

Farr@Aberdeen Research Themes: Reproductive Health; Prediction Modelling (external funding but benefiting from Farr Infrastructure/Network)

Development and validation of prognostic models for subfertility

Dr David McLernon, Prof Amanda Lee, Professor S Bhattacharya

Funder: Chief Scientist Office, Scotland

Contact: d.mclernon@abdn.ac.uk

The aim of this postdoctoral research programme was to develop clinical prediction models to improve the management of couples with a fertility problem.

The first piece of work used national data on all licensed in vitro fertilisation (IVF) clinics in the UK from the Human Fertilisation and Embryology Authority. Two models were developed to estimate the chances of having a baby over multiple complete cycles of IVF based on a couple's specific characteristics and treatment information. One used information available before starting IVF and the other was based on additional information collected during the first IVF attempt.

For example, a 30 year old woman who has never been pregnant before and has been trying to conceive for about two years with no medically diagnosed reason for her infertility has a 46% chance of having a baby over one complete cycle of IVF (includes the transfer of a fresh embryo plus any associated frozen embryos) and a 79% chance over 3 cycles. She decides then undergoes IVF, has 5 eggs collected in her first cycle and only one embryo develops from these 5 eggs. This embryo is then transferred when it is 3 days old. Her chances then change to 29% over one complete cycle and 59% over 3 complete cycles.

Impacts:

The models were converted into an online calculator called OPIS (Outcome Prediction In Subfertility) that will help shape couples' expectations and help them prepare emotionally and financially for their IVF journey (<https://w3.abdn.ac.uk/clsm/opis>). This project was published in the BMJ and Human Reproduction with the former publication generating national and global interest from radio, press and online blogs/news sites. It was also reported on BBC Reporting Scotland and STV News. Our work was also cited in the Scottish Government National Infertility Group Report (<http://www.gov.scot/Resource/0050/00501403.pdf>) where it contributed evidence which led to the recommendation, and subsequent policy change, of increasing the number of NHS funded complete cycles of IVF in Scotland to three.

Subsequent work has led to collaborations with researchers in the Netherlands, USA, Vietnam and Australia and New Zealand to externally validate the OPIS model on their national or clinic level IVF registries with a view to it being updated and utilised in those locations.

The second piece of work used record-linked population based databases (Aberdeen Fertility Clinic Databases, the Aberdeen Maternity and Neonatal Databank and the SMR02 maternity admission database) to predict the chances of live birth at different points in time in couples with unexplained subfertility accounting for different fertility treatments. Dynamic prediction using a landmarking approach was used to predict a pregnancy (leading to a live birth) within six months after registration at the fertility clinic. Prognosis was then updated monthly from three months post-registration up to 24 months. Predictors included female age, duration of infertility, and initiation of fertility treatment (clomifene, intra-uterine insemination (IUI) or IVF), the latter as a time-varying covariate. This work is ongoing and is currently being written up for publication.

Impacts:

Throughout and subsequent to my CSO funded Postdoctoral Fellowship I have been involved as the prediction modelling expert on several other projects both externally and within the University/Farr@Aberdeen. In August 2016 I was invited to deliver a lecture on 'Developing accurate prediction models and capturing the impact of time in subfertility' at the European Society of Human Reproduction and Embryology (ESHRE) Capri Workshop 2016 and have presented at the ESHRE and International Society for Clinical Biostatistics conferences. I am a member of the STRengthening Analytical Thinking for Observational Studies (STRATOS) Initiative Group on 'Evaluating diagnostic tests and prediction models', an ISCB committee which is chaired by world experts in prognostic modelling, and the Farr Frontiers Prediction Modelling group which is being established.

Publications:

McLernon DJ, te Velde E, Steyerberg E, Lee AJ, Bhattacharya S. Predicting the chances of a live birth after one or more complete cycles of in-vitro fertilisation: an population-based study of linked cycle data from 113,873 women. *BMJ* 2016; 355:i5735. <http://dx.doi.org/10.1136/bmj.i5735>

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Black M, Bhattacharya S, Philip S, Norman J, McLernon DJ¹. Planned repeat cesarean section at term and adverse childhood health outcomes: a record-linkage study. *PLoS Med* 2016; 13(3):e1001973.

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