of HCV RNA within 3 months of age.Serum samples of the children born to Ab1 mothers were tested for anti-HCV antibody, HCV RNA, and liver function approximately every 3 months during the first year and biannually thereafter.  | Not Reported | Minimum followup period was 6 months | Pregnant women were screened for anti-HCV antibody in Tottori Prefecture, Japan. None of the mothers had risk factors for HIV infection | Not Reported | 21791/NR Eligible/NR Enrolled/59 | **Mode of delivery (n=84)**Vaginal: 56 (66%) Cesarean: 28 (33%) | **Maternal HCV/RNA status (n=84)**Positive: 50 (60%)**Maternal viral load (n=84)** **high (≥ 2.5 x 106 copies/mL):** 21 (25%) | 7/84 (8%) | Not Reported |
| Pipan, 1996168ItalyPoor | Prospective cohort | HCV/RNA detection in children over a period of 12 months | none | Every three months for one year | Anti-HCV positive pregnant women, no history of Hepatitis B, no apparent source of HCV exposure | History of Hepatitis B, apparent source of HCV exposure | 1338/36/25/25 | **Maternal age (n=25)** Median (range)26.4 (19-35) | **Maternal HCV/RNA+ (n=25)**Positive**:**18 (72%) | **Infant HCV/RNA+ at birth** **(n=25)**None**Infant HCV/RNA+ at 12 months** **(n=25)** 0  | Not Reported |
| Resti, 1998169ItalyFair | Prospective cohort study | Children were considered infected when hepatitis C virus RNA was detected or when anti­bodies to the virus persisted beyond age 2 years or reappeared after having disappeared. Alanine aminotransferase concentrations were defined as raised if they were higher than twice the upper limit of normal | Study data suggests that there may be a higher risk of vertical transmission in mothers with a higher viral titre, but theresults were not significant.IV drug users were not excluded from analysis, but authors suggest inclusion of these mothers did not significantly impact findings | Median followup in the 403 children who completed the study was 28 (24-38) months | 19 centres participated in the studyWomen (and their babies) with confirmed hepatitis C antibodies but negative for HIV­1 | History of blood product transfusions or IV drug use was carefully investigated by face to face interviewswith experienced pediatricians using standardizedquestionnaires, but these individuals were not excluded | NR/442/403/403 & 403 infants (275 RNA+ mothers) | **RNA+/HIV- mothers (n=275)Mode of delivery** Vaginal: 213 (77%) Caesarean: 62 (23%)**Breastfeeding** Yes: 87 (32%) No: 188 (68%) | **Maternal IVDU (n=275)**111 (80%) | 13/275 (4.7%) | Not Reported |
| Spencer, 1997170AustraliaPoor | prospective cohort study | Presence of HCV RNA in serum collected from infant anytime during followup. | Potential maternal risk factors assessed: duration/type of drug use, alcohol, smoking, past HBV infection, age | At least 6 months, up to 6 years when possible | HCV positive and HCV negative pregnant women, IVDU on methadone maintenance program and their infants | Not Reported | Not Reported/Not Reported/131/125 anti-HCV+, 63 HCV RNA+ | **Maternal age** mean: 30  | **Maternal HCV RNA status (n=125)** **Positive:** 63 (62.4%)**Maternal genotype****transmitting mothers**Type 1a: 5 (83.3%)Type 3a: 1 (16.7%)**Non-transmitting mothers**Type 1: 1 (1.6%)Type 1a: 36 (57.1%)Type 1b: 4 (6.3%)Type 2a: 1 (1.6%) Type 2b: 2 (3.2%)Type 3a: 18 (28.6%)Untypeable: 1 (1.6%)**HIV infection**None **IVDU** 131 (100%) | 6/63 (9.5%) (at 18 months) | Not Reported |
| Syriopoulou, 2005171GreecePoor  | Prospective cohort study  | HCV/RNA+ more than 2 times after 3 months and/or anti-HCV+ after 18 months  | Univariate analysis of IVDU, mother's age, mode of delivery, genotype, type of feeding (but no multivariate analysis) | Every three months until 1 year of age, then every 6 months | Anti-HCV positive pregnant women | Not Reported | NR/86/86/86 mother-child pairs | **Mean age at delivery** (SD): 29.6 (+/- 3 yrs)**Mode of delivery (n=86)**Vaginal: 53 (62%)Cesarean: 33 (38%) | **Maternal HCV genotype (n=54)**3a: 23 (42%)1a: 10 (19%)1b: 7 (13%)1a/1b: 6 (11%)2a/2c: 6 (11%)4c/4d: 2 (4%)**Maternal HCV/RNA status (n=86)**Positive:56 (65%)**Maternal HIV infection (n=86)**Yes:1 (1%)**IVDU (n=86)**during pregnancy:2 (2%)before pregnancy: 6 (7%) | **Overall transmission (n=86):**2 (2.3%) | Not Reported |
| Tajiri, 2001172Japan (seven hospitals in the Osaka metropolitan area)Poor | Prospective cohort study | Babies were tested for serum alanine aminotransferase (ALT) activity, anti-HCV antibodies and HCV RNA at 0, 3, 6, 9, 12 months and every year thereafter. Babies with repeated positive HCV RNA tests were considered infected. | Not Reported | All infants were followed 9 to 61 months | Pregnant women who tested positive for anti-HCV antibodies  | Not Reported | 16800/154/141/114 | **Route of transmission (n=141)**Mother-to-child: 9/141 (6%)Blood transfusion: 31/141 (22%)Accidental needle stick injury: 3/141 (2%)HCV carriers in their families: 11/141 (8%)Other/unidentified: 87/141 (62%)**Mode of delivery (n=114)**Vaginal: 90 (21%)Cesarean: 24 (79%) | **Maternal IVDU**None**Maternal HIV infection (n=73)**Positive: 0Negative: 73Not tested: 68(68 not tested because HIV infection is not endemic in Japan including the areas studied (adult rate of infection, 0.01%)**Maternal HCV viral load**High: 46 (63%)Low: 27 (37%) | 9/114 (7.8%) | Not Reported |
| Tanzi, 1997173ItalyPoor | Prospective cohort study | presence of antibodies for one or more HCV antigens at birth, 3, 6, 10, and 18 months | None | 18 months | Women admitted to the Maternity Clinic of University of Parma from January to December 1993, those who tested positive for antibodies were invited to submit their children for period checks | Not Reported | 1347/1347/1347/1347  | NR | **Maternal anti-HCV+ (n=1347)**31 (2.3%)**Maternal** **HCV-RNA+ (n=1347)**18 (1.3%)**Maternal HIV infection (n=1347)** 4 (.27%) | **Overall transmission (n=32)Infant HCV/RNA+**at birth: 2 (6%)at 3, 6, 10, 18 months: 0 (0%)**Infant anti-HCV+**at birth: 32 (100%)at 18 months: 0 (0%) | Not Reported |
| Zanetti, 1998174(Intervirology)ItalyA prospective Study on Mother-to-Infant Transmission of Hepatitis C virusZanetti, 1999175(Journal of Hepatology)ItalyMother-to-infant transmission of hepatitis C virusPoor | Prospective cohort study | Detection of HCV-RNA, persistence of anti-HCV beyond 18 months of age or ex novo production of antibody were assumed to represent evidence of infection | Not Reported | For babies born to HCV seropositive mothers,peripheral blood sampling, laboratory and clinical evaluations werescheduled at birth, about every 3 months during the 1st year of lifeand then every 6 months. | Infants born to HCV-infected mothers, including mothers with history of IV drug use who were screened for HIV antibodies. | Not Reported | 40000+/482/291/291 & 291 infants | Not Reported | **Maternal HIV infection (n=291)**Yes: 40 (14%)**Maternal HCV/RNA status**(n=291)Positive: 251 (86%)**Maternal genotype (n=17)**3a: 6/17 1a: 4/172a: 3/171b: 2/174a: 1/174c/4d: 1/17 | HCV+: 17/291 (5.8%) HCV+/HIV+: 3/17 (17.6%) | Not Reported |

| **Author, yearCountryStudy NameOverall Quality** | **Transmission by labor mgmt:Fetal monitoring** | **Transmission by mgmt:Rupture of membranes**  | **Transmission by route of delivery** | **Transmission by type of infant feeding** | **Transmission by other risk factors (maternal)** | **Transmission by other risk factors (child)** | **Sub-group analyses** | **Adverse events** | **Funding source** | **(Cont'd)Transmission rate by other risk factors (maternal)** | **(Cont'd)Transmission rate by other risk factors (maternal)** |
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| Ceci, 2001156ItalyFair | Not Reported | Not Reported | No association (data NR) | Not Reported | Transmission from women with no known risk of infection was significantly lower (RR=0.17%, 0.04-0.73%; p=0.0063)  | Not Reported  | Not Reported | Not Reported | Not Reported | **By maternal blood transfusion (n=38)2+ positive tests vs. 0 positive tests**3/8 (37.5%) vs. 2/30 (6.7%), p<0.05**By maternal viremia (n=38)2+ positive tests vs. 0 positive tests**6.90 +/- 5.87 x 106vs. 3.93 +/- 2.94 x 106 |   |
| Conte, 2000157ItalyPoor | Not Reported | Not Reported | **Cesarean vs. vaginal (n=365)**1/106 (1%) vs. 7/259 (2.7%) \*RR: .245 (.275- 49.463) | **Breast vs. formula (n=370)**2/90 (2%) vs. 6/280 (2%)\*RR: 1.02 (.305-3.45) | Not Reported | Not Reported | Not Reported | Not Reported | Not Reported |   |   |
| European Pediatric Hepatitis C Virus Network, 2001 (Pembrey)158Italy, Spain, Germany, Ireland, Scotland, Belgium, SwedenGood | **Fetal scalp monitoring during delivery (yes vs. no) (n=724)**11/93 (11.8%) vs. 58/631 (9.2%)OR=1.33 (95% CI 0.63-2.74)\*not adjusted | Not Reported | **Cesarean vs. Vaginal (n=1400)** 28/382 (7.3%) vs. 101/1018 (9.9%)OR: .739 (.467-1.163)\*type of cesarean (CS) or vaginal deliveryelective CS: 20/192 (10.4%)Emergency CS: 7/115 (6.1%)Unspecified CS: 1/75 (1.3%)Vaginal, spontaneous: 81/825 (9.8%)Vaginal, instrumented: 12/79 (15.2%)Vaginal, unspecified: 8/114 (7%)**HIV- mothers (n=884)****Cesarean vs. vaginal** 15/218 (6.9%) vs. 39/666 (5.9%)OR 1.17 (0.59-2.31, p=.66)\*Adjusted for breastfeeding status, maternal age at delivery, and center category\*info on type of CS or vaginal delivery NR for HIV- | **Breast vs. formula (n=1424)**29/351 (8.3%) vs. 102/1073 (9.5%)**HIV- mothers****Breast vs. formula (n=887)**21/319 (6.6%) vs. 36/568 (6.3%)OR 1.07 (0.57-2.02, p=0.83)\*Adjusted for mode of delivery, maternal age at delivery**HIV+ mothersbreast vs. Formula (n=497)** 5/13 (38.5%) vs. 64/484 (13.2%)OR 6.41 (1.25-32.94), p=0.03\*Adjusted for mode of delivery, maternal age at delivery | **Mother HIV positive vs. negative (n=1419)**70/503 (13.9%) vs. 60/916 (6.6%), OR 2.31 (1.58-3.37)**No** **maternal drug use ever vs. not during pregnancy vs. during pregnancy (n=1384)** 43/567 (7.6%) vs. 49/455 (10.8%) vs. 33/362 (9.1%), OR=0.82 (.50-1.35) vs. OR=1.20 (.74-1.97)**Maternal history of hepatitis (yes vs. no) (n=1038)**50/421 (11.9%) vs. 55/617 (8.9%), OR=1.38 (0.90-2.10)**Other infections during pregnancy (yes vs. no) (n=996)**7/90 (7.8%) vs. 84/906 (9.3%), OR=0.83 (0.38-1.81)\*Not adjusted  | **<36 weeks gestational age vs. >36 weeks (n=1248)**7/105 (6.7%) vs. 109/1143 (9.5%), OR 0.68 (0.26-1.50) **Birth weight <2500g vs. >2500 g (n=1362)**49/523 (9.4%) vs. 109/1143 (9.5%), OR 1.05 (0.71-1.56) | Not Reported | Not Reported | European Commission DG XII Biomed2 Programme |   |   |
| European Pediatric Hep C Virus Network, 2005 (Tovo)176Italy, Spain, Germany, Ireland, UK, Norway, SwedenGood |   |   | **Elective cesarean vs. emergency cesarean or vaginal delivery (n=1220)**OR 1.66 (1.00-2.74) unadjusted, p=.05OR 1.46 (0.86-2.48)adjusted, p=.16**HIV- mothers elective vs. emergency cesarean or vaginal delivery (n=1034)**1.57 (0.88-2.83) unadjusted, p=0.131.59 (0.88-2.86) adjusted, p=0.13\*adjusted for sex, mode of delivery, prematurity, and infant feeding type  | **Breast vs. formula (n=1220)**OR 0.74 (0.42-1.31) unadjusted, p=.30OR .88 (0.48-1.61) adjusted, p=.68**HIV- mothers breast vs. formula (n=1034)**OR 0.88 (0.48-1.61) unadjusted, p=.68OR 0.92 (0.50-1.70) adjusted, p=.60 | **Mother HIV positive vs. negative (n=1220)**OR 1.89 (1.05-3.40) unadjusted, p=.03OR 1.82 (0.94-3.52) adjusted, p=.06 | **Female vs. male (n=1220)**OR 2.12 (1.27-3.56) unadjusted, p=.004OR 2.07 (1.23-3.48) adjusted, p=.006**Premature vs. term (n=1220)**OR 0.54 (0.23-1.26) unadjusted, p=.15OR 0.45 (0.19-1.08) adjusted, p=.07**HIV- mothersfemale vs. male (n=1034)**OR 1.79 (1.00-3.22) unadjusted, p=.05OR 1.80 (1.00-3.24) adjusted, p=.07**HIV- motherspremature vs. term (n=1034)**OR 0.83 (0.32-2.13) unadjusted, p=.690.83 (0.32-2.15) adjusted, p=.80 | Not Reported | Not Reported | European Commission Regione Piemonte, Italy; UK Medical Research Council |   |   |
| Gibb, 2000161Ireland, UKFair | Not Reported | Not Reported | **Elective cesarean vs. emergency cesarean vs. vaginal (n=424)**0% (0-7.4) vs. 5.9% (1.0-17.8) vs. 7.7% (4.5-11.9) OR elective cesarean 0 (95% CI 0-0.86) vs. OR emergency cesarean 0.84 (95% CI 0.12-3.63) vs. \*Adjusted for HIV status and breastfeeding**Elective cesarean vs. vaginal/emergency cesarean (n=424)**0% (0-7.4) vs. 7.4% (4.5-11.3) OR 0 (0-0.87)\*Adjusted for HIV status and breastfeeding | **Breast vs. formula (n=414)**7.7% (2.2-17.8) vs. 6.7% (3.7-10.6) OR 1.52 (0.35-5.12)\*Adjusted for HIV status and mode of delivery | **HIV positive vs. negative (n=441)**18.6% (5.8-38.6) vs. 6.4% (3.5-10.3) OR= 3.8 (0.92-13.2)\*Adjusted for breastfeeding and HIV status | Not Reported | Not Reported | Not Reported | UK Department of Health | Not Reported |   |
| Garland, 1998160 AustraliaPoor | Not Reported | Not Reported | **Vaginal vs. cesarean (n=83)** 3/61 (4.9%) vs. 0/22 (0%)  | Viral RNA detected in breast milk: 0/18 (0%) | Not Reported | Not Reported | Sibling HCV RNA+: 1/16 (6%) | Not Reported | Not Reported |   |   |
| LaTorre, 1998162ItalyPoor  | Not Reported | Not Reported | **Vaginal vs. cesarean (n=80)**1/66 (1.5%) vs. 1/14 (7%) | **Breastfed vs. formula fed (n=80)**0/24 (0%) vs. 2/56 (3.6%) \*none of the HCV-RNA positive mothers breastfed | **By maternal HCV RNA status (n=80)**mother positive: 2/56 (3.6%)mother negative: 0/24 (0%)\*not adjusted | Not Reported | Not Reported | Not Reported | Not specified, research and testing took place at Careggi Hospital, University of Florence |   |   |
| Lin, 1995163Republic of ChinaPoor | Not Reported | Not Reported | Not Reported | Breast feeding transmission rate: (n=11 breast fed) None (0%) | IVDU during pregnancy: 1/12 (8.3%) infants HCV+ | Not Reported | Not Reported | Not Reported | National Science Council, Yuan, China |  |  |
| Mast, 2005164US (Houston and Honolulu)Good | **\* Results are for HCV RNA+/HIV- mothers (n=181)Internal vs. external** 3/16 (18.8%) vs. 4/165 (2.4%), RR 7.7 (1.9-31.6), p=.02**Internal fetal monitoring**\*Adjusted OR, 6.7 (1.1-35.9) | **\* Results are for HCV RNA+/HIV- mothers (n=182)Rupture of membranes before onset of laboryes vs. no** 4/45 (8.9%) vs. 3/137 (2.2%), RR 4.1 (0.9-17.5), p=.06**Duration of membrane rupture** <1 vs. 1-5 vs. 6-12 vs. >=130/53 vs. 1/59 (1.7%) vs. 4/40 (10%) vs. 2/30 (6.7%), p=.02**Membrane rupture >6 hrs**OR, 9.3 (1.5-179.7)\*adjusted | **\* Results are for HCV RNA+/HIV- mothers (n=181)Elective cesarean vs. emergency cesarean vs. vaginal delivery**0/12 (0%) vs. 1/18 (5.5%) vs. 6/151 (4%), elective cesarean RR undefined, emergency cesarean RR 1.4 (0.2-1.1), p=.55**Elective cesarean vs. emergency cesarean/vaginal** 0/12 vs. 7/169 (4%), RR 0.87 (0.05 to 14) | **\* Results are for HCV RNA+/HIV- mothers (n=182)Breast vs. formula** 2/62 (3.2%) vs. 5/120 (4.2%), RR 0.8 (0.2-3.9), p=1.0 | **Maternal** **HCV/RNA status at delivery**positive vs. negative9/190 (4.6%) vs. 0/54, RR undefined**\*Remaining results are for HCV/RNA+ mothers (n=190)maternal HIV status**positive vs. negative2/8 (25%) vs. 7/182 (3.8%), RR 6.5 (1.6-26.4)**Maternal HCV RNA level, genome copies/mL** <=106 vs. >106, <107 vs. >=1071/61 (1.6%) vs. 2/87 (2.3%) vs. 4/34 (11.8%), p=.03**Maternal age at delivery, years**>=30 vs. <305/100(5) vs. 2/81(2.5), RR 2.0(0.4-10.2), p=0.46**(results continued in last 2 columns)** | **\*Results for infants born to HCV/RNA+ mothers (n=190)Sex**Male vs. female2/85 (2.3%) vs. 5/96 (5.2%),RR 0.45 (0.09-2.27), p=.45**Gestational age**<37 vs. >=370/27 vs. 7/155 (4.5%),RR undefined, p=.6**Birth weight**<2500g vs. >=2500g1/22 (4.6%) vs. 6/160 (3.8%),RR 1.2 (0.2-9.6), p=1**Apgar score at 5 min**<=8 vs. >80/21 vs. 7/161 (4.4%),RR undefined, p=1 | Not Reported | Not Reported | Centers for Disease Control | **Prior pregnancies**>4 vs. <=42/73 vs. 5/109, RR 0.6(0.1-3.0)**ALT level at delivery, U/L**>35 vs. <=353/45(6.7) vs. 4/137, RR 2.3(0.5-9.8)**Duration of membrane rupture**<1 vs. 1-5 vs. 6-12 vs. >=130/53(0) vs. 1/59(1.7) vs. 4/40(10) vs. 2/30(6.7), (p=.02)adjusted OR for membrane rupture >6h, 9.3(1.5-179.7)**Duration of labor, h**<=6 vs. 7-12 vs. >=132/84(2.4) vs. 4/48(8.3) vs. 1/44(2.3), (p=.78) | **Cigarette smoking during** pregnancyyes vs. no1/99(1) vs. 6/83(7.23), RR 0.14(0.02-1.1)**Alcohol intake during pregnancy**yes vs. no1/42(2.4) vs. 6/140(4.3), RR 0.6(0.1-4.5)**History of IVDU**yes vs. no1/94(1.1) vs. 6/88(6.8), RR 0.2 (0.02-1.27)**Amniotic fluid**clear (ref) vs. meconium vs. bloody2/129(1.6) vs. 4/40(10) vs. 1/10(10), RR 6.5(1.2-33.9) RR 6.5 (0.6-65.2) |
| McMenamin, 2008165Ireland Fair | **Fetal scalp electrode (n=23)**Infant HCV RNA+: 0/11 (0%)infant not tested: 12 | Not Reported | **Elective cesarean vs. emergency cesarean or vaginal delivery (n=441):** 1/33 (3%, 95% CI 0% - 8%) vs. 17/408 (4.2%, 95% CI 2.3%-6.2%) p=NS\*Not adjusted\*same results if limited to HIV- mothers**Elective cesarean vs. emergency cesarean or vaginal delivery HCV-RNA+ women (n=295)**5.3% vs. 7.2%p=NS\*Not adjusted\*Authors didn't provide raw numbers | Not Reported | **HCV RNA positive vs. negative vs. unknown (n=441)**Positive vs. negative vs. unknown: 18/255 (7.1%, 95% CI 6.3%-7.9%, p<.05) vs. 0/17 (0%, p<.05) vs. 0/69 (0%)\*not adjusted**HIV positive vs. negative (n=441)** 1/17 (5.9%, 95% CI 0%-17.2%, p=NS)vs. 17/418 (4.1%, 95% CI 2.2%-6.0%, p=NS)Mother status unknown: 0/6 (0%) | Not Reported | Not Reported | Not Reported | Not specified, retrospective review of data from National Maternity Hospital and Rotunda Hospital |  |  |
| Moriya, 1995166JapanPoor | Not Reported | Not Reported | Not Reported | Breast feeding transmission rate (n=74): 5/6 infected received breast milk (83%%) vs. 54/68 uninfected (79%)OR 1.3 (0.14 to 12.0) | Not Reported | Not Reported | Not Reported | Not Reported | Ministry of Health & Welfare, Japan |   |   |
| Okamoto , 2000167 Japan (Tottori University & Medical Center)Poor | Not Reported | Not Reported | **Vaginal vs. cesarean**7/41 (17%) vs. 0/18 (0%), p=089**High Viral Load mothers** (>2.5x106 copies/mL):7/16 (44%) vs. 0/10 (0%), p=.023  | The sample size was too small to test the effect of breast-feeding. | History of blood transfusion, history of clinical hepatitis NS, data NR | HCV-RNA+ titers of vaginally delivered infants born to RNA+ mothers:Mothers (Geometric average, 95% CI):Infectious: 5, (7.0, 2.4–20.0) vs.Noninfectious: 31, (1.5, 0.9–2.3), p<.001Children (Geometric average, 95% CI):Infected: 7, (8.0, 3.8–16.7) vs.Uninfected: 34, (1.4 0.9–2.2), p<.001 | Not Reported | Research on Children and Families of the Ministry of Welfare of Japan | Not Reported |   |   |
| Pipan, 1996168Italy Poor | Not Reported | Not Reported | Not Reported | **Breast vs. formula (n=25)**0/6 (0%) vs. 0/19 (0%) | Not Reported | Not Reported | Not Reported | Not Reported | MURST grant and the FVG Branch of Italian League against Virus Disease |   |   |
| Resti , 1998169ItalyFair | Not Reported | Not Reported | **Vaginal vs. cesarean (n=275)** 9/213 (4%) vs. 4/62 (6%), RR 0.65 (0.21-2.05), p=0.498  | **Breast vs. formula (n=275)**6/87(7%) vs. 7/188(4%), RR = 1.85 (0.64 to 5.35), p=0.358. 3/6 infected breast fed children had hepatitis C virus RNA detected on the day of birth | Transmission from women with no known risk of infection was significantly lower (RR=0.17%, 0.04-0.73%; P=0.0063) **IVDU during pregnancy** 1/12 (8.3%) infants HCV+**HCV viral load**No significant difference (z=0.380; P=0.704) in RNA load between mothers who transmitted the virus and those who did not (3.8 (0.02 to 56)×105 RNA copies/ml v 2.4 (0.01 to 92.7)×105 RNA copies/ml) | 6 babies had hepatitis C virus RNA immediately after birth. The transmission rate was higher in 20 recipients of blood transfusions (RR=10%, 95% CI 3-17%)  | Not Reported | Not Reported | Partially supported by grant 394/A from Regione Toscana, III Programma Ricerca Sanitaria and by a grant from Ministero della Ricerca Scientifica | Not Reported |   |
| Spencer, 1997170AustraliaPoor | Not Reported | **Viremic mothers (mean hours ± SD) (n=63)**Transmitted vs. not transmitted: 28±10 vs. 16±4, p=.03 | **Viremic mothers, cesarean (n=63) transmitted vs. not transmitted**1/6 (14%) vs. 6/56 (9%), p=.5**Cesarean vs. vaginal**1/7 (14%) vs. 5/55 (9%) | **Viremic mothers breastfeeding (n=63)**transmitted vs. not transmitted 2/6 (33%) vs. 31/57 (54%) p=0.4 **Breast fed vs. formula fed**2/33 (6%) vs. 4/30 (13%) Viral RNA detected in breast milk: (n= 38) 0% | Viremic mothers transmitting vs. non-transmitting**Viral load at delivery** 8.9x105 vs. 3.9x105, p=0.04**Drug use, mean years** 8.8±1.4 vs. 10±0.8, p=0.7**Past HBV infection**4/6 (66%) vs. 34/55 (62%), p<0.9**Heroin use during pregnancy**2/2 (100%) vs. 38/45 (84%), p<0.9 | **Birth weight (mean g)**2698 (transmitted n=6) vs. 3020 (no transmission n=57)p= 0.4**Gestational Age** transmitting vs. non-transmitting: 37±0.9 weeks vs. 39±0.3 weeks, p=0.3 | Not Reported | Not Reported | Not Reported |   |   |
| Syriopoulou, 2005171GreecePoor | Not Reported | Not Reported | **Vaginal vs. cesarean (n=56)**2/39 (5%) vs. 0/17 (0%), p=0.34 | **Breast vs. formula (n=56)**0/15 (0%) vs. 2/41 (5%), p=0.38 | **HCV/RNA+ vs. HCV/RNA- (n=86)**2/56 (3.6%) vs. 0/30 (0%)**HIV+ vs. HIV- (n=56)**1/2 (50%) vs. 1/54 (2%) (p<.001)**IVDU use during pregnancy, yes vs. no (n=56)**2/3 (67%) \*1 mother was HIV+ vs. 0/54 (0%)(p<.001)**IVDU ever, yes vs. no (n=56)**2/8 (25%) vs. 0/48 (0%)(p<.001) | Not Reported | Not Reported | Not Reported | Not Reported |   |   |
| Tajiri , 2001172Japan (seven hospitals in the Osaka metropolitan area)Poor | Not Reported | Not Reported | **Vaginal vs. cesarean (n=114)** 8/90 (8.8%) vs. 1/24 (4.2%), p = 0.396\*RR: 2.04 (.284 - 43.42) | **Breast vs. formula (n=114)** 9/98 (9.2%) vs. 0/16, p=0.243 | Maternal HCV Viremia:positive: 9/81 vs. negative: 0/33, p=.040Maternal viral load:High: 8/46 vs. Low: 0/27, p=0.019 | Not Reported | Not Reported | Not Reported | Not Reported |   |   |
| Tanzi, 1997173ItalyPoor | Not Reported | Not Reported | Not Reported | HCV RNA+ mothers (n=18)12/18 HCV/RNA+ mothers breastfed, none infected at 3 month followup | Not Reported | Not Reported | Not Reported | Not Reported | Not Reported |   |  |
| Zanetti , 1998174(Intervirology)ItalyA prospective Study on Mother-to-Infant Transmission of Hepatitis C virusZanetti et al, 1999175(Journal of Hepatology)ItalyMother-to-infant transmission of hepatitis C virusPoor | Not Reported | Not Reported | **Vaginal vs. cesarean (HCV+)** 7/193 (3.6%) vs. 1/58 (1.7%), p = 0.7**(HCV+/HIV+)** 0/4(0%) vs. 9/36(25%), p = 0.5 | **HIV- mothers breast vs. formula (n=251)** 3/127 (2.4%) vs. 5/124 (4.0%), p = 0.5**HIV+ mothers breast vs. formula** **(n= 40)** 0 vs. 9/40 (22.5%) | Transmission by History of IVDU: HCV+: Yes: 3/67 (4.5%) vs. No: 5/184 (2.7%), p=0.4HCV+/HIV+: Yes: 9/40 (22.5%) vs. No: 0Transmission by History of Chronic Liver Disease or elevated ALT:HCV+: Yes: 3/85 (3.5%) vs. No: 5/166 (3%), p=1HCV+/HIV+: Yes: 4/10 (40%) vs. No: 5/30 (16.7%), p=0.2 | Not Reported | Not Reported | Not Reported | Not Reported |   |   |

Abbreviations: HCV, hepatitis C virus; SVR, sustained virologic response.