

Pregnancy Prognosis in Infertile Couples on the DuoFertility Programme Compared with *In Vitro* Fertilisation/Intracytoplasmic Sperm Injection

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Abstract

This article describes an assessment of the pregnancy rate resulting from the combined use of a medical device and a consultancy service to assist infertile couples in achieving natural pregnancy. A retrospective cohort study was performed on the first 500 couples using the DuoFertility (Cambridge Temperature Concepts Ltd, Cambridge, UK) expectant management programme in comparison with UK statistics on assisted reproductive technology. Of the 242 couples who qualified for or had previously undergone *in vitro* fertilisation or intracytoplasmic sperm injection, but had not been diagnosed as absolutely sterile (as opposed to infertile), the DuoFertility programme resulted in an average clinical pregnancy rate of 39 % after 12 months of use. This is significantly higher than both UK (25.6 %) and European (27.9 %) average *in vitro* fertilisation clinical pregnancy rates as well as the European intrauterine insemination clinical pregnancy rate (8.2 %) at the 95 % confidence level. We conclude that DuoFertility, as a method of aiding pregnancy in infertile couples, deserves further evaluation.

Keywords

DuoFertility, infertility, fertility, *in vitro* fertilisation, intracytoplasmic sperm injection, intrauterine insemination, pregnancy, retrospective field trial

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In the UK, one in seven couples experience difficulty conceiving.¹ The British Fertility Society defines infertility as the inability to conceive despite regular unprotected sexual intercourse over a period of at least two years. Assisted reproductive technology (ART) has made it possible for many infertile couples to conceive. The ART treatment proposed to the patient can vary from intrauterine insemination (IUI), stimulated or not, *in vitro* fertilisation (IVF) or intracytoplasmic sperm injection (ICSI). In Europe, the number of IVF and ICSI procedures has trebled over the last decade.² However, several studies have shown that considerable spontaneous pregnancy potential may be present in the population starting ART.^{3–6} To maximise the chances of pregnancy, couples can be advised to time intercourse with the fertile window.^{7,8} This has been identified as a potential source of stress.⁹ Assessment of the knowledge of fertility awareness and how the information can be used to enhance the chance of conception has shown that only 26 % of women attending a fertility clinic for treatment have an adequate understanding of their fertility.¹⁰ The use of fertility monitors may be a suitable approach to allow women to identify these fertile days accurately.^{4,11} This retrospective study was conducted using the DuoFertility system (Cambridge Temperature Concepts Limited, Cambridge, UK), which consists of a stick-on patch that captures up to 20,000 temperature measurements every day and a monitoring device that automatically analyses the data to indicate to the woman the days with the maximum chances of conception. The woman can record additional parameters, such as luteinising hormone test results, cervical mucus observations,

cervical position, menstruation, spotting, intercourse and even free-form text notes, which are taken into account in the analysis if relevant. All data are transferred via the internet from the woman's home to a central Fertility Centre where fertility consultants can review the data and advise the woman if required.

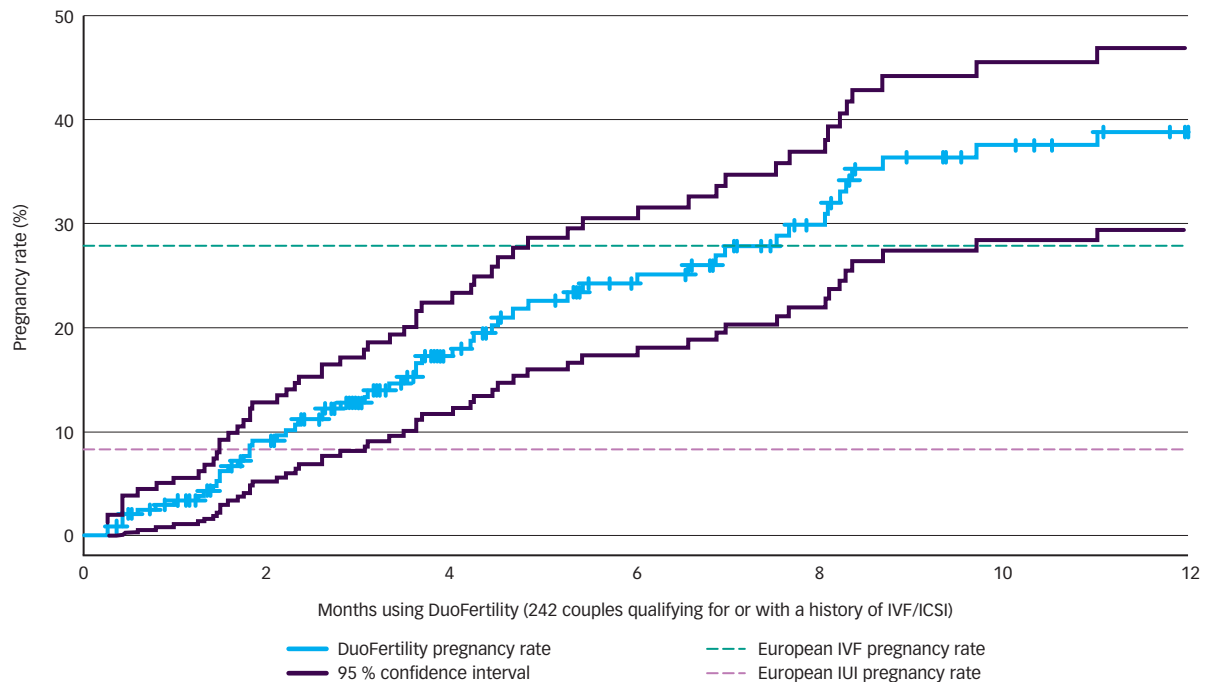
Materials and Methods

Study Design and Procedures

We performed a retrospective cohort study of the first 500 couples who began using the DuoFertility monitor in 2009–2010 (DuoFertility only became available to the public in mid-2009). Each couple's medical history was collected during the first month after purchase. Four hundred and ninety-seven couples provided sufficient information (each partner's age, duration of infertility, diagnosis, tubal patency, semen parameters, primary or secondary infertility, previous fertility treatment or previous referral for fertility treatment) to estimate their eligibility for IVF and pregnancy rate through a cycle of IVF/ICSI. All data from the DuoFertility monitor are transferred from the patient's home to the Fertility Centre via the internet, allowing identification of the number of cycles and time during which the DuoFertility monitor was used.

Patient Inclusion Criteria

The field of expectant management of infertility suffers from the potential criticism, owing to the non-invasive nature of the intervention, that any woman who achieves pregnancy could have

Figure 1: Pregnancy Rate with DuoFertility

IVF = in vitro fertilisation; IUI = intrauterine insemination.

done so by chance – which is necessarily true for any one individual woman. It is well reported that the vast majority of couples conceive within one year of trying; however, this success rate drops for subsequent years of failure to conceive.¹² Therefore, it is critical to focus analysis on statistically significant groups of women who would be expected to have a reduced probability of treatment-free pregnancy. The inclusion criteria used in this study are:

- patients must have provided medical information allowing for the estimation of success rate with IVF;
- women must be eligible for IVF/ICSI treatment or have been through one of these treatments in the past with their current partner;
- at least one fallopian tube must be patent (unobstructed);
- the female partner must menstruate at least six times a year; and
- the male partner must have a sperm count over five million.

Statistical Analysis

A retrospective cohort study was performed using the first 500 couples on the DuoFertility programme in comparison with European and UK statistics on ART.^{13,14} The primary outcome measure was pregnancy, defined as patient-reported delayed period, continued elevated temperature and a positive chemical pregnancy test either in blood or urine. Note that several couples stopped using DuoFertility, and did not respond to questions regarding potential pregnancy so were assumed non-pregnant, indicating a possible under-reporting of pregnancy rates. Couples who responded to fertility questionnaires (497 out of 500) were assessed against the patient inclusion criteria above, resulting in 242 included couples (over 1,370 cumulative months of use) for analysis. The date of commencement with DuoFertility, patient-reported pregnancy and last date of use of DuoFertility (either because of pregnancy or loss to follow-up) was recorded. These data were used to compute the Kaplan-Meier estimator, which was then graphed as cumulative event data using the R statistical package¹⁵ and displayed together with the 95 % confidence interval (see Figure 1). This technique was then used to calculate the 12-month

clinical pregnancy rate and confidence intervals for various segments of the data, as described below and represented in Figures 2 and 3.

Results

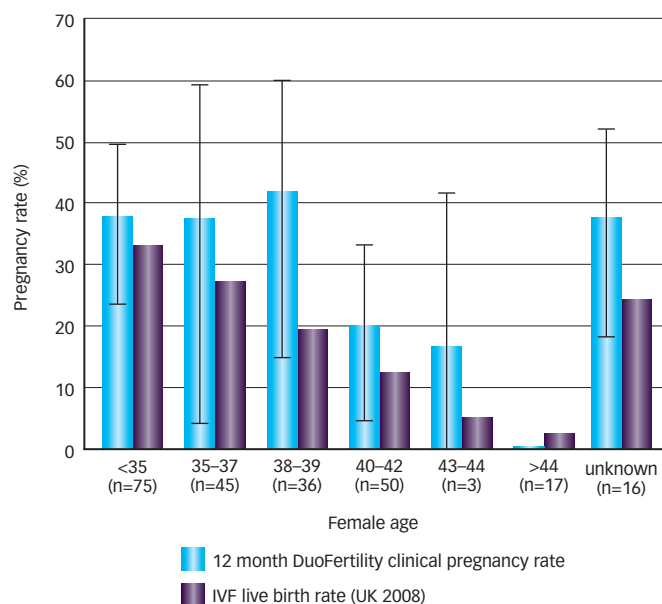
Pregnancy Rate

The 12-month patient-reported pregnancy rate, accounting for right-censoring of the data, was 38.8 %, with a 95 % confidence interval of 29.4–47.0 % (hereafter presented as 39±9 %). A comparison may be drawn with the effectiveness of ART as well as with the expected treatment-free pregnancy rate within the infertile population. The National Institute for Clinical Excellence guidance on fertility¹² indicates that approximately 84 % of couples will conceive naturally within one year of trying, and about half of those remaining will conceive during the second year of trying, whilst only one in eight of those remaining after two years of trying will conceive in the following year. Other studies have found that, on average, 9.1–14.3 % of infertile couples achieve treatment-free pregnancy per year.^{3,5,17} In the UK, the clinical pregnancy rate for one cycle of IVF/ICSI is 25.6 %, ¹³ while the respective rate for Europe is 27.9 % ¹⁴ and 8.2 % for IUI. ¹⁶ By way of comparison, an earlier and more limited study of clinical pregnancy rate with DuoFertility found a six-month pregnancy rate of 19±9 %, ⁴ whilst the current study shows a slight but not significant increase to 24±7 % over six months. In both cases, the six-month clinical pregnancy rate is not statistically different from the European IVF clinical pregnancy rate of 27.9 %. Of the 242 couples who met the inclusion criteria, 90 had previously undergone a cycle of IVF/ICSI. Although the average pregnancy success rate for these couples (26±13 %) was lower than the average, this is insignificantly different from the pregnancy rate with a further cycle of IVF/ICSI.

Age Groups

The pregnancy rate decreases with increased maternal age both in expectant management programmes³⁻⁵ and with IVF/ICSI treatment.¹³ Figure 2 displays the 12-month pregnancy rate for DuoFertility, segmented by female age at first use of DuoFertility, alongside the UK live birth rate for IVF/ICSI at each age. Live birth rate is used here as unfortunately the

Figure 2: DuoFertility Pregnancy Rate Versus Female Age



IVF = in vitro fertilisation.

Human Fertility & Embryology Authority data on clinical pregnancy rate are not segmented by age. Women who are eligible for IVF/ICSI under the NICE guidelines (younger than 39 years of age; n=142 in the current study) have a significantly higher chance of getting pregnant compared with older women with a similar fertility history (over 39 years of age; n=84 in the current study), as shown in *Figure 2*. However, it appears that the drop-off in pregnancy rate with maternal age (from <35 to >44) may be less steep for the DuoFertility programme than for IVF/ICSI.

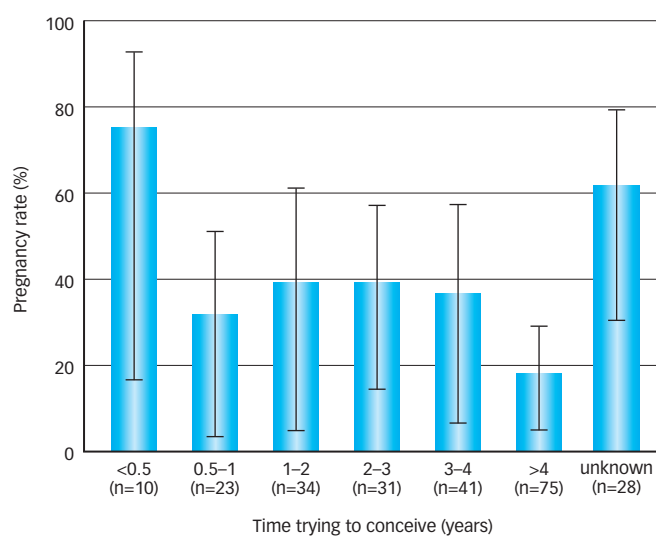
Parity

The data were further segmented according to whether a couple had previously had a child (secondary infertility) or not (primary infertility). The average pregnancy rates were 31±12 % for primary infertility, and 47±22 % for secondary infertility; however, this difference is not significant at the 95 % confidence level. A similar trend has been observed in other expectant management studies³ in which the pregnancy rate was lower in couples with primary infertility than in those with secondary infertility (15.1 versus 28.5 %).

Time Trying to Conceive

The chance of natural pregnancy decreases with the length of time trying to conceive,¹² as sterile (as opposed to infertile) couples make up an increasing proportion of the population. The DuoFertility pregnancy rate is segmented by time trying to conceive in *Figure 3*.

Figure 3: DuoFertility Pregnancy Rate Versus Time Trying to Conceive



The drop observed after four years, although not statistically significant, may indicate an increased likelihood of the couples having an undiagnosed underlying condition by this stage.

Conclusions

This study supports previous findings on the natural pregnancy potential of infertile couples.³⁻⁵ The results suggest that use of the DuoFertility monitor, in combination with the support provided by consultants, enhances the natural pregnancy rate in specific patient groups. Around one-third of couples seeking IVF have no identified underlying cause for their infertility ('unexplained infertility'),¹³ whilst a further significant group have mild-to-moderate underlying causes such as decreased sperm count, or a single blocked fallopian tube, which although increasing time to pregnancy would not preclude natural pregnancy. This study suggests that for many IVF or ICSI candidate couples, the possibility of natural pregnancy should not be discounted, and indeed may be significantly improved with an appropriate monitoring and support programme. The authors recognise that the sample size of this study is relatively small and by nature self-selecting and retrospective; however, if these findings are confirmed in larger studies, such a programme could be offered to couples with a good prognosis before they undergo invasive^{1,18} and expensive procedures such as ART if those procedures would not provide a significantly higher chance of conceiving. The authors also recognise that live birth rate is preferable to pregnancy rate as the primary outcome measure; however, this information was not available at the time the article was written owing to the recent availability of DuoFertility. ■

- Hull MG, Glazener CM, Kelly NJ, et al., Population study of causes, treatment, and outcome of infertility, *Br Med J (Clin Res Ed)*, 1985;291:1693-7.
- Terävä AN, Gissler M, Hemminki E, Luoto R, Infertility and the use of infertility treatments in Finland: prevalence and socio-demographic determinants, *Eur J Obstet Gynecol Reprod Biol*, 2008;136:61-6.
- Eijkemans MJ, Lintsen AM, Hunault CC, et al., Pregnancy chances on an IVF/ICSI waiting list: a national prospective cohort study, *Hum Reprod*, 2008;23:1627-32.
- Chausiaux OE, Hayes JM, Long CD, et al., Better than IVF? Pregnancy rates of the DuoFertility programme over six cycles of use, Presented at: the 13th COG Congress, 4-7 November 2010.
- Collins JA, Burrows EA, Wilan AR, The prognosis for live birth among untreated infertile couples, *Fertil Steril*, 1995;64:22-8.
- Greil AL, Infertility and psychological distress: a critical review of the literature, *Soc Sci Med*, 1997;45:1679-704.
- Dunson DB, Colombo B, Baird DD, Changes with age in the level and duration of fertility in the menstrual cycle, *Hum Reprod*, 2002;17:1399-403.
- Wilcox AJ, Weinberg CR, Baird DD, Timing of sexual intercourse in relation to ovulation - Effects on the probability of conception, survival of the pregnancy, and sex of the baby, *N Engl J Med*, 1995;333:1517-21.
- Kopitzke EJ, Berg BJ, Wilson JF, Owens D, Physical and emotional stress associated with components of the infertility investigation: perspectives of professionals and patients, *Fertil Steril*, 1991;55:1137-43.
- Blake D, Smith D, Bargiacchi A, et al., Fertility awareness in women attending a fertility clinic, *Aust N Z J Obstet Gynaecol*, 1997;37:350-2.
- Genius SJ, Bouchard TP, High-tech family planning: reproductive regulation through computerized fertility monitoring, *Eur J Obstet Gynecol Reprod Biol*, 2010;153:124-30.
- National Institute for Health and Clinical Excellence, *Fertility: assessment and treatment for people with fertility problems*, London: NICE, 2004.
- Human Fertilisation and Embryology Authority, A long term analysis of the HFEA Register data (1991-2006), Version 1 Rev 2, 11/07/2007. Available at: www.hfea.gov.uk/docs/LateSt_long_term_data_analysis_report_91-06.pdf (accessed 12 September 2011).
- de Mouzon J, Goossens V, Bhattacharya S, et al., Assisted reproductive technology in Europe, 2006: results generated from European registers by ESHRE, *Hum Reprod*, 2010;25:1851-62.
- R Development Core Team, R: A language and environment for statistical computing, Austria, R Foundation for Statistical Computing, 2009.
- Andersen AN, Goossens V, Ferraretti AP, et al., Assisted reproductive technology in Europe, 2004: results generated from European registers by ESHRE, *Hum Reprod*, 2008;23:756-71.
- Snick HK, Snick TS, Evers JL, Collins JA, The spontaneous pregnancy prognosis in untreated subfertile couples, *Hum Reprod*, 1997;12:1582-8.