

CO-MORBIDITY DIAGNOSIS AND THE UTILIZATION OF ASSISTED REPRODUCTIVE TECHNOLOGY SERVICES IN NORTH CENTRAL ZONE OF NIGERIA

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Abstract

The purpose of this study was to assess co-morbidity diagnosis and the utilization of assisted reproductive technology services among infertile couples in North Central Zone of Nigeria. To achieve this purpose, one (1) research question and one (1) hypothesis was developed. The ex-post facto research design was used for the study. The population of the study was two million, nine hundred and fifteen thousand, seven hundred and twenty nine (2,915,729) infertile couples in North Central Zone of Nigeria. To obtain adequate data for representation, a sample size of seven hundred and sixty eight (768) respondents comprising of males and females was drawn from the target population representing 4% of the target population. Stratified sampling technique, simple random sampling technique, purposive sampling technique and proportionate sampling technique were adopted to have proper representation of respondents for the study. A validated questionnaire of 4 point modified Likert scale of Strongly Agreed (SA), Agreed (A), Disagreed (D) and Strongly Disagreed (SD) was used as instrument to elicit information from the selected respondents. The questionnaire consisted of Section A and B. Spearman Brown Rank Order (SBRO) and Gutman Split Half method were used to determine the reliability of the instrument. 0.801 and 0.789 reliability coefficient was obtained respectively. A total of seven hundred and sixty eight copies of the questionnaire were randomly distributed among infertile couples in North Central Zone of Nigeria for data collection out of which seven hundred and fifty one (751;97.4%) were duly completed and used for analysis. Descriptive statistics of frequencies and simple percentages were used to describe the demographic characteristics of the respondents. Descriptive statistics of mean and standard deviation were used to answer the research question, and an inferential statistics of one sample t-test was used to test the hypothesis at 0.05 alpha level of significance. The results revealed that co-morbidity diagnosis significantly determine the utilization of Assisted Reproductive Technology services among infertile couples in North Central Zone of Nigeria ($t=52.212$; $p=0.000$). Based on the finding of the study, it was concluded that co-morbidity diagnosis is determinant for the utilization of Assisted Reproductive Technology services among infertile couples in North Central Zone of Nigeria. Based on the conclusion drawn, it was recommended that reproductive health technology experts should initiate collaborative efforts that bring the innovation and development of new treatment procedures to public knowledge, in order to disabuse the minds of people of the assumed notion that infertile couples with malformation infections and other reproductive health concerns such as tubal factor infertility cannot conceive and

give birth in their lives. This will go a long way to reduce the burden of infertility treatment on couples seeking ART treatment.

Keywords: Co-morbidity, Diagnosis, Infertile Couples, Utilization, Assisted Reproductive Technology.

Introduction

The causes of infertility in general, and female and male infertility in particular, are mainly preventable through utilization of assisted reproductive technology services. Of adult couples in African countries it is estimated that 10%–25% are sub-fertile and of these sub-fertile couples female factors account for about 55%, male factors for 30%–40% of causes, while 5%–15% of causes are unexplained (Giwa-Osagie, 2015; Cha, Koo & Ko 2017). The most common cause of infertility in Africa is infection of which the two sexually transmitted infections (STIs), gonorrhoea and chlamydia are the main culprits in both males and females. According to Osian, Afemiki, Olorunfemi and Eweka (2019), infertile couples delay in utilization of assisted reproductive technology (ART) services such as diagnosis of sexually transmitted infections (STIs), lack of diagnosis, incomplete therapy, no therapy, or inappropriate therapy will further compound the problems of STIs among infertile couples in Africa. After STIs, infections during or after abortion and during and after child birth represent the next major cause of female infertility in Africa thus requiring medical investigation to conceive again. In comparison, the developed countries of Europe and North America have more endocrine causes of infertility and have better facilities for the diagnosis and appropriate therapy of STIs and can therefore be expected to have better prognosis in infertility management and treatment through the use of ART services (Giwa-Osagie, 2015; Osian, Afemiki, Olorunfemi & Eweka 2019).

Traditionally, it has been claimed that for every fourth couple the reason for childlessness is the female factor, every third the male factor, every second the reason is in both members and for the rest the reason remains unexplained and would further require medical utilization to resolve the issue (Jegade, 2018). Up to 30–75% of women with Polycystic Ovary Syndrome (PCOS) are obese (Ehrmann 2015), which in turn also reduces fecundity and may result to ART uptake by the couples. Moreover, morbidly obese women (BMI 40 kg/m²) with PCOS had significantly lower pregnancy rates than PCOS women whose body mass index (BMI) was less than 40 who sought for ART services (Jungheim, Lanzendorf, Odem, Moley, Chang & Ratts 2019).

WHO (2016) described obesity as one of the most serious public-health threats and it is considered as the main preventable cause of illness and premature death. According to the data, a total of 20.6% of women aged 25-64 years were obese and the proportions of viscerally obese (waist circumference over 88 cm) women was even higher, (40%). Generally, body mass index (BMI) is categorized into four subgroups: underweight (BMI less than 18.5 kg/m²), normal weight (BMI 18.5–24.9 kg/m²), overweight (BMI 25.0–29.9 kg/m²) and obesity (BMI of 30 kg/m² or more). Overweight and underweight women are therefore at a risk of decreased fertility leading to the use of ART services to aid conception. Usually, the mechanism accounting for sub-fertility among over- and underweight women is ovulatory dysfunction (Rich-Edwards, Spiegelman, Garland,

Hertzmark, Hunter, Colditz, Willett, Wand, & Manson, 2018). The prevalence of anovulation increases with increasing BMI in overweight women, and with decreasing BMI in underweight women (Haslam & James 2015). However, the effect of obesity on fecundity seems to persist even in women with regular cycles (Gesink-Law, Maclehose, & Longnecker, 2017). The increment of one BMI unit above 29kg/m^2 in obese ovulatory women seems to be equivalent to a one year increment in a woman's age on fecundity (vanderStee, Steures, Eijkemans, Habbema, Hompes, Burggraaff, Oosterhuis, Bossuyt, van der Veen, & Mol, 2018). Several studies (Crosignani, Colombo, Vegetti, Somigliana, Gessati & Ragni, 2018; Tang, Glanville, Hayden, White, Barth, & Balen, 2016) have indicated that weight loss can improve fertility among obese, anovulatory patients. If changes in lifestyle do not sufficiently reduce BMI, then bariatric surgery can be performed in morbidly obese women ($\text{BMI} > 40\text{ kg/m}^2$) or in women with infertility with $\text{BMI} > 35\text{ kg/m}^2$ and whose infertility is due to obesity, for example PCOS. Weight reduction after bariatric surgery seems to improve fecundity (Tan & Carr 2018).

Obesity can therefore inform couples' decision to utilize ART services. There are several studies (Farhiet al., 2018, Luke, Brown, Stern, Missmer, Fujimoto, Leach & SART, 2018; Pinborg, Gaarslev, Hougaard, Nyboe-Andersen, Andersen, Boivin & Schmidt, 2017) indicating that obesity is associated with prolonged ovarian stimulation, decreased sensitivity to gonadotrophins, increased cancellation rates and lower number of retrieved oocytes. The findings are parallel with those of underweight women (Pinborget al., 2017). The higher requirements of gonadotrophins maybe related to aberrations in levels of estrogen and SHBG and also to the greater amount of body surface, which leads to different absorption and distribution of the gonadotrophins and altered peripheral steroid metabolism (Tamer, Erel & Senturk, 2019).

A meta-analysis of 22 studies demonstrated a significant risk of miscarriage after ART utilization among women with $\text{BMI} 25\text{ kg/m}^2$ compared to women whose BMI was less than 25 kg/m^2 (RR 1.31, 95% CI 1.18–1.45) (Rittenberg, Seshadri, Sunkara, Sobaleva, Oteng-Ntim & El-Toukhy, 2018). Not only overweight women, but also underweight women have an increased risk of suffering miscarriage (Vercellini, Fedele, Aimi, De Giorgi, Consonni & Crosignani, 2016). In addition, overweight women seem to have a significantly lower live birth rate in BMI group 25 kg/m^2 versus $\text{BMI} < 25\text{ kg/m}^2$ according to the pooled data from nine studies (RR 0.84, 95% CI 0.77–0.92) (Rittenberg, Seshadri, Sunkara, Sobaleva, Oteng-Ntim & El-Toushy, 2018). The effect of BMI is even more significant among obese women than in overweight women; the reductions in the live birth rate being 9% in overweight women but 20% in obese women compared with normal weight women (Rittenberg et al., 2018). In young women undergoing ART, the effect of an increased BMI is more prominent on fertility than in women aged 36 or more, in these older women BMI has only a minimal impact on fertility (Sneed, Uhler, Grotjan, Rapisarda, Lederer & Beltsos, 2018).

According to Balen and Anderson, and Policy and Practice Committee of the BFS (2017) the British Fertility Society recommended avoidance of any fertility treatment until a woman's BMI is $< 35\text{ kg/m}^2$ in order to achieve a more favourable outcome in fertility

treatment and a safer course of pregnancy, not to mention the health of the newborn. It has been calculated that a weight loss of one BMI unit could improve the odds of pregnancy by a factor of 1.19 (Ferlitsch, Sator, Gruber, Rucklinger, Gruber & Huber, 2019). In addition, before any fertility treatments, BMI should be $>18 \text{ kg/m}^2$ and the woman cannot have an eating disorder.

These challenges associated with infertility have necessitated different healthcare seeking behaviours, ranging from spiritual, traditional/alternative health care to orthodox medical types, including bio-technological devices such as ART services. This study therefore, purposed to assess co-morbidity diagnosis and the utilization of assisted reproductive technology services among infertile couples in North Central Zone of Nigeria.

Research Question

1. Will co-morbidity diagnosis determine the utilization of Assisted Reproductive Technology services among infertile couples in North Central Zone of Nigeria?

Research Hypothesis

1. Co-morbidity diagnosis among infertile couples in North Central Zone of Nigeria is not significant determinant for the utilization of Assisted Reproductive Technology services.

Methodology

The research design adopted for this study was ex-post facto research design. Ex post facto research design is ideal for conducting social research when it is not possible or acceptable to manipulate the characteristics of human participants (Simon & Goes, 2013). The population of the study comprised of all infertile couples who are affected by either primary or secondary infertility in North Central Zone of Nigeria. The population consisted of 2,915,729 with a sample size of 768 infertile couples representing 4% of the target population per hospital attendance as suggested by Research Advisor (2006) that in a population of 2,915,729, a sample size of 384 can be used at 0.05 levels, 5% margin error and 99% confidence interval. However, the researchers doubled the figure to have a wider coverage of respondents for the purpose of generalization of findings to the target population (The higher the number, the better generalization of results).

To arrive at the sample size of 768, a multi-stage sampling procedure that involves stratified sampling technique, purposive sampling technique, simple random sampling technique, proportionate and systematic sampling techniques were used for the study as follows: Stratified sampling technique was used to divide the zone (6 States and the FCT) into three strata 1. (Niger, Kwara), 2. (Benue, Kogi), 3. (Plateau, Nasarawa) and the FCT based on the geopolitical distribution that is North Central North (NCN), North Central East (NCE), and North Central West (NCW), that is, (NCN = Niger, Kwara; NCE = Benue, Kogi, NCW = Plateau, Nasarawa) respectively. Purposive sampling technique was used to select the FCT Abuja, since it was the Federal Capital Territory of Nigeria and that because it has the highest number of assisted reproductive technology hospitals

situated therein. The third stage involved the use of simple random sampling technique to select 3 States, thus, Kwara, Plateau, and Benue using fish bowl method. Consequently, a total of 3 states and the FCT were selected, making a total of 4 states being selected for the study. Purposive sampling technique was used to select all the 3 ART hospitals in Plateau State; 2 in Benue State; and 3 in Kwara State, since the hospitals situated in the selected states were not many. And a simple random sampling technique was used to select 9 ART hospitals out of 17 ART hospitals situated in FCT Abuja. Consequently, a total number of 17 ART hospitals were selected and used for the study. Proportionate sampling technique was then employed to calculate the number of respondents per hospital attendance by using 4% of the population to form the sample size. Proportionate sampling was calculated by multiplying the target population per hospital attendance by 4% to get the sample size per hospital. The choice of proportionate sampling procedure was to enable randomization of the respondents to have equal opportunity to all infertile couples sample based on the availability. The instrument used for data collection was questionnaire which was divided into two (2) Sections (Sections A& B) and comprised of 14 items. Section A contained four (4) items designed to obtain information on demographic characteristics of the respondents while Section B contained ten (10) items that seek to elicit information on psycho-social factors and the utilization of assisted reproductive technology services among infertile couples, designed on a 4-point modified Likert scale of Strong Agreed (SA), Agreed (A), Disagreed (D) and Strongly Disagreed (SD). Data was collected using close ended questionnaire that was transformed into a digital questionnaire form and 768 copies of the questionnaire were administered on line. The submitted questionnaire form were exported, coded and analysed using statistical package for social science SPSS version 27 and the following statistical tools were used: Descriptive statistics of mean and standard deviation was used to answer the research question on assessment of co-morbidity diagnosis as determinants for the utilization of assisted reproductive technology services among infertile couples in North Central Zone of Nigeria, thus, any response that has a mean aggregate of 2.50 and above was accepted as positive and any response that has a mean score of less than 2.50 was considered negative or not accepted. Inferential statistics of One Sample t-test was used to test the formulated null hypothesis at 0.05 alpha level of significance.

Results

Assessment of co-morbidity diagnosis factors as determinants for the utilization of assisted reproductive technology services among infertile couples.

Responses of respondents on co-morbidity diagnosis like smoking, alcohol consumption among others as determinant for the utilization of assisted reproductive technology services among the infertile couples were scored in means and standard deviations in Table 4.7.

Table 2: Mean response of respondents onco-morbidity diagnosis factors as determinants for the utilization of assisted reproductive technology services among infertile couples

Sn	Co-morbidity diagnosis factors	Mean	Std. Dev.
1	Smoking has led me to use ART in order to reproduce	3.10	0.663
2	I am using ART services because duration of smoking has hindered my natural conception for some years	3.24	0.729
3	I am using ART because drinking alcohol has hampered my natural conception	3.12	0.512
4	I am using ART services because duration of drinking has hindered my natural conception for some years	3.22	0.607
5	I am using ART services because alcohol only influence my sexual desire and satisfaction but cannot conceive	3.12	0.428
6	I am using ART services because my habitual smoking is after sex for relaxation which causes lack of natural conception	3.24	0.676
7	Sexually transmitted infections such as chlamydia and gonorrhea significantly increase the use of ART services in order to make children	3.02	0.421
8	Because a woman has had prior dilation and curettage (D&C) she cannot get pregnant through the natural way (sexual intercourse)	3.16	0.670
9	Because women had prior abdominopelvic surgeries, making children through the natural way (sexual intercourse) is difficult	3.06	0.501
10	Infertile couples with sexually transmitted infections have higher miscarriages in their attempt to make children the natural way (sexual intercourse)	3.27	0.631
Aggregate mean		3.15	0.343

(Benchmark = 2.50)

The aggregate mean for the Table was 3.15 which was far higher than the benchmark of 2.50. The implication for this is that most respondents agreed that co-morbidity diagnosis factors could be major determinants for the utilization of assisted reproductive technology services among infertile couples in the study area. As indicated in the table above, these included smoking and the duration involved, drinking and the duration involved and the influences induced by such practices. Others included pelvic inflammation, fibroid, Negative embryo implantation and impaired oocyte maturation. From the aggregate mean score of 3.15, it could be concluded that respondents generally agreed that co-morbidity diagnosis factors could be major determinants for the utilization of assisted reproductive technology services among infertile couples in North Central Zone of Nigeria.

This hypothesis was tested by comparing the scores of respondents on co-morbidity in Table 1 with the benchmark (2.50). The result of the one sample t-test used for the hypothesis is summarized in Table 2.

Table 2: One sample t-test on co-morbidity diagnosis as determinants for the utilization of assisted reproductive technology services among infertile couples.

Variables	N	Mean	Std. Dev.	Std. Error	t-value	df	p-value
Co-morbidity factor	751	3.15	0.343	0.013	52.212	750	0.000
Test mean	751	2.50	0.000	0.000			

(t-critical = 1.96, p < 0.05)

The result in Table 2 revealed that respondents responded that co-morbidity diagnosis is major and significant determinant for the utilization of assisted reproductive technology services among infertile couples in North Central Zone of Nigeria. This is because the observed t-value (52.212) for the test is higher than the critical value of 1.96 indicated at the bottom of the table. The p-value obtained at 750, degree of freedom (df) was 0.000 ($p < 0.05$). These observations provided enough evidence for rejecting the null hypothesis. Therefore the null hypothesis which states that, co-morbidity diagnosis (smoking, alcohol consumption, tubal factor infertility, endometriosis, ovulatory dysfunction and polycystic ovary syndrome) among infertile couples in North Central Zone of Nigeria are not significant determinants for the utilization of assisted reproductive technology services is hereby rejected and conclude that co-morbidity diagnosis could be a major determinant for the utilization of assisted reproductive technology services among infertile couples in North Central Zone of Nigeria.

Discussions

Co-morbidity diagnosis was found to be significant ($p=0.000$) determinants for the utilization of assisted reproductive technology services among infertile couples in this study. The study found that most respondents agreed (3.10) that co-morbidity diagnosis factors could be major determinants for the utilization of assisted reproductive technology services among infertile couples in the study area. Such factors were found ($x=3.20$) to include smoking and the duration involved, drinking and the duration involved ($x=3.12$), the influences induced by such practices. Others included pelvic inflammation ($x=3.22$), fibroid ($x=3.12$), negative embryo implantation ($x=3.24$) and impaired oocyte maturation ($x=3.16$). This finding is in line with studies by Chambers, Sullivan, Ishihara, Chapman & Adamson, (2016) that the most common cause of infertility in Africa is infection of which the two sexually transmitted infections (STIs), gonorrhoea and chlamydia are the main culprits in both males and females. Delayed diagnosis of STIs, lack of diagnosis, incomplete therapy, no therapy, or inappropriate therapy compound the problems of STIs in Africa After STIs, infections during or after abortion and during and after child birth represent the next major cause of female infertility in Africa. The latter explains the preponderance of secondary infertility over primary infertility in Africa (Giwa-Osagie, 2015). In comparison, the developed countries of Europe and North America have more endocrine causes of infertility and have better facilities for the diagnosis and appropriate therapy of STIs and can therefore be expected to have better prognosis in infertility management. In Africa, there are more tubal factors, more irreversible oligo- or azoospermia and less resources for the

management of infertility due to economic, political, capacity-building factors and the severity of disease (Chambers, Sullivan, Ishihara, Chapman & Adamson, 2016).

Conclusion

Based on the results of this study and its limitations, it was concluded that:

Co-morbidity diagnosis determines the utilization of assisted reproductive technology services among infertile couples in North Central Zone of Nigeria.

Recommendations

On the basis of the conclusion drawn, recommendation was made to improve on the utilization of assisted reproductive technology services:

1. Since ART services has increased both in variety and quantity to include treatment of tubal factor infertility, endometriosis, ovulatory dysfunction and polycystic syndrome, in order for infertile couples to conceive and make life birth, there is need to train more specialists on the use of ART services and intensify capacity building of other adjunct service providers. As this makes ART utilization very difficult for many prospective clients to have timely access to treatment. Those that can endure the waiting period are made to pay exorbitantly because of oligopolistic tendency of few specialists who are presently in the practice. Therefore, it is important to increase the training capacity of tertiary health care institutions to train more medical practitioners, especially gynecologists in general and ART specialists specifically.

References

- Balen, A.H., Anderson, R.A., & Policy and Practice Committee of the BFS, (2017). Impact of obesity on female reproductive health: British Fertility Society, Policy and Practice Guidelines. *Human Fertility (Camb)*, 10:195-206.
- Cha, K., Koo, J., & Ko, J. (2017). Pregnancy after in vitro fertilization of human follicular oocytes collected from nonstimulated cycles, their culture in vitro and their transfer in a donor oocyte program. *Fertility Sterility*, 55:109-113.
- Chambers, G.M., Sullivan, E.A., Ishihara, O., Chapman, M.G., & Adamson, G.D. (2016). The economic impact of assisted reproductive technology: a review of selected developed countries. *Fertility Sterility*, 91:2281-2294.
- Crosignani, P.G., Colombo, M., Vegetti, W., Somigliana, E., Gessati, A., & Ragni, G. (2018). Overweight and obese anovulatory patients with polycystic ovaries: parallel improvements in anthropometric indices, ovarian physiology and fertility rate induced by diet. *Human Reproduction*, 18:1928-1932.
- Ehrmann, O., (2015). First intention IVF protocol for polycystic ovaries: does oral contraceptive pill pretreatment influence COH outcome? *Reproduction BiolEndocrinol*, 11:54-59.
- Farhi, A., Reichman, B., Boyko, V., Hourvitz, A., Ron-El, R., & Lerner-Geva, L. (2018). Maternal and neonatal health outcomes following assisted reproduction. *Reproductive Biomed* 26(5):454-61.
- Ferlitsch, K., Sator, M.O., Gruber, D.M., Rucklinger, E., Gruber, C.J., & Huber, J.C. (2019). Body mass index, follicle-stimulating hormone and their predictive value in in vitro fertilization. *Journal of Assisted Reproduction Genetics*, 21:431-436.

- Gesink Law, D.C., Maclehose, R.F., & Longnecker, M.P. (2017). Obesity and time to pregnancy. *Human Reproduction*, 22:414-420.
- Giwa-Osagie, O.F. (2015). ART in developing countries with a particular reference to sub Saharan Africa, In: *Current Practices and Controversies in Assisted Reproduction: Report of a WHO Meeting*, Vayena, E., Rowe P. J. and Griffin P.D. (Eds.). World Health.
- Haslam, D. W., & James, W.P., (2015). Obesity. *Lancet*; 366:1197-1209.
- Jegede, A.S., & Fayemiwo, P. (2018). Cultural and Ethical Challenges of Assisted Reproductive Technologies in the Management of Infertility among the Yoruba of South Western Nigeria. *African Journal of Reproductive Health*; 14(2): 115-127.
- Jungheim, E.S., Lanzendorf, S.E., Odem, R.R., Moley, K.H., Chang, A.S., & Ratts, V.S. (2019). Morbid obesity is associated with lower clinical pregnancy rates after in vitro fertilization in women with polycystic ovary syndrome. *Fertility Sterility*; 92:256-261.
- Luke, B., Brown, M.B., Stern, J.E., Missmer, S.A., Fujimoto, V.Y., Leach, R., & SART (2018). Writing group female obesity adversely affects assisted reproductive technology (ART) pregnancy and live birth rates. *Human Reproduction*; 26:2452-252.
- Osian, E.A., Afemikhe, J.A., Olorunfemi, O., & Eweka, A. (2019). Knowledge and perception of assisted reproductive technology among women attending the University of Benin Teaching Hospital, Benin City, Nigeria. *Journal of Nursing Midwifery Sci*; 6:125-130.
- Pinborg, A., Gaarslev, C., Hougaard, C.O., Nyboe Andersen, A., Andersen, P.K., Boivin, J., & Schmidt, L. (2017). Influence of female bodyweight on IVF outcome: a longitudinal multicentre cohort study of 487 infertile couples. *Reprod Biomed*; 23:490-499.
- Research Advisor, (2006). <http://research-advisors.com/tools/SampleSize.htm>
- Rich-Edwards, J.W., Spiegelman, D., Garland, M., Hertzmark, E., Hunter, D.J., Colditz, G.A., Willett, W.C., Wand, H., & Manson, J.E. (2018). Physical activity, body mass index, and ovulatory disorder infertility. *Epidemiology*; 13:184-190.
- Rittenberg, V., Seshadri, S., Sunkara, S.K., Sobaleva, S., Oteng-Ntim, E., & El-Toukhy, T. (2018). Effect of body mass index on IVF treatment outcome: an updated systematic review and metaanalysis. *Reprod Biomed*; 23:421-439.
- Simon, M.K., & Goes, J. (2013). Dissertation and scholarly research: recipe for success. Seattle, W.A: Dissertation Success LLC.
- Sneed, M.L., Uhler, M.L., Grotjan, H.E., Rapisarda, J.J., Lederer, K.J., & Beltsos, A.N. (2018). Body mass index: impact on IVF success appears age-related. *Hum Reprod*; 23:1835-1839.
- Tamer, R.C., Erel, C., & Senturk, L.M. (2019). The impact of body mass index on assisted reproduction. *Curr Opin Obstet Gynecol*; 21:228-235.
- Tan, O., & Carr, B.R. (2018). The impact of bariatric surgery on obesity-related infertility and in vitro fertilization outcomes. *Semin Reprod Med*; 30:517-528.
- Tang, T., Glanville, J., Hayden, C.J., White, D., Barth, J.H., & Balen, A.H. (2016). Combined lifestyle modification and metformin in obese patients with polycystic ovary syndrome. A randomized, placebo-controlled, double-blind multicentre study. *Human Reproduction*; 21:80-89.
- van der Steeg, J.W., Steures, P., Eijkemans, M.J., Habbema, J.D., Hompes, P.G., Burggraaff, J.M., Oosterhuis, G.J., Bossuyt, P.M., van der Veen, F., & Mol, B.W. (2018). Obesity affects spontaneous pregnancy chances in subfertile, ovulatory women. *Hum Reprod*; 23:324-328.

- Vercellini, P., Fedele, L., Aimi, G., De Giorgi, O., Consonni, D., & Crosignani, P.G. (2016). Reproductive performance, pain recurrence and disease relapse after conservative surgical treatment for endometriosis: the predictive value of the current classification system. *Hum Reprod*; 21:2679-2685.
- World Health Organisation (2016). *Interpreting Reproductive Health – ICDP +5 Forum* The Hague, Netherlands, 8-12 February.