

# Minutes

## Stillbirth Clinical Studies Group

3 November 2016, 14:00–17:00



**Present:** Gordon Smith (GS; Chair); Jane Sandall (JaS), Steve Charnock-Jones (SCJ), David Cromwell (DC), Janet Scott (JSc), Hannah Knight (HK), Sarah Stock (SS; phone), Clare Francis (CF), Julia Sanders (JuS), Clea Harmer (CH; CEO, Sands) and Laura Price (LP; Sands) **Apologies:** Alex Heazell (AHe), Peter Brocklehurst (PB), Dimitrios Siassakos (DS), Neil Sebire (NS), Alyson Hunter (AHu), Tracey Mills (TM), Basky Thilaganathan (BT), Jim Thornton (JT)

- 1) **Welcome, introductions and apologies.** There were some organisational difficulties with the meeting that meant that PB and AHe were unable to join as they had planned.
- 2) **Minutes of the last meeting and matters arising** (GS). Minutes confirmed. Action summary: [2] minutes sent to Sands and BMFMS websites, LP continuing to remind BMFMS to post. [6] RCOG breech guideline consultation comments submitted. [10] Sands continuing to work with CSG to unravel data issues. [11] SS, JuS and CF invited and present.
- 3) **Ongoing projects**
  - a) MiNESS (AHe) (Questionnaire-based study of sleeping habits/activities in 300 women who had a stillbirth and 700+ gestation-matched controls). Final data expected Spring 2017
  - b) AFFIRM (SS) (Stepped wedge trial of fetal movements awareness and management protocol). Going well, with all units now randomised. Protocol paper has been submitted. Main funder has agreed a 6-month no-cost extension. Trial Steering Committee meets in December 2016
  - c) POP study (GS) (Serial ultrasound and blood sampling in 4,500 nulliparous pregnant women). Data analysis likely to result in multiple papers. One looking at DLK1 association with FGR and *Dlk1* deletion in mice was published in *Nature Genetics* in October (see appendix)
  - d) Minimally invasive autopsy study, HTA (NS). No report
  - e) DESiGN (JSc) (Stepped wedge trial of GAP programme in units in London/SE). An amendment to the primary outcome has been proposed. CSG to consider
  - f) Parents2. New Health Foundation grant to develop and pilot test a national process for parental involvement in perinatal mortality reviews. Study started, finishing the approvals (ethics etc). 15 months expected duration. Health Foundation likely to support further steps
  - g) Development of Core Outcome Set (COS) for research into care after stillbirth - new springboard grant to pump-prime research to develop a COS in collaboration with CROWN and COMET. Study set-up phase. DS's Academic Clinical Fellow is applying to NIHR for a fellowship/grant to complete the COS. DS to circulate an outline to the CSG members and Sands next month for comment

**Actions:**

1. DESiGN amendment to be circulated to CSG for review and comment (subsequent comments were positive and the amendment was agreed)
2. Parents 1/2 studies to be added to agenda for future meetings
3. DS to circulate CORE project outline to CSG for comment (Dec 16)

**4) Completed projects**

- a) Stillbirth Autopsy Study (NS) (Sands-funded study of 1000 anonymised post mortems and creation of database of objective findings). Series of papers published in *Ultrasound in Obstetrics and Gynecology* in November (see appendix). NS summarised findings at last meeting
- b) Insight (Sands-funded study of current bereavement care). Submitted for publication in *BJOG*
- c) Parents1 (Pilot of parental involvement in perinatal mortality reviews). Paper in preparation for submission to an open access journal

**5) Applications (planned/pending/awarded)**

- a) [HTA call for macrosomia trial](#). Follows Boulvain et al (2015). Applications considered Nov 2016. Full proposals being considered March 2017
- b) HTA call for scoping exercise re difficult delivery of fetal head at Caesarean. Not within remit of this CSG
- c) HTA late pregnancy ultrasound: examining validity in the UK. Call for proposals subsequent to PICO submission from the Stillbirth CSG. GS lead applicant, successful. Now in contract phase. Study will start 1 March 2017 and run for 2 years
- d) TRUFFLE 2 (JT/BT) (Prospective feasibility study examining third trimester monitoring protocols for high-risk pregnancies): exploring funding opportunities
- e) ReMIT2 (AHe). No report

**6) Future PICOs to the HTA**

- a) Induction: 35/39 trial collected 5 years of routine observational data for women 35 years+, had results similar to those reported by Stock et al (2012) (included women with complications, but adjusted for this): no increase in C section. Given that induction is the only disease-modifying intervention to prevent stillbirth, it is timely to consider whether there are ways to support the use of induction without impacting on hospital resources. SS to draft PICO
- b) Whole-genome sequencing of placentas: variations between placentas supporting healthy vs stillborn babies. SCJ to discuss with NS

**Actions:**

1. GS to send SS previous PICO
2. SS to draft PICO looking at non-pharmaceutical outpatient induction vs hormone-mediated induction and circulate to CSG for comment
3. LP to investigate timelines for PICO submission
4. SCJ to discuss placenta PICO with NS

**7) Update on Sands research funding cycle and next steps, incl planned evaluation (LP).**

18 applications at final stage. LP currently sourcing peer reviewers. Perinatal Expert Panel to meet on 18 Jan 2017. Evaluation of first funding cycle planned for March 2017, to include views of PEP members. Sands to research ways of measuring impact. Suggestions on means of assessing shared.

**Action:**

1. JaS to send links on impact research to LP

**8) Current and upcoming consultations**

- a) Exceptional review of NICE fetal monitoring recommendations (paper circulated). Not in remit of Stillbirth CSG

**9) Each Baby Counts and National Maternity and Perinatal Audit update (HK)**

- a) EBC. Team will examine three topics in greater detail in next report: fetal monitoring, human factors, delays in neonatal resuscitation. Topics will be rotated annually. Will present quantitative results on overall incidence, quality of reviews and proportion of cases for which different care might have made a difference to outcome
- b) National Maternity and Perinatal Audit. Three major components: (1) organisational survey to provide an up-to-date overview of maternity care provision, women's access to recommended services and options available to them (to be sent out Jan 2017); (2) continuous prospective clinical audit of 20-30 key interventions and outcomes, which will identify unexpected variation between service providers/regions (published annually from late 2017); (3) a series of in-depth time-limited topic-specific sprint audits. 3 year contract with HQIP, with possible 2-year extension. Resulting database will include linked mother–baby data in England, Scotland and Wales. An English Maternity Services Dataset is being implemented by NHS Digital and 100 of 140 trusts are submitting – this will be used for the audit from year 2 onwards if data quality allows. There is the potential to link maternity records with child's health and educational outcomes, which would be extremely helpful for research.

**10) ISA**

- a) Report from ISA meeting 2016 (AHe). No report
- b) Plans for ISA 2018 in Glasgow (AHe/JSc). Suggestions for scientific programme/bereavement programme should be sent to JSc

**Action:**

1. CSG members' suggestions for ISA 2018 programme to be sent to JSc

**11) AOB**

- a) JSa expressed concerns that messaging to women (e.g. Mama Academy wallets) was being delivered with no evidence for impact (positive or negative). Wales are rolling out safer pregnancy initiative. AFFIRM will also provide data on this
- b) It would be helpful if those unable to attend could add bullet point updates

## 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