

Minutes
Stillbirth Clinical Studies Group
8 June 2016, 14:00–17:00



Present: Gordon Smith (GS; Chair); Sarah Stock (SS; incoming Chair); Peter Brocklehurst (PB); Steve Charnock-Jones (SCJ); Alex Heazell (AHe, by phone); Hannah Knight (HK); Tracey Mills (TM, by phone), Jane Sandall (JaS); Janet Scott (JSc); Jim Thornton (JT); and Laura Price (LP)

Apologies: David Cromwell (DC); Alyson Hunter (AHu); Julia Sanders (JuS); Neil Sebire (NS); Dimitrios Siassakos (DS); and Basky Thilaganathan (BT)

- 1) **Welcome, introductions and apologies.** SS was welcomed as the incoming CSG Chair.
- 2) **Minutes of the last meeting and matters arising.** Actions discharged. Re SCJ/NS PICO, HTA consider proposals for interventions, diagnostic effectiveness, etc, so PICO would have to be structured accordingly.
- 3) **Ongoing projects**
 - a) MiNESS (AHe) Finished recruiting last year. Analysis continues. Results meeting 9 June 2017. Two papers submitted to *BJOG*. Discussing peer review comments re methods with editor. Once paper has been accepted, highlight cumulative evidence to devolved governments, NHS England, RCM and RCOG to ensure public health messages can be promoted and supported by front-line health professionals. CSG to consider methods and results.
 - b) AFFIRM (SS/AHe) Protocol accepted by *BMJ Open*. Analysis plan written. Awaiting data from participating sites. Closed results meeting on 20 October. Have surveyed % implementation by sites to inform ITT analysis.
 - c) HTA-funded evidence synthesis/health economic analysis of universal late pregnancy ultrasound. Surveying via professional bodies to ascertain the ultrasound markers being used. Systematic review protocol to be submitted to Prospero. Investigators meeting in December to discuss early results.
 - d) Each Baby Counts (HK) Second report to be published 21 June, with full results for 2015 and thematic analysis on three aspects of care: fetal monitoring; human factors; and neonatal care. Media interest expected.

National maternity and perinatal audit (HQIP-funded) (HK) 100% of maternity units in Scotland and Wales, 98% England (three trusts without electronic records) supplying information for 88 data points (direct from hospitals in England). By the end of 2018, will have a research resource that includes information on practically all births over a 2 year period (~3 million deliveries). Meeting with MBRRACE in Autumn to discuss linkage.

Study using HES data to replicate 35/39 study with perinatal death as primary outcome: 77000 deliveries in nulliparous women 35+. *JAMA* rejected, submitting to *BMJ*.
 - e) PARENTS 2 (DS) study on designing a new process for involving parents (alongside the MBRRACE project): 1st phase completed (staff and stakeholders focus groups in two cities; consensus meeting 9 June); two papers in preparation (consensus paper and thematic analysis paper). Pilot intervention to start this summer. CSG members invited to join a large bid (NIHR/HF) early next year for a dissemination and evaluation project.

- f) International consensus on bereavement care (DS) Working to agree basic principles of respectful bereavement care for LMICs and HICs. Any CSG member aware of ongoing research in LMICs to contact DS.
- g) Core outcome set for trials of bereavement care interventions (DS) Prior to potential award of NIHR fellowship, the Bristol team are exploring appropriate parent engagement in COS development.
- h) DESiGN (JSc/JaS) Study started Nov 2016. 11 units randomised, with a further two units to randomise. JSa is leading an analysis of implementation and training. First results likely end 2018.

Action:

1. (a) AHe to circulate MiNESS paper to CSG
2. (e) CSG members interested in joining bid for dissemination/evaluation project for involving parents in review to contact DS
3. (f) CSG members aware of LMIC bereavement care research to contact DS

4) Completed projects

- a) INSIGHT (DS) Paper on bereavement care practices and behaviours to inform training accepted by *BJOG*.
- b) PARENTS (DS) Paper on parental views on perinatal mortality review accepted for publication by *BMC Pregnancy and Childbirth*

5) Applications

- a) RfPB Wales application: under-representation of women with associated social risk factors presenting with RFM (JuS) Awaiting result. CSG would have been interested to see proposed application.
- b) HTA call for macrosomia trial (JT) JT application unsuccessful; awarded to a trial using customised growth charts/GROW software led from Warwick.
- c) HTA call for scoping exercise re difficult delivery of fetal head at Caesarean (JT) Not successful. Commissioning brief may be revised and call re-opened.
- d) ReMIT2 (AH) [should appear under Ongoing projects] Multicentre RCT of PIGF as marker of poor outcome (composite) in RFM pregnancies from 36 weeks (sample size ~750 women). More blood samples currently being tested in pilot. Starting Autumn at earliest.

6) PICOs

RCOG Research Committee has asked for 1 PICO/CSG meeting.

- a) Planned Caesarean delivery at 39 weeks to improve outcome in nullips $\geq 40y$ (GS) Objective is to show it does not cause harm. Only tangentially related to SB.
- b) Computerised CTG (AH) Agreed cluster trial would be preferential to stepped-wedge design, with 'all women seeking additional medical care' as population. CSG opted to support the development of this PICO and submission to the Research Committee.
- c) Induction for all at 39 weeks (JT) HTA unlikely to consider while US trial is under way. Re-assess in light of remaining uncertainties when US trial publishes (data at end 2017).
- d) Use of new techniques of intermittent IP fetal monitoring to improve perinatal outcomes (JuS) Raises important questions but work is needed to scope out interventions and what a trial would look like. CSG suggest submitting to HTA as a suggestion for a scoping exercise, with an explanatory note.

Action:

1. (b) AH to develop PICO for submission to Research Committee
2. (d) JaS and JuS to liaise to develop scoping suggestion for HTA

- 7) **Development of a national research strategy (JSc/LP)** PB will chair a meeting of a Pregnancy Research Review Group that will bring together funding bodies, ABPI, charities, Royal Colleges, government agencies and the devolved nations to consider their strategies for pregnancy research and devise models to 'de-risk' pregnancy research for pharmaceutical companies. Invitations to be sent by Chris Whitty on behalf of CMO.

The Health Futures 20/30 consultation represents a further opportunity to raise the area of pregnancy research. All CSG members are encouraged to complete the consultation exercise by 16 June deadline. HK to follow-up with RCOG.

Action:

1. JaS to circulate Health Futures link via LP
2. HK to follow up with RCOG

8) **ISA 2017/2018**

ISA 2017: University College Cork, 22–24 September (Fetal Growth conference 20–22 Sept)

2018 International Conference on Stillbirth, SIDS and Baby Survival (ISPID-ISA 2018), Glasgow, 7–9 June

- 9) **Update on Sands research funding cycle and evaluation (LP)** Four studies funded: improving communication skills around limiting life-sustaining support in neonatal unit (Marlow); outcomes for resuscitated babies with no heart rate at 10 mins (Sullivan); meta-narrative review of impact of socioeconomic factors and stillbirth risk (Kingdon); prediction and prevention of perinatal death (IPD meta-analysis and COS development; Khalil). Will be monitored via interim reports linked with payment schedule and with advice from PEP Chair/Vice Chair. PEP members will be asked for their views and advice in forthcoming evaluation exercise.

- 10) **BJOG Stillbirth-themed issue (DS)** No report

11) **AOB**

- a) JSa asked for a record of thanks to Sands' staff involved in ReAssure project, particularly for the support and debriefing of research staff. Now conducting follow-up research into how it is being seen and used by health professionals.
- b) The CSG welcomed SS as the new Chair and thanked GS for 6 years in the Chair.

Appendix: papers published from CSG-supported studies

Post mortem study

1. Man, J., Hutchinson, J. C., Heazell, A. E., Ashworth, M., Levine, S. and Sebire, N. J. (2016), Stillbirth and intrauterine fetal death: factors affecting determination of cause of death at autopsy. *Ultrasound Obstet Gynecol*, 48: 566–573. doi:10.1002/uog.16016
2. Man, J., Hutchinson, J. C., Ashworth, M., Heazell, A. E., Jeffrey, I. and Sebire, N. J. (2016), Stillbirth and intrauterine fetal death: contemporary demographic features of >1000 cases from an urban population. *Ultrasound Obstet Gynecol*, 48: 591–595. doi:10.1002/uog.16021
3. Man, J., Hutchinson, J. C., Ashworth, M., Judge-Kronis, L., Levine, S. and Sebire, N. J. (2016), Stillbirth and intrauterine fetal death: role of routine histological organ sampling to determine cause of death. *Ultrasound Obstet Gynecol*, 48: 596–601. doi:10.1002/uog.16020
4. Man, J., Hutchinson, J. C., Ashworth, M., Heazell, A. E., Levine, S. and Sebire, N. J. (2016), Effects of intrauterine retention and postmortem interval on body weight following intrauterine death: implications for assessment of fetal growth restriction at autopsy. *Ultrasound Obstet Gynecol*, 48: 574–578. doi:10.1002/uog.16018
5. Man, J., Hutchinson, J. C., Heazell, A. E., Ashworth, M., Jeffrey, I. and Sebire, N. J. (2016), Stillbirth and intrauterine fetal death: role of routine histopathological placental findings to determine cause of death. *Ultrasound Obstet Gynecol*, 48: 579–584. doi:10.1002/uog.16019
6. Man, J., Hutchinson, J. C., Ashworth, M., Jeffrey, I., Heazell, A. E. and Sebire, N. J. (2016), Organ weights and ratios for postmortem identification of fetal growth restriction: utility and confounding factors. *Ultrasound Obstet Gynecol*, 48: 585–590. doi:10.1002/uog.16017

POP study/data

7. Cleaton MA, Dent CL, Howard M, Corish JA, Gutteridge I, Sovio U, Gaccioli F, Takahashi N, Bauer SR, Charnock-Jones DS, Powell TL, Smith GC, Ferguson-Smith AC, Charalambous M. Fetus-derived DLK1 is required for maternal metabolic adaptations to pregnancy and is associated with fetal growth restriction. *Nat Genet* 2016 Oct 24. doi: 10.1038/ng.3699. [Epub ahead of print]
8. Sovio U, Murphy HR, Smith GCS. Accelerated fetal growth prior to diagnosis of gestational diabetes mellitus: a prospective cohort study of nulliparous women. *Diabetes Care* 2016;39:982-7
9. Salvatari N, Sovio U, Pitman Mayo R, Charnock-Jones DS, Smith GCS. The relationship between human placental morphometry and ultrasonic measurements of utero-placental blood flow and fetal growth. *Placenta* 2016;38:41-8
10. Partap U, Sovio U, Smith GCS. Fetal growth and the risk of spontaneous preterm birth in a prospective cohort study of nulliparous women. *American Journal of Epidemiology* 2016;184:110-119
11. Sovio U, White IR, Dacey A, Pasupathy D, Smith GCS. Screening for fetal growth restriction with universal third trimester ultrasonography in nulliparous women in the Pregnancy Outcome Prediction (POP) study: a prospective cohort study. *Lancet* 2015;386:2089-97