

## **2015 application for project support for research targeting disadvantaged groups**

**Applicant:** Dr Alice Rumbold

### **Project aims**

For the years 1986 to 2002:

1. To examine the proportion of women who received treatment for infertility at an assisted reproductive technology (ART) clinic in South Australian (SA) and/or the Northern Territory (NT), who are identified as Aboriginal and/or Torres Strait Islander (Indigenous);
2. To compare the frequency of infertility resulting from PCOS between Indigenous and non-Indigenous clients;
3. To describe the characteristics of Indigenous women with PCOS seeking ART treatment (e.g. age, BMI) and the main treatments utilised; and
4. To assess any differences in live births and other perinatal outcomes between Indigenous and non-Indigenous women with PCOS receiving ART treatment.

### **Alignment with New Knowledge Program activities**

This study will document, for the first time, use of and response to infertility treatment within an ART clinic among Indigenous women with PCOS. This will contribute new knowledge about the natural history of the disease in this high risk group of women, and identify any potential gaps in infertility service delivery. Thus, it aligns with two of the CRE topic areas: *Defining the natural history of PCOS* and *Improving fertility treatments*.

### **Background**

PCOS is a major risk factor for infertility. Recent analysis of the Australian Longitudinal Study on Women's Health found PCOS was reported by almost 6% of participants, and of these, 72% also reported infertility, compared with just 16% of women who did not report PCOS (Joham et al. 2015).

Indigenous women are at particularly high risk of PCOS. In a study of urban dwelling women in Darwin, PCOS was detected in 15% of Indigenous women and this figure rose to 31% among women who were obese (Boyle et al. 2012). However, very little is known about the impact of PCOS on fertility in this group, or about the occurrence of infertility overall, despite Indigenous women experiencing a high burden of a range of risk factors for infertility (PCOS, obesity and sexually transmitted infections).

In 2000, Kildea and Bowden published an audit of medical records of 342 Indigenous women of reproductive age residing in a remote community in the Northern Territory. Documented infertility was present in 26% of all women's records, and among these, there was evidence of medical assistance for infertility in 43% of records. For the majority of women (65%), the cause of infertility was unknown, "menstrual irregularities" or PCOS was noted in 15% of cases, for the remaining 20%, "tubal damage resulting from infectious causes" was recorded.

It is difficult to draw firm conclusions from this study as it is based on data from one community. Incomplete medical investigation of subfertility was also present in many records, therefore, the impact of PCOS on fertility among these women is likely to have been underestimated. However, the findings demonstrate that Indigenous women are willing to seek medical assistance for subfertility. The extent to which this includes assisted reproductive technologies (ART) is however, unclear.

Indigenous women are likely to face a number of barriers to accessing ART treatments. There may be financial pressures associated with the out of pocket costs of ART treatment or geographical isolation, particularly for remote-dwelling women who may find it hard to be away from their community for the duration of ART treatment. Poor engagement with ART clinics may also occur

because services are considered to be culturally inappropriate. However, to our knowledge, there has been no study documenting Indigenous women's access to infertility treatment provided by an ART clinic, nor the main medical reasons why Indigenous women may seek ART treatment (e.g. PCOS or other causes of infertility).

### **Rationale**

Assessing Indigenous women's access to infertility treatment and their main reasons for treatment will provide important information about the consequences of PCOS for fertility in this high risk group. This study will also examine responses to ART treatment among Indigenous women with PCOS. This is important as there is emerging evidence from the United Kingdom that the effectiveness of ART interventions varies across ethnic groups (Jayaprakasan et al 2014).

There are few existing datasets that have the ability to assess infertility treatment among Indigenous women. For example, Indigenous status of clients is not currently collected in the Australia and New Zealand Assisted Reproduction Database (ANZARD), the national dataset for surveillance of ART treatments and outcomes. Prof Michael Davies has assembled a whole of population cohort, the SA Birth Cohort, in which medical records from ART clinics in SA have been linked to perinatal data for the years 1986-2002. As the major provider of ART services in SA during this time (Repromed) also provided services to women living in the NT, Prof Davies also has access to all data for NT-based clients for the same time period. Maternal ethnicity has been assessed in previous studies using this dataset (e.g. Davies et al. 2012), and these analyses confirm that Indigenous status is available both in the ART data as well as the perinatal records. However, to date, no analyses of treatments and outcomes specifically among Indigenous women have been undertaken.

### **Methods**

**Design:** Cross-sectional study of Indigenous women in the SA Birth Cohort, as well as Indigenous female clients of the Darwin Repromed ART clinic.

**Methods & Analysis:** Data are available about all ART treatment cycles in SA and the NT for the period January 1986 - December 2002. All SA cycles have already been linked to the contemporary statewide perinatal outcomes database as part of the establishment of SA Birth Cohort (more than 99% of births resulting from ART were linked to the corresponding birth record, indicating minimal loss to follow up). The data for NT treatment cycles has not been analysed previously, and therefore, based on our previous experiences, will require some cleaning to identify duplicated records, data entry errors and other discrepancies. Analyses will first describe and compare Indigenous and non-Indigenous women overall (e.g. total number of clients, primary reason for infertility) (Aims 1 & 2). Analyses will then be restricted to women with identified PCOS, and compare the demographic characteristics (e.g. maternal age, BMI etc.) as well the frequency of each ART treatment (e.g. ovulation induction (OI) only, OI with in vitro fertilisation (IVF) etc.), between Indigenous and non-Indigenous women (Aim 3). Parametric and non-parametric analyses will be used as appropriate. To address Aim 4, logistic regression will be used to determine if Indigenous status is an independent predictor of live birth and other perinatal outcomes among women with PCOS, after adjustment for confounding variables (age, BMI, smoking, SES). In these analyses, data will be restricted to SA residents only, as perinatal data for NT clients is not available.

### **Significance**

Indigenous women are at much higher risk of subfertility than other Australian women, due to a high prevalence of PCOS, as well as other risk factors such as obesity and sexually transmitted infections. However, very little is known about the extent and causes of infertility in this group or whether Indigenous women with subfertility seek treatment in ART clinics. This work will generate evidence of the impact of PCOS on fertility among Indigenous women and is likely to highlight gaps in access

to ART treatment. The study will also determine, for the first time, whether Indigenous women with PCOS who seek ART treatment have similar pregnancy and birth outcomes to their non-Indigenous counterparts. This information is likely to contribute to our understanding of PCOS aetiology and may also lead to modifications of treatment strategies specifically for Indigenous women.

### **Expected outcomes**

A peer reviewed publication describing the frequency of Indigenous women seeking infertility treatment for PCOS as well as their response to treatment will be submitted at the completion of this project. The work may also lead to applications to the relevant stakeholders (ART clinics, SA Health, NT Health) for access to more recent data, to assess trends in access as well as outcomes.

### **Selection criteria**

**Competitiveness:** Dr Rumbold holds a NHMRC Career Development Fellowship and has a strong publication and grant record relative to opportunity; see attached brief CV summary.

**Rationale/appropriateness of the design:** This study will utilise a population cohort comprising 17 years of ART and perinatal data with good identification of Indigenous status.

**Feasibility:** The dataset (the SA Birth Cohort) has already been assembled and linked by Prof Davies (the applicant's supervisor), data for NT clients is already available and requires minimal cleaning.

**Research & translation plan:** cleaning of NT data, statistical analyses, manuscript preparation, presentation of work at select conferences (e.g. FSA, PSANZ), and preparation of research summary for dissemination to clinics, PCOS alliance and FSA.

### **Additional selection criteria for disadvantaged groups applications**

**Commitment and experience relevant to Indigenous health:** Since 2005, Dr Rumbold has led a range of collaborative projects with Aboriginal communities in the NT and SA, spanning sexual, reproductive and perinatal health (see publications listed in the brief CV summary).

**Merit/relevance to Indigenous health:** This project will contribute significantly to improving our understanding of the impact of PCOS on fertility among Indigenous women. This will be achieved by undertaking secondary analyses of an already assembled dataset. Therefore, the planned work will not contribute to any research burden on communities.

### **Summary budget**

Funding is requested for biostatistical salary support to undertake the planned analyses (including cleaning of NT data). The salary and increments as per the University of Adelaide schedule (Sept 2015), are as follows: Data manager/biostatistician at HEO7, Step 5 (\$87,880 p.a., \$114,244 total salary with on-costs). Funding is requested for 2 months' salary based on 0.2 FTE, therefore, the total costs for proposed analysis are: \$3,808.

### **References**

Boyle JA, *et al.* Prevalence of polycystic ovary syndrome in a sample of Indigenous women in Darwin, Australia. *Med J Aust* 2012;196:62–6.

Davies MJ, *et al.* Reproductive technologies and the risk of birth defects. *NEJM*. 2012;366:1803-13.

Jayaprakasan K, *et al.* Effect of ethnicity on live birth rates after in vitro fertilisation or intracytoplasmic sperm injection treatment. *BJOG*. 2014;121(3):300-6.

Joham AE, *et al.* Prevalence of infertility and use of fertility treatment in women with polycystic ovary syndrome: data from a large community-based cohort study. *J Womens Health*. 2015;24(4):299-307.

Kildea S, Bowden FJ. Reproductive health, infertility and sexually transmitted infections in indigenous women in a remote community in the Northern Territory. *Aust N Z J Public Health*. 2000;24(4):382-6.