

Monitoring Health Concerns Related to Marijuana in Colorado: 2015 Update

Appendix: Marijuana Use During Pregnancy and Breastfeeding

Retail Marijuana Public Health Advisory Committee
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Epidemiology of Marijuana use in Pregnancy:

- Roberson EK, 2014: (ADDED 5/18/15) Marijuana Use and Severe Nausea, Hawaii 4,735 women PRAMS secondary analysis
 - 6.0% report use in month prior to pregnancy, 2.6% report use during pregnancy
 - 21.2% report severe nausea during pregnancy, those who reported severe nausea were significantly more likely to report marijuana use (3.7% vs. 2.3%; PR=1.63, 95%CI: 1.08-2.44)
- Salas-Wright CP, 2015 (ADDED 5/18/15) Substance Use and Teen Pregnancy: NSDUH 2002-2012
 - n= 97,850 women between 12-17, 810 of whom were pregnant
 - Controlling for age, race/ethnicity, household income, and the absence of a mother/father in the household, pregnant teens were significantly more likely than non-pregnant teens to report using cannabis (AOR = 1.79, 95%CI 1.45-2.20)
 - Compared to non-pregnant early adolescents, pregnant early adolescents [12-14 years] were significantly more likely to report have use cannabis in the previous 12 months than non-pregnant teens, (AOR= 7.18, 95% CI= 3.46 -14.91). Older pregnant teens [15-17 years] report much lower marijuana use (AOR=1.57, 95%CI = 1.27-1.93), however still report significantly higher use than non-pregnant teens.
- The National Survey on Drug Use and Health reported in 2012-2013, 4.9% of pregnant 15-44 year old women used marijuana in the past month. National Household Survey on Drug Use and Health (2003-2004), 10% of American women aged 15-44 years reported use of an illicit drug in the past month. Of pregnant women in the same age group, 4.6% reported any illicit drug use, 3.6% reported cannabis use.
- Schauburger 2014 (Prevalence of illicit drug use in pregnant women): 200 prenatal women in a private practice in Wisconsin had urine tests at intake- 7% positive for MJ. Only 4.5% of this sample self-reported ANY drug use, while 13% had a positive urine test for one or more drugs.
- Hayatbakhsh et al 2012: large cross-sectional study (24,874 women) at a tertiary public hospital in Australia (2000-2006)
 - 2.6% of women used cannabis during pregnancy (based on interview at 12-16 weeks of pregnancy)
- Moore 2010 (During pregnancy, recreational drug-using women. . . continued to smoke tobacco and cannabis): This study in the UK found that: among women who reported using marijuana in the month before getting pregnant, about 2/3 reported continued use after finding out they were pregnant, and throughout pregnancy, but at around half the volume.
- Fergusson 2002: Avon Longitudinal Study of Pregnancy and Childhood (UK), a large cohort study (12,129 women)
 - 4.8% of mothers self-reported smoking cannabis before pregnancy and 2.6% in 1st trimester, 2.1% in mid-pregnancy
- Saurel-Cubizolles MJ et al 2014: Cannabis use in France, 13,545 women
 - 1.2% of women reported cannabis use during pregnancy

- 40% reported use less than once a month, 26% reported 1-9 times per month and 15% at least 10 times per month (19% didn't answer frequency question)

Birth Outcome Risks

Stillbirth

We found limited evidence that maternal use of marijuana during pregnancy is associated with an increased risk of stillbirth. (REVIEWED 5/18/2015)

- Varner et al 2014 - Stillbirth Collaborative Research Network
 - *medium quality evidence based on strengths and limitations*
 - Findings:
 - Screening positive for tetrahydrocannabinolic acid was associated with an OR of 2.34 (95%CI 1.13-4.81, p=0.021) for stillbirth with partial confounding by cotinine (tobacco exposure).
 - Strengths:
 - population based case-control study (March 2006-September 2008)
 - 663 stillbirth deliveries (cases), 1932 live births (controls)
 - sample was racially and ethnically diverse
 - utilized maternal self-report + medical record review + toxicology screen
 - Tested umbilical cord segments from both cases and controls for drugs including THC and obtained maternal blood samples
 - adjusted for stillbirth risk factors at baseline using a modification to a risk factor score, including maternal characteristics: age, race/ethnicity, education, tobacco, alcohol, illicit drug use, comorbidities etc
 - Limitations:
 - relatively small number of women tested positive for individual drugs and therefore lacked sample size to make definitive conclusions
 - participants who did not have cotinine and toxicology testing differed in race, ethnicity and gestational age from those who had samples available for testing
 - Unable to determine if exposure was before or after occurrence of stillbirth.

Preterm Delivery

We found mixed evidence for whether or not maternal use of marijuana during pregnancy is associated with preterm delivery. (REVIEWED 5/18/2015)

- [Mark K et al 2015 - \(ADDED 2015\) Marijuana use and pregnancy: prevalence, associated characteristics, and birth outcomes](#)

- *Low quality evidence based on strengths and limitations.*
 - Findings:
 - Marijuana screen by either self-report or urine toxicology, continued screening throughout the pregnancy, by self-report or urine toxicology.
 - At intake 116/396 screened positive: 27(23.3%) by urine only, 35 (30.2%) by self-report only, and 54 (46.6%) by both urine and self-report
 - Marijuana use was not related to incidence of preterm delivery 17.7% vs. 12.0%, p=.0325.
 - Strengths:
 - Included all pregnant women seen at the hospital from July 1, 2009 to June 30, 2010.
 - Primary exposure was marijuana use, assessed each trimester.
 - At intake 116/396 patients (29.3%) screened positive for marijuana
 - All patients received same prenatal care
 - Limitations:
 - Few marijuana positive by urine screen at end of pregnancy 3/170, but decreased urine testing over the trimesters (160 first trimester, 9 third trimester) limits general applicability of findings.
 - Retrospective cohort requires provider documentation
 - Frequency of marijuana use not measured and quit date not confirmed.
- Day et al 1991: Maternal Health Practices and Child Development Study (Pittsburgh)
 - *low quality evidence based on strengths and limitations*
 - Findings:
 - non significant relationship between prenatal marijuana use and prematurity
 - Strengths:
 - longitudinal study with large sample size (n=519 live born singleton births)
 - quantified marijuana use and assessed use in each trimester
 - study nurses were blinded to the exposure status of the infant
 - adjusted for tobacco and alcohol use
 - Limitations:
 - no statistical data included in the paper to support the finding with regards to prematurity
 - Inner city, outpatient clinic population with low socioeconomic status of women, 60% completed high school, 57% of population were black, 43% white
 - Fergusson 2002: Avon Longitudinal Study of Pregnancy and Childhood (UK)
 - *low quality of evidence based on strengths and limitations*
 - Findings:

- No significant association between cannabis use before and during pregnancy and perinatal death, preterm delivery or need for special care admission of the newborn
 - Strengths:
 - large cohort study (12,129 women) in UK
 - Limitations:
 - cannabis use assessed by self-completion questionnaires mailed to mothers
 - the analysis for preterm delivery did not include an adjusted multivariate analysis
 - 70% of women who used cannabis also used tobacco, tobacco was adjusted for but unable to perform a stratified analysis of cannabis users only
- Hayatbakhsh et al 2012:
 - *medium quality of evidence based on strengths and limitations*
 - Findings:
 - Adjusted analysis: Significant association of cannabis use preterm birth (OR 1.5, 95%CI 1.1-1.9),
 - Using adjusted ORs, the population-attributable risk for preterm birth was 1.5%.
 - Strengths:
 - large cross-sectional study (24,874 women) at a tertiary public hospital in Australia (2000-2006)
 - adjusted for multiple variables including cigarette smoking, alcohol and other illicit drug use
 - Limitations:
 - self reported data on substance use
 - no quantification of amount of cannabis use during pregnancy
 - only looked at cannabis use at 1st prenatal visit (12-16 weeks)
 - potential inadequate confounding variables
- Dekker GA et al 2012 - Risk factors for preterm birth
 - *low quality evidence based on strengths and limitations*
 - Findings:
 - Use of marijuana pre-pregnancy was an independent risk factor for spontaneous preterm birth (birth <37 weeks gestation) with intact membranes (OR 2.34, 95% CI 1.22-4.52)
 - Strengths:
 - large prospective multicenter cohort of 3234 nulliparous women with singleton pregnancies (November 2004-August 2008)
 - Limitations:
 - only looked at pre-pregnancy marijuana use, many women stop using during pregnancy and rates of use are not likely the same
 - study conducted in New Zealand and Australia, potentially limiting

- generalizability of findings.
- Bada HS et al 2005 - prenatal drug exposure and LBW/preterm births
 - *low quality evidence based on strengths and limitations*
 - Findings:
 - The preterm group had significantly higher proportions of mothers who used cocaine, opiates or marijuana during pregnancy
 - In the adjusted analysis for risk factors associated with prematurity, marijuana was not significantly associated (OR 0.9, 95%CI 0.73-1.11)
 - Strengths:
 - secondary data analysis from a large multicenter study (Maternal Lifestyle Study (4 centers of the National Institute of Child Health and Human Development Neonatal Research Network) - recruitment May 1993-May 1995
 - adjusted for tobacco, alcohol and other drug use, prenatal care, maternal medical risk factors
 - Limitations:
 - 16,988 mother/child dyads met eligibility criteria, only 70% were consented (11,811)
 - large percentage of Medicaid patients (64.2%), 43.4% of mothers were black, 29.3% had education <12 years, 34% had no/intermediate prenatal care
 - unable to determine the effect of each prenatal drug exposure independent of other substance exposures
 - Shiono PH et al 1995 - Cocaine and MJ effect on LBW and preterm birth
 - *medium quality evidence based on strengths and limitations*
 - Findings:
 - 11% of women had THC-COOH in serum or self-reported using marijuana
 - 7.8% had positive serum
 - 5.6% had positive self-report
 - 2.4% had positive serum and positive self-report
 - No significant association with marijuana use and preterm birth (OR 1.1, 95%CI 0.8-1.3) or abruptio placentae (OR 1.3, 95%CI 0.6-2.8)
 - Strengths:
 - prospective multicenter cohort study in US
 - large multi-ethnic sample - 7470 women enrolled (43% African American, 24% Hispanic, 33% white or other)
 - interviewed women at 23-26 weeks gestation about risk factors
 - serum collected at study entry and also for a randomly selected subsample of 12% of women at 31-36 weeks gestation (3rd trimester)
 - serum tested for THC-COOH, any positive sample was confirmed by gas chromatography-mass spectrometry
 - adjusted for tobacco smoking
 - Limitations:

- study conducted 1984-1989
 - drug use categorized as yes/no variable
 - no adjustment for alcohol use as described
- Saurel-Cubizolles MJ et al 2014: Cannabis use in France and preterm birth, small for gestational age
 - *low quality evidence based on strengths and limitations*
 - Findings:
 - 1.2% of women reported cannabis use during pregnancy
 - 40% reported use less than once a month, 26% reported 1-9 times per month and 15% at least 10 times per month (19% didn't answer frequency question)
 - Preterm (before 37 weeks) birth rate higher in cannabis users (10.9%) than non-users (5.3%)
 - For births before 32 weeks (1.3% for cannabis users and 0.5% in non-users)
 - - Preterm birth rate in users (using less than once per month) 9.9%
 - Preterm birth rate in users (using >1 time per month) 12.3%
 - adjusted OR for cannabis users who were non-tobacco smokers was non-significant for cannabis use less than once per month and preterm birth (OR 1.24, 95% CI 0.44-3.49) and small for gestational age
 - adjusted OR for cannabis users who were tobacco users was statistically significant for preterm birth (OR 2.68, 95%CI 1.16-6.20) and spontaneous preterm birth (OR 3.50, 95%CI 1.28-9.58)
 - Strengths:
 - Large sample size (13,545 women), national sample in France
 - Analyzed tobacco smokers and non-tobacco smokers separately
 - Limitations:
 - self-report of drug use
 - Interview done after delivery, could cause recall bias
 - Small percentage of cannabis users in the sample (1.2%)
 - limited sample size of cannabis-only users who used more than once per month - didn't allow for analysis of this group
 - large confidence intervals

Low Birth Weight (birth weight <2500g regardless of gestational age)

We found mixed evidence for whether or not maternal use of marijuana during pregnancy is associated with low birth weight infants. (REVIEWED 5/18/2015)

- Mark K et al 2015 (ADDED 2015) - Marijuana use and pregnancy: prevalence, associated characteristics, and birth outcomes
Low quality evidence based on strengths and limitations.

- Findings:
 - Marijuana screen by either self-report or urine toxicology, continued screening throughout the pregnancy, by self-report or urine toxicology.
 - At intake 116/396 screened positive: 27(23.3%) by urine only, 35 (30.2%) by self-report only, and 54 (46.6%) by both urine and self-report
 - Marijuana use was not related to incidence of low birth weight (13.8% vs. 14.0%, p=1.00)

- Strengths:
 - Included all pregnant women seen at the hospital from July 1, 2009 to June 30, 2010.
 - Primary exposure was marijuana use, assessed each trimester.
 - At intake 116/396 patients (29.3%) screened positive for marijuana
 - All patients received same prenatal care
- Limitations:
 - Few marijuana positive by urine screen at end of pregnancy 3/170, .but decreased urine testing over the trimesters (160 first trimester, 9 third trimester) limits general applicability of findings.
 - Retrospective co-hort requires provider documentation
 - Frequency of marijuana use not measured and quit date not confirmed.

- Conner et al 2015 (**ADDED 2015**) - Maternal marijuana use and neonatal morbidity
 - *medium quality evidence based on strengths and limitations.*
 - Findings:
 - Composite and individual markers of poor neonatal outcome were not significantly higher in women who used marijuana during pregnancy (birth-weight less than 2500gm, NICU admission, 5 minute APGAR score less than seven, and umbilical artery pH<7.10)

 - Strengths:
 - Included all consecutive, non-anomalous, term, deliveries at one institution over a 4 year period (Washington University, St. Louis, MO)
 - 8138 women, 680 (8.4%) used marijuana during pregnancy
 - Adjusted for other drug use, smoking, and African American race.
 - Limitations: Retrospective cohort
 - Marijuana use recorded by either self report or positive urine drug screen
 - No measure of amount of marijuana use.
 - No measure of trimester(s) of use

- Hayatbakhsh et al 2012:
 - *medium quality of evidence based on strengths and limitations*
 - Findings:

- 2.6% of women used cannabis during pregnancy (based on interview at 12-16 weeks of pregnancy)
 - Adjusted analysis: Significant association of cannabis use with low birth weight (OR 1.7, 95%CI 1.3-2.2)
 - Using adjusted ORs, the population-attributable risk for low birth weight, was 2.5%.
 - Strengths:
 - large cross-sectional study (24,874 women) at a tertiary public hospital in Australia (2000-2006)
 - adjusted for multiple variables including cigarette smoking, alcohol and other illicit drug use
 - Limitations:
 - self reported data on substance use
 - no quantification of amount of cannabis use during pregnancy
 - only looked at cannabis use at 1st prenatal visit (12-16 weeks)
 - potential inadequate confounding variables
- Schempf et al 2008
 - *medium quality evidence based on strengths and limitations*
 - Findings:
 - Unadjusted OR for marijuana use and low birth weight: OR 1.94, 95% CI 1.23-3.06, when adjusted for other drug use and social, psychosocial, behavioral and biomedical factors OR decreased to 1.07, 95%CI 0.60-1.92 (non-significant)
 - Strengths:
 - large sample (808 women with singleton, live births)
 - Drug use measurement: universal urine toxicologic screen at admission to L&D, self-report or report in the medical record
 - conducted sensitivity analyses with no change in drug effect
 - adjusted for social, psychosocial, behavioral (tobacco and alcohol use, early prenatal care) and biomedical factors (hypertensive disorders, STIs, medical risk factors etc)
 - Limitations:
 - retrospective cohort study of low income women who delivered at Johns Hopkins (1995-1996)
 - possible over-adjustment of factors
 - did not assess for differences in gestational age
 - 63% of the sample did not have early prenatal care (1st visit within the 1st trimester with 4 or more total visits)
- Bada HS et al 2005 - prenatal drug exposure and LBW/preterm births
 - *low quality evidence based on strengths and limitations*
 - Findings:
 - The LBW and IUGR groups had significantly higher proportions of mothers who used cocaine, opiates or marijuana during pregnancy

- In the adjusted analysis for risk factors associated with LBW (OR 1.21, 95%CI 0.9-1.61) and IUGR (OR 1.08, 95%CI 0.85-1.36), marijuana was not statistically significant
 - Strengths:
 - secondary data analysis from a large multicenter study (Maternal Lifestyle Study (4 centers of the National Institute of Child Health and Human Development Neonatal Research Network) - recruitment May 1993-May 1995
 - adjusted for tobacco, alcohol and other drug use, prenatal care, maternal medical risk factors
 - Limitations:
 - 16,988 mother/child dyads met eligibility criteria, only 70% were consented (11,811)
 - large percentage of Medicaid patients (64.2%), 43.4% of mothers were black, 29.3% had education <12 years, 34% had no/intermediate prenatal care
 - unable to determine the effect of each prenatal drug exposure independent of other substance exposures
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 - No significant association with marijuana use and low birth weight (OR 1.1, 95%CI 0.9-1.5)
 - Strengths:
 - prospective multicenter cohort study in US
 - large multi-ethnic sample - 7470 women enrolled (43% African American, 24% Hispanic, 33% white or other)
 - interviewed women at 23-26 weeks gestation about risk factors
 - serum collected at study entry and also for a randomly selected subsample of 12% of women at 31-36 weeks gestation (3rd trimester)
 - serum tested for THC-COOH, any positive sample was confirmed by gas chromatography-mass spectrometry
 - adjusted for tobacco smoking
 - Limitations:
 - study conducted 1984-1989
 - drug use categorized as yes/no variable
 - no adjustment for alcohol use as described

Small for Gestational Age (birth weight less than 10th percentile for gestational age)

We found mixed evidence for whether or not maternal use of marijuana during pregnancy is associated with infants being born small for gestational age. (REVIEWED 5/18/2015)

- Day et al 1991: Maternal Health Practices and Child Development Study (Pittsburgh)
 - *low quality of evidence based on strengths and limitations*
 - Findings:
 - non significant relationship between marijuana use and small for gestational age (SGA) status.
 - Strengths:
 - longitudinal study with long term follow up (519 live born infants)
 - quantified marijuana use and assessed use in each trimester
 - study nurses were blinded to the exposure status of the infant
 - adjusted for tobacco and alcohol use
 - Limitations:
 - no statistical data included in the paper to support the finding with regards to SGA
 - Inner city, outpatient clinic population with low socioeconomic status of women, 60% completed high school, 57% of population were black - may limit generalizability of findings
- Hayatbakhsh et al 2012:
 - *medium quality of evidence based on strengths and limitations*
 - Findings:
 - 2.6% of women used cannabis during pregnancy (based on interview at 12-16 weeks of pregnancy)
 - Adjusted analysis: Significant association of cannabis use with small for gestational age (OR 2.2, 95% CI 1.8-2.7) and NICU admission (OR 2.0, 95%CI 1.7-2.4)
 - Strengths:
 - large cross-sectional study (24,874 women) at a tertiary public hospital in Australia (2000-2006)
 - adjusted for multiple variables including cigarette smoking, alcohol and other illicit drug use
 - Limitations:
 - self reported data on substance use
 - no quantification of amount of cannabis use during pregnancy
 - only looked at cannabis use at 1st prenatal visit (12-16 weeks)
 - potential inadequate confounding variables
- Saurel-Cubizolles MJ et al 2014: Cannabis use in France and preterm birth, small for gestational age
 - *low quality evidence based on strengths and limitations*
 - Findings:

- 1.2% of women reported cannabis use during pregnancy
 - 40% reported use less than once a month, 26% reported 1-9 times per month and 15% at least 10 times per month (19% didn't answer frequency question)
- adjusted OR for cannabis users + non-tobacco smokers showed no significant association between cannabis use less than once per month and small for gestational age
- Strengths:
 - Large sample size (13,545 women), national sample
 - Analyzed tobacco smokers and non-tobacco smokers separately
- Limitations:
 - self-report of drug use
 - Interview done after delivery, could cause recall bias
 - Small percentage of cannabis users in the sample (1.2%)
 - limited sample size of cannabis-only users who used more than once per month - didn't allow for analysis of this group
 - large confidence intervals

Decreased Birth Weight

We found mixed evidence for whether or not maternal use of marijuana during pregnancy is associated with decreased birth weight. (REVIEWED 5/18/2015)

- Day et al 1991: Maternal Health Practices and Child Development Study (Pittsburgh)
 - *low quality of evidence based on strengths and limitations*
 - Findings:
 - No significant effect of prenatal marijuana use on birth weight, head or chest circumference.
 - There was a significant effect of prenatal marijuana use in months 1 or 2 of pregnancy on infant birth length.
 - Smoking 1 joint per day during the 1st month of pregnancy was associated with a reduction of 1.5mm in birth length (95%CI - 2.74mm to -0.28mm)
 - Strengths:
 - subsample of a large longitudinal study, this study included 519 live born infants of women who reported marijuana use at the rate of >2 joints per month or more during their 1st trimester and an equal number using less than that was selected randomly from the original sample
 - quantified marijuana use and assessed use in each trimester
 - adjusted for alcohol and tobacco use, gestational age, infant sex, race and maternal height and pregnancy weight gain
 - Limitations:
 - Inner city, outpatient clinic population with low socioeconomic status of women, 60% completed high school, 57% of population were black

- data not presented for findings reported
 - The small changes observed may not be clinically significant
- El Marroun 2009 - Generation R study
 - *medium quality of evidence based on strengths and limitations*
 - Findings:
 - 214 women (2.9% of total sample) used cannabis before and during pregnancy, 41 of those women continued use throughout the pregnancy
 - Adjusted analysis
 - continued cannabis use during pregnancy was significantly associated with decreased fetal weight in late pregnancy (-96.44g, 95% CI -152.45g to -40.43) and decreased birth weight (-277.27g, 95% CI -409.15g to -145.39g) as compared to nonusers
 - use in early pregnancy was significantly associated with decreased fetal weight in late pregnancy (-57.66g, 95% CI -86.68g to -28.65g) and birth decreased weight (-156.61g, 95% CI -224.0g to -89.23g) as compared to nonusers
 - Cannabis use before pregnancy was not significantly associated with decreased fetal weight or birth weight.
 - Cannabis use in early pregnancy was significantly associated with a decrease in head circumference in mid-pregnancy (-1.01mm, 95% CI -2.02mm to -0.01mm) and late pregnancy (-1.78mm, 95% CI -3.21mm to -0.34mm)
 - Cannabis use before pregnancy was significantly associated with a decrease in head circumference in late pregnancy (-1.29mm, 95% CI -2.48mm to -0.09mm)
 - Using infants exposed to tobacco only as a reference group, birth weight of cannabis exposed infants in early pregnancy (-95.4g; 95%CI -168.27 to -22.54) and continued exposure (-171.68g; 95%CI -308.29 to -35.07) were both significantly less. The same was true for fetal weight in late pregnancy, with decreased fetal weight in late pregnancy for fetuses exposed to cannabis in early pregnancy, -40.56g; 95%CI -71.53 to -9.60 and for fetuses continuously exposed to cannabis -67.12g; 95% CI -124.32 to -9.92) as compared to those only exposed to tobacco.
 - Using cannabis in early pregnancy or throughout pregnancy resulted in significantly decreased fetal growth (11.18g/week and 14.44 g/week, respectively) as compared to non users (based on slope of the estimated growth curve).
 - Strengths:
 - large population-based cohort study in Netherlands (enrolled 2002-2006), analysis included 7,452 pregnant women)
 - adjusted for gestational age, maternal age, BMI, height education, national origin, maternal alcohol use, parity, gravidity, fetal sex and maternal psychopathology

- utilized ultrasound assessment in early, mid and late pregnancy to estimate fetal growth
 - Limitations:
 - self report data for drug use
 - adjusted for tobacco use, but study was not able to look at effect of cannabis alone (85% of cannabis users also used tobacco)
 - small sample size of cannabis users
 - The small changes observed may not be clinically significant
- Fried et al 1987: Ottawa Prenatal Prospective Study (OPPS)
 - *medium quality of evidence based on strengths and limitations*
 - Findings:
 - 15.14% of mothers used cannabis, mean amount: 6.64 +/- 19.19 joints/week (range 0.33-151.7)
 - Cannabis use during pregnancy did not have a significant negative effect on any birth growth parameter (birth weight, length, head circumference)
 - Strengths:
 - longitudinal study of 667 newborns and their mothers
 - conducted maternal interviews in each trimester
 - quantified cannabis use in terms of number of joints used per week
 - adjusted for factors including use of tobacco, alcohol, caffeine, maternal height, weight and pregnancy weight gain, gestational length
 - Limitations:
 - study initiated in 1978
 - self report data on substance use
- Fergusson 2002: Avon Longitudinal Study of Pregnancy and Childhood (UK)
 - *low quality of evidence based on strengths and limitations*
 - Findings:
 - 3 categories: cannabis use at least once/week before and throughout pregnancy, once/week before or during pregnancy but not throughout pregnancy and < once/week both before and throughout pregnancy
 - Adjusted for covariates and gestation:
 - women who used cannabis once per week before or during pregnancy but not throughout pregnancy had significantly increased effect size for both mean birth weight (89.22g, 95%CI 12.98-165.30) and birth length (0.58cm, 95%CI 0.19-0.97) as compared to nonusers
 - use < once per week before and throughout pregnancy had significantly increased effect size for birth weight (58.6g, 95%CI 12.91-165.32)
 - Strengths:
 - large cohort study (12,129 women) in UK

- adjusted for tobacco use, alcohol and caffeine consumption, other drug use, maternal height and weight, demographic factors and gestation
- Limitations:
 - cannabis use assessed by self-completion questionnaires mailed to mothers
 - 70% of women who used cannabis also used tobacco, tobacco was adjusted for but unable to perform a stratified analysis of cannabis users only
 - number of cannabis users was relatively small which limits statistical power
 - small changes in birth parameters observed may not be clinically significant
- English DR et al 1997: Meta-analysis of cannabis use and birth weight
 - *low quality of evidence based on strengths and limitations*
 - Findings:
 - Pooled estimates for decrease in mean birth weight associated with any cannabis use during pregnancy varied from 35g-48g.
 - “inadequate evidence that maternal cannabis use, at the levels of consumption typically reported, causes low birth weight.”
 - Strengths:
 - only included studies which adjusted for cigarette smoking (10)
 - Limitations:
 - only searched Medline for articles
 - many studies do not quantify cannabis use, therefore it is difficult to combine the results
 - articles included from 1966 to November 1995 (doesn't include newer studies)
- Hingson R et al 1982: Study of effect of maternal alcohol use
 - *low quality of evidence based on strengths and limitations*
 - Findings:
 - 14% of mothers used marijuana during pregnancy (8% >1x/week)
 - Infants of mothers who used marijuana during pregnancy averaged 105 g smaller than babies of nonusers.
 - Evidence of dose response: mothers who used marijuana <3x/week had babies which were 95g smaller and mothers who used marijuana >3x/week had babies who were 139g smaller (both statistically significant)
 - Strengths:
 - large sample: 1690 mother/newborn pairs at Boston City Hospital
 - adjusted for gestational age, tobacco, alcohol or other drug use, maternal height, weight and pregnancy weight gain
 - Limitations:
 - study conducted 1977-1979

- Study conducted to evaluate effect of alcohol
 - Of all marijuana users during pregnancy, 25% had between 1-1.99 drinks/day and 44% had >2 drinks per day (may have confounding present)
 - maternal interview done after birth, which could lead to recall bias
 - The small changes observed may not be clinically significant
- Linn et al 1983: Delivery Interview Program at Brigham and Women's Hospital
 - *low quality of evidence based on strengths and limitations*
 - Findings:
 - 1246 women reported usage of marijuana during pregnancy (~10% of total interviewed)
 - 880 women reported occasional use (7.1%), 229 reported weekly use (1.8%), 137 reported daily use (1.1%)
 - Adjusted analysis showed no statistically significant association with birth weight (OR 1.07, 95% CI 0.87-1.31)
 - Strengths:
 - adjusted for demographic characteristics, tobacco and alcohol use and maternal OB history
 - large sample of women (n=12424), 1246 women with marijuana usage during pregnancy
 - Limitations:
 - maternal interview after birth regarding drug usage, may lead to potential recall bias (mothers who have undesirable outcome more likely to report prior use of marijuana)
 - this is an early paper about the effect of prenatal marijuana use (study conducted 1977-1980)
 - marijuana use characterized by use/non-use, may have limited findings
- Gray et al 2010: Prenatal cannabis exposure and concurrent tobacco exposure
 - *low quality of evidence based on strengths and limitations*
 - Findings:
 - Cannabis exposure (by positive meconium analysis - i.e. 3rd trimester use) was associated with significantly decreased birth weight, reduced length and smaller head circumference as compared to non-exposed neonates
 - however most neonates were within the expected range for weight, head circumference, and length
 - If exposure was expanded to include any self-report, oral fluid test or meconium result, growth parameters were no longer significantly affected by cannabis exposure
 - Strengths:
 - maternal interview and testing during pregnancy (oral fluid at end of each trimester and postpartum) and neonatal meconium testing (from birth, twice daily until the appearance of milk stool)

- adjusted for tobacco use
- Limitations:
 - Small sample size to detect difference (86 mother/child dyads) - only 38 self-reported cannabis use during pregnancy
 - excluded women with heavy cannabis consumption (>5 joints per day or >4 joints on a single occasion after pregnancy recognition)
- Janisse et al 2014 - gestational duration, birth weight and fetal growth
 - *low quality of evidence based on strengths and limitations*
 - Findings:
 - 24.2% of women in study used marijuana during pregnancy
 - maternal marijuana use was negatively related to growth ($\beta = -0.05$, $p < 0.004$)
 - for marijuana, the effect on infant birth weight was due to restricted fetal growth
 - Strengths:
 - prospective study - 3090 women followed from entry to prenatal care to delivery
 - only included pregnancies with ultrasound supported estimate of gestational age
 - Limitations:
 - Study also included alcohol, tobacco and cocaine use
 - participants enrolled 1986-1998
 - study limited to urban African American women at a single institution which could limit generalizability
 - Women who reported at least 0.5oz of alcohol consumption per day were all invited to participate, so moderate to heavy drinkers were overrepresented in the sample
 - high percentage of participants used marijuana, sample not representative of national averages
 - marijuana use was categorized into 4 levels according to the % of prenatal visits in which use was reported

Birth Defects

We found mixed evidence for whether or not maternal use of marijuana during pregnancy is associated with neural tube defects such as anencephaly. (REVIEWED 5/18/2015)

- David, AL, et al. 2014 (ADDED 2015) A Case-Control Study of Maternal Periconceptual and Pregnancy Recreational Drug Use and Fetal Malformation Using Hair Analysis, London, Birmingham, Bristol UK
 - *Medium quality based on study design and strengths and limitations*
 - Findings:
 - THC use alone was not significantly associated with neural tube defect
 - Cannabis is the most reported recreational drug used during pregnancy

(13.2 % study population)

- Strengths:
 - Prospective case-control, 517 pregnant women total
 - Objective assessment of cannabis use in all trimesters
 - Adjustment for social factors
 - Limitations:
 - Hair analysis not used routinely, no way to determine exposure amount or exact timing relative to important developmental timepoints in pregnancy
- van Gelder M et al 2009: data from National Birth Defects Prevention Study
- *Medium quality of evidence based on strengths and limitations*
 - Findings:
 - Periconceptional cannabis use not significantly associated with an increased risk of anencephaly (adjusted OR 1.7, 95%CI 0.9-3.4)
 - When restricting analysis to cannabis use in 1st month after conception (time of neural tube closure), adjusted OR 2.5 (95% CI 1.3-4.9), showing a significant association.
 - Strengths:
 - population-based, case-control study in US (1997-2003)
 - 10,241 case infants with selected congenital malformations and 4967 control infants
 - exposure if mother reported use of substance starting 1 month before pregnancy to the end of the 3rd month (periconceptional period)
 - adjusted for maternal confounders including age at delivery, tobacco and alcohol use, race/ethnicity, education, pre-pregnancy BMI and any periconceptional folic acid use
 - Limitations:
 - Average postpartum telephone interview 10 months after estimated date of delivery (range 1.5-24 months), no difference between cases and controls, leading to potential recall bias
 - Likely underestimate of use of illicit drugs in study (self-report, respondents often falsely deny use due to social stigma, possible incomplete recall)
 - stated that a stratified analysis was done for frequency of cannabis use however results are not reported/mentioned in the paper
- Shaw et al 1996 - Parental drug use and neural tube defects (NTD)
- *medium quality evidence based on strengths and limitations*
 - Findings:
 - Marijuana/hash use was associated with a non-significant adjusted OR 0.74 (95%CI 0.46-1.2) for a NTD-affected pregnancy from maternal periconceptional drug use (use in period 3 months before through 3 months after conception)

- No significantly increased NTD odds for paternal marijuana use (OR 0.86, 95%CI 0.63-1.2)
 - Strengths:
 - population-based case control study of fetuses and live born infants with neural tube defects (NTDs) between 1989-1991 in California (California Birth Defects Monitoring Program)
 - Sample: 538 face to face interviews with cases and 539 with controls, average of 4.9 months after actual or estimated date of delivery and 4.6 months for controls
 - adjusted for maternal vitamin use, race/ethnicity, education, income, age, income
 - Limitations:
 - based on self-report, potential reporting bias
 - use of prevalent (did not include spontaneous abortions) instead of incident cases
- Suarez L et al 2007 - Maternal exposures and neural tube defects
 - *low quality evidence based on strengths and limitations*
 - Findings:
 - Found no significant effect of street drug use on NTD risk when adjusted for cigarette smoking.
 - Strengths:
 - population-based case-control study, Mexican-American women in Texas
 - compared NTD-affected pregnancy (1995-2000) to controls in the same area
 - adjusted for tobacco use
 - Limitations:
 - 175 cases and 221 controls
 - small number of marijuana users (2% of women in study reported marijuana use)
 - did not look at marijuana separately (street drug use included cocaine and marijuana)

We found mixed evidence for whether or not maternal use of marijuana during pregnancy is associated with gastroschisis. (REVIEWED 5/18/2015)

- David, AL, et al. 2014 (ADDED 2015) A Case-Control Study of Maternal Periconceptual and Pregnancy Recreational Drug Use and Fetal Malformation Using Hair Analysis, London, Birmingham, Bristol UK
 - *Medium quality based on study design and strengths and limitations*
 - Findings:
 - THC use alone was not significantly associated with gastroschisis
 - Cannabis is the most reported recreational drug used during pregnancy (13.2 % study population)

- Strengths:
 - Prospective case-control, 517 pregnant women total
 - Objective assessment of cannabis use in all trimesters
 - Adjustment for social factors
- Limitations:
 - Hair analysis not used routinely, no way to determine exposure amount or exact timing relative to important developmental timepoints in a pregnancy
- Forrester MB 2006 - Gastroschisis and prenatal drug use
 - *low quality evidence based on strengths and limitations*
 - Findings:
 - prenatal marijuana use rate was significantly higher among gastroschisis cases than among the total population (275.23 per 10,000 live births for gastroschisis cases and 26.19 per 10,000 live births for total cases)
 - pattern of prenatal marijuana use showed the highest rates in the youngest age group and decreased with increasing maternal age (similar to the gastroschisis rates)
 - Strengths:
 - use of Hawaii birth defects registry, infants and fetuses delivered during 1986-2002 (total of 316,508 live births, 109 total gastroschisis cases)
 - prenatal drug use based on positive toxicology screen of mother or infant during or shortly after delivery or report of drug use in the medical record
 - Limitations:
 - small sample size to form conclusions (3 gastroschisis cases with marijuana use out of 109 total gastroschisis cases)
 - limited information on when drug use occurred during pregnancy
 - toxicology screening was done around delivery and gastroschisis likely occurs within the first several months of pregnancy, so cannot know if the mother was using at that time, also used self-report data
 - didn't adjust for other potential risk factors
- van Gelder M et al 2009: data from National Birth Defects Prevention Study
 - *Medium quality of evidence based on strengths and limitations*
 - Findings:
 - increased crude OR for having a child with gastroschisis with periconceptional use of cannabis, but maternal age was a strong confounder and adjusted OR showed no statistically significant association (OR 1.3, 95% CI 0.9-1.8)
 - Strengths:
 - population-based, case-control study in US (1997-2003)
 - 10,241 case infants with selected congenital malformations and 4967 control infants
 - exposure if mother reported use of substance starting 1 month before

pregnancy to the end of the 3rd month (periconceptional period)

- Limitations:
 - Average postpartum telephone interview 10 months after estimated date of delivery (range 1.5-24 months), no difference between cases and controls, potential recall bias
 - Likely underestimate of use of illicit drugs in study (self-report, often falsely deny use due to social stigma, possible incomplete recall)
 - stated that a stratified analysis was done for frequency of cannabis use however results are not reported/mentioned in the paper

We found limited evidence that maternal use of marijuana during pregnancy is associated with isolated, simple ventricular septal defects (heart defects). (REVIEWED 5/18/2015)

- Williams et al 2004: Maternal lifestyle factors and Risk for Ventricular Septal Defects (VSD)
 - *medium quality evidence based on strengths and limitations*
 - Findings:
 - Maternal cannabis use was associated with a crude OR of 2.35 (95%CI 1.43-3.86) of isolated, simple VSD when utilizing maternal self-report and crude OR of 2.21 (95%CI 1.11-4.38) when utilizing paternal proxy report
 - Frequency of use analysis: ≤ 2 days per week, crude OR 2.20 (95%CI 1.22-3.93) and ≥ 3 days per week, crude OR 3.73 (95%CI 1.56-8.96) for maternal self-report data, not statistically significant when utilizing paternal proxy report data
 - Adjusted OR for maternal cannabis use (adjusted for maternal age, race, overt diabetes and multivitamin use) 1.90 (95%CI 1.29-2.81) [comparing no use, light use (≤ 2 days per week) and heavy use (≥ 3 days per week)]
 - Strengths:
 - population-based case-control study
 - 122 infants with isolated simple VSD for this analysis(out of larger study of 4929 case infants with birth defects), 3029 control infants
 - Metropolitan Atlanta Congenital Defects Program utilized active case-finding procedures which have previously been shown to be highly sensitive
 - use of maternal and paternal questionnaires, self-report and proxy report
 - Data analyzed for women who reported marijuana use with other drugs and separately for women who only reported marijuana use (and results did not change)
 - Limitations:
 - Only included infants who had a defect noted in the first year of life
 - self-report/proxy report data only, no biological samples collected

- cases identified in infants born between 1968-1980)

We found mixed evidence for whether or not maternal use of marijuana during pregnancy is associated with birth defects.

- Linn et al 1983: Delivery Interview Program at Brigham and Women's Hospital
 - *low quality evidence based on strengths and limitations*
 - Findings:
 - Adjusted analysis showed a non-significant OR of 1.36, 95% CI 0.97-1.91 for major malformations in marijuana users vs non-users
 - Strengths:
 - large sample (12424 women, 1246 of those who reported use of marijuana)
 - adjusted for demographic characteristics, tobacco and alcohol use and maternal OB history
 - Limitations:
 - major malformations included were those that were diagnosed during the delivery hospitalization (many present at a later time)
 - potential recall bias (mothers who have undesirable outcome more likely to report prior use of marijuana)
 - this is an early paper about the effect of prenatal marijuana use (study conducted 1977-1980)
- Day et al 1991: Maternal Health Practices and Child Development Study (Pittsburgh)
 - *low quality of evidence based on strengths and limitations.*
 - Findings:
 - no significant association between marijuana use in any trimester or any of the first 3 months and minor physical anomalies.
 - Number of major physical anomalies seen in the study was insufficient for analysis.
 - Strengths:
 - longitudinal study with large sample size (519 live born infants)
 - quantified marijuana use and assessed use in each trimester
 - adjusted for tobacco and alcohol use
 - Limitations:
 - based on examinations of the infant between 24 and 48 hours of life (many anomalies present later)
 - Inner city, outpatient clinic population with low socioeconomic status of women, 60% completed high school, 57% of population were black
- Forrester MB and Merz RD 2007: Birth defects and prenatal drug use in Hawaii
 - *low quality evidence based on strengths and limitations*
 - Findings:
 - Prenatal marijuana rates were significantly higher than expected for 21 (39%) of the 54 types of birth defects
 - mainly CNS defects, cardiovascular system defects, oral clefts,

GI system and limbs

- If other drug use was excluded, than rates of prenatal marijuana use were significantly higher than expected for 19 (35%) of the 54 types of birth defects
- Strengths:
 - use of statewide, populations-based registry for adverse pregnancy outcomes (total live births 316,508, total cases with one of 54 birth defects was 7293 infants or fetuses and 829 cases of prenatal marijuana use among deliveries 1986-2002)
 - cases included all infants and fetuses delivered 1986-2002 with a report of drug use (meth, cocaine or marijuana) or a diagnosis of 54 selected birth defects
 - Drug use based on mention of illicit drug use in medical record or positive toxicology screen for the mother or infant during or shortly after delivery
- Limitations:
 - small number of cases for many birth defects categories which limited the ability to identify statistically significant differences and resulting in large confidence intervals
 - no adjustment for confounding factors (ex: demographics, health behaviors or prenatal care)
 - use of illicit drugs at any time during pregnancy
 - no dose or frequency information on drug use

HEALTH EFFECTS OF PRENATAL USE ON EXPOSED OFFSPRING

SIDS

We found a limited body of research that failed to show association between maternal use of cannabis during and after pregnancy and SIDS. (REVISED 9/21/2015)

- Scragg RKR et al - Maternal cannabis use and SIDS
 - *low quality evidence based on strengths and limitations*
 - Findings:
 - Maternal use of cannabis in pregnancy
 - adjusted for main confounders, OR 1.3 (95%CI 0.69-1.87)
 - multivariate OR 1.18 (95%CI 0.76-1.85)
 - attributable risk of SIDS from cannabis exposure (from univariate analysis) was 14% (lower than tobacco - 51%)
 - Strengths:
 - reviewed obstetric records and completed in home interviews with parents

- adjusted for main confounders: ethnicity, maternal tobacco, SES, mother's marital status, age at first pregnancy, infant's age
 - multivariate analysis controlled for region, time of day, season, age mother left school, mother's age, parity, attendance at antenatal clinic and educational classes, infant's sex, birth weight, gestation, sleep position, breastfeeding and bed sharing
 - Limitations:
 - New Zealand case-control study (485 cases, 1800 controls), births October 1, 1987-September 30, 1990
 - possible underreporting of cannabis use (social desirability bias, marijuana is illegal in New Zealand)
 - missing data from uninterviewed parents (81% of parents of cases interviewed and 88.4% of controls interviewed), ethnic differences in non-respondents (more likely to be Maori)
- Klonoff-Cohen H et al 2001: Maternal/Paternal Drug use and SIDS
 - *low quality evidence based on strengths and limitations*
 - Findings:
 - SIDS outcome was not significantly associated with maternal cannabis use during conception (OR 1.1, 95% CI 0.6-2.0) or pregnancy (OR 0.6, 95%CI 0.3-1.6)
 - maternal smoking during pregnancy was a confounder
 - Strengths:
 - case-control study of 239 infants who died with a diagnosis of SIDS in southern CA between 1989-1992 matched with 239 healthy infants by birth hospital, date of birth, age and sex
 - adjusted for maternal socioeconomic status, alcohol use during pregnancy, sleep position, bed sharing, infant risk factors
 - Limitations:
 - small number of mothers who reported drug use during conception or pregnancy, low power to detect statistically significant associations
 - 100 eligible cases were unable to be located
 - self-report drug histories
 - telephone interviews 6-12 months after infant's death (common protocol), possible recall bias
 - large confidence intervals for adjusted OR

We found mixed evidence for whether or not maternal use of marijuana during pregnancy is associated with newborn behavior issues. (REVIEWED 5/18/2015)

- de Moraes Barros et al 2006:
 - *low quality evidence based on strengths and limitations*
 - Findings:
 - Compared exposed to non-exposed infants, exposed infants were more irritable, less responsive to calming maneuvers by the examiner, cried more during exam and exhibited more jitteriness and startles. Exposed

infants had higher arousal scores after adjusting for sex, gestational age and postnatal age and a higher excitability score after adjusting for gestational age.

- Strengths:
 - cross-sectional study
 - Infants had Neonatal ICU Network Neurobehavioral Scale (NNNS) neurobehavioral assessment between 24 and 72 hours of life.
- Limitations:
 - small sample size: 26 full term neonates born to adolescent mothers (July 2001-November 2002) who had used marijuana (4.6% of adolescent mothers) at one city hospital in Brazil.
 - no quantification of marijuana use (just positive hair testing which shows use in last 3-5 months)
- Hayes 1996: Study of prenatal marijuana exposure in rural Jamaica, offspring outcomes to five years
 - *low quality evidence based on strengths and limitations*
 - Findings:
 - No significant difference in developmental testing outcomes between exposed and non-exposed infants, except
 - At 30 days, exposed infants had more favorable scores on Autonomic Stability and Reflex clusters on the Brazelton Scales as compared to non-exposed infants
 - Developmental scores at 4 and 5 years were significantly correlated to specific aspects of home environment and consistency of school (pre-school) attendance.
 - Strengths:
 - Five year follow-up.
 - use of Brazelton Neonatal Behavioral Assessment Scale
 - use of McCarthy Scales of Children's Abilities
 - use of the Caldwell Home Observation for Measurement of the Environment Scale
 - Recruited population from same environment, rural lower income class.
 - Limitations:
 - Small sample size (30 exposed and 26 non-exposed infants)
 - No explanation of other potential risk factors: alcohol consumption, tobacco use, polydrug use.
- Dreher 1994: Study of prenatal marijuana exposure in rural Jamaica
 - *low quality evidence based on strengths and limitations*
 - Findings:
 - No significant difference at day 3 in performance between exposed and non-exposed infants
 - At 1 month, exposed infants had significantly higher scores on the Autonomic and Reflex clusters as well as the General Irritability item

- (they were less irritable) as compared to non-exposed infants
 - On further analysis, maternal education was significantly correlated with this finding of higher autonomic scores.
- Strengths:
 - use of Brazelton Neonatal Behavioral Assessment Scale
- Limitations:
 - Small sample size (24 exposed and 20 non-exposed infants)
 - no adjusted analysis performed
 - In the area of rural Jamaica this study was conducted in, heavy use of marijuana by women is associated with a higher education level and greater financial independence (capacity to create a supportive postnatal environment)
 - short term follow up of infants (1 month)
- Richardson GA et al 1989:
 - *medium quality evidence based on strengths and limitations*
 - Findings:
 - prenatal marijuana use was not a significant predictor of Neonatal Behavioral Assessment Scale (NBAS) performance on day 2 of life
 - infants of women who continued to use a substance (alcohol, tobacco or marijuana) did not show differential NBAS performance from infants whose mothers never used or stopped using the substance
 - Strengths:
 - longitudinal prospective study (373 infants)
 - NBAS examiners were blinded of infants' exposure status
 - interviews done at fixed time points during pregnancy
 - multivariate analysis adjusted for alcohol, tobacco and marijuana use as well as demographic and socioeconomic factors
 - Limitations:
 - Sample with low socioeconomic status, average educational level of 11.8 years, 51% white and 49% black
 - NBAS examiner was the strongest predictor of neonatal behavior in this study. 5 examiners were used in this study, 4 separate regression analyses were performed, each eliminating one of the examiners and results were unchanged
- Lester and Dreher 1989: Marijuana use in Pregnancy and newborn cry (Jamaica)
 - *low quality evidence based on strengths and limitations*
 - Findings:
 - Infants of women who used marijuana during pregnancy had higher-pitched and more variable cry
 - could suggest respiratory involvement or an effect of marijuana on the central nervous system
 - Frequency of marijuana smoking was inversely correlated with the median first formant (F1) of the cry
 - Strengths:

- at the time of the study (late 1980's), marijuana in Jamaica had higher concentration of THC than that seen in the US
- marijuana use determined for each trimester
- rare use of tobacco, alcohol or other drugs by pregnant women in this sample
- Limitations:
 - small sample size (20 exposed and 20 non-exposed infants)
 - study conducted in Jamaica in the late 1980's which limits generalizability
 - users smoked marijuana cigars or drank marijuana tea
 - marijuana use based on self-report or direct observation

We found moderate evidence that maternal use of marijuana during pregnancy is associated with decreased growth in exposed offspring. (REVIEWED 5/18/2015)

- Cornelius et al 2002: cohort of adolescent mothers and their offspring (part of MHPCD project, Pittsburgh)
 - *medium quality evidence based on strengths and limitations*
 - Findings:
 - 39% reported use of marijuana in year before pregnancy, 15% in 1st trimester, 4% in 2nd trimester, 3.5% in 3rd trimester
 - At age 6, 2nd trimester use predicted lower height (-1.13 inches, $p < 0.01$)
 - No significant effect of prenatal exposure to alcohol, tobacco or marijuana on BMI, ponderal index or weight for height z scores
 - Strengths:
 - longitudinal study of adolescent mothers and their offspring
 - 345 offspring evaluated at 6 years, out of original 413 eligible from prenatal phase
 - adjusted for tobacco, alcohol use (prenatal and current use), maternal factors (demographic, psychosocial, height), current home environment
 - Limitations:
 - 69% African-American, 31% Caucasian, low SES, 78% completed HS which may limit generalizability
 - recruitment, prenatal and delivery phases 1990-1994
 - 2nd and 3rd trimester use was characterized as use/nonuse due to low numbers of users in these trimesters
- Fried et al 1999: Ottawa Prenatal Prospective Study 12 year follow up
 - *low quality evidence based on strengths and limitations*
 - Findings:
 - 3 groups of prenatal usage: no use, mild/moderate use (up to 6 joints/week), heavy use (at least 6 joints per week)
 - Average scores for head circumference at each age were smallest for the heavy marijuana group, intermediate for

moderate group and largest for non-users (statistically significant in 9-12 year olds, remained significant after adjusting for cigarette and alcohol use)

- First year weight gain was positively related to maternal marijuana prenatal use, children of heavy users gained more weight than other groups.
- Female children in heavy marijuana group were significantly lighter than male children at 12 months old (significant after adjustment for tobacco and alcohol use)

○ Strengths:

- adjusted for maternal demographic, social and height/weight factors, paternal weight and height as well as method and length of time of breast feeding (also tobacco and alcohol use)

○ Limitations:

- small sample size (follow up cohort of 140 children of women who reported any use of marijuana, alcohol >0.85oz average daily or smoked an average of 16 mg nicotine per day +50 children of women with no substance use)
- actual measurements of groups at each age not listed, calculated standardized z scores
- assessed exposure of child to secondhand tobacco smoke postnatally, however paper does not state that exposure to marijuana postnatally was recorded or considered

We found moderate evidence that maternal use of marijuana during pregnancy is associated with decreased IQ scores in exposed offspring. (REVIEWED 5/18/2015)

- Day et al 1994: relationship between prenatal marijuana exposure and performance on Stanford-Binet Intelligence Scale at age 3

○ *medium quality of evidence based on strengths and limitations*

○ Findings:

- For total cohort: no significant effects of marijuana use during any trimester on composite score of Stanford-Binet.
- For offspring of African-American women: 1st trimester marijuana use significantly predicted a decrease of 1.3 IQ points per joint smoked per day on the verbal reasoning subscale, 2nd trimester use was a significant predictor of performance on the short term memory subscale (decrease of 1.6 points per joint per day).
- For offspring of white women: no significant effect of prenatal marijuana use in any trimester.
- Preschool/day care attendance was a significant predictor of better performance on the Stanford-Binet Scale.
 - For total cohort: (considering interaction)
 - interaction of 1st trimester marijuana use by preschool/daycare attendance was significant and

- positive for composite and verbal reasoning subscale
- effect on of 2nd trimester use was a significant 2.3 point decrease per joint per day (not significant with interaction term)
- For African-American offspring:
 - 1st trimester use had 0.9 points/joint/day decrease on composite score, 1.1 points/joint/day decrease on short-term memory subscale and 1.5 points/joint/day decrease on verbal reasoning subscale.
 - 2nd trimester use had decrease of 1.8 points/joint/day for short term memory. Interaction between marijuana use and preschool/daycare attendance not significant in this group
- For white offspring:
 - For composite score, 2nd trimester effect showed a decrease of 8.9 points/joint/day if a child did not attend preschool/daycare and was offset by an increase in IQ score among children who did attend preschool/daycare.
 - Also was a significant main effect of 2nd trimester use on abstract/visual reasoning subscale (decrease of 7.6 points/joint/day) after controlling for the effect of the interaction.
 - Authors summarize: for both white and African-American offspring, prenatal marijuana use was associated with significantly decreased scores on the Stanford-Binet, but the decrease was offset by preschool/daycare attendance only in white children.
- Strengths:
 - high retention rate of MHPCD study (analyzed 655 of original 763 infants)
 - categorization of marijuana use into average daily joints (ADJ)
 - assessment of drug use at each trimester and each follow up point
 - comprehensive assessment of current factors that influence cognitive development (home environment, maternal cognitive ability, social and demographic factors) and adjusted for those factors
- Limitations:
 - Initial recruitment for study was 1983-1985
 - mothers were generally low income with a high school education and sample was 48% white, 52% black (could limit generalizability)
- Goldschmidt L et al 2008 - Prenatal MJ and Intelligence at Age 6 (MHPCD)
 - *medium quality evidence based on strengths and limitations*
 - Findings:
 - 2nd trimester heavy marijuana exposure (>1 joint cigarette per day) was significantly associated with the child's Stanford-Binet Intelligence Scale (SBIS) composite score after controlling for other predictors (5

- point deficit in composite score as compared to non-exposed)
 - 1st trimester heavy marijuana exposure significantly related to verbal reasoning (deficit of 2.6 points as compared to non-exposed)
 - Heavy marijuana exposure in 2nd (deficit of 8 points) and 3rd (deficit of 5 points) trimester significantly predicted performance on the quantitative reasoning subscale after controlling for other predictors
 - 2nd trimester heavy exposure was significantly associated with a decreased score on short-term memory subscale (-4.5 points)
- Strengths:
 - high retention rate of MHPCD study (648 children in this analysis)
 - categorization of marijuana use into average daily joints (ADJ)
 - assessment of drug use at each trimester and each follow up point
 - comprehensive assessment of factors that influence cognitive development (home environment, maternal cognitive ability, social and demographic factors)
- Limitations:
 - participants tended to be low income, most only had high school education and were 47% white, 53% African-American - may limit generalizability
 - use of SBIS - does not measure specific aspects of cognition such as learning, memory, problem solving and concept formation

We found moderate evidence that maternal use of marijuana during pregnancy is associated with reduced cognitive function in exposed offspring. (REVIEWED 5/18/2015)

- Willford et al 2010: MHPCD f/u age 16-18
 - *medium quality evidence based on strengths and limitations*
 - Findings:
 - prenatal marijuana use was significantly associated with decrease in processing speed and interhemispheric coordination
 - Strengths:
 - long term follow up cohort, 320 mother/child dyads for this analysis
 - prenatal marijuana use measured during each month of the 1st trimester and in 2nd and 3rd trimester
 - average daily joints calculated for each trimester
 - adjusted for home environment, prenatal exposure to alcohol or tobacco and age, life events, maternal depression, anxiety and hostility, also maternal intellectual ability (measured at 10 year f/u)
 - also considered adolescent drug use, depression and anxiety
 - Limitations:
 - low socioeconomic status of sample
 - sample contained less than half of the original sample due to inability to get 269 of the subjects to complete the bimanual coordination task (BCT) for various reasons
- Fried et al 2003 - Cognitive functioning in 13-16 year olds (OPPS f/u)

- *low quality of evidence based on strengths and limitations*
- Findings
 - Compared children of heavy users (≥ 6 joints/week) vs none/light users (< 6 joints/week)
 - After adjustment, there was a significant association found with children of heavy users having slower response times on the Abstract Designs latency section (visual memory task) than none/light users ($p \leq 0.05$)
 - After adjustment, there was a significant negative association with performance on the Peabody Spelling assessment ($p \leq 0.05$)
- Strengths
 - 157 children tested out of long term follow up cohort (190 children)
 - multiple tests used to assess multiple aspects of cognition
 - adjusted test scores for age of subject
 - adjusted for prenatal exposure, SES, maternal age, maternal drug use (tobacco, alcohol, other drugs), postnatal variables (SES, current maternal tobacco and marijuana use, home environment)
- Limitations
 - small sample sizes for marijuana analysis ($n=25$ for heavy users)
 - achievement tests are more highly dependent on formal learning experiences in school or home
 - study started in 1978
 - children of non-users and light users included in the same comparison group
- Smith AM et al 2004 - Effects of prenatal use on response inhibition - an fMRI study
 - *low quality of evidence based on strengths and limitations*
 - Findings:
 - there was a significant positive relationship between bilateral prefrontal cortex activity (mediates inhibitory functions) and the amount of prenatal marijuana exposure
 - there was an attenuation of activity in the left cerebellum with increase prenatal exposure to marijuana during response inhibition
 - After adjustment, prenatally exposed participants had significantly more errors of commission than the non-exposed group
 - Strengths:
 - controlled for current drug use (urine testing prior to imaging and completion of a drug questionnaire), participant excluded if positive for cocaine, opiates or amphetamine), also adjusted for current marijuana, nicotine, alcohol and IQ
 - adjusted for prenatal exposure to nicotine, alcohol and caffeine
 - Limitations:
 - small sample size - 35 participants from the OPPS f/u sample (16 exposed to prenatal marijuana, 15 not exposed)

- sample is predominantly white, middle class which could limit generalizability
- 13 of the 31 participants tested positive for cannabis, however there were no significant differences between the prenatally exposed and the non-prenatally exposed groups in the amount of cannabinoids in their urine and current use of marijuana was adjusted for

We found limited evidence that maternal marijuana use during pregnancy is associated with decreased academic ability of exposed offspring. (REVISED 5/18/2015)

- Fried et al 1997: Ottawa Prenatal Prospective Study f/u
 - *low quality of evidence based on strengths and limitations*
 - Findings:
 - Prenatal marijuana exposure was not significantly related to either the reading or language outcomes at age 9-12
 - Strengths:
 - multiple tests to assess reading and language/auditory domains were administered to the children as well as 2 brief questionnaires to examine depression and anxiety levels
 - adjusted for maternal demographic factors and educational level as well as postnatal variables such as current maternal marijuana use, socio-demographic characteristics
 - Limitations
 - small sample size (long term follow up cohort of 131 children of women who reported any use of marijuana, alcohol >0.85oz average daily or smoked an average of 16 mg nicotine per day +50 children of women with no substance use)
 - separated users into 3 groups (≤ 1 joint per week, >1 and <6 joints per week and ≥ 6 joints per week) and cell sizes were small for the more frequent use groups (n=11 and n=20, respectively)
- Goldschmidt L et al 2004 - Prenatal exposure and academic achievement at age 10 (MHPCD study f/u)
 - *medium quality evidence based on strengths and limitations*
 - Findings:
 - After adjustment, 1st trimester heavy use significantly predicted deficits in the WRAT-R reading and spelling scores and a lower rating on the teacher's evaluations
 - 1st trimester heavy use also significantly associated with the child's self-reported depression and anxiety symptoms.
 - When these scores were included in the regression analysis, 1st trimester heavy use was no longer a significant predictor of academic performance as measured in this study
 - After adjustment, 2nd trimester use was a significant predictor of

reading comprehension scores (PIAT-R) and 2nd trimester heavy use was significantly associated with a lower rating teachers' evaluation.

- 2nd trimester exposure was not significantly related to depression or anxiety symptoms

- 2nd trimester marijuana use also significantly predicted underachievement, after adjustment OR 2.0 (95% CI 1.05-3.8, p=0.04) as compared to non-users

○ Strengths:

- high retention rate of MHPCD study (606 children evaluated)
- categorization of marijuana use into average daily joints (ADJ)
- assessment of maternal drug use at each trimester and each follow up point
- utilized the Wide Range Achievement Test - Revised (WRAT-R), reading comprehension subtest of the Peabody Individual Achievement Test - Revised (PIAT-R) and teacher's report of child's performance
- also assessed child's depression and anxiety symptoms
- adjusted for maternal prenatal tobacco use, maternal current substance use, socio-demographic factors, child characteristics and environment,

○ Limitations:

- for regression analysis, marijuana use dichotomized to heavy use (≥ 1 joint per day) and no use + non-heavy use (< 1 joint per day)
- women were not heavy users of marijuana
- variables such as motivation, social skills and parent involvement in child's education (all predictors of school achievement) were not included in the analysis
- sample was predominantly low socioeconomic status

- Goldschmidt et al 2012: School achievement in 14 year olds (MHPCD f/u)

○ *medium quality evidence based on strengths and limitations*

○ Findings:

- after adjustment, 1st trimester maternal marijuana use (> 1 joint per day) was significantly associated with lower Weschsler Individual Achievement Test (WIAT) Screener (basic reading, math reasoning and spelling) composite score (-2.9 points, p<0.05)
- 1st trimester use (> 1 joint per day) significantly associated with a deficit in the basic reading subscale (-3.3 points, p<0.05)

○ Strengths:

- long term follow up cohort, 524 mother/child dyads for this analysis
- marijuana use measured during each month of the 1st trimester and in 2nd and 3rd trimester
- average daily joints calculated for each trimester
- adjusted for current maternal substance use, home environment, prenatal exposure to alcohol or tobacco and age
- also considered IQ, depression symptoms, inattention and effects of early initiation of marijuana use (results from previous studies)

- Limitations:
 - low socioeconomic status of the sample

We found moderate evidence that maternal use of marijuana during pregnancy is associated with attention problems in exposed offspring. (REVIEWED 5/18/2015)

- El Marroun 2011: Generation R study (Rotterdam, Netherlands) - 18 month f/u
 - *low quality evidence based on strengths and limitations*
 - Findings:
 - Prenatal exposure to cannabis was associated with increased scores on the aggressive behavior scale and the attention problem scale in girls only at 18 months old (using Child Behavior Checklist for toddlers CBCL 1 ½-5yrs).
 - In a logistic regression analyses using the cut-off score of the CBCL, the only significant result was that girls had an increased odds for developing attention problems (OR 2.75, 95% CI: 1.27-5.96, p=0.01)
 - Strengths:
 - large general population birth cohort (4077 for 18 month f/u out of 5512 initial study population)
 - Limitations:
 - even with a large cohort, only 88 women used cannabis in pregnancy, therefore there was a small sample size for analysis (especially with stratifying by gender)
 - ethnic differences in sample may limit generalizability to US population (i.e. women using cannabis during pregnancy were more often of Surinamese and Antillean national origin and women that continued use throughout pregnancy were more likely to be Turkish and less likely to be Moroccan)
- Noland JS et al 2005 - Prenatal drug use and selective attention in preschoolers
 - *low quality of evidence based on strengths and limitations*
 - Findings:
 - there was a non-significant positive correlation between the average severity of marijuana exposure and the rate of omission errors on the picture deletion task (PDT)
 - severity of first trimester marijuana use was identified as the best marijuana exposure predictor of PDT omission error rate (p=0.03)
 - When adjusting for severity of current caregivers use of marijuana, 1st trimester marijuana severity of use was not longer statistically significant
 - Strengths:
 - longitudinal prospective study (Case Western Reserve University), n=330 children (long term follow up for prenatal exposure to cocaine)
 - child testers blinded to substance exposure of children

- prenatal exposure assessed via biological samples taken during the birth hospital stay and a post partum interview (2 weeks post partum)
 - Limitations:
 - high percentage of marijuana users also used other substances (tobacco, alcohol or cocaine) - participants in a longitudinal study evaluating effects of prenatal cocaine exposures
 - use of severity score for marijuana - frequency estimate (days/week) multiplied by the daily amount of joints for each of 4 time periods which were averaged into a single average severity score
- Goldschmidt L et al 2000 - Prenatal exposure and behavior problems at age 10
 - *medium quality of evidence based on strengths and limitations*
 - Findings:
 - After adjustment, 1st trimester marijuana use remained a significant predictor of the attention scale of the SNAP ($p < 0.01$)
 - After adjustment, 3rd trimester marijuana use was significantly associated with higher scores on the hyperactivity ($p < 0.001$), attention ($p < 0.01$) and impulsivity ($p < 0.01$) scales of the SNAP
 - 1st trimester heavy use associated with significantly higher scores on the delinquency scale of the CBCL.
 - inattention symptoms mediated the effect of prenatal marijuana exposure on delinquency
 - No significant associations between prenatal marijuana use and the TRF scales
 - Strengths:
 - high retention rate of MHPCD study (635 children evaluated)
 - assessment of maternal drug use at each trimester and each follow up point
 - categorization of marijuana use into average daily joints (ADJ)
 - assessed child behavior problems with Swanson Noland and Pelham assessment (SNAP, elicits symptoms for DSM-III ADD with hyperactivity) and Child Behavior Checklist (CBCL) -both completed by mother/caregiver and Teacher's Report Form (TRF) - completed by teacher
 - adjusted for SES, maternal psychosocial characteristics, child's home environment, current maternal substance use, prenatal substance use
 - Limitations:
 - Only 575 children had teacher's reports
 - sample was predominantly low socioeconomic status
- Fried et al 2001: OPPS f/u 13-16 yrs
 - *medium quality evidence based on strengths and limitations*
 - Findings:
 - maternal marijuana use was significantly associated with poorer performance on the stability factor (one of the 5 factors of the model of attention)

- Heavy maternal marijuana use (≥ 6 joints per week) was associated with factor scores reflecting less consistent reaction time over blocks and more omissions
- Maternal marijuana use was not significantly associated with the other 4 factors (shift/flexibility, encode/retain, impulsivity, focus/execute)
- Strengths:
 - long term follow up of longitudinal study (152 of original 190 children)
 - adjusted for prenatal and current: parental education, family income, maternal drug use, secondhand smoke exposure (maternal and child), family status, adolescent's current smoking habits
 - subjects completed 11 tests that consisted of tasks to assess the 5 models of attention
- Limitations:
 - no measures of attentional deficits for the mother or father were available
 - study initiated in 1978

We found limited evidence that maternal use of marijuana during pregnancy is associated with increased depression symptoms in exposed offspring. (REVIEWED 5/18/2015)

- Gray KA et al. 2005 - Prenatal exposure and effect on child depressive symptoms at age 10 (MHPCD f/u study)
 - *medium quality of evidence based on strengths and limitations*
 - Findings:
 - prenatal marijuana exposure in 1st and 3rd trimesters significantly predicted more symptoms of depression in children after controlling for significant prenatal predictors and current correlates of child depression
 - Strengths:
 - high retention rate of MHPCD study (prospective study with long term follow up) n=636
 - categorization of marijuana use into average daily joints (ADJ)
 - assessment of drug use at each trimester and each follow up point
 - mother and child interviewed separately in a non-clinical environment
 - staff interviewers were unaware of mother's prenatal and current substance use history
 - conducted 3 regression analyses, one controlling for significant prenatal covariates, one controlling for the 10 year significant covariates and a 3rd with significant variables from the 1st and 2nd analyses
 - Limitations:
 - study looked at depression symptoms, not depression diagnosis
 - possible limited generalizability of study - sample was predominantly low socioeconomic status

We found insufficient evidence to suggest that maternal marijuana use during pregnancy is associated with psychosis symptoms in exposed adolescent offspring. (REVIEWED

5/18/2015)

- Zammit S et al 2009 - Avon Longitudinal Study f/u (UK)
 - *low quality of evidence based on strengths and limitations*
 - Findings:
 - after adjustment, maternal cannabis use during pregnancy was not significantly associated with psychosis-like symptoms (adjusted OR 0.94, 95% CI 0.62-1.41, p=0.755) based on the PLIKSi (psychosis like symptoms semi-structured interview)
 - Strengths:
 - 12 year follow up of large longitudinal study
 - Limitations:
 - poor retention at 12 year time point - sample consisted of 6356 children from original cohort of 14,062
 - did not assess current maternal substance use (only assessed maternal substance use up to 47 months after birth)
 - children who did not complete the assessment were more likely to have mothers who smoked tobacco and used cannabis as compared to those who did complete it

We found limited evidence that maternal marijuana use during pregnancy is associated with delinquent behaviors in exposed offspring. (REVIEWED 5/18/2015)

- Day et al 2011: Prenatal exposure and delinquent behaviors
 - *medium quality evidence based on strengths and limitations*
 - Findings:
 - After adjustment, offspring of heavier marijuana users (>1 joint per day) were significantly more likely to report delinquent behavior at age 14 (OR 1.76, 95%CI 1.05-2.96) as compared to non-users or those who used lower amounts
 - Association between prenatal marijuana exposure and delinquent behavior was mediated by depressive symptoms and attention problems at age 10
 - Strengths:
 - long term follow up cohort, 525 mother/child dyads for this analysis
 - marijuana use measured during each month of the 1st trimester and in 2nd and 3rd trimester
 - average daily joints calculated for each trimester
 - adjusted for current maternal substance use, home environment, prenatal exposure to alcohol or tobacco and age
 - also considered IQ, depression symptoms, inattention (results from previous studies)
 - utilized maternal report (Child Behavior Checklist) and adolescent self-report (Self-Report Delinquency Scale)
 - Limitations
 - low socioeconomic status of the sample

- there are multiple pathways to delinquency and the effects of prenatal marijuana exposure only explain a portion of the delinquency in the adolescent population

We found mixed evidence for whether or not maternal marijuana use during pregnancy is associated with frequency of marijuana use by the exposed offspring during adolescence. (REVIEWED 5/18/2015)

- Day et al 2006: Prenatal marijuana use and marijuana use by offspring at age 14
 - *medium quality of evidence based on strengths and limitations*
 - Findings:
 - When adjusted for significant current child behavioral characteristics:
 - prenatal marijuana exposure was not significantly associated with age of onset of offspring marijuana use
 - prenatal marijuana exposure was significantly associated with frequency of offspring marijuana use (OR 1.3 for adolescents who were exposed to 1 joint/day as compared to those with no exposure)
 - Strengths:
 - 580 of original 763 offspring evaluated at 14 years
 - participants evaluated at time point with a standardized protocol (maternal psychological, social and environmental factors, demographics, substance use, child's cognitive, behavioral, psychological and physical development)
 - adjusted for prenatal substance use, maternal and child factors
 - Limitations
 - low socioeconomic status of participants
 - original cohort was weighted to substance-using women, therefore results may be less generalizable
- Porath AJ and Fried PA 2005 - Prenatal marijuana use and later drug use in offspring (OPPS follow up)
 - *low quality of evidence based on strengths and limitations*
 - Findings:
 - no significant association between prenatal exposure to marijuana and offspring's regular use of marijuana
 - no significant association between prenatal marijuana exposure and gender of offspring and initiation or regular use of marijuana
 - Strengths:
 - longitudinal study with long term follow up (152 adolescents), 16-21 years old)
 - use was determined via self-report and verified with a urine test
 - Limitations:
 - relatively small sample size (especially for gender-specific analyses) - 190 children selected from original cohort for follow up studies
 - sample predominantly white, middle class

- Study started in 1978
- no data collected on parent's current use of substances
- use of marijuana in pregnancy categorized into use and no use

We found insufficient evidence that maternal marijuana use during pregnancy is associated with initiation of marijuana use by exposed offspring during adolescence. (REVIEWED 5/18/2015)

- Porath AJ and Fried PA 2005 - Prenatal marijuana use and later drug use in offspring (OPPS follow up)
 - *low quality of evidence based on strengths and limitations*
 - Findings:
 - Significant association between prenatal exposure to marijuana and offspring's initiation of marijuana use (OR 2.76, 95%CI 1.11-6.86)
 - no significant association between prenatal marijuana exposure and gender of offspring and initiation or regular use of marijuana
 - Strengths:
 - longitudinal study with long term follow up (152 adolescents), 16-21 years old)
 - use was determined via self-report and verified with a urine test
 - Limitations:
 - relatively small sample size (especially for gender-specific analyses) - 190 children selected from original cohort for follow up studies
 - sample predominantly white, middle class
 - Study started in 1978
 - no data collected on parent's current use of substances
 - use of marijuana in pregnancy categorized into use and no use
 - large confidence interval (95%CI 1.11-6.86)

MARIJUANA USE AND BREASTFEEDING

Epidemiology of marijuana use and breastfeeding:

- There is limited epidemiologic information about marijuana use in breastfeeding women, as distinct from data in pregnant women.

Biological evidence shows that THC is present in the breast milk of women who use marijuana.

Biological evidence shows that infants who drink breast milk containing THC absorb and metabolize the THC.

- Two women who used marijuana while breastfeeding had THC in their breast milk. One of them had plasma tested as well, with 8x higher concentration in the breast milk compared with plasma. (Perez-Reyes 1982)

Strengths:

- Biological finding

- Both THC and metabolites were tested

Minor limitations:

- No information about temporal relationship between use and presence in breast milk.
 - Only two women were tested for presence of THC. Only one was tested for ratios between plasma and breast milk.
- One baby's feces was tested, with much higher metabolite-to-THC proportion than was present in its mother's breast milk. (Perez-Reyes 1982)

Strengths:

- Biological finding
- Both THC and metabolites were tested

Limitations:

- Could conversion to metabolites occur in the gut, without absorption?
- Infant's urine was not tested.
- Only one mother and child were tested.

We found **mixed** evidence for whether or not an association exists between maternal use of marijuana while breastfeeding and motor development in exposed infants. (REVIEWED 5/18/2015)

- Infants whose mothers used marijuana while breastfeeding during the first month of life (on at least 15 of 30 days) had poorer motor development at 1yr of age, but no significant difference in mental development (Astley 1990) *Medium quality evidence based on strengths and limitations.*
- Infants whose mothers used marijuana while breastfeeding during the third month of life had no significant difference in mental or motor development at 1yr of age (Astley 1990) *Medium quality evidence based on strengths and limitations.*

Strengths:

- Longitudinal study - marijuana use during the 1st and 3rd month of lactation and follow up testing of infant at 1yr
- Controls matched on multiple factors, including duration of lactation, prenatal marijuana exposure and month of birth
- Marijuana exposure was a continuous variable (days exposed)
- Good tools used to measure development at 1yr (Bayley Scales of Infant Development)
- Adjusted for many variables - maternal age, race, income, education, marital status, pregnancy history, and weight gain; maternal tobacco, coffee, alcohol and other drug use during pregnancy or lactation; marijuana use during pregnancy; infant gestational age and sex
- Mean change of a 12% decrease in scores

Limitations:

- Matching for prenatal marijuana exposure was unable to reduce the strong correlation between prenatal and lactation exposure (of women who reported marijuana use during pregnancy, 84% continued to use marijuana during lactation).

- No confidence interval was given for the change
 - Mother-child interaction was not measured or adjusted for
- Infants whose mothers used marijuana while breastfeeding had no significant difference in mental or motor development at 1yr of age (Tennes 1985) *Low quality evidence based on strengths and limitations.*

Strengths:

- Longitudinal study
- Good tools used to measure development at 1yr (Bayley Scales of Infant Development)

Major limitations:

- No statistics were given - mean, CI, etc., nor were statistical methods given. It was simply stated "Comparison of infant outcomes on growth, or on mental and motor development, revealed no apparent effects of postnatal marijuana exposure."

Minor limitations:

- Over 50% of "heavy users" were lost at 1 year.
- Controls were chosen randomly from among non-exposed (not matched), and were demographically different from marijuana users
- 62 total breastfeeding mothers, with only 6 who used marijuana more than weekly
- Time period of exposure was not clarified - it appears to be any concurrent marijuana use and breastfeeding
- Did not say anything about adjusting for potential confounding variables

We found insufficient evidence to determine whether or not infant exposure to marijuana (either from maternal marijuana use during breastfeeding or infant exposure to marijuana smoke) is associated with SIDS. (REVIEWED 5/18/2015)

- Infants exposed to marijuana postnatally did not have different risk of SIDS than those not exposed. (Klonoff-Cohen 2001) *Low quality evidence based on strengths and limitations.*

Strengths:

- Controls were matched on multiple factors
- Cases and controls clearly defined
- Adjusted for multiple potential confounders

Major limitations:

- Retrospective case-control study interviewing parents whose baby had died, about their drug use relative to the lost baby
- Postnatal exposure defined as EITHER breastfeeding while using MJ, or exposing infant to marijuana smoke

Minor limitations:

- Reports "tremendous effort to locate" some cases, consisting of "14 strategies" - some might not have wanted to participate

- Quantity of postnatal marijuana exposure not clarified - appears to be any vs none
- Wide confidence interval for OR (0.4-2.9)

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