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## ARTICLE

# Assisted reproduction using donor spermatozoa in women aged 40 and above: the high road or the low road?


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Dr De Brucker received his medical degree in 2008. He is currently working as a gynaecologist in the service of the Centre for Reproductive Medicine in Brussels. He has a special interest in female age and fertility.

**Abstract** The effect of age on outcome is one of the most intriguing areas in the assisted reproduction field. In older patients using donor spermatozoa to reproduce, it remains undefined as to which is the treatment of choice: intrauterine insemination (IUI) or IVF/intracytoplasmic sperm injection (ICSI). Since life-table analysis provides data that are easy to use for patient counselling, this study analysed cumulative delivery rates (CDR) in patients using donor spermatozoa undergoing either primarily IUI or IVF/ICSI and patients who eventually switched from IUI to IVF/ICSI. Crude and expected CDR after six IUI cycles and three primary ICSI cycles (no previous IUI) were similar in both groups (24% versus 26% and 29% versus 35%, respectively). Since time-to-pregnancy is an important factor in these older patients, ICSI treatment is advised to be started immediately, since a single cycle of ICSI will achieve the same success rate as a much longer period with at least six IUI cycles. If patients switch to ICSI after failed IUI, this only adds marginal benefit in CDR. Nearly all deliveries in the primary ICSI group were achieved in the first cycle. 

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**KEYWORDS:** age, cumulative delivery rate, delivery, ICSI, IUI, life-table analysis

## Introduction

Female fertility starts to decline at least 10 years prior to the onset of menopause (Broekmans et al., 2007). Although there is no strict definition of advanced reproductive age in women, subfertility becomes more pronounced after the age of 35 years. The effect of female age on fertility was reported more than 20 years ago (Menken et al., 1986). Over the past few decades, postponing childbirth has become a social trend as more women have pursued higher education and careers. This has led to an increase in treatments for age-related female subfertility (Broekmans et al., 2007). However, an age-related decrease in success rates of these treatments has been well documented (Hull et al., 1996; van Noord-Zaadstra et al., 1991). Therefore, it is important for both candidate couples and fertility specialists to describe the probability of delivery after a defined number of treatment cycles. In this perspective, providing the cumulative chances of achieving a live birth after a given number of cycles is more meaningful than live birth rates per cycle. As important as success rate is the choice of treatment to achieve success. Should clinicians opt for intrauterine insemination (IUI) or for IVF/intracytoplasmic sperm injection (ICSI) as primary treatment in women with advanced age requiring donor spermatozoa to reproduce?

Only limited data are available for IUI (CECOS, 1982; Barratt and Cooke, 1993; Botchan et al., 2001; Custers et al., 2008; Dovey et al., 2008). Previously, the present study group reported on a large study describing the cumulative delivery rate (CDR) in different age groups after artificial insemination with donor spermatozoa and this study revealed crude and expected CDR of 26% and 52% after 12 cycles in older age subgroups (40–45 years; De Brucker et al., 2009).

The most common indications for using donor spermatozoa are severe male infertility including azoospermia, lesbian couples and single-parent requests. While for husband spermatozoa, life-table data are available in literature for IVF and ICSI (Elizur et al., 2006; Malizia et al., 2009; Osmanagaoglu et al., 1999, 2002), no study in the literature reports cumulative data for IVF/ICSI with donor spermatozoa. While most women undergoing assisted reproduction treatment with donor spermatozoa have patent tubes, aged women may opt for IVF/ICSI because of an anticipated decline in ovarian reserve after age 40. Indeed, ovarian reserve determines the number of oocytes that can be obtained after hormonal stimulation, and this is more important for IVF than IUI outcome. Hence, in a setting where both IUI and IVF are reimbursed, women may prefer IVF/ICSI over IUI, hoping to 'buy time'.

Thus, an important factor for these older patients not covered in the current literature, apart from the question whether IVF/ICSI has a role, is the question of when to refrain from IUI and switch to IVF/ICSI. Various recommendations for all ages have been made about the maximum number of IUI cycles that should be performed, but good data is lacking (Custers et al., 2008). Therefore, this study analysed CDR in patients using donor spermatozoa undergoing IUI or IVF/ICSI. Moreover, IVF/ICSI CDR after failed IUI was analysed.

## Materials and methods

### Patients

A retrospective study was performed on patients enrolled in our programme between January 2003 and December 2007. All patients were treated with frozen–thawed donor spermatozoa. In total, 173 patients aged  $\geq 40$  years at the time of their first assisted reproduction cycle were included; the oldest patient was 45 years old. This study analysed 764 IUI cycles in 150 patients and 46 primary ICSI cycles in 23 patients. Since 63 patients opted for ICSI after failed IUI treatment, this group will be referred to as 'switchers'. Switchers underwent 129 ICSI cycles. Switchers were further divided into three subgroups: 1–3 IUI cycles; 4–6 IUI cycles; and 7–12 IUI cycles prior to their switch (Figure 1).

Ovarian reserve was assessed by measurement of FSH concentration on day 3 of the menstrual cycle and by antral follicle count. Tubal patency was examined by hysterosalpingography.

Live birth after 25 weeks of gestation was taken as the primary endpoint. All patients without a delivery after 25 weeks in an IUI or ICSI cycle were eligible for a subsequent cycle, including patients with cancelled cycles and those with a pregnancy that did not result in a live birth.

Follow up was ensured by sending questionnaires to patients and their doctor or by telephone queries whenever questionnaires were incomplete or in case of missing data. The following information was obtained from patients that stopped their treatment: status with regards to treatment (no further treatment or still continuing treatment); occurrence of a pregnancy with or without infertility treatment outside of the study clinic; and reasons for discontinuing treatment.

### Clinical and laboratory procedures

#### Intrauterine insemination

Although patients had normal menstrual cycles, some patients received mild ovarian stimulation either using clomiphene citrate 50–100 mg from day 3 until day 7 of their menstrual cycle or human menopausal gonadotrophin 75–150 U from day 3 of their cycle onwards. Although there is no evidence that adding mild ovarian stimulation to

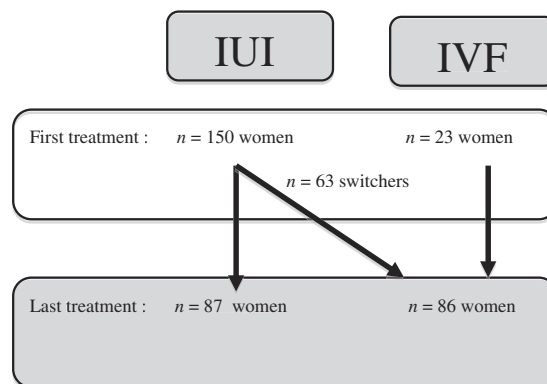


Figure 1 Treatment groups.

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