

*AHRQ's Effective Health Care Program: Applying Existing Evidence to
Obstetric Care*

Wednesday, November 10, 2010

12:00-1:00 pm ET

Transcript

OPERATOR: Katherine, the floor is yours.

KATHERINE GRIFFITH: Thank you. Good afternoon, ladies and gentlemen. Thank you for standing by. On behalf of the Agency for Healthcare Research and Quality, also known as A-H-R-Q or AHRQ, welcome to today's Web conference, *Applying Existing Evidence to Effective Obstetric Care*, held by AHRQ's Effective Health Care Program. My name is Katherine Griffith, and I am a contractor for AHRQ's Office of Communications and Knowledge Transfer, and I will be moderating today's event.

This event is part of a series of Web conferences we are holding on Effective Health Care Program research and training. So, we are especially happy you are able to join us today and hope that you will join us for future events.

Before we get started, I want to review some information about the Web conference technology. If you have questions during the presentation, you may submit them electronically by entering them via the "Ask Question" button. The "Ask Question" button is located at the bottom of your screen. When you click on the button, a box will appear in which you can type your question. Once completed, press the "Submit" button. A selection of submitted questions will be addressed during the moderated Q&A session at the end of the Web conference.

Also if you are experiencing technical difficulties, please open the Web conference FAQ document under the "Downloadable Files" button on the bottom of your screen for troubleshooting ideas. You can also contact technical support by submitting your issue in the "Ask Question" box, and someone will get back to you via your e-mail.

Under the "Downloadable Files," you also find the slides for this event, and a document with speaker bio sketches. Today's Web conference includes closed-captioning. The captioning appears in the box below the slides. Finally, this presentation is being recorded and will be available on the AHRQ's Effective Health Care Program Web site shortly.

Let's start with the presentations. During this Web conference, Effective Health Care Program investigator Dr. Wanda Nicholson and I will highlight the benefits of using patient-centered outcomes research in clinical decisionmaking. I will kick off the conference by giving a brief overview of AHRQ's Effective Health Care Program before I turn it over to Dr. Wanda Nicholson to share her research findings on treatments for gestational diabetes and the prevention of the type 2 diabetes postpartum.

As a reminder, you can send your questions electronically by entering them via the “Ask Question” button at the bottom of your screen. Once you enter your question into the box, press the “Submit” button. You can ask either of us questions about the research, the Effective Health Care Program, the specific findings shared today, but we will not address questions until the end of the event. I encourage you to ask them throughout the event as you think of them. We will do our best to address as many questions as we can during the Q&A session.

I will begin discussing the Effective Health Care Program and how you can use patient-centered outcomes research in practice. Patient-centered outcomes research is also known as comparative effectiveness research, which delivers unbiased practical evidence-based information to help you and your patients weigh different options to make the most informed health care decision. It compares drugs, devices, procedures, tests and methods of health care delivery. Patient-centered outcomes research shows which treatment has been shown to work best in different clinical situations and how they compare when it comes to benefits, harms, and side effects.

It will also tell us what is known and what is not. Most importantly, patient-centered outcomes research is descriptive, not prescriptive. It does not tell you how to practice medicine, it does not mandate a particular test or treatment for anyone, nor does it prohibit any tests or treatment. It gives you tools, not rules, that you and your patients can use to make the best possible decisions.

Here at AHRQ, the investment for patient-centered outcomes research has been built around the framework displayed here. The colored boxes and ovals show the different types of work involved with patient-centered outcomes research. Underneath is the research platform that supports the work—including research infrastructure, method development, and training of researchers.

The research process starts at scanning the horizon to identify new and emerging clinical interventions that may impact health care in the U.S. That leads to a systematic review and synthesis of current medical research to compare effectiveness. Evidence synthesis often tells us where the gaps lie between existing medical research and the needs of clinical practice. We also promote and generate new scientific evidence and analytic tools to fill those critical gaps.

All the information gained needs to be communicated in a way that makes sense to the health care decisionmakers. This includes translating the research into plain language and making it accessible and useful to diverse audiences in order to improve health care. We also have a commitment to reach out to stakeholders and communities for input to make sure we get the research right. If it isn't relevant and applicable, then we can't expect it to have an impact.

The Effective Health Care Program has a cradle to grave research agenda that focuses on 14 priority conditions listed here. As you can see, one of the priority conditions is pregnancy. As you can see here, the research focuses on key population. The goal is to fill the gap that traditional clinical trials have left out—including women—to produce pragmatic evidence-based information to help inform everyday clinical decisions by you and your patients.

Since the inception of the Effective Health Care Program, AHRQ has funded and completed dozens of patient-centered comparative effectiveness research projects. These projects include

comprehensive review of diagnostic or treatment options for breast and prostate cancers, atrial fibrillation, diabetes, osteoarthritis, depression, and many other conditions.

The Effective Health Care Program creates a variety of projects that are based on these research reviews and reports. These include executive summaries, plus summary guides written for clinicians, consumers, and policymakers. We recently added to our portfolio a number of materials to support clinician's education, including continuing education modules, interactive key space and faculty slide sets. We will soon be adding patient decision aids as well.

I would like to highlight our consumer guides that summarize the evidence in plain language in an easy-to-read format. These guides are paired with our clinician guides to promote shared decisionmaking. Most of our consumer guides have also been translated into Spanish. The consumer guides can be found online or are available in print. We also have audio podcasts of the guides online as well. Currently, the Effective Health Care Program offers decisionmaking resources related to gestational diabetes and elective induction of labor.

Today, Dr. Wanda Nicholson will be discussing the research that she conducted leading to the EHC findings presented in the clinician and consumer guides related to gestational diabetes. The elective induction of labor research highlights, which discuss the benefits and harms of the practice and their implications on maternal and fetal outcomes, can also be found in the materials on the Effective Health Care Program Web site.

We want to encourage you to get involved in the Effective Health Care Program. Your participation is mutually beneficial. There are multiple points of involvement in our program before, during, and after the research is completed. Before, you can nominate a topic for research on our Web site. If there is a women's health topic you feel you should be addressed, we will give you instructions on how to nominate the topic at the end of the conference. During, you can give input on draft key questions and reports. This kind of involvement helps you get the type of research that will really help answer those controversial questions and it helps us by getting the research right.

If it isn't relevant and applicable, then we can't expect it to have an impact. After the research is completed, you can disseminate the information to your colleagues and patients. You can implement the findings in your clinical decisions. This helps you and us by creating an opportunity for better and more informed decisionmaking and making an impact on the quality of health care.

Well, let's start with the main presentation. We now have the pleasure of hearing from Dr. Wanda Nicholson. Dr. Nicholson is an associate professor in the Department of Obstetrics and Gynecology at the University of North Carolina in Chapel Hill. Dr. Nicholson is a board-certified obstetrician and gynecologist and a perinatal epidemiologist. She is a fellow in the American College of Obstetricians and Gynecologists, ACOG. Her research focuses on epidemiology of chronic conditions in women, including gestational diabetes, type 2 diabetes, obesity, and the effect of depressive symptoms on health-related quality of life. She was previously an investigator with the Johns Hopkins Evidence-based Practice Center, where she

was the principal investigator of this report on labor and postpartum management of gestational diabetes.

Dr. Nicholson?

WANDA NICHOLSON: Thank you. And let me say thank you to the Agency for Healthcare Research and Quality and the Effective Health Care Program as well as everyone who has signed up for the Web conference series today, for the opportunity to speak and to participate.

So, we'll go forward with gestational diabetes, caring for women during and after pregnancy. A brief outline of the materials for today's presentation is that we will first just briefly review the background of gestational diabetes and move toward the process for developing evidence-based or comparative effectiveness review. Then we will delve into the questions addressed in the evidence-based review, look at the results for each question, and then finally end with a brief discussion about the resources that are available that Katherine mentioned earlier in her presentation to guide patients and physicians through shared decisionmaking.

And finally, I know that we are limited in our time period today. So, I did include the Web site through AHRQ, where anyone can find the complete final report.

So, what is gestational diabetes, and what is its health impact in the United States? As I am sure most of us on the call know, gestational diabetes, or GDM, is defined as carbohydrate intolerance that is first recognized or diagnosed in pregnancy. And it's one of the most common medical complications that we find in pregnancy, affecting an estimated 7 percent of annual births in the United States.

Gestational diabetes is known to affect both maternal and neonatal outcomes including Cesarean delivery and maternal hypoglycemia, as well as neonatal hypoglycemia, birth trauma, and neonatal intensive care unit admissions.

NICHOLSON: It's also well established that up to 60 percent of women with a history of gestational diabetes will subsequently develop type 2 diabetes within 5 to 15 years of delivery, emphasizing further the need for postpartum followup and testing. Certainly the practice patterns that are related to medical therapy, delivery management, and postpartum surveillance have the potential to affect millions of women and to affect maternal and neonatal health both during and after pregnancy.

Next slide. So, in response to this need for evidence-based practice in gestational diabetes, the American College of Obstetrics and Gynecology in partnership with AHRQ and the Effectiveness Health Care program derived four key clinical questions that are focused on clinical management, delivery management, and postpartum surveillance in the patient with gestational diabetes.

As I mentioned, there are four key questions that are addressed in this report. Question one is, what is the evidence for the risks and benefits of oral diabetes agents, and specifically looking at second-generation sulfonylureas and the specific one we looked at was glyburide, as well as

metformin, as compared to all types of insulin, for both the mother and the neonate in the treatment of women with gestational diabetes?

A subquestion for question one then followed, which is, what is the appropriate threshold for initiation of therapy? In other words, what is the glucose threshold by which we should say that a patient should then transfer from diet therapy alone to initiation of an oral diabetes medication or insulin?

Next slide. Question number two focused on delivery management and what is the evidence that elective Cesarean delivery or choice of timing of induction in women with GDM results in beneficial or harmful maternal or neonatal outcomes?

A secondary question: how are estimated fetal weight and gestational age related to the outcomes of management of GDM with elective Cesarean delivery or timing of induction?

Next slide. And then the last two questions, three and four, focus on the gestational diabetic after delivery. And those questions are, what are risk factors that are associated both long-term and short-term development of type 2 diabetes after a history of gestational diabetes?

And question four, in regard to postpartum surveillance and screening for type 2 diabetes, what are the performance characteristics of diagnostic tests for diagnosing type 2 diabetes in women with a history of gestational diabetes?

So, in conducting this evidence-based review, I will briefly review the process. I can certainly answer any detailed questions about it in the question-and-answer session, but in the interest of time, I will be brief here.

Our team searched several large national databases including MEDLINE and The Cochrane Library from inception through 2007. This initial review was then augmented with hand searches of 13 additional relevant journal articles, and then a final update was also done just prior to submission of the report. We conducted two independent reviews of all the titles. There we identified abstracts from four articles. Any disagreements by the team in terms of which article should or should not be included or excluded were then resolved by consensus.

Part of the process also in our review with evidence-grading, which you will see at different points since we go through the results of our review. And the grading scale varied from high to moderate, low, very low, and insufficient. And I won't go into detail here because you can see the definitions of each one of those evidence-grade categories listed here.

And I think as it relates to obstetrical management of the gestational diabetic, unfortunately at this time, you will see as we go to the review that a large amount of the available data was categorized as a low level of evidence, very low, or insufficient. But we will focus on that more specifically as we get to the data result slides.

Next slide. And briefly, the results of our literature research. And I have to say that I think this slide was very humbling to our research team. You can see, based on the four questions that we were challenged to review, we identified initially over 11,000 titles.

Through review, we then reduced that to only eight—I am sorry, a little bit over 2,500 abstracts. And then after further review, additional titles and abstracts were included, and we were down to 551 articles, and then with further review based on our inclusion and exclusion criteria, all of which could be found in detail on the report, we excluded another 507 articles. So, a response to those four key very relevant, very important questions when we applied our evidence-based inclusion and exclusion criteria, we were down to 44 included studies across all four questions.

Next slide. So, let's look at the results. In regard to key question one, again, our focus was on the use of oral diabetes medications compared to insulin. Again our question: What is the evidence for the risks and benefits of the use of oral diabetes meds, glyburide and metformin, as compared to all types of insulin? And then second: Is there a difference in outcome based on what glucose levels that medical therapy is initiated?

And in phrasing or in framing the results, what I have done here is to first list the conclusions in a broad fashion, and then we will move toward—go forward in delving more into the actual data that was abstracted.

Our overall conclusions were based on this data that we were unable to draw firm conclusions on any of our comparisons, specifically glyburide compared to insulin, metformin compared to insulin. From three randomized trials a combination—I am sorry—of three randomized trials and five observational studies.

There was limited evidence of no substantial benefit or harm, however, of the use of glyburide compared to insulin. Only a small difference in infant birth weight. There was no evidence of any substantial harms of the use of metformin compared to insulin. But unfortunately, it was really no evidence on a threshold value for when medical therapy should be initiated. And so, we graded this overall body of evidence with a low grade of evidence.

Next slide. And I hope everyone can see this clearly. I did include a substantial amount of data here on this table, and let me walk you through. This table shows the effect of diabetes medications specifically on maternal outcome from randomized clinical trials. And what you will see is this table summarizes the detailed evidence from a comparative effectiveness review. And if you look at the first three studies that we have listed there, they compare maternal outcomes in glyburide in women treated with glyburide compared to women treated with insulin.

And there are three primary outcomes that we have listed here: glycemic control of the mother, the Cesarean delivery, and any episodes of maternal hypoglycemia. And then if you look to the right, you will see an overall summary of the findings from each of the particular studies. A thing of note here, in general, you note that in the first randomized trial that there was no difference in the maternal glucose levels between women who were in the insulin group compared to women who were in the glyburide group.

One of the limitations of this study, however, was that it was a very small randomized trial with a total sample size of only 23 women. No other information was really available on Cesarean delivery or episodes of hypoglycemia in the mother.

If you look at Bertini and Associates, you will see that there was no difference in glucose control in women between the two groups. There was also no difference in the proportion or percentage of women who underwent Cesarean delivery who were treated with insulin or glyburide, and really no difference in the number of hypoglycemic episodes between the two groups.

The largest study to date, in which we will focus a bit more specifically here, is a study by Langer and colleagues that was published in 2000. And this large RCT included over 400 women who were randomized to insulin and glyburide. In the Langer study, I have limited the number of outcomes that we were able to review in our short period of time today, but it does provide the most extensive list of outcome comparisons, both maternal and neonatal.

But specifically here you will see that there was no difference when they looked at the final fasting blood glucose between the two treatment groups, no difference in Cesarean delivery between women treated with insulin or glyburide. However, there was a higher number of hypoglycemic episodes in mothers treated with insulin compared to moms treated with glyburide.

And finally, if you look at the bottom of the slide, you will see the one large randomized trial to date that's comparing metformin to insulin and this was published by Rowan in 2008. A very large, very strong randomized trial of 751 women and you will see here, between the two groups of metformin and insulin, no difference in average fasting blood glucose or Cesarean delivery.

Next slide.

Here we again look at these four trials and look specifically at neonatal outcomes. And again one of the limitations for the first two trials is that there is a very small sample size and therefore may not be sufficient power in these studies to really detect differences between the groups. But as you will see if you move to the far right, in terms of the summary of findings, there was no difference in infant birth weight in the first study from Anjalakshi. But there was no information, unfortunately, on any congenital anomalies, any birth trauma, or any hypoglycemic episodes in the neonate.

If you look at Bertini, there was a higher proportion of incidence with macrosomia actually in insulin group compared to the glyburide group. And there was also a higher proportion of incidence with NICU admissions in the glyburide group, but no cases of any perinatal mortality, but there was no report of any congenital abnormalities in this group as well.

Finally, we get back to our premier study, Langer. Again the largest randomized controlled trial of these comparisons, and we see no difference in—no substantial difference in infant birth weight. Women in the—who were treated with glyburide had infants who were slightly larger at birth than the infants born to women treated with insulin, but it was not a clinically significant difference.

Langer also reported congenital anomalies as outcomes, and you can see if you look in the second column there was really no difference in congenital anomalies between the two groups in very small absolute numbers. And if you look to the middle of the table, you will see again no differences really in neonatal hypoglycemic episodes or NICU admissions.

When we look at the Rowan study, again another large trial comparing metformin and insulin. What's important here is again, no significant differences in infant birth weight. No significant differences in congenital abnormalities, birth trauma, or any NICU admissions. There was a higher proportion however of neonates who experienced a hypoglycemic episode in the insulin group compared to the glyburide group.

Next slide. Now, in addition, the randomized controlled trials certainly are considered a gold standard comparing oral diabetes medications and looking at maternal and infant outcomes; however, we did in addition include five observational studies that compare glyburide to insulin with the total overall five studies—study sample of over 900 women. I won't go into detail into each of the five studies because of time, but I have included the information here.

One that I did want to emphasize is the study by Jacobson that includes a large number of women—504 women, and this—each of the five trials this was the most—I am sorry—each of the observational studies, this was the best designed or best adjusted multivariate study. If you can see here, you will see if you compare insulin to glyburide there were actually higher maternal glucose levels in the insulin group compared to the glyburide group.

There was a higher number of maternal episodes of hypoglycemia, however, in the glyburide group compared to the insulin group. However, glyburide was not associated with any adverse neonatal outcomes, including neonatal hypoglycemia, macrosomia, large or small for gestational age infants compared to the insulin group.

And the reason why I emphasized the Jacobson study in addition to its large sample size, they also conduct the multivariate analysis where they adjusted for full maternal characteristics including race, ethnicity, maternal glucose levels, as well as maternal obesity. If you look at the subsequent studies, Conway and Yogeve, these are definitely studies that are relevant and contribute to our knowledge.

And if we go to the next slide, these two additional studies by Chmait and Rochon, again very important and relevant studies. However, they have smaller sample size and most importantly these other four studies did not adjust for maternal characteristics. And one of the key factors for adjustment would have been maternal obesity. And while I think that the results of these studies are reported, the results of the Jacob study, I think we have more confidence that these are firm conclusions.

Next slide. So, conclusions and limitations in terms of key question one. The limited number of randomized clinical trials that we found—it should say “shows no”—I am sorry—shows no substantial differences in maternal or neonatal outcomes with glyburide compared to insulin. And I apologize for that typo.

Those three RCTs show no substantial differences in maternal or neonatal outcomes with glyburide compared to insulin. However, there is only one RCT with an appropriate sample size as we mentioned, the RCT authored by Langer. And so these smaller RCTs, comparing those two medications may have not been able to detect overall small differences.

When we look at glyburide and insulin in regard to observational studies, again, they are also limited, but they also do not suggest any adverse effects of glyburide. And as I mentioned, there is only one observational study that included a multivariate analysis for adjustment for confounders.

When we look at the one trial by Rowan that compared metformin and insulin, again a large clinical trial, well designed, and which shows also those substantial differences in maternal and neonatal outcomes if we compare metformin use with insulin.

Next slide.

So, if we look at key question two with the focus on the effect of elective Cesarean delivery, timing of induction, or the use of estimated fetal weight on outcomes, our specific question is, what is the evidence that elective Cesarean delivery or the choice of timing of induction in women with gestational diabetes result in beneficial or harmful maternal and neonatal outcomes? And how are estimated fetal weight and gestational age related to the outcomes for management of GDM, with elective cesarean or timing of induction?

And I think that this particular key question was a very crucial one that definitely affects the day-to-day lives of our patients as well as clinicians who are managing them. If you see at the bottom of the slide, our conclusions are that there is very little evidence. And what we will be able to review is actually just one randomized clinical trial that compares the effect of labor induction on maternal and perinatal outcomes.

We will also look at just briefly at four additional observational studies that focused on the effect of estimated fetal weight and/or gestational age on delivery management. But in general, as you will see, as we go through the next few slides that we were unable to draw firm conclusions based on the available data. And in general, overall there is just an insufficient number of studies that target this particular key question.

Next slide. The one and only randomized trial comparing delivery management is a trial by Kjos actually published in 1993 that compares two labor induction protocols for women with gestational diabetes. And as you will see if you look in the table, there was a controlled group, which was randomized to expectant management compared to an intervention group in which induction occurred at 38 weeks gestation following confirmation of fetal lung maturity.

If you look at the key conclusions of this randomized trial is that women who were randomized to the intervention group or induction at 38 weeks did have a decreased macrosomia, which you would expect, as well as a decrease in birth weight or lower birth weight delivery compared to those women who were randomized to the control group.

If you look at the limitation column, I think that you would see what we would expect to encounter. In general, in randomized—in efforts for randomized clinical trials in terms of labor management. There was a lot of crossover between the two groups. There was a high number of women who were randomized to expectant management, who for various clinical reasons did in fact undergo induction at an earlier gestational age and/or Cesarean delivery.

However, for Kjos and colleagues in terms of analyzing this clinical trial, they did analyze it based on an intention-to-treat analysis, in which they based the analysis on the original groups that the women were originally randomized to. And based on that, then we saw the lower rate of macrosomia and birth weight in the steady group.

What is also important about this clinical trial is that there was no difference in the final analysis in Cesarean delivery rates among women randomized to the control group of expectant management compared to women who were randomized in the intervention group. And I think that's an important take-home because it suggests that there isn't a substantial difference in maternal morbidity in women who undergo expectant management compared to women who undergo earlier induction.

Next slide. Just briefly, I have included detail for four additional studies that were a combination of prospective cohort retrospective analysis looking at effect of estimated fetal weight and gestational age on delivery management and outcomes. We would have to caution our interpretation of these four studies.

If you look at the initial study by Conway and colleagues, they looked prospectively at a group of women who were expectantly managed versus women who were induced or either—who either underwent Cesarean delivery based on an estimated fetal weight, by ultrasound. And as you can see there was an increase in the cesarean delivery rate in the study population. However, there was a decrease in the incidence of macrosomia and shoulder dystocia in that study group.

What's important here though is that in each of these cohort studies, there was no, again, no adjustment for maternal characteristics including maternal BMI, which should be a key confounder in any other results. Also what's important in each of these four studies is that they included a combination of women who were both diet-controlled gestational diabetics as well as insulin-requiring gestational diabetics. And so, we do have some concern as to what the conclusions or outcome may have been or how they may have differed if the studies had been powered appropriately for a stratified analysis based on whether you are a mild gestational diabetic with diet or an insulin-requiring diabetic.

The last study in this table, Peled in 2004, also deserves further comment. Although the findings showed a decreasing rate of macrosomia and shoulder dystocia in the women in the intervention group, this study actually spanned over a 19-year period. The women in the intervention group were compared to historical controls pulled from a database and certainly we know there will be wide variations in practice patterns over the course of the last 19 years. So, again, the conclusions are promising, but I think we have to view these conclusions with caution.

Next slide. So, conclusions for key question two, limitations as I mentioned are generally severity of GDM, whether the study was done in patients with insulin-requiring or diet-controlled. Again, the wide timeframe and finally again, no adjustment for confounders, in particular, maternal characteristics, so the findings presented may not be entirely valid.

Next slide. Predicting type 2 diabetes after gestational diabetes, this is our question that focused on what risk factors are associated with short-term and long-term development of type 2 diabetes following a pregnancy with gestational diabetes.

And fortunately in this question we found consistent evidence that supported maternal weight and adiposity as important risk factor. We looked overall at 16 observational studies to obtain this data. And I think also of importance is that unfortunately we found no studies that particularly looked at lifestyle factors or lifestyle interventions such physical activity as a risk factor for type 2 diabetes. So, let's go forward and look at what we were able to find.

Next slide. Here we look at antepartum as well intrapartum maternal obesity. And as you can see, there's several measures across several studies. If we look at our graph here across the x-axis, you will see that number one, any estimates of risks that are to the right of one show an increased risk; any point to the left basically show no increased risk. But as you look here, you can see, it's fairly consistent across these six studies, that an increase in prepregnancy at adiposity measures including weight and BMI is associated with the development of type 2 diabetes after gestational diabetes.

Next slide. We also looked at postpartum obesity and found the same results. One of the premier studies in this area is a study by Cho published in 2005 who looked at a variety of measures of adiposity ranging from BMI to weight to measures of skin-fold thickness. And as you can see here, each of those point estimates are to the right of one suggesting an increase in the odds of developing type 2 diabetes ranging from two up to 3.3.

Next slide. And finally, just briefly we looked at the metabolic factors that could be associated or predictive of the development of type 2 diabetes, and I don't think these come as a surprise. We try to emphasize those in these slides; if you look at the rectangular box at the top, several studies that looked at the fasting blood glucose during the 3-hour OGTT, and you will see that each of these studies show an increase with the development of type 2 diabetes.

I think this is an interesting find because from a clinical standpoint, we typically we have a patient who in particular had an elevated fasting on the 3-hour OGTT. We are particularly concerned about issues around shoulder dystocia and macrosomia. So, I think it's also very relevant here that this particular measure is hardly predictive of subsequent development of type 2 diabetes.

And here at the bottom of the slide, the second rectangular box, you will see again that the overall OGTT response during pregnancy is also highly predictive of development of type 2 diabetes.

Next slide. Our last key question, key question four, was, how do we move toward diagnosing type 2 diabetes after GDM, and what are the performance characteristics, specifically the sensitivity and specificity of past for diagnosing type 2 diabetes after pregnancy?

Our conclusions from this review, we identified eight observational studies. Unfortunately, we were unable to draw firm conclusions on the accuracy of the use of the fasting blood glucose in diagnosing type 2 diabetes, compared with the current gold standard of the 75 gram 2-hour oral glucose tolerance test.

Next slide. Briefly here you will see a summary of the studies that we looked at. There were 8 studies with 10 comparisons. And if you look at the table you will see that the top two rows have been marked out. And that's because these were studies we identified in the literature, but they were not relevant because the threshold values for diagnosing type 2 diabetes are very different than the current threshold values that are advocated by the American Diabetes Association as well as the American College of Obstetrics and Gynecology. So, we were left really with three comparisons of comparing the fasting blood glucose to the 75 gram OGTT.

Next slide. Just briefly, if we look at those three studies, you will see here the sensitivity if we compare fasting blood glucose of greater than 126, which is the current standard for diagnosing type 2 diabetes in a nonpregnant population compared to the 2-hour OGTT. And you will see here that there are wide ranges of sensitivity rates from a low of 46 percent to a high of 89 percent.

In these particular studies, the specificity was very high, nearing 98 percent to 99 percent. But again the sensitivity range here varied, and so again, walking away from this data without firm conclusion about the performance of the fasting blood glucose in the presence of the postpartum period in women with gestational diabetes.

Next slide. So, study limitations now for questions three and four. As I mentioned, the evidence currently supports a consistent relationship between measures of obesity or adiposity in type 2 diabetes. Overall, we still graded that level of evidence as low because, you know, there were several studies but not in a large number studies. And there were studies that did not—again did not have complete adjustment for confounders. And as I alluded to in key question four, again, difficult to assess the performance of the fasting blood glucose compared to our standard 75 gram oral glucose tolerance test. So, again, a low grade of evidence for key question four at this point as well.

Next slide. So, what do we have in terms of our key findings? Number one, there is no substantial return of neonatal outcome differences with glyburide or metformin compared to insulin, specifically we found no increased risk with the use of oral diabetes medicines, whether it was glyburide or metformin compared to insulin. Number two, from key question two, no clear evidence yet about the timing of induction or elective Cesarean delivery in the management of the gestational diabetic.

We are unable to draw confident conclusions on the effect of the estimated fetal weight or gestational age based on current studies. Key finding four, measures of adiposity are consistently

associated with development of type 2 diabetes. Our final point, we are unable at this point to adequately assess the fasting blood glucose compared to the 75 gram. And our overall evidence grade for the entire body of evidence regarding all four key questions is still low, meaning that the planning and implementation of additional studies will likely enhance and change treatment management.

Next slide. So let me end with areas of future research. First, we need well-designed clinical trials with sufficient sample size to detect small differences. And as I mentioned earlier in the area for diabetes medication, we really only have two large well-designed clinical trials. These trials would need to follow an intention-to-treat analysis to reduce bias and also include consistent outcomes with consistent definitions.

We also need either randomized clinical trials or prospective studies with appropriate control and adjustment for confounders. These are urgently needed to assess key question two in terms of choice and timing of delivery in GDM.

Third, identifying the most important risk factors for developing type 2 diabetes will require large prospective studies with long-term follow up. And finally in terms of diagnostic testing, we need additional studies that will assess the timing and frequency of screening using current threshold and also assessing performance in different subgroups. But we are not clear, however, at this point do diagnostic tests perform differently based on race, ethnicity or based on your original response to prenatal testing.

Next slide. I won't delay with this point in the interest of time, because I know Katherine alluded to the resources that the Effective Health Care Program provides for clinicians in counseling their patients about gestational diabetes.

Next slide. At acknowledgments, let me finish by acknowledging the Gestational Diabetes Evidence-based Practice Team that I work, Johns Hopkins, also the American College of OBGYN Committee on Obstetric Practice from which these questions originated. And again, as I alluded to earlier, AHRQ, the Effective Health Care Program, and the Eisenberg Center. Thank you.

GRIFFITH: Oh, yes, that was great. Thank you so much. It is now time for questions. If you have a question, please type your question into the "Ask Question" box at the bottom of the screen. I will go ahead and get started with one question for Dr. Nicholson. In regards to key question number two, what factors account for the limited data on delivery management?

NICHOLSON: Well, I think it reflects our—from a clinician standpoint or any provider who is providing care to the one with gestational diabetes, the overwhelming concern about delivery in terms of avoiding macrosomia, avoiding shoulder dystocia and birth trauma. And so, I think that in regard to that particular key question, it might be very difficult to conduct randomized clinical trials, both from an acceptance standpoint on the part of the patient as well as other providers at your particular site.

So it is—I think it responds back to the point that it is somewhat difficult sometimes to conduct well-designed clinical trials in an area where there's already a lot of variation in management and major concerns about outcome.

Having said that, I think there is room to readdress key question two in the design of prospective observational studies that have clear protocols based on the clinical changes that may occur over the course of pregnancy.

I think you would also have to address it from a multicenter perspective. I think it would be difficult to recruit a sufficient number of women at any one particular site. So, I think any funding priorities would also have to look at funding multiple sites to really design a study and include all of the important and relevant outcomes that we would be interested in.

GRIFFITH: Great, thank you. We have another question for you. How do we move forward with clinical trials to determine the efficacy of oral agents in managing maternal glucose?

NICHOLSON: Well, I think again in order to, as—it's not included on the site here. There are some short small survey studies that show that increasingly clinicians who provide care to women with gestational diabetes are using oral diabetes medications more and more; and that's despite the fact that we have few trials and that it hasn't been officially approved by the FDA for use in this regard. I think the way to move forward is in the way that one would normally move forward in looking at gathering data to obtain FDA approval. And that again would be through the conduct of one of the large multicenter trial where you are randomizing women to oral therapy or insulin.

I think what would also help with that would be perhaps the establishment of a registry of patients who have been treated with oral diabetes medications as a way of reporting any adverse outcomes as well, in particular, any congenital anomalies. Congenital anomalies in particular are very important, but they are also somewhat difficult to ascertain even in the context of a well-designed trial in terms of getting a high number of (INAUDIBLE) to make a true comparison.

GRIFFITH: Great. And actually related to that question, we have a question that is: Do you use oral agents in treating gestational diabetic? If so, how do you counsel the patient? And what do the medical endocrinologists do within your communities?

NICHOLSON: That was a great question, and I don't know whether there has been a large—I don't think there's large genetic practice patterns in the use of oral diabetes meds and insulin. In general, I think our institution still tends to favor the use of insulin in the management of gestational diabetics. So, I think if you were to look overall at our population, you would see a very large number of proportion who are managed with insulin.

At the same time, we do also use oral diabetes medicines, particularly glyburide, in patients who don't quite meet our glucose targets with diet alone and who, you know, may be adverse to or unwilling to try insulin therapy. So, I think our prescription of the glyburide certainly tends to be applied to really targeted patients who we believe will be compliant with and who we believe we

can get some success with using it. It's not that we use glyburide in a broad fashion across all the gestational diabetics. I think it is on an individual patient-by-patient basis.

In regard to the second question of counseling, I covered many of the points that we covered in the talk today. One, that there—the mainstay of therapy traditionally has been insulin. We know how it works, we know how it affects the mother. We know that it doesn't cross the placenta, so it's not going to affect the fetus. And we have a long history of use with insulin and its safety in pregnancy. I counsel them that glyburide is the choice that we have a limited data on its long-term effects and to what extent it may cross to the placenta.

I certainly quote them the result, particularly the article by Langer, that large trial. And so, I think when you go into the exam room and you are having a discussion, a big part of it is focused on the shared decisionmaking between the physician—I am sorry—between the clinician and the patient. And having said that, I think, that's where the resources from the Eisenberg Center, I believe, can certainly play a key role because they take all of the data that we've talked about for the last hour, and are able to present it, I think, in an easily understood fashion that a provider can use with the patient in having this discussion.

GRIFFITH: OK. Thank you so much. I think our time is almost up. If we did not get to your question today, or you have a question for Dr. Nicholson or me, please e-mail at ehc_clinicians@ahrq.hhs.gov. To access all the research mentioned today and print them out, you can find them on the Effective Health Care Program Web site, as I mentioned before. The link is listed here.

You can also call the publications clearinghouse at the number here. Also, on the Web site, you can become involved in the topic nomination and refinement process that I described earlier, as well as comment on the draft and review report. All these features, in addition to signing up for e-mail updates, can be easily navigated in the panel on the left-hand side of the Effective Health Care Program Web site.

Finally, I would like to thank Dr. Nicholson for sharing her research findings with us today. I think we all agree it was very helpful. I would like to thank our many participants for joining today. We hope the information presented here informed you about how you can implement patient-centered outcomes research into everyday practice and how the Effective Health Care Program resources are available to you and your patients with decisionmaking.

As we conclude this Web conference, let me remind you that this event will be archived and available in a few weeks on the Effective Health Care Program Web site, which should pop up on your screen right about now.

Finally as you leave the event, please answer the one feedback question posed. Your feedback is very important to us as we develop more resources and plan for similar events. Have a nice day. Thank you so much.

OPERATOR: Thank you ladies and gentlemen. This does conclude today's Web conference. We thank you for your participation, and you may disconnect your lines at this time, and have a great day.

END