

adequately the expectations of the pregnant woman may be one of these strategies cited by the authors.

This is not a simple task. A systematic review that analyzed the validated instruments that measure the women's childbirth experiences verified great heterogeneity of content and quality of the instruments and did not include studies that assessed the expectations of the pregnant women.<sup>3</sup> Although some tools have already been developed with this purpose, such as the Delivery Experience And Expectancy Questionnaire (known by the Portuguese acronym) from Portugal, Wijma Delivery Expectancy Questionnaire from Sweden, and the Salmon Questionnaire from Spain, such instruments were not validated for the reality of several countries, and, up to this moment, there is no consensus for the investigation of these phenomena.

The humanization of the practices of childbirth care is still a great challenge.<sup>4</sup> Thereby, health professionals responsible for obstetric care, upon being aware of the expectations of the women, may think of new strategies to care for pregnant women to improve the care for the mother-baby binomial and therefore the satisfaction of the women. An instrument that measures the expectation of the pregnant women may be a tool that reduces the number of unnecessary cesarean deliveries and that aid in the adequate delivery; after all, each woman is different and bears different expectations, and thereby each delivery is also different. ■

Gabriela M. Marques, MD, BSc  
Diego Z. Nascimento, MD, BSc  
Betine P. M. Iser, MD, PhD  
Postgraduate Program in Health Sciences  
University of Southern Santa Catarina at Tubarão  
Av. José Acácio Moreira Santa Catarina  
787 - Dehon  
Tubarão SC, Brazil 88704-900  
[gabii\\_moreno@hotmail.com](mailto:gabii_moreno@hotmail.com)

The authors report no conflict of interest.

#### REFERENCES

1. Gregory KD, Korst LM, Saeb S, McCulloch J, Greene N, Fink A, Fridman M. Childbirth-specific patient-reported outcomes as predictors of hospital satisfaction. *Am J Obstet Gynecol* 2019;220:201.e1–19.
2. Ledford CJW, Canzona MR, Womack JJ, Hodge JA. Influence of provider communication on women's delivery expectations and birth experience appraisal: a qualitative study. *Fam Med* 2016;48:523–31.
3. Nilvér H, Begley C, Berg M. Measuring women's childbirth experiences: a systematic review for identification and analysis of validated instruments. *BMC Pregnancy Childb* 2017;17:1–19.
4. Pereira RM, Fonseca GDO, Pereira ACCO, Gonçalves GA, Mafra RA. New childbirth practices and challenges for the humanization of assistance in southern and southeastern Brazil. *Cien Saude Colet* 2018;25:3517–24.

© 2019 Elsevier Inc. All rights reserved. <https://doi.org/10.1016/j.ajog.2019.02.005>

## Twin-twin transfusion syndrome: need for mechanistic studies



**TO THE EDITORS:** We commend the systematic review and meta-analysis of Mackie et al<sup>1</sup> in which they assessed the ability of first-trimester pregnancy-related factors to predict complications in monochorionic (MC) pregnancies. Among the factors assessed were ultrasound measurements, maternal characteristics, and biomarkers, whereas the outcomes were primarily consequences of twin-twin transfusion syndrome (TTTS), including discrepancy in amniotic fluid volumes, growth discordance, and intrauterine fetal demise. Not surprisingly, the authors found that “it is not currently possible to predict adverse outcomes in MC twin pregnancies.”

The primary pathophysiology of MC adverse outcomes is vascular anastomoses, which result in transfusion of blood from donor to recipient, and subsequent nutrient, hematologic, and fluid dynamic alterations. Nearly all MC pregnancies have vascular anastomoses, with an average of 5–7 superficial (artery-artery, vein-vein) or deep (artery-vein/vein-artery) anastomoses, with artery-artery and vein-vein providing a protective effect from TTTS.

As the fetus grows, the linear growth of vessel diameters combined with increased cardiac output results in an approximate fourth-power increase in the net transfusion.<sup>2</sup> Thus, relatively compensated anastomoses in early

pregnancy may rapidly become imbalanced, resulting in the sudden appearance of TTTS findings.<sup>3</sup> Additional effects of placental resistance, arterial pressure, amniotic fluid volume and pressure, blood viscosity, and unequal placental sharing may markedly alter both fluid and growth alterations.<sup>3</sup>

Accordingly, it is most important that future studies explore the detection, type, and quantification of anastomotic flow and placental sharing as well as pregnancy characteristics that may predict the likelihood of these anastomoses.<sup>4</sup> It is only with a more mechanistic hypothesis-based study that one may develop truly prognostic approaches. ■

Michael G. Ross, MD, MPH  
Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center  
Geffen School of Medicine  
University of California, Los Angeles  
10833 Le Conte Avenue  
Los Angeles, CA 90095  
[mikeros@ucla.edu](mailto:mikeros@ucla.edu)

Martin van Gemert, PhD  
Department of Biomedical Engineering and Physics  
Academic Medical Center

University of Amsterdam  
Amsterdam, The Netherlands

Jeroen P. Wijngaard, PhD  
Department of Clinical Chemistry Hematology and Immunology  
Diaconessenhuis  
Utrecht, The Netherlands

The authors report no conflict of interest.

## REFERENCES

1. Mackie FL, Hall MJ, Morris RK, Kilby MD. Early prognostic factors of outcomes in monochorionic twin pregnancy: systematic review and meta-analysis. *Am J Obstet Gynecol* 2018;219:436–46.
2. Van Gemert MJ, Umur A. Trends of discordant fetal growth in monochorionic twin pregnancies. *Phys Med Biol* 2000;45:N85–93.
3. Van Den Wijngaard JP, Umur A, Ross MG, Van Gemert MJ. Twin-twin transfusion syndrome: mathematical modelling. *PrenatDiagn* 2008;28:280–91.
4. Nakata M, Martinez JM, Diaz C, Chmait R, Quintero RA. Intra-amniotic Doppler measurement of blood flow in placental vascular anastomoses in twin-twin transfusion syndrome. *Ultrasound Obstet Gynecol* 2004;24:102–3.

© 2019 Elsevier Inc. All rights reserved. <https://doi.org/10.1016/j.ajog.2019.02.007>

## REPLY TO: TWIN–TWIN TRANSFUSION SYNDROME: NEED FOR MECHANISTIC STUDIES



**TO THE EDITORS:** We thank Professor Ross et al. for their interest in our publication “Early prognostic factors of outcomes in monochorionic twin pregnancy: systematic review and meta-analysis,”<sup>1</sup> and for kindly highlighting important areas of future research.

We agree that unbalanced placental vascular anastomoses are pivotal to the pathophysiology of twin–twin transfusion syndrome (TTTS). Computational and mathematical studies, including those performed by Professor Ross, have demonstrated that fluid mechanics are involved in TTTS and have improved knowledge surrounding TTTS. However, to our knowledge there have been no studies able to translate the models’ findings into real-life measurable parameters, as it is very difficult to visualize placental anastomoses, irrespective of type, using color flow or power Doppler, especially in the first trimester. Professor Christoph Lees is examining the use of advanced dynamic flow (ADF) and superb microvascular imaging (SMI) Doppler, although this is an early-stage research tool (personal communication).

The study by Nakata et al<sup>2</sup> that Professor Ross et al reference, which evaluates invasive intra-amniotic Doppler placental anastomoses blood flow measurement, received criticism regarding the lack of validation of the technique and

the findings,<sup>3</sup> as far as the authors are aware, these findings have not been validated in real life, nor have the findings of the computational modeling studies. Thus the search continues for novel first-trimester predictive markers for TTTS, which is hampered by the lack of animal models. We are exploring other aspects of TTTS pathogenesis, by investigating the use of maternal serum analytes and microRNA as predictive tests, which would be evaluated in conjunction with ultrasound assessment.<sup>4</sup> Currently, as there is no prevention for TTTS, even with the identification of a “high-risk” group, sequential ultrasound monitoring of the amniotic fluid deepest vertical pools would be required. ■

Fiona L. Mackie, MBChB  
Centre for Women’s & Children Health  
Institute of Metabolism and Systems Research  
University of Birmingham  
Mindelsohn Way Edgbaston  
Birmingham, B15 2TT, UK  
[fionamackie@doctors.org.uk](mailto:fionamackie@doctors.org.uk)

R. Katie Morris, PhD  
Centre for Women’s & Children Health  
Institute of Metabolism and Systems Research  
University of Birmingham, Birmingham, B15 2TT, UK  
West Midlands Fetal Medicine Centre  
Birmingham Women’s and Children’s NHS Foundation Trust  
Mindelsohn Way, Edgbaston, B15 2TG, UK

Mark D. Kilby, DSc  
Centre for Women’s & Children Health  
Institute of Metabolism and Systems Research  
University of Birmingham, Birmingham, B15 2TT, UK  
West Midlands Fetal Medicine Centre  
Birmingham Women’s and Children’s NHS Foundation Trust  
Mindelsohn Way, Edgbaston, B15 2TG, UK

The authors report no conflicts of interest.

F.L.M. is funded by the Richard and Jack Wiseman Trust, who had no involvement in the Reply.

## REFERENCES

1. Mackie F, Hall M, Morris R, Kilby M. Early prognostic factors of outcomes in monochorionic twin pregnancy: systematic review and meta-analysis. *Am J Obstet Gynecol* 2018;219:436–46.
2. Nakata M, Martínez J, Diaz C, Chmait R, Quintero R. Intra-amniotic Doppler measurement of blood flow in placental vascular anastomoses in twin-twin transfusion syndrome. *Ultrasound Obstet Gynecol* 2004;24:102–3.
3. Taylor M, Wee L, Denbow M, Fisk N. Re: Intra-amniotic Doppler measurement of blood flow in placental vascular anastomoses in twin-twin transfusion syndrome. *Ultrasound Obstet Gynecol* 2004;24:479–81.
4. Mackie F, Morris RK, Kilby MD. The prediction, diagnosis and management of complications in monochorionic twin pregnancies: the OMMIT (Optimal Management of Monochorionic Twins) study. *BMC Pregnancy Childbirth* 2017;17:153.

© 2019 Elsevier Inc. All rights reserved. <https://doi.org/10.1016/j.ajog.2019.02.008>