

Reply to: Twin-twin transfusion syndrome: need for mechanistic studies

Mackie, Fiona; Morris, R. Katie; Kilby, Mark

DOI:

[10.1016/j.ajog.2019.02.008](https://doi.org/10.1016/j.ajog.2019.02.008)

License:

Creative Commons: Attribution-NonCommercial-NoDerivs (CC BY-NC-ND)

Document Version

Peer reviewed version

Citation for published version (Harvard):

Mackie, F, Morris, RK & Kilby, M 2019, 'Reply to: Twin-twin transfusion syndrome: need for mechanistic studies: Twin-twin transfusion syndrome: need for mechanistic studies', *American journal of obstetrics and gynecology*, vol. 220, no. 5, pp. 508. <https://doi.org/10.1016/j.ajog.2019.02.008>

[Link to publication on Research at Birmingham portal](#)

General rights

Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

- Users may freely distribute the URL that is used to identify this publication.
- Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
- User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
- Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

Take down policy

While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact UBIRA@lists.bham.ac.uk providing details and we will remove access to the work immediately and investigate.

Accepted Manuscript

Reply to: Twin-twin transfusion syndrome: Need for mechanistic studies

Fiona L. Mackie, MBChB, R. Katie Morris, PhD, Professor Mark D. Kilby, DSc

PII: S0002-9378(19)30349-7

DOI: <https://doi.org/10.1016/j.ajog.2019.02.008>

Reference: YMOB 12550

To appear in: *American Journal of Obstetrics and Gynecology*

Received Date: 15 January 2019

Accepted Date: 3 February 2019

Please cite this article as: Mackie FL, Morris RK, Kilby MD, Reply to: Twin-twin transfusion syndrome: Need for mechanistic studies, *American Journal of Obstetrics and Gynecology* (2019), doi: <https://doi.org/10.1016/j.ajog.2019.02.008>.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



Title: Reply to: Twin-twin transfusion syndrome: Need for mechanistic studies

Fiona L MACKIE MBChB, Centre for Women's & Children Health, Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, B15 2TT, 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.

Professor 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.

Conflict of interest: the authors report no conflicts of interest

Funding: FLM is funded by the Richard and Jack Wiseman Trust but they had no involvement in the reply.

Corresponding author: Fiona L MACKIE MBChB, Centre for Women's & Children Health, Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, B15 2TT, UK. +441216264535 (work) fionamackie@doctors.org.uk

Word count: 293

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' (Mackie 2018), 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 visualise placental anastomoses, irrespective of type, using colour flow or power Doppler, especially in the first trimester. Professor Christoph Lees is examining the use of advanced dynamic flow (ADF) and superb micro-vascular imaging (SMI) Doppler, although this is an early-stage research tool (personal communication).

The study by Nakata et al. (Nakata 2004) that Professor Ross et al. reference that evaluates invasive intra-amniotic Doppler placental anastomoses blood flow measurement received criticism regarding the lack of validation of the technique and the findings (Taylor 2004), and as far as the authors are aware, these findings have not been validated in real-life, nor have the findings of the computational modelling 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 (Mackie 2017). 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.

References

- Mackie F, Hall M, Morris R and Kilby M (2018). "Early prognostic factors of outcomes in monochorionic twin pregnancy: systematic review and meta-analysis." *Am J Obstet Gynecol*: epub ahead of print.
- Mackie F, Morris RK and Kilby MD (2017). "The prediction, diagnosis and management of complications in monochorionic twin pregnancies: The OMMIT (Optimal Management of Monochorionic Twins) study." *BMC Pregnancy Childbirth* **17**(1): 153.
- Nakata M, Martínez J, Díaz C, Chmait R and Quintero R (2004). "Intra-amniotic Doppler measurement of blood flow in placental vascular anastomoses in twin-twin transfusion syndrome." *Ultrasound Obstet Gynecol* **24**(1): 102-103.
- Taylor M, Wee L, Denbow M and Fisk N (2004). "Re: Intra-amniotic Doppler measurement of blood flow in placental vascular anastomoses in twin-twin transfusion syndrome." *Ultrasound Obstet Gynecol* **24**(4): 479-481.