October 2015 Literature Alert

1.
Ann Intern Med. 2015 Oct 6;163(7):529-36. doi: 10.7326/M15-1707.
Screening for Iron Deficiency Anemia and Iron Supplementation in Pregnant Women to Improve Maternal Health and Birth Outcomes: U.S. Preventive Services Task Force Recommendation Statement.
Siu AL; U.S. Preventive Services Task Force.

Abstract
DESCRIPTION:
Update of the 2006 U.S. Preventive Services Task Force (USPSTF) recommendation on screening for iron deficiency anemia.
METHODS:
The USPSTF reviewed the evidence on the association between change in iron status as a result of intervention (oral supplementation or treatment) in pregnant women and adolescents and improvement in maternal and infant health outcomes.
POPULATION:
This recommendation applies to pregnant women and adolescents living in the United States who do not have symptoms of iron deficiency anemia. It does not address pregnant women who are malnourished, have symptoms of iron deficiency anemia, or have special hematologic conditions or nutritional needs that may increase their need for iron.
RECOMMENDATIONS:
The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for iron deficiency anemia in pregnant women to prevent adverse maternal health and birth outcomes. (I statement). The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of routine iron supplementation for pregnant women to prevent adverse maternal health and birth outcomes. (I statement).
PMID: 26344176

2.
J Neonatal Perinatal Med. 2015 Jul 31;8(2):105-12. doi: 10.3233/NPM-15814102.
Neonatal outcomes of macrosomic infants of diabetic and non-diabetic mothers.
Cordero L, Paetow P, Landon MB, Nankervis CA.

Abstract
OBJECTIVE:
To compare neonatal outcomes (including breastfeeding (BF) initiation) of 170 macrosomic IDM with that of 739 macrosomic nIDM.
DESIGN/METHODS:
Retrospective cohort investigation of all macrosomic infants born consecutively over a four-year period (2008-2011). Macrosomic (birth weight ≥4000 g) IDM included 100 infants whose mothers had gestational diabetes and 70 whose mothers had pregestational diabetes.
RESULTS:
IDM were more likely to be delivered by cesarean to obese women while nIDM were more likely to be delivered vaginally to younger women with a higher level of education. Ethnic distribution (60% white, 20% black, 10% Hispanic and 10% Asian or African) was similar in each group. Forty-nine percent of IDM and 7% of nIDM required NICU admission. Respiratory disorders (mainly TTNB) affected 21% of IDM and 3% of nIDM while hypoglycemia was observed in 36% of IDM and 15% of nIDM. Of the 35 IDM delivered vaginally, 10 were complicated by shoulder dystocia without injury. Conversely, 70 of the 458 nIDM delivered vaginally experienced shoulder dystocia that resulted in 6 limb fractures and 3 brachial plexus injuries. On arrival to labor and delivery, 75% of all women intended to BF; however, at the time of discharge, 65% of women with diabetes and 92% of those without diabetes who intended to BF had initiated BF.
CONCLUSIONS:
Both macrosomic IDM and macrosomic nIDM are at risk for significant morbidities. Macrosomic IDM carry a higher risk for NICU admissions, leading to maternal-infant separation, and lower BF initiation rates.
KEYWORDS:
Macrosomia; breastfeeding; diabetes
PMID: 26410433

3.
J Pediatr. 2015 Sep;167(3):579-585.e2. doi: 10.1016/j.jpeds.2015.05.043. Epub 2015 Jun 27.
Gestational Weight Gain in Adolescent Compared with Adult Pregnancies: An Age-Specific Body Mass Index Approach.
Elchert J, Beaudrot M, DeFranco E.

Abstract
OBJECTIVE:
To determine current trends in gestational weight gain (GWG) in adolescents, using adolescent specific body mass index (BMI), in relation to the 2009 Institute of Medicine GWG guidelines.
STUDY DESIGN:
Population-based retrospective cohort using Ohio birth records (2006-2012). Analyses were limited to primiparous women with singleton nonanomalous live births and available data on BMI and GWG. GWG percentiles were stratified by maternal age (less than 15, 15-17, 18-19,

and 20-34 years old) and prepregnancy BMI category. Adolescent specific BMI definitions were used for mothers less than 19 years.
RESULTS:
A total of 1 034 552 births occurred during the study period; 326 368 were included for analysis. Less than one-quarter of women gained the recommended amount of weight (20.6%). A large proportion of pregnancies had excessive GWG: 59.8% of mothers less than 15 years of age, compared with older adolescent (59.9%, 62.6%) and adult mothers (64.6%), P < .001. Average, median, and IQRs of GWG were similar for all women within the same BMI category, regardless of age. Except in underweight women, the average GWG was at the high end or above the 2009 Institute of Medicine recommendations, for adolescents in all BMI groups, similar to adults, median 35 (IQR 24-47) pounds.
CONCLUSIONS:
Current GWG trends indicate that excessive weight gain is nearly as common in adolescents as in adult mothers.

PMID: 26130111

4.
N Engl J Med. 2015 Sep 10;373(11):1032-9. doi: 10.1056/NEJMoa1502950.
Eculizumab in Pregnant Patients with Paroxysmal Nocturnal Hemoglobinuria.
Kelly RJ, Höchsmann B, Szer J, Kulasekararaj A, de Guibert S, Röth A, Weitz IC, Armstrong E, Risitano AM, Patriquin CJ, Terriou L, Muus P, Hill A, Turner MP, Schrezenmeier H, Peffault de Latour R.

Abstract
BACKGROUND:
Eculizumab, a humanized monoclonal antibody against complement protein C5 that inhibits terminal complement activation, has been shown to prevent complications of paroxysmal nocturnal hemoglobinuria (PNH) and improve quality of life and overall survival, but data on the use of eculizumab in women during pregnancy are scarce.
METHODS:
We designed a questionnaire to solicit data on pregnancies in women with PNH and sent it to the members of the International PNH Interest Group and to the physicians participating in the International PNH Registry. We assessed the safety and efficacy of eculizumab in pregnant patients with PNH by examining the birth and developmental records of the children born and adverse events in the mothers.
RESULTS:
Of the 94 questionnaires that were sent out, 75 were returned, representing a response rate of 80%. Data on 75 pregnancies in 61 women with PNH were evaluated. There were no maternal deaths and three fetal deaths (4%). Six miscarriages (8%) occurred during the first trimester. Requirements for transfusion of red cells increased during pregnancy, from a mean of 0.14 units per month in the 6 months before pregnancy to 0.92 units per month during pregnancy. Platelet transfusions were given in 16 pregnancies. In 54% of pregnancies that progressed past

the first trimester, the dose or the frequency of use of eculizumab had to be increased. Low-molecular-weight heparin was used in 88% of the pregnancies. Ten hemorrhagic events and 2 thrombotic events were documented; both thrombotic events occurred during the postpartum period. A total of 22 births (29%) were premature. Twenty cord-blood samples were examined for the presence of eculizumab; the drug was detected in 7 of the samples. A total of 25 babies were breast-fed, and in 10 of these cases, breast milk was examined for the presence of eculizumab; the drug was not detected in any of the 10 breast-milk samples.
CONCLUSIONS:
Eculizumab provided benefit for women with PNH during pregnancy, as evidenced by a high rate of fetal survival and a low rate of maternal complications. (ClinicalTrials.gov number, NCT01374360.).
PMID: 26352814

5.
Prenat Diagn. 2015 Sep;35(9):919-22. doi: 10.1002/pd.4645. Epub 2015 Jul 16.
The hippocampal commissure: a new finding at prenatal 3D ultrasound in fetuses with isolated complete agenesis of the corpus callosum.
Contro E, Nanni M, Bellussi F, Salsi G, Grisolia G, Sanz-Cortès M, Righini A, Rizzo N, Pilu G, Ghi T.

Abstract
OBJECTIVE:
The aim of this research was to determine the prevalence and sonographic appearance of the hippocampal commissure in fetuses with isolated complete agenesis of the corpus callosum by three-dimensional neurosonography in the multiplanar mode.
METHODS:
This was a multicenter observational study. Stored volume datasets of fetuses with isolated complete agenesis of the corpus were retrospectively retrieved for analysis in three tertiary centers. The presence or absence of the hippocampal commissure was independently evaluated in the coronal and midsagittal planes by two operators. Postnatal follow-up was obtained in all cases.
RESULTS:
From November 2007 to February 2013, 41 cases between 19 and 30 weeks of gestation were retrieved for analysis. The hippocampal commissure was visible in the coronal and sagittal planes in 27/41 (65.8%), absent or not clearly recognizable in the remaining 14 cases. The qualitative analysis of the two operators was concordant in 100% of cases.
CONCLUSIONS:
In more than half of fetuses with complete callosal agenesis, the hippocampal commissure may be visualized at prenatal ultrasound. This is a residual interhemispheric connection, which in normal cases is hidden by the corpus callosum itself. Further research is needed to establish if this has an impact on postnatal outcome. © 2015 John Wiley & Sons, Ltd.

PMID: 26126648

6.
J Perinatol. 2015 Sep;35(9):768-72. doi: 10.1038/jp.2015.44. Epub 2015 May 7.
Outcomes of neonates with birth weight⩽500 g: a 20-year experience.
Upadhyay K, Pourcyrous M, Dhanireddy R, Talati AJ.
Author information
Abstract
OBJECTIVE:
Ethical dilemmas continue regarding resuscitation versus comfort care in extremely preterm infants. Counseling parents and making decisions regarding the care of these neonates should be based on reliable, unbiased and representative data drawn from geographically defined populations. We reviewed survival and morbidity data for our population at the edge of viability.
STUDY DESIGN:
A retrospective review of our perinatal database was carried out to identify all infants born alive and admitted to the neonatal intensive care unit (NICU) with BW⩽500 g between 1989 and 2009. Data from the initial hospital stay and follow-up at 24 months were collected.
RESULT:
Out of 22 672 NICU admissions, 273 were eligible: 212 neonates were reviewed after excluding infants with comfort care. BW ranged from 285 to 500 g (mean 448 g) and gestational age range 22 to 28 weeks (median 24 week). Sixty-one (28.8%) survived until discharge. Only 13.8% males survived compared with 39.2% females (P<0.05). Half (49%) were discharged with home oxygen/monitor. Fifty (82%) patients' charts were available to review at the 24-month follow-up. Thirty-three percent of surviving infants had a normal neurodevelopmental assessment at 24 months. Forty-three percent had weight/head circumference<5th percentile at 24 months.
CONCLUSION:
About a third of neonates admitted to NICU with ⩽500 g BW survived, with 33% of those surviving, demonstrating age-appropriate development at a 24-month follow-up visit.
PMID: 25950920

7.
BJOG. 2015 Sep;122(10):1303-11. doi: 10.1111/1471-0528.13324. Epub 2015 Mar 6.
A whole-of-population study of term and post-term gestational age at birth and children's development.
Smithers LG, Searle AK, Chittleborough CR, Scheil W, Brinkman SA, Lynch JW.

Abstract
OBJECTIVE:
To examine the risk of poor child development according to week of gestation at birth, among children born ≥37 weeks' gestation.
DESIGN:
Population-based study using linked data (n = 12 601).
SETTING:
South Australia.

POPULATION:
All births ≥37 weeks' gestation.
METHODS:
Relative risks of developmental vulnerability for each week of gestation were calculated with adjustment for confounders and addressing missing information.
MAIN OUTCOME MEASURES:
Child development was documented by teachers during a national census of children attending their first year of school in 2009, using the Australian Early Development Index (AEDI). Children scoring in the lowest 10% of the AEDI were categorised as developmentally vulnerable.
RESULTS:
The percentage of children vulnerable on one or more AEDI domains for the following gestational ages 37, 38, 39, 40, 41, 42-45 weeks was 24.8, 22.3, 20.6, 20.0, 20.4 and 24.2, respectively. Compared with children born at 40 weeks, the adjusted relative risks [(95% confidence interval (CI)] for vulnerability on ≥1 AEDI domain were; 37 weeks 1.13 (0.99-1.28), 38 weeks 1.05 (0.96-1.15), 39 weeks 1.02 (0.94-1.12), 41 weeks 1.00 (0.90-1.11) and 42-45 weeks 1.20 (0.84-1.72).
CONCLUSIONS:
Children born at 40-41 weeks' gestation may have the lowest risk of developmental vulnerability at school entry, reinforcing the importance of term birth in perinatal care. Early term or post-term gestational age at birth can help clinicians, teachers and parents recognise children with potential developmental vulnerabilities at school entry.

KEYWORDS:
Child development gestational age
PMID: 25754325

8.
Pediatrics. 2015 Aug 24. pii: peds.2015-1043. [Epub ahead of print]
Preterm Birth and Poor Fetal Growth as Risk Factors of Attention-Deficit/Hyperactivity Disorder.
Sucksdorff M, Lehtonen L, Chudal R, Suominen A, Joelsson P, Gissler M, Sourander A.

Abstract
BACKGROUND:
Previous studies have shown an association between prematurity and attention-deficit/hyperactivity disorder (ADHD). Results concerning late preterm infants are controversial, and studies examining fetal growth represented by weight for gestational age are scarce. Our objective was to examine the association between gestational age by each week of fetal maturity, weight for gestational age, and ADHD.
METHODS:
In this population-based study, 10 321 patients with ADHD, diagnosed according to the International Classification of Diseases and 38 355 controls individually matched for gender, date and place of birth, were identified from Finnish nationwide registers. Perinatal data were obtained from the Finnish Medical Birth Register. Conditional logistic regression was used to

examine the association between gestational age, weight for gestational age, and ADHD after controlling for confounding factors.
RESULTS:
The risk of ADHD increased by each declining week of gestation. The associations were robust after adjusting for confounders. An elevated risk also was seen among late preterm and early term infants. As for fetal growth, the odds ratio showed a U-shaped curve with an increased risk seen when the weight for gestational age was 1 SD below and 2 SD above the mean.
CONCLUSIONS:
Our findings suggest that each gestational week has significance for child's subsequent neurodevelopment and risk for ADHD. We also showed that poor fetal growth increased the risk of ADHD. This highlights the importance of taking into account both prematurity and poor fetal growth when planning the timing of birth as well as later follow-up and support policies.

PMID: 26304830

9.
Eur J Obstet Gynecol Reprod Biol. 2015 Oct;193:34-9. doi: 10.1016/j.ejogrb.2015.06.024. Epub 2015 Jul 9.
Folic acid in pregnant women associated with reduced prevalence of severe congenital heart defects in their children: a national population-based case-control study.
Czeizel AE, Vereczkey A, Szabó I.

Abstract
OBJECTIVE:
Previous Hungarian intervention trials have shown an association between periconceptional folic-acid-containing multivitamin supplementation and significantly reduced risk of congenital heart defects (CHDs). These findings were confirmed in observational multivitamin studies in the USA, and studies in the Netherlands and China regarding folic acid. The objective of this observational population-based study was to estimate the possible preventive effect of folic acid supplementation for different CHDs during their critical period of development.
STUDY DESIGN:
Evaluation of medically recorded use of folic acid (calculated daily average 5.6mg) during the critical period of development of eight types of CHD (verified through autopsy reports or after catheter examination and/or surgical correction) in the population-based Hungarian Case-Control Surveillance of Congenital Abnormalities (HCCSCA), 1980-1996, containing 22,843 cases with congenital abnormalities and 38,151 population controls without any CHDs, including 5395 matched controls of 3567 live-born cases with various CHDs. A conditional logistic regression model was used to estimate the relative risk/protection [odds ratio (OR) with 95% confidence intervals (CI)] of folic acid in the mothers of cases with various types of CHD and their matched controls.
RESULTS:
There was a significant decrease in the prevalence of cases with ventricular septal defect (OR 0.57, 95% CI 0.45-0.73), tetralogy of Fallot (OR 0.53, 95% CI 0.17-0.94), d-transposition of great arteries (OR 0.47, 95% CI 0.26-0.86) and atrial septal defect secundum (OR 0.63, 95% CI 0.40-

0.98) in infants born to mothers who had taken high doses of folic acid during the critical period of CHD development.
CONCLUSIONS:
The risk of development of certain types of CHD was significantly reduced in pregnant women who were supplemented with folic acid. Thus, CHDs should be included as a secondary assessment in neural-tube-defect preventive programs.

KEYWORDS:
Congenital heart defect; Folic acid; Population-based case–control study; Tetralogy of Fallot; Ventricular septal defect; d-Transposition of great arteries
PMID: 26225846

10.
Ultrasound Obstet Gynecol. 2015 Sep;46(3):350-5. doi: 10.1002/uog.14728.
Prevention of postpartum hemorrhage and hysterectomy in patients with morbidly adherent placenta: a cohort study comparing outcomes before and after introduction of the Triple-P procedure.
Teixidor Viñas M, Belli AM, Arulkumaran S, Chandraharan E.

Abstract
OBJECTIVES:
To evaluate patient outcomes and need for further interventions in women with a morbidly adherent placenta (MAP), before and after introduction of the Triple-P procedure involving placental non-separation, myometrial excision and reconstruction of the uterine wall.
METHODS:
Between December 2007 and February 2014, 30 patients with MAP were treated at our center. In 2007, we instituted a policy of bilateral prophylactic occlusion balloon catheter placement in both internal iliac arteries followed by Cesarean section with non-placental separation and preservation of the uterus. In 2010, the surgical technique was modified and the Triple-P procedure introduced. As a result, 19 women in our study received the Triple-P protocol (study group) and 11 did not (control group). The quantity of blood replacement products, estimated blood loss, and necessity for uterine arterial embolization and/or hysterectomy were recorded retrospectively and compared between the two groups.
RESULTS:
Placenta percreta was confirmed in six (54.5%) patients in the control group and 13 (68.4%) in the study group. Estimated mean blood loss during the procedure was lower in the study group than in the control group (1.70 L vs 2.17 L, respectively), but the difference was not statistically significant (P = 0.445). The risks of postpartum hemorrhage (PPH) and hysterectomy were statistically significantly lower in the study group (PPH, 54.5% vs 15.8%; P = 0.035; hysterectomy, 27.3% vs 0.0%; P = 0.045). As a consequence, there was a significant decrease in duration of inpatient stay in the study group (P = 0.044).
CONCLUSION:

Introduction of the Triple-P procedure conveyed a significantly reduced rate of hysterectomy, PPH and duration of hospital stay in patients with MAP. Copyright © 2014 ISUOG. Published by John Wiley & Sons Ltd.

KEYWORDS:
hysterectomy prevention; massive postpartum hemorrhage; prophylactic percutaneous occlusion balloon catheter placement; uterine artery embolization
PMID: 25402727

11.
Am J Obstet Gynecol. 2015 Sep;213(3):410.e1-6. doi: 10.1016/j.ajog.2015.05.022. Epub 2015 May 14.
The risk of fetal death in nonanomalous pregnancies affected by polyhydramnios.
Pilliod RA, Page JM, Burwick RM, Kaimal AJ, Cheng YW, Caughey AB.

Abstract
OBJECTIVE:
The objective of the study was to evaluate the ongoing risk of intrauterine fetal demise (IUFD) in nonanomalous pregnancies affected by polyhydramnios.
STUDY DESIGN:
We analyzed a retrospective cohort of all singleton, nonanomalous births in California between 2005 and 2008 as recorded in a statewide birth certificate registry. We included all births between 24+0 and 41+6 weeks' gestational age, excluding multiple gestations, major congenital anomalies, and pregnancies affected by oligohydramnios. Polyhydramnios was identified by International Classification of Diseases, ninth revision, codes. $\chi(2)$ tests were used to compare the dichotomous outcomes, and multivariable logistic regression analyses were then performed to control for potential confounders. We analyzed the data for pregnancies affected and unaffected by polyhydramnios. The IUFD risk was expressed as a rate per 10,000.
RESULTS:
The risk of IUFD in pregnancies affected by polyhydramnios was greater at every gestational age compared with unaffected pregnancies. The IUFD risk in pregnancies affected by polyhydramnios was more than 7 times higher than unaffected pregnancies at 37 weeks at a rate of 18.0 (95% confidence interval [CI], 9.0-32.6) vs 2.4 (95% CI, 2.0-2.5) and was 11-fold higher by 40 weeks' gestational age at a rate of 66.3 (95% CI, 10.8-68.6) vs 6.0 (95% CI, 5.1-6.3) in unaffected pregnancies. When adjusted for multiple confounding variables, the presence of polyhydramnios remained associated with an increased odds of IUFD in nonanomalous singleton pregnancies, with an adjusted odds ratio of 5.5 (95% CI, 4.1-7.6).
CONCLUSION:
Ongoing risk of IUFD is greater in low-risk pregnancies affected by polyhydramnios at all gestational ages compared with unaffected pregnancies with the greatest increase in risk at term. Although further study is needed to explore the underlying etiology of polyhydramnios in these cases, the identification of polyhydramnios alone may warrant increased antenatal surveillance.

KEYWORDS:
antenatal testing; intrauterine fetal demise; polyhydramnios; stillbirth
PMID: 25981851

12.
Am J Obstet Gynecol. 2015 Sep;213(3):373.e1-7. doi: 10.1016/j.ajog.2015.03.051. Epub 2015 Mar 28.
The significance of base deficit in acidemic term neonates.
Knutzen L, Svirko E, Impey L.

Abstract
OBJECTIVE:
Much emphasis is placed on the metabolic component of umbilical cord acidemia at birth, with an importance attached to an arterial level of <7.00 accompanied by a base deficit of 12 mmol/L. We hypothesized that in acidemic neonates, the level of arterial base deficit provides no prognostic information beyond that provided by the level of arterial pH.
STUDY DESIGN:
This is a cohort study using a database of deliveries from a major teaching hospital, with additional information from neonatal records. A total of 8797 term, singleton, nonanomalous neonates were identified who had paired and validated cord blood gas analysis. Of these, 520 were acidemic (pH <7.1) and 84 were severely acidemic (pH <7.0). Outcomes examined were encephalopathy grade 2/3 and/or death, Apgar <7 at 5 minutes, neonatal unit admission, and composite outcomes of neurological and systemic involvement. Hierarchical logistic regressions were done using IBM SPSS Statistics 20.0 (Armonk, NY) to assess the predictive value of arterial pH and arterial base deficit.
RESULTS:
For each outcome the median pH and base deficit of those neonates affected by the adverse outcome was significantly lower than for those who were unaffected. Hierarchical logistic regressions showed that pH is a significant predictor of all adverse outcomes studied (P < .001 for all outcomes). When base deficit, and then the cross-product, are added to the model, neither add predictive value.
CONCLUSION:
In acidemic neonates, the metabolic component does not predict those at risk of adverse outcomes once pH is taken into account. The apparently worse outcomes with greater base deficit simply reflect a greater degree of acidemia. The prognostic significance attached to the base deficit among acidemic neonates is questionable.

KEYWORDS:
adverse neonatal outcome; base deficit; metabolic acidosis; pH; umbilical cord
PMID: 25827502