



## March 2016 Literature Alert

1.

Am J Obstet Gynecol. 2016 Feb;214(2):225-34. doi: 10.1016/j.ajog.2015.09.080. Epub 2015 Oct 9.

[Celiac disease and obstetric complications: a systematic review and metaanalysis.](#)

Saccone G, Berghella V, Sarno L, Maruotti GM, Cetin I, Greco L, Khashan AS, McCarthy F, Martinelli D, Fortunato F, Martinelli P.

### Abstract

The aim of this metaanalysis was to evaluate the risk of the development of obstetric complications in women with celiac disease. We searched electronic databases from their inception until February 2015. We included all cohort studies that reported the incidence of obstetric complications in women with celiac disease compared with women without celiac disease (ie, control group). Studies without a control group and case-control studies were excluded. The primary outcome was defined a priori and was the incidence of a composite of obstetric complications that included intrauterine growth restriction, small for gestational age, low birthweight, preeclampsia and preterm birth. Secondary outcomes included the incidence of preterm birth, intrauterine growth restriction, stillbirth, preeclampsia, small for gestational age, and low birthweight. The review was registered with PROSPERO (CRD42015017263) before data extraction. All authors were contacted to obtain the original databases and perform individual participant data metaanalysis. Primary and secondary outcomes were assessed in the aggregate data analysis and in the individual participant data metaanalysis. We included 10 cohort studies (4,844,555 women) in this metaanalysis. Four authors provided the entire databases for the individual participant data analysis. Because none of the included studies stratified data for the primary outcome (ie, composite outcome), the assessment of this outcome for the aggregate analysis was not feasible. Aggregate data analysis showed that, compared with women in the control group, women with celiac disease (both treated and untreated) had a significantly higher risk of the development of preterm birth (adjusted odds ratio, 1.35; 95% confidence interval, 1.09-1.66), intrauterine growth restriction (odds ratio, 2.48; 95% confidence interval, 1.32-4.67), stillbirth (odds ratio, 4.84; 95% confidence interval, 1.08-21.75), low birthweight (odds ratio, 1.63; 95% confidence interval, 1.06-2.51), and small for gestational age (odds ratio, 4.52; 95% confidence interval, 1.02-20.08); no statistically significant difference was found in the incidence of preeclampsia (odds ratio, 2.45; 95% confidence interval, 0.90-6.70). The risk of preterm birth was still significantly higher both in the subgroup analysis of only women with diagnosed and treated celiac disease (odds ratio, 1.26; 95% confidence interval, 1.06-1.48) and in the subgroup analysis of only women with undiagnosed and untreated celiac disease (odds ratio, 2.50; 95% confidence interval; 1.06-5.87). Women with diagnosed and treated celiac disease had a significantly lower risk of the development of preterm birth, compared with undiagnosed and untreated celiac disease (odds ratio, 0.80; 95% confidence interval, 0.64-0.99). The individual participant data metaanalysis showed that women with celiac disease had a significantly higher risk of composite obstetric complications compared with control subjects (odds ratio, 1.51; 95% confidence interval, 1.17-1.94). Our individual participant data concurs with the aggregate analysis for all the secondary outcomes. In summary, women with celiac disease had a significantly higher risk of the development of

obstetric complications that included preterm birth, intrauterine growth restriction, stillbirth, low birthweight, and small for gestational age. Since the treatment with gluten-free diet leads to a significant decrease of preterm delivery, physicians should warn these women about the importance of a strict diet to improve obstetric outcomes. Future studies calculating cost-effectiveness of screening for celiac disease during pregnancy, which could be easily performed, economically and noninvasively, are needed. In addition, further studies are required to determine whether women with adverse pregnancy outcomes should be screened for celiac disease, particularly in countries where the prevalence is high. Copyright © 2016 Elsevier Inc. All rights reserved.

**KEYWORDS:**

celiac disease; metaanalysis; pregnancy; preterm birth; small for gestational age

PMID: 26432464 [PubMed - in process]

2.

Circulation. 2016 Feb 9;133(6):566-75. doi: 10.1161/CIRCULATIONAHA.115.019089. Epub 2016 Jan 14.

[Congenital Heart Defects and Indices of Fetal Cerebral Growth in a Nationwide Cohort of 924 422 Liveborn Infants.](#)

Matthiesen NB, Henriksen TB, Gaynor JW, Agergaard P, Bach CC, Hjortdal VE, Østergaard JR.

**Abstract**

**BACKGROUND:**

Neurodevelopmental disorders are the most common and distressful comorbidities associated with congenital heart defects (CHD). Head circumference at birth (HC), a proxy for prenatal cerebral growth, is an established risk factor for neurodevelopmental disorders.

**METHODS AND RESULTS:**

In a nationwide cohort, we included all 924 422 liveborn Danish singletons, 1997 to 2011. CHD was present in 5519. The association between CHD and growth indices was analyzed by multivariable linear regression, adjusted for potential confounders. We report mean differences in gestational age-specific z scores in comparison with the general population. CHD was associated with lower HC z scores, -0.10 (95% confidence interval [CI], -0.13 to -0.08). Several CHD subtypes were associated with smaller HC, eg, hypoplastic left heart syndrome, -0.39 (95% CI, -0.58 to -0.21); common arterial trunk, -0.41 (95% CI, -0.74 to -0.09); and major ventricular septal defects, -0.25 (95% CI, -0.35 to -0.15). Other single-ventricle defects, transposition of the great arteries, tetralogy of Fallot, and anomalous pulmonary venous return, were also associated with smaller HC. Transposition of the great arteries was associated with smaller HC relative to birth weight, -0.26 (95% CI, -0.39 to -0.13). Major ventricular septal defects were associated with larger HC relative to birth weight. The results were consistent under various conditions, eg, when siblings of infants with CHD (n=5311) or infants with other major malformations (n=24 974) were used as the reference.

**CONCLUSIONS:**

Several subtypes of CHD were associated with smaller HC. The associations with major ventricular septal defects, common arterial trunk, and anomalous pulmonary venous return have not previously been described. Only infants with transposition of the great arteries had smaller HC relative to birth weight.

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**KEYWORDS:**

brain; epidemiology; heart defects, congenital; pediatrics

PMID: 26769743 [PubMed - in process]

3.

Science. 2016 Feb 26;351(6276):933-9. doi: 10.1126/science.aad0314. Epub 2016 Jan 28.

[The maternal interleukin-17a pathway in mice promotes autism-like phenotypes in offspring.](#)

Choi GB, Yim YS, Wong H, Kim S, Kim H, Kim SV, Hoeffler CA, Littman DR, Huh JR.

Abstract

Viral infection during pregnancy has been correlated with increased frequency of autism spectrum disorder (ASD) in offspring. This observation has been modeled in rodents subjected to maternal immune activation (MIA). The immune cell populations critical in the MIA model have not been identified. Using both genetic mutants and blocking antibodies in mice, we show that retinoic acid receptor-related orphan nuclear receptor gamma t (ROR $\gamma$ t)-dependent effector T lymphocytes [for example, T helper 17 (TH17) cells] and the effector cytokine interleukin-17a (IL-17a) are required in mothers for MIA-induced behavioral abnormalities in offspring. We find that MIA induces an abnormal cortical phenotype, which is also dependent on maternal IL-17a, in the fetal brain. Our data suggest that therapeutic targeting of TH17 cells in susceptible pregnant mothers may reduce the likelihood of bearing children with inflammation-induced ASD-like phenotypes.

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Comment in

IMMUNOLOGY. [Maternal TH17 cells take a toll on baby's brain.](#) [Science. 2016]

PMID: 26822608 [PubMed - indexed for MEDLINE] PMCID: PMC4782964

4.

Lancet. 2016 Feb 6;387(10018):558-65. doi: 10.1016/S0140-6736(15)00990-3. Epub 2015 Dec 3.

[Weight change between successive pregnancies and risks of stillbirth and infant mortality: a nationwide cohort study.](#)

Cnattingius S, Villamor E.

Abstract

BACKGROUND:

Maternal overweight and obesity are risk factors for stillbirth and infant mortality. Whether temporal changes in maternal weight affect these risks is not clear. We aimed to assess whether change of BMI between first and second pregnancies affects risks of stillbirth and infant mortality in the second-born offspring.

METHODS:

In a Swedish population-based cohort of women who gave birth to their first and second child between Jan 1, 1992, and Dec 31, 2012, we investigated associations between change in maternal body-mass index (BMI) during early pregnancy from first to second pregnancies and risks of stillbirth and neonatal, postneonatal, and infant mortality after the second pregnancy. Relative risks (RRs) for each outcome according to BMI change categories were calculated with binomial regression.

FINDINGS:

Complete information was available for 456,711 (77.7%) of 587,710 women who had their first and second single births in the study period. Compared with women with a stable BMI (change between -1 kg/m<sup>2</sup> and <1 kg/m<sup>2</sup>) between pregnancies, the adjusted RRs for women who gained at least 4 BMI units between pregnancies were 1.55 (95% CI 1.23-1.96) for stillbirth and 1.29 (1.00-1.67) for infant mortality. Stillbirth risks increased linearly with increased BMI gain. Risks of infant mortality in second

pregnancy only increased with BMI gain in women with healthy BMI (<25 kg/m<sup>2</sup>) during first pregnancy; the adjusted RR for healthy weight women who gained 2 to less than 4 BMI units was 1.27 (1.01-1.59) and for those who gained 4 BMI units or more the adjusted RR was 1.60 (1.16-2.22). In overweight women (BMI ≥25 kg/m<sup>2</sup>), weight loss before pregnancy reduced risk of neonatal mortality.

#### INTERPRETATION:

Our findings emphasise the need to prevent weight gain before pregnancy in healthy and overweight women and that weight loss should be promoted in overweight women.

#### FUNDING:

Swedish Research Council for Health, Working Life and Welfare, and Karolinska Institutet.

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Comment in

Interpregnancy weight gain--a modifiable cause of stillbirth? [Lancet. 2016]

PMID: 26651225 [PubMed - indexed for MEDLINE]

5.

N Engl J Med. 2016 Feb 4;374(5):434-43. doi: 10.1056/NEJMoa1509819.

[Metformin versus Placebo in Obese Pregnant Women without Diabetes Mellitus.](#)

Syngelaki A, Nicolaides KH, Balani J, Hyer S, Akolekar R, Kotecha R, Pastides A, Shehata H.

Abstract

#### BACKGROUND:

Obesity is associated with an increased risk of adverse pregnancy outcomes. Lifestyle-intervention studies have not shown improved outcomes. Metformin improves insulin sensitivity and in pregnant patients with gestational diabetes it leads to less weight gain than occurs in those who do not take metformin.

#### METHODS:

In this double-blind, placebo-controlled trial, we randomly assigned pregnant women without diabetes who had a body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) of more than 35 to receive metformin, at a dose of 3.0 g per day, or placebo (225 women in each group) from 12 to 18 weeks of gestation until delivery. The BMI was calculated at the time of study entry (12 to 18 weeks of gestation). The primary outcome was a reduction in the median neonatal birth-weight z score by 0.3 SD (equivalent to a 50% reduction, from 20% to 10%, in the incidence of large-for-gestational-age neonates). Secondary outcomes included maternal gestational weight gain and the incidence of gestational diabetes and of preeclampsia, as well as the incidence of adverse neonatal outcomes. Randomization was performed with the use of computer-generated random numbers. The analysis was performed according to the intention-to-treat principle.

#### RESULTS:

A total of 50 women withdrew consent during the trial, which left 202 women in the metformin group and 198 in the placebo group. There was no significant between-group difference in the median neonatal birth-weight z score (0.05 in the metformin group [interquartile range, -0.71 to 0.92] and 0.17 in the placebo group [interquartile range, -0.62 to 0.89],  $P=0.66$ ). The median maternal gestational weight gain was lower in the metformin group than in the placebo group (4.6 kg [interquartile range, 1.3 to 7.2] vs. 6.3 kg [interquartile range, 2.9 to 9.2],  $P<0.001$ ), as was the incidence of preeclampsia (3.0% vs. 11.3%; odds ratio, 0.24; 95% confidence interval, 0.10 to 0.61;  $P=0.001$ ). The incidence of side effects was higher in the metformin group than in the placebo group. There were no significant between-group

differences in the incidence of gestational diabetes, large-for-gestational-age neonates, or adverse neonatal outcomes.

**CONCLUSIONS:**

Among women without diabetes who had a BMI of more than 35, the antenatal administration of metformin reduced maternal weight gain but not neonatal birth weight. (Funded by the Fetal Medicine Foundation; ClinicalTrials.gov number, NCT01273584; EudraCT number, 2008-005892-83.).

PMID: 26840133 [PubMed - indexed for MEDLINE]

6.

N Engl J Med. 2016 Feb 18;374(7):647-55. doi: 10.1056/NEJMoa1511048. Epub 2016 Feb 4.

[A Randomized Trial Comparing Skin Antiseptic Agents at Cesarean Delivery.](#)

Tuuli MG, Liu J, Stout MJ, Martin S, Cahill AG, Odibo AO, Colditz GA, Macones GA.

Abstract

**BACKGROUND:**

Preoperative skin antisepsis has the potential to decrease the risk of surgical-site infection. However, evidence is limited to guide the choice of antiseptic agent at cesarean delivery, which is the most common major surgical procedure among women in the United States.

**METHODS:**

In this single-center, randomized, controlled trial, we evaluated whether the use of chlorhexidine-alcohol for preoperative skin antisepsis was superior to the use of iodine-alcohol for the prevention of surgical-site infection after cesarean delivery. We randomly assigned patients undergoing cesarean delivery to skin preparation with either chlorhexidine-alcohol or iodine-alcohol. The primary outcome was superficial or deep surgical-site infection within 30 days after cesarean delivery, on the basis of definitions from the Centers for Disease Control and Prevention.

**RESULTS:**

From September 2011 through June 2015, a total of 1147 patients were enrolled; 572 patients were assigned to chlorhexidine-alcohol and 575 to iodine-alcohol. In an intention-to-treat analysis, surgical-site infection was diagnosed in 23 patients (4.0%) in the chlorhexidine-alcohol group and in 42 (7.3%) in the iodine-alcohol group (relative risk, 0.55; 95% confidence interval, 0.34 to 0.90; P=0.02). The rate of superficial surgical-site infection was 3.0% in the chlorhexidine-alcohol group and 4.9% in the iodine-alcohol group (P=0.10); the rate of deep infection was 1.0% and 2.4%, respectively (P=0.07). The frequency of adverse skin reactions was similar in the two groups.

**CONCLUSIONS:**

The use of chlorhexidine-alcohol for preoperative skin antisepsis resulted in a significantly lower risk of surgical-site infection after cesarean delivery than did the use of iodine-alcohol. (Funded by the National Institutes of Health and Washington University School of Medicine in St. Louis; ClinicalTrials.gov number, NCT01472549.).

PMID: 26844840 [PubMed - indexed for MEDLINE] PMCID: PMC4777327 [Available on 2016-08-18]

7.

Prenat Diagn. 2016 Feb;36(2):148-53. doi: 10.1002/pd.4756. Epub 2015 Dec 27.

[The performance of an intermediate 16th-week ultrasound scan for the follow-up of euploid fetuses with increased nuchal translucency.](#)

Le Lous M, Bouhanna P, Colmant C, Rozenberg P, Quibel T.

## Abstract

### OBJECTIVE:

The objective of the study is to assess the utility of an intermediate ultrasound scan at 16(+0) to 18(+6) weeks of gestation in euploid fetuses with increased nuchal translucency  $\geq 3.5$  mm.

### METHODS:

Three hundred eighty-nine fetuses with nuchal translucency (NT)  $\geq 3.5$  mm were identified in two prenatal centers between January 2008 and December 2012. Pregnancy work-up included karyotyping, monthly detailed ultrasound scan starting with a 16th-week scan, a cardioechography, and a genetic counseling. Abnormal findings and pregnancy outcomes were analyzed retrospectively.

### RESULTS:

Of the 389 fetuses included, 52% had normal karyotype. Among euploid fetuses, 51 (30.7%) structural defects were identified overall. First-trimester scan was useful to identify 16 of the major defects (31.3%), and the 16th-week scan was useful to identify an additional 21 of them (41.2%), whereas the 22nd-week pregnancy scan discovered an additional 14 (27.4%). Structural defects discovered with the 16th-week scan were cardiac defects (n = 7), polymalformative syndromes (n = 3), left diaphragmatic hernias (n = 3), limbs abnormalities (n = 2), genitourinary (n = 2), microretrognathism (n = 2), hydrops (n = 1), and exomphalos (n = 1). If the intermediate scan was normal, the chances of a favorable outcome were as high as 85% and were close to 100% after 20 weeks, irrespective of initial NT.

### CONCLUSION:

The intermediate ultrasound was useful in fetuses with increased NT pregnancy work-up. © 2015 John Wiley & Sons, Ltd.

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PMID: 26661276 [PubMed - in process]

8.

J Perinatol. 2016 Feb;36(2):95-9. doi: 10.1038/jp.2015.130. Epub 2015 Dec 10.

[A randomized controlled trial of differing doses of postcesarean enoxaparin thromboprophylaxis in obese women.](#)

Stephenson ML, Serra AE, Neepser JM, Caballero DC, McNulty J.

## Abstract

### OBJECTIVE:

To compare two enoxaparin dosing strategies at achieving prophylactic anti-Xa levels in women with a body mass index (BMI)  $\geq 35$  (kg m<sup>-2</sup>) postcesarean delivery.

### STUDY DESIGN:

Women with BMI  $\geq 35$  were randomized to receive prophylactic enoxaparin at a fixed dose of 40 mg daily or weight-based dosing of 0.5 mg kg<sup>-1</sup> twice daily. The primary outcome was the proportion of subjects with peak anti-Xa levels in the prophylactic range of 0.2 to 0.6 IU ml<sup>-1</sup>.

### RESULT:

From August 2013 through February 2014, 84 demographically similar women completed the protocol. In the weight-based group, 88% (37/42) of the women reached prophylactic anti-Xa levels versus 14% (6/42) in the fixed dose group (odds ratio 44.4, 95% confidence interval 12.44, 158.48, P<0.001). No anti-Xa level exceeded 0.48 IU ml<sup>-1</sup>. There were no venous thromboembolic or bleeding events requiring reoperation or transfusion in either group.

### CONCLUSION:

Compared with fixed dosing daily, weight-based dosing twice daily more effectively achieved prophylactic anti-Xa levels without reaching the therapeutic range.

PMID: 26658126 [PubMed - in process]

9.

J Ultrasound Med. 2016 Feb;35(2):263-9. doi: 10.7863/ultra.15.03020. Epub 2015 Dec 11.

[Sonographic Findings of Morbidly Adherent Placenta in the First Trimester.](#)

Rac MW, Moschos E, Wells CE, McIntire DD, Dashe JS, Twickler DM.

Abstract

OBJECTIVES:

The purpose of this study was to evaluate the association between first-trimester sonographic findings and morbidly adherent placenta at delivery.

METHODS:

We conducted a retrospective review of all first-trimester sonographic examinations from pregnancies that underwent third-trimester sonography for placenta previa or low-lying placenta between September 1997 and October 2011. Only women with a prior cesarean delivery were included. Transabdominal and transvaginal images from these first-trimester studies were reviewed for the following sonographic parameters: distance from the inferior border of the gestational sac to the external cervical os, location of the decidua basalis, presence of anechoic areas, uterine-bladder interface irregularity, and smallest anterior myometrial thickness. Morbidly adherent placentation was confirmed on histologic examination of hysterectomy specimens. Statistical methods included univariate and multivariate analyses.

RESULTS:

Thirty-nine patients met inclusion criteria, of whom 14 (36%) had confirmed placental invasion. The number of prior cesarean deliveries was significantly associated with placental invasion ( $P < .0001$ ). The only first-trimester sonographic finding associated with invasion was the smallest anterior myometrial thickness measured in the sagittal plane ( $P < .02$ ). Multivariate analysis based on these two variables yielded an area under the receiver operating characteristic curve of 0.94 (95% confidence interval, 0.87-1.00) and significantly improved the prediction of placental invasion compared to using the number of prior cesarean deliveries alone.

CONCLUSIONS:

In women with persistent placenta previa or low-lying placenta and prior cesarean delivery, the smallest anterior myometrial thickness on first-trimester sonography significantly improved detection of morbidly adherent placenta.

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KEYWORDS:

first trimester; morbidly adherent placenta; obstetric ultrasound; sonography

PMID: 26657748 [PubMed - in process]

10.

BJOG. 2016 Feb;123(3):356-66. doi: 10.1111/1471-0528.13753. Epub 2015 Nov 24.

[Clinical pharmacokinetic properties of magnesium sulphate in women with pre-eclampsia and eclampsia.](#)

Okusanya BO, Oladapo OT, Long Q, Lumbiganon P, Carroli G, Qureshi Z, Duley L, Souza JP, Gülmezoglu AM.

Abstract

BACKGROUND:

The pharmacokinetic basis of magnesium sulphate (MgSO<sub>4</sub>) dosing regimens for eclampsia prophylaxis and treatment is not clearly established.

OBJECTIVES:

To review available data on clinical pharmacokinetic properties of MgSO<sub>4</sub> when used for women with pre-eclampsia and/or eclampsia.

SEARCH STRATEGY:

MEDLINE, EMBASE, CINAHL, POPLINE, Global Health Library and reference lists of eligible studies.

SELECTION CRITERIA:

All study types investigating pharmacokinetic properties of MgSO<sub>4</sub> in women with pre-eclampsia and/or eclampsia.

DATA COLLECTION AND ANALYSIS:

Two authors extracted data on basic pharmacokinetic parameters reflecting the different aspects of absorption, bioavailability, distribution and excretion of MgSO<sub>4</sub> according to identified dosing regimens.

MAIN RESULTS:

Twenty-eight studies investigating pharmacokinetic properties of 17 MgSO<sub>4</sub> regimens met our inclusion criteria. Most women (91.5%) in the studies had pre-eclampsia. Baseline serum magnesium concentrations were consistently <1 mmol/l across studies. Intravenous loading dose between 4 and 6 g was associated with a doubling of this baseline concentration half an hour after injection. Maintenance infusion of 1 g/hour consistently produced concentrations well below 2 mmol/l, whereas maintenance infusion at 2 g/hour and the Pritchard intramuscular regimen had higher but inconsistent probability of producing concentrations between 2 and 3 mmol/l. Volume of distribution of magnesium varied (13.65-49.00 l) but the plasma clearance was fairly similar (4.28-5.00 l/hour) across populations.

CONCLUSION:

The profiles of Zuspan and Pritchard regimens indicate that the minimum effective serum magnesium concentration for eclampsia prophylaxis is lower than the generally accepted level. Exposure-response studies to identify effective alternative dosing regimens should target concentrations achievable by these standard regimens.

TWEETABLE ABSTRACT:

Minimum effective serum magnesium concentration for eclampsia prophylaxis is lower than the generally accepted therapeutic level.

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KEYWORDS:

Eclampsia; magnesium sulphate; pharmacokinetics; pre-eclampsia; serum magnesium

PMID: 26599617 [PubMed - in process] PMCID: PMC4737322

11.

BJOG. 2016 Feb;123(3):400-7. doi: 10.1111/1471-0528.13274. Epub 2015 Jan 27.

[Prenatal detection of congenital heart disease-results of a national screening programme.](#)



van Velzen CL, Clur SA, Rijlaarsdam M, Bax CJ, Pajkrt E, Heymans MW, Bekker MN, Hruda J, de Groot C, Blom NA, Haak MC.

Abstract

OBJECTIVE:

Congenital heart disease (CHD) is the most common congenital malformation and causes major morbidity and mortality. Prenatal detection improves the neonatal condition before surgery, resulting in less morbidity and mortality. In the Netherlands a national prenatal screening programme was introduced in 2007. This study evaluates the effects of this screening programme.

DESIGN:

Geographical cohort study.

SETTING:

Large referral region of three tertiary care centres.

POPULATION:

Fetuses and infants diagnosed with severe CHD born between 1 January 2002 and 1 January 2012.

METHODS:

Cases were divided into two groups: before and after the introduction of screening.

MAIN OUTCOME MEASURES:

Detection rates were calculated.

RESULTS:

The prenatal detection rate (n = 1912) increased with 23.9% (95% confidence interval [95% CI] 19.5-28.3) from 35.8 to 59.7% after the introduction of screening and of isolated CHD with 21.4% (95% CI 16.0-26.8) from 22.8 to 44.2%. The highest detection rates were found in the hypoplastic left heart syndrome, other univentricular defects and complex defects with atrial isomerism (>93%). Since the introduction of screening, the 'late' referrals (after 24 weeks of gestation) decreased by 24.3% (95% CI 19.3-29.3).

CONCLUSIONS:

This is the largest cohort study to investigate the prenatal detection rate of severe CHD in an unselected population. A nationally organised screening has resulted in a remarkably high detection rate of CHD (59.7%) compared with earlier literature.

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KEYWORDS:

Congenital heart defects; detection rate; fetal echocardiography; prenatal anomaly screening; prenatal diagnosis

PMID: 25625301 [PubMed - in process]

12.

J Pediatr. 2016 Feb;169:214-220.e1. doi: 10.1016/j.jpeds.2015.10.083. Epub 2015 Dec 2.

[Improved Survival in Down Syndrome over the Last 60 Years and the Impact of Perinatal Factors in Recent Decades.](#)

Glasson EJ, Jacques A, Wong K, Bourke J, Leonard H.

Abstract

OBJECTIVE:

To calculate the survival of people with Down syndrome over the past 60 years and the influence of major perinatal factors by using linked population-based data.

#### STUDY DESIGN:

A data linkage between 2 Western Australian (WA) data sets (the Register for Developmental Anomalies and the Intellectual Disability Exploring Answers database) was used to identify 772 children born with Down syndrome in WA from 1980-2010. Perinatal and mortality data were extracted from the WA Midwives Information System and WA death registrations and compared with the remaining WA population born during that same era. An additional 606 children with Down syndrome living in WA prior to 1980 were available from a disability services database and were used for predicting survival into adulthood.

#### RESULTS:

Overall, for cases born 1953-2010, 88% (95% CI 86%, 90%) survived to 5 years of age, 87% (95% CI 85%, 89%) to 10 years, and 83% (95% CI 80%, 85%) to 30 years. Children live-born with Down syndrome were significantly more likely (all  $P > .001$ ) to have mothers older than 35 years (32.7% vs 13.4%), a gestational age less than 37 weeks (23.8% vs 7.9%), a cesarean delivery (28.9% vs 23.0%), and a birth weight less than 2500 g (20.4% vs 6.1%). Down syndrome survival was reduced in the presence of a cardiovascular defect, younger gestational age, low birth weight, or earlier birth years.

#### CONCLUSIONS:

Improved survival for children born with Down syndrome over the last 60 years has occurred incrementally, but disparities still exist for children who are preterm or have low birth weight.

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PMID: 26651430 [PubMed - in process]

13.

Eur J Obstet Gynecol Reprod Biol. 2016 Mar;198:30-4. doi: 10.1016/j.ejogrb.2015.12.004. Epub 2016 Jan 4.

#### [Does anal sphincter injury preclude subsequent vaginal delivery?](#)

Fitzpatrick M, Cassidy M, Barassaud ML, Hehir MP, Hanly AM, O'Connell PR, O'Herlihy C.

Abstract

#### OBJECTIVE:

To assess continence and anal sphincter integrity during a subsequent pregnancy and delivery in women known to have a previous anal sphincter injury.

#### DESIGN:

Prospective observational study.

#### SETTING:

The National Maternity Hospital, Dublin, Ireland.

#### POPULATION:

Antenatal patients with a documented obstetric anal sphincter injury at a previous delivery.

#### METHODS:

Women underwent symptom scoring, endoanal ultrasound and manometry.

#### MAIN OUTCOME MEASURES:

Recommended and actual mode of delivery, continence scores and endoanal ultrasound findings after index delivery.

#### RESULTS:

557 women were studied. 293 (53%) had no symptoms of faecal incontinence, 189 (34%) had mild symptoms and 75 (13%) moderate or severe symptoms. 408 (73%) had an endoanal ultrasound.

383(94%) had a normal or small (<1 quadrant) defect in the internal anal sphincter and 390 (96%) had a scar or small (<1e quadrant) defect in the external anal sphincter. 393 (70%) delivered vaginally. 164 (30%) were delivered by caesarean section. 197/557 (35%) returned for follow-up. There was no significant change in continence following either vaginal or caesarean delivery. 20 (5.1%) women had a recognised second anal sphincter tear during vaginal delivery.

#### CONCLUSIONS:

The majority of women who sustain a third degree tear have minimal or no symptoms of faecal incontinence when assessed antenatally in a subsequent pregnancy. 70% go on to have a vaginal delivery, with little impact on faecal continence. These findings provide reassurance for patients and clinicians about the safety of vaginal delivery following anal sphincter injury in appropriately selected patients.

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#### KEYWORDS:

Endoanal ultrasound; Faecal incontinence; Obstetric anal sphincter injury; Subsequent delivery  
PMID: 26773248 [PubMed - in process]

14.

JAMA. 2016 Feb 23;315(8):775-87. doi: 10.1001/jama.2016.0289.

[Developing a New Definition and Assessing New Clinical Criteria for Septic Shock: For the Third International Consensus Definitions for Sepsis and Septic Shock \(Sepsis-3\).](#)

Shankar-Hari M, Phillips GS, Levy ML, Seymour CW, Liu VX, Deutschman CS, Angus DC, Rubenfeld GD, Singer M; Sepsis Definitions Task Force. Collaborators (19)

#### Abstract

##### IMPORTANCE:

Septic shock currently refers to a state of acute circulatory failure associated with infection. Emerging biological insights and reported variation in epidemiology challenge the validity of this definition.

##### OBJECTIVE:

To develop a new definition and clinical criteria for identifying septic shock in adults.

##### DESIGN, SETTING, AND PARTICIPANTS:

The Society of Critical Care Medicine and the European Society of Intensive Care Medicine convened a task force (19 participants) to revise current sepsis/septic shock definitions. Three sets of studies were conducted: (1) a systematic review and meta-analysis of observational studies in adults published between January 1, 1992, and December 25, 2015, to determine clinical criteria currently reported to identify septic shock and inform the Delphi process; (2) a Delphi study among the task force comprising 3 surveys and discussions of results from the systematic review, surveys, and cohort studies to achieve consensus on a new septic shock definition and clinical criteria; and (3) cohort studies to test variables identified by the Delphi process using Surviving Sepsis Campaign (SSC) (2005-2010; n = 28,150), University of Pittsburgh Medical Center (UPMC) (2010-2012; n = 1,309,025), and Kaiser Permanente Northern California (KPNC) (2009-2013; n = 1,847,165) electronic health record (EHR) data sets.

##### MAIN OUTCOMES AND MEASURES:

Evidence for and agreement on septic shock definitions and criteria.

##### RESULTS:

The systematic review identified 44 studies reporting septic shock outcomes (total of 166,479 patients) from a total of 92 sepsis epidemiology studies reporting different cutoffs and combinations for blood

pressure (BP), fluid resuscitation, vasopressors, serum lactate level, and base deficit to identify septic shock. The septic shock-associated crude mortality was 46.5% (95% CI, 42.7%-50.3%), with significant between-study statistical heterogeneity ( $I^2 = 99.5\%$ ;  $\tau^2 = 182.5$ ;  $P < .001$ ). The Delphi process identified hypotension, serum lactate level, and vasopressor therapy as variables to test using cohort studies. Based on these 3 variables alone or in combination, 6 patient groups were generated. Examination of the SSC database demonstrated that the patient group requiring vasopressors to maintain mean BP 65 mm Hg or greater and having a serum lactate level greater than 2 mmol/L (18 mg/dL) after fluid resuscitation had a significantly higher mortality (42.3% [95% CI, 41.2%-43.3%]) in risk-adjusted comparisons with the other 5 groups derived using either serum lactate level greater than 2 mmol/L alone or combinations of hypotension, vasopressors, and serum lactate level 2 mmol/L or lower. These findings were validated in the UPMC and KPNC data sets.

#### CONCLUSIONS AND RELEVANCE:

Based on a consensus process using results from a systematic review, surveys, and cohort studies, septic shock is defined as a subset of sepsis in which underlying circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than sepsis alone. Adult patients with septic shock can be identified using the clinical criteria of hypotension requiring vasopressor therapy to maintain mean BP 65 mm Hg or greater and having a serum lactate level greater than 2 mmol/L after adequate fluid resuscitation.

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[Effect of hyperemesis gravidarum on gestational diabetes mellitus screening.](#)

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Abstract

#### OBJECTIVE:

To clarify the effect of starvation due to hyperemesis gravidarum on the screening of gestational diabetes mellitus (GDM).

#### METHODS:

A retrospective study was undertaken of pregnant women who delivered at Tsukuba University Hospital, Japan, between October 1, 2010, and September 30, 2013. GDM screening was performed in the first trimester using the random blood glucose test with a cutoff value of 5.2mmol/L and in the second trimester using a 50-g glucose challenge test with a cutoff value of 7.8mmol/L. If the screening was positive, a 75-g oral glucose tolerance test was performed for a definite diagnosis.

#### RESULTS:

Among 2112 eligible women, 33 (1.6%) required hospitalization for hyperemesis; the remaining 2079 women formed the control group. In the first trimester, the positive GDM screening rate was significantly higher in the hyperemesis group than in the control group (13 [39.4%] vs 115 [5.5%];  $P < 0.001$ ). Additionally, the positive predictive value was significantly lower in the hyperemesis group (23.1% vs 73.9%;  $P < 0.001$ ). In the second trimester, no significant differences were observed between groups.

#### CONCLUSION:

Hyperemesis gravidarum affects the positive GDM screening rate in the first trimester.

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KEYWORDS:

Gestational diabetes mellitus; Hyperemesis gravidarum; Screening

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