

OB/GYN Clinical [ALERT]

Evidence-based commentaries
on women's reproductive health

SPECIAL FEATURE

The Changing Face of Labor Management

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Dr. Hobbins reports no financial relationships relevant to this field of study.

Our understanding of the conduct of labor has undergone periodic re-evaluation. In the 1950s, cesarean delivery was a major operation. Today, the procedures are shorter, accompanied by less surgical fanfare, and associated with fewer days in the hospital. Nevertheless, as the only other option to vaginal delivery, the operation, performed in 35% of cases for failure to progress, still should be considered “major” considering its potential for maternal complications.

ARREST OF LABOR IN THE FIRST STAGE

In 1954, Emmanuel Friedman published a study that laid the groundwork for quantifying time limits for normal latent and active phases of labor.¹ It was based on data from 500 women whose labors were unaccompanied by epidurals. Only 13% of the women had oxytocin for induction or augmentation. The Friedman curve defined the upper limits of normal for the latent phase (> 20 hours for multiparas and > 46 hours for nulliparas) and for progress in the active phase (< 1.5 cm/hour for multiparas and

< 1.2 cm/hour for nulliparas). Arrest of labor in the active phase was defined as no change in cervical dilation for two hours or more in the active stage once 4 cm of dilation was attained.

These data were challenged later because Friedman's pure cohort might not represent today's laboring patients. The Consortium for Safe Labor published data from 19 hospitals and 62,000 patients showing that the steepest slope of cervical dilation did not occur until 6 cm and that some patients attaining successful vaginal deliveries could take up to six hours to progress between 4 cm and 5 cm and three hours to progress between 5 cm and 6 cm dilation.² This caused the Society for Maternal-Fetal Medicine to suggest the following contemporary guidelines:³

- A prolonged latent phase should not be reason alone for cesarean delivery since amniotomy and/or oxytocin augmentation should move most patients into the active phase.
- Active phase arrest should not be diagnosed before 6 cm.

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[INSIDE]

Staged Preeclampsia Screening
in Early Pregnancy

page 4

Should All Pregnant Women Be Screened
for Hepatitis C?

page 6

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Thank You, John Hobbins; Welcome Camille Hoffman

This issue marks the end of an era for *OB/GYN Clinical Alert*. John Hobbins, the last member of the original editorial board, presents his last regular contribution with his Special Feature. After a long and distinguished career, Dr. Hobbins is retiring to spend more time in Key West. Of the many talented scholars that Leon Speroff assembled for this newsletter, John has been the most prolific and durable. I have always admired John's writing. He consistently selects topics of high relevance to clinical practice. He writes clearly and with great precision, emphasizing the known and not yet known. His brief and highly focused contributions create a clinical connection and tell a story that sticks in our memory. This final Special Feature is a great example. Please join me in thanking John for his many years of service to *OB/GYN Clinical Alert* and wishing him well in his retirement. Perhaps we can coax an occasional guest commentary out of him in the future.

With each change comes new opportunities. This issue presents the first contribution by Dr. Camille Hoffman, an Associate Professor of Maternal-Fetal Medicine at the University of Colorado. She will take over the responsibility of reporting on the maternal-fetal medicine literature. I am pleased to report that Dr. Hobbins helped train Dr. Hoffman and highly recommended her for a position on our Editorial Board. This contribution on preeclampsia is truly "Hobbinesque" in focus and relevance for clinical practice. Please join me in welcoming Dr. Hoffman to *OB/GYN Clinical Alert*.

— Jeffrey T. Jensen, MD, MPH, Editor

• Cesarean delivery is not advised unless no progress in cervical dilation has been made for four hours of documented adequate contractions post-amniotomy or after more than six hours of adequate oxytocin-assisted contractions.

ARREST OF LABOR IN THE SECOND STAGE

For years, failure of descent represented a patient's inability to achieve an increase in fetal head station after two hours of pushing or, in some definitions, to attain delivery. However, published opinions from the Consortium for Safe Labor included a more liberal approach to defining arrest in the second stage as > 2 hours in a multipara and > 3 hours in a nullipara.² Even more time was allowed for those with epidurals or malpresentations.

In 2016, Wilson-Leedy et al compared 200 patients managed with the new guidelines and 200 patients not managed this way.⁴ They found the overall cesarean delivery rate decreased from 26.9% to 18.9%, and the cesarean delivery rate in patients with cervixes < 6 cm decreased from 7.1% to 1.1% with the newer guidelines.

In addition to achieving vaginal delivery more frequently, are there any greater risks with the new guidelines? Several studies addressed this question, but perhaps the most attention-getting study challenging the newer guidelines was conducted on 7,800 laboring patients.⁵ Rosenbloom

et al compared patients who delivered between 2010 and 2014 and those who delivered after the new guidelines were applied in 2014. The cesarean delivery rate actually rose from 15.8% to 17.3%, and there were 1.6- and 1.8-fold increases in adverse maternal and neonatal outcomes, respectively. However, as with any before-and-after study, some non-guideline practices or factors introduced or deleted during the "after" group's care could have affected the results.

The problem with any type of rigid guideline that reduces myriad variables into a generic recommendation is that one size does not always fit all. For example, some patients without red flags might need even more than six hours to make progress. Yet others with unfavorable factors might benefit more from the old guidelines rather than prolonging an inevitable surgical conclusion. This has caused some authors to construct computer-generated formulas that consider many favorable or unfavorable factors to predict outcomes for individual patients.⁶ Various methods can help better attain a vaginal delivery.

Epidural anesthesia: Epidurals may help to shorten labor in some anxious patients, but one study has shown that first-stage labors last an average of 26 minutes longer and second stages last an average of 15 minutes longer.⁷ Often, first-stage times are increased when epidurals are administered before the active phase is attained.

Amniotomy: This method has been a staple of obstetricians for either improving success of labor induction or augmenting contraction strength if first-stage progress has stalled. In 1995, amniotomy was found to shorten labor but also to increase the rate of amnionitis.⁸ In a 2008 publication based on a Cochrane database, Neilson found no statistically significant effect on first-stage length, Apgar scores, or cesarean delivery rate.⁹

Hydration: In some centers, the NPO (nothing by mouth) policy remains for patients in labor. Some data show that intravenous fluids shorten labor in this setting, particularly if the infusion is given at a rate of 250 mL/hour vs. 125 mL/hour.¹⁰ However, it is unclear if infusion is any better than liberal ingestion of clear fluids in shortening labor or avoiding cesarean delivery.

Ambulation: These results are mixed. Lawrence et al found a halving of the cesarean delivery rate and the need for operative vaginal delivery when ambulation was encouraged.¹¹

The importance of nursing support: In one often-quoted study, labor nurses were tracked according to the cesarean delivery rates of patients they cared for while on duty.¹² Those in the lower quartile had patients with shorter labors (4.4 hours vs. 5.6 hours) and fewer forceps deliveries (13% vs. 26%) than nurses in the highest cesarean delivery quartile. This implies that motivation does make a difference.

ASSESSMENT OF FETAL STATION

Fetal station is an important variable in predicting a successful vaginal delivery or in making the ultimate decision for cesarean delivery for “failure of descent” in the second stage. However, our assessment of station is one of the most subjective endeavors a provider undertakes. The ritual requires the examiner to construct an imaginary line between the two ischial spines and then, with the same finger, to determine how many centimeters the leading part of the fetal skull is below or above this line. No provider’s brain has the three-dimensional capability to determine this precisely, especially when the head is well below the level of the spines. Throw in 2-3 cm of caput and it is impossible to tell if progress is being made in descent of the fetal skull.

In 2009, Barbera et al described an alternative method using ultrasound.¹³ It entailed applying a standard curvilinear transducer to the vulva (trans-perineal ultrasound) to get a midline sagittal image that incorporates the length of the median raphae of the symphysis pubis and the leading edge of the fetal skull. The “angle of progression” is constructed from two lines directed from the inferior border of the symphysis, one along the long axis of this structure and another to the leading edge of the fetal skull. The quantified angle of progression that is created represents an objective method to assess fetal station. Most importantly, the

method can be used serially to determine whether there has been true descent of the head through the pelvis. Following its introduction, many papers have appeared from Europe showing the efficacy of trans-perineal ultrasound in predicting successful vaginal delivery^{14,15} or operative delivery.¹⁶ Interestingly, although the concept arose in the United States, it has not been taken up here where, with our heads in the sand, we continue “winging it” with a wholly subjective method.

PARTING COMMENTS

Here are some unsolicited thoughts from someone who has spent the last 50 years going with the flow, but also sometimes bucking it. Protocols, computerized models, and even ultrasound-derived methods can help with managing labor. However, decisions to perform a cesarean delivery also should be based on trends in a patient’s clinical course rather than on one isolated snapshot. The art of medicine involves decisions based on information that the provider has filed while watching the whole story unfold and by employing, on occasion, an approach of “been there, done that” or, alternatively, “been there and wish I had not done that.”

Today, we also frequently depend on evidence-based guidelines and formulas that are designed to protect our patients and us from disastrous missteps. Protocols are particularly important to keep providers on the same page as we enter an era of shift medicine, where “laborists” are replacing primary providers for in-hospital activities.

I get it. Despite the “highs” of participating in one of the most important events in people’s lives, the camaraderie on the labor deck, and the occasional, but addictive, jolts of adrenaline, I gave up labor and delivery coverage when I realized that long shifts, interspersed with regular daytime requirements, were not making me a better decision-maker in either job.

I thought patients would revolt against the laborist concept, but they seem to have accepted it, or maybe they just have become inured to it, along with some patient-unfriendly aspects of our present healthcare system. However, as we move forward, the motto that pregnancy is not an illness, including the part that involves delivery, should not be forgotten. Unless a woman strays off course, there is no need to engage in unnecessary meddling. Most importantly, she should be involved in fashioning her delivery plan and must be properly informed about why any change in that plan is being contemplated. For me, the nurse midwife delivery model, with physicians called only if problems arise, makes sense for low-risk women and, frankly, even in some higher-risk women.

Finally, delivering patients empirically at 39 weeks intuitively seems wrong, despite early evidence that cesarean delivery, as well as rates of some maternal and neonatal complications, is lower.¹⁷ What has not

been studied is the cost and anxiety created by inducing patients with no obvious risks, often accompanied by methods of cervical ripening, IVs, monitors, reallocation of nursing coverages, etc. Also, while we are in the wake of these new findings, it may be too easy to say, “you should have this,” rather than “you could have this.” This needs further evaluation.

I have loved writing these Alerts and Special Features ever since my good friend, Leon Speroff, asked me to help with them 237 Alerts ago. However, it is now time for me to put my yellow-lined pads and pencils to another use. Yes, I still use them. While not missing the monthly deadlines, I certainly will miss these opportunities to cover new information and to share my thoughts with you. Thanks for listening. ■

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ABSTRACT & COMMENTARY

Staged Preeclampsia Screening in Early Pregnancy

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Dr. Hoffman reports no financial relationships relevant to this field of study.

SYNOPSIS: The use of 150 mg of daily aspirin from 11 to 14 weeks through 36 weeks of gestation reduces the rate of early preeclampsia (PE) in approximately 90% of at-risk pregnancies. In addition, aspirin also provides the benefit of reducing the risk of PE < 37 weeks by about 60% and the length of NICU stay by about 70%, primarily by reducing the number of neonates delivered before 32 weeks. What constitutes a high-risk patient and what quantifies patient-specific risks before PE develops remain to be answered.

SOURCES: Wright D, Tan MY, O'Gorman N, et al. Predictive performance of the competing risk model in screening for preeclampsia. *Am J Obstet Gynecol* 2019;200:199.e1-13.

Wright A, Wright D, Syngelaki A, et al. Two-stage screening for preterm preeclampsia at 11-13 weeks' gestation. *Am J Obstet Gynecol* 2019;220:197.e1-11.

Preterm preeclampsia (PE) remains a large contributor to maternal and fetal/neonatal morbidity and mortality worldwide. Traditionally, women have been considered high risk for PE based on obstetric

history and maternal medical risk factors,¹ including a history of early severe PE, multiple gestation, chronic hypertension, systemic lupus erythematosus, underlying renal disease, and other maternal comorbidities. Based

on the current categorization strategy, PE is predicted accurately less than 50% of the time.² Using this traditional prediction approach, low-dose aspirin (81 mg) is recommended, starting prior to 16 weeks. When low-dose aspirin is given at ≥ 100 mg/day and taken consistently starting at < 16 weeks, the rates of very early and early-PE are reduced by 80% to 90% and the rate of preterm-PE is reduced by about 60%.³

Investigators from the United Kingdom completed three prospective studies evaluating the addition of the “triple test.” The triple test includes further assessment of women with preexisting risk factors for PE with a mean arterial blood pressure (MAP), uterine artery Dopplers (UtA-PI, average pulsatility index of both uterine arteries), and a placental growth factor (PLGF) maternal serum assessment between 11 weeks 0 days’ and 13 weeks 6 days’ gestation. The objective of the study by D. Wright et al (study 1) was “to examine the predictive performance of the competing risks model in screening for PE with delivery < 34 weeks (early-PE), < 37 weeks (preterm-PE), and delivery at any gestation (all-PE) by maternal factors alone and in combination of maternal factors, MAP, UtA-PI, and PLGF (the triple test).” This study included 61,174 singleton pregnancies with an overall rate of PE of 2.9% ($n = 1,770$). In this study, which used a set screen positive rate of 10% overall, the detection rates of early-PE, preterm-PE, and all-PE were 90%, 75%, and 50%, respectively. There was excellent agreement, close to 1.0 (100%) between overall predicted risk and observed incidence of early and preterm PE. On the other hand, prediction of all-PE was poor.

In study 2, using the same population, A. Wright et al looked more closely at a two-stage screening model in which the whole population (mostly low-risk women) was compared with a high-risk population selected based on traditional categorization to determine if triple testing can be reserved for a higher-risk group. In this analysis, the authors found that “if ... first-stage screening is maternal factors, then measurements of MAP, UtA-PI, and PLGF can be reserved for only 70% of the population.” Detection rates for PE (and 10% screen positive rate) were similar to whole-population screening with the triple test, with an overall 85% detection rate for PE < 32 weeks. For the two-stage screening model (study 2), the ability to triage women who traditionally would have been high risk to undergo various combinations of the triple test remained highly predictive of actual development of early and preterm PE, while becoming more cost effective and less labor intensive by eliminating 30% of the overall population who were low risk. The ability of the triple test, in combination with preexisting maternal risk factors, to predict PE, especially the worst type (that which necessitates delivery prior to 32 weeks) was particularly high for black and South Asian women at 100% (95% confidence interval, 93.6-100 and 66.4-100, respectively).

■ COMMENTARY

A targeted attack on PE, and the suffering that it causes, is long overdue. After reviewing these studies, it is difficult to understand why we are not moving more eagerly toward this two-staged approach in the United States. A number of patients now have an automatic “preeclampsia risk score” included in their sequential screening. This is based on PLGF levels and reported out as a 1 in “x” risk, just as sequential or quad screen results are listed. Hopefully, clinicians at least will heed the preeclampsia risk score based on PLGF levels alone and recommend low-dose aspirin. In addition, it is easy and routine to collect a maternal blood pressure; therefore, MAP can be assessed and recorded easily. As for the uterine artery Dopplers, most perinatal sonographers and sonologists are familiar with these studies, and the fetal medicine foundation provides online instructions. They are certainly no more difficult than nuchal translucency measurements.

While we are missing cases of early and preterm PE with severe features with our current protocols — something that occurred in 0.36% and 0.81% of the 2.9% of overall diagnoses of PE in these studies — we continue to screen all patients for conditions (trisomy 21, open neural tube defects) that affect far fewer pregnancies overall. Why is this? Have we embraced the mantra for too long that preeclampsia is curable only by delivery and failed to recognize the risk reduction and prevention that the early advent of low-dose aspirin can accomplish?

Based on established research and supported by these studies, the following suggestions are offered to reduce the risk of early or preterm PE:

1. ACOG Committee Opinion no. 743 recommends that clinicians stratify patients by the following risks: a history of PE, multifetal gestation, renal disease, autoimmune disease, type 1 or type 2 diabetes, and chronic hypertension. If the patient has at least one risk factor, then the clinician should recommend a daily low-dose aspirin (81 to 150 mg/day).

- Bedtime dosing is best and women should start prior to 16 weeks’ gestation.

- U.S. aspirin formulations are 81 mg or 325 mg per tablet, but the U.K. studies suggest more significant benefit from a dose ≥ 100 mg/day. Women at particularly high risk could opt for two 81 mg tablets daily, one and one-half 81 mg tablets daily, or one-half 325 mg tablet daily. All approach this goal.

2. If the patient has other known maternal risk factors, such as advanced maternal age, high body mass index, black and South Asian ethnicity, and the patient’s mother had PE, then checking a MAP and either doing UtA or adding a PLGF (or both) into your office’s sequential screen is worthy of consideration. If any of these are “positive,” proceed with the aspirin recommendations noted above. ■

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ABSTRACT & COMMENTARY

Should All Pregnant Women Be Screened for Hepatitis C?

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Dr. Allen reports she receives grant/research support from Bayer and is a consultant for Merck.

SYNOPSIS: In this cost-effectiveness analysis using Markov modeling, investigators found that universal antenatal screening for hepatitis C was cost-effective, with a mean incremental cost-effectiveness ratio of approximately \$3,000 per quality-adjusted life years gained compared to risk-based screening.

SOURCE: Chaillon A, Rand EB, Reau N, Martin NK. Cost-effectiveness of universal hepatitis C virus screening of pregnant women in the United States. *Clin Infect Dis* 2019; Jan. 28. doi: 10.1093/cid/ciz063. [Epub ahead of print].

In this Markov model cost-effectiveness analysis, the authors compared universal antenatal screening for hepatitis C followed by treatment after pregnancy to risk-based screening (the current practice in the United States). As with most cost-effectiveness modeling, assumptions were made based on national estimates and knowledge of disease.

Chaillon et al assumed an average age of 27 years for pregnant women and a chronic hepatitis C virus (HCV) prevalence of 0.73%, with annual loss to follow-up rates after HCV diagnosis of 12%. They estimated that 18% of HCV-infected pregnant women have been diagnosed previously and linked to care. The current risk-based testing and linkage rate per year was estimated to be 5%, and the cost of anti-HCV and HCV RNA confirmatory lab testing was based on the 2018 national fee schedule. Drug costs were estimated to be \$25,000 per treatment course, with 90% sustained virological response. They classified chronic liver disease using the METAVIR system (F0 = no fibrosis, F1 = portal fibrosis without septa, F2 = few septa, F3 = numerous septa without cirrhosis, F4 = cirrhosis) and based fibrosis distribution and liver disease stage transition rate per year on U.S. national estimates for women. They did not assume treatment restrictions by fibrosis stage, and calculated annual costs for nontreatment medical expenses among HCV-infected patients by stage.

The authors also calculated a mean incremental cost-effectiveness ratio (mean incremental costs divided by the mean incremental quality-adjusted life years) for antenatal screening compared to risk-based screening. The assumed willingness to pay threshold was \$50,000

per quality-adjusted life year gained. They also estimated the effect of routine antenatal HCV screening on the U.S. population.

Chaillon et al found that the incremental cost of universal hepatitis C screening was \$53.20 for the testing, and the incremental increase in quality-adjusted life years was 0.019 per pregnant woman screened compared to risk-based screening. That calculated to a mean incremental cost-effectiveness ratio of \$2,826 per quality-adjusted life years gained compared to risk-based screening, falling below the \$50,000 willingness-to-pay threshold. Sensitivity analyses showed that universal screening still was cost-effective under different treatment eligibility scenarios, different prevalence rates of HCV, different fibrosis progression rates, 85% vs. 90% sustained virological response, higher proportion of women already diagnosed and linked at baseline (40%), higher loss to follow-up rates (50%), lower liver transplant costs, higher background testing rates, and lower proportion of cirrhosis in the baseline cohort. The estimated effect to the U.S. population was that screening 5.04 million pregnant women in 2018 would result in the detection and treatment of 33,000 women overall, with an incremental detection and treatment of 7,000 women.

■ COMMENTARY

There has been a debate as to whether we should screen all pregnant women for HCV infection in the United States.¹ HCV causes chronic liver disease in 75% to 85% of those infected and can progress to liver failure and death. The incidence of HCV infection has been increasing among young adults because of the opioid epidemic.² At the same time, we now finally have

treatments (direct-acting antiviral therapies) that are more than 90% effective in clearing the virus. Based on testing recommendations from the Centers for Disease Control and Prevention and endorsed by the American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine (SMFM), the following prenatal patients should be screened for HCV:³

- Women who have been injection drug users, even those who injected only once;
- Women who received clotting factor concentrates made prior to 1987;
- Women who received blood transfusions or solid organ transplants before July 1992;
- Chronic hemodialysis patients;
- Women who have been exposed to HCV, such as healthcare workers after needle sticks involving HCV-positive blood and those who have received blood or organs from a donor who tested HCV-positive;
- Women with HIV infection;
- Women seeking evaluation or care for sexually transmitted infections;
- Incarcerated women;
- Women who use intranasal drugs;
- Women who have had a tattoo or piercing at an unregulated facility without strict infection control policies.

The main reason the SMFM has not recommended universal screening is because no treatments are safe for use in pregnant women; therefore, there is no way to affect vertical transmission rates.³ As a result, any woman testing positive would have to wait until the postpartum period to initiate therapy. Additionally, there are concerns regarding its cost-effectiveness and the low prevalence of HCV infection. Nevertheless, the American Association for the Study of Liver Diseases and the Infectious Diseases Society of America recently called for universal screening of pregnant women.⁴ Arguments in favor of universal screening include using prenatal care as an opportunity to diagnose HCV in reproductive-age women, as pregnant women typically are insured and then can be linked to HCV care postpartum (if their insurance continues to be active after the postpartum period). With a vertical transmission rate of about 5%, the infants of pregnant women with HCV also could be identified and tested. Furthermore, the earlier identification of women infected with HCV would allow treatment before the next pregnancy, reducing vertical transmission. Finally, studies have shown that the risk-based screening, as currently practiced, is not effective.⁴

The outcomes of cost-effectiveness analyses depend highly on the assumptions in the model. Chaillon et al demonstrated that universal screening is cost-effective with the newer drug prices for direct-acting antiviral medications. Another recent study using a different cost-effectiveness model also showed that universal prenatal screening for HCV was cost-effective.⁵

This model estimated the mean incremental cost-effectiveness ratio to be \$41,000 per quality-adjusted life years gained compared to risk-based screening. For comparison, the mean incremental cost-effectiveness ratio for gestational diabetes screening is estimated at \$20,000 and postpartum depression screening is \$14,000. In terms of what is considered a worthwhile

[Despite the lack of a treatment available during pregnancy, and given that testing for HCV is not too expensive and can be added to prenatal labs easily, I suspect this will become part of the prenatal lab panel in the future.]

investment, the willingness-to-pay threshold per quality-adjusted life years gained for healthcare interventions varies in the literature from \$50,000 to \$100,000. Basically, a willingness-to-pay threshold is the amount the healthcare system (patient, insurance company, or society) would be prepared to pay for a health benefit. Therefore, both studies calculated an incremental cost-effectiveness ratio less than \$50,000 per quality-adjusted life years gained, indicating that universal prenatal screening is cost-effective.

Despite the lack of a treatment available during pregnancy, and given that testing for HCV is not too expensive and can be added to prenatal labs easily, I suspect this will become part of the prenatal lab panel in the future. This would parallel the transition that HIV testing took, from risk-based to universal screening in prenatal care. Some changes to obstetric practice would occur if a patient tested positive for HCV, such as avoiding internal fetal monitoring, prolonged rupture of membranes, and episiotomy in managing labor.³ Additionally, the infant could be tested after birth. Testing would change management even if the patient did not follow up postpartum for HCV treatment. Nevertheless, it remains to be seen if SMFM will change its recommendations in its next guideline revision. ■

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CME/CE QUESTIONS

- In the study by Wright et al, what was the detection rate of preeclampsia using historical risks factors plus the triple test?**
 - 90% of early preeclampsia cases
 - 90% of preterm preeclampsia cases
 - 75% of all preeclampsia cases
 - 30% of all preeclampsia cases
- In the study by Chaillon et al, universal antenatal screening for hepatitis C was found to be cost-effective, with a mean incremental cost-effectiveness ratio of how much per quality-adjusted life years gained compared to risk-based screening?**
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- Explain the latest data regarding diagnosis and treatment of various diseases affecting women;
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- Discuss the advantages, disadvantages, and cost-effectiveness of new testing procedures in women's health.

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