Treatment-independent live birth after in-vitro fertilisation: a retrospective cohort study of 2,133 women

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Running title: Treatment independent live birth after IVF

Abstract

Study question: What is the chance of a treatment-independent live birth following IVF (including ICSI) treatment?

Summary answer: Over five years of follow-up, the treatment-independent live birth rate was 17% in unsuccessfully treated women and 15% in those who had a live birth after IVF.

What is known already: A limited number of studies have investigated the chance of treatment-independent conception following completion of IVF, but most of them have been based on surveys with poor response rates and limited sample sizes.

Study design, size, duration: This is a population-based, retrospective cohort study of 2,133 women who received IVF treatment between 1998 and 2011 at a single regional IVF Unit and were followed for a minimum of one year and maximum of 15 years after their last IVF or ICSI treatment cycle.

Participants/materials, setting, methods: This study included all women, residing in the North-East of Scotland, who attended the Aberdeen Fertility Clinic and received IVF treatment between 1998 and 2011. Clinical and diagnostic information of all women were linked with treatment and pregnancy outcome data. A total of 2,133 women were divided into two groups: a) those who achieved a live birth following successful IVF or ICSI treatment (n=1,060); and b) those in whom treatment was unsuccessful i.e. resulted in either no pregnancy or pregnancy loss (n=1,073). The two groups were followed from the date of the last embryo transfer until the first treatment-independent live birth or 31st December 2012, whichever came first. The primary outcome was the treatment-independent live birth rate at one, two and a half, five and ten years of follow up. Cox regression was used to determine factors associated with treatment-independent live birth in each group.

Main results and the role of chance: Within five years of follow up, the treatment-independent live birth rate was 17% (95% CI, 15%-19%) among women whose IVF or ICSI treatment was unsuccessful and 15% (95% CI, 12%-17%) among women whose treatment resulted in live birth. In both groups, shorter duration of infertility, younger female age and IVF as compared to ICSI were associated with a higher chance of achieving treatment-independent live birth. Among unsuccessfully treated women, the chance of post-IVF live birth was reduced in those with tubal factor infertility. Three or more previous IVF or ICSI embryo transfers were associated with a lower chance of treatment-independent live birth among successfully treated women.

Limitations, reasons for caution: The study was conducted in a single fertility centre, which could compromise the generalisability of the findings. Moreover, data were unavailable on the women's use of contraception or active attempts to get pregnant, both of which could influence treatment-independent live birth rates.

Wider implications of the findings: This study provides a better understanding of the long-term prognosis for treatment-independent live birth after completion of IVF or ICSI treatment. The results will inform women of their chances of a treatment-independent live birth following failed or successful treatment and the factors which are associated with it.

Study funding/competing interest(s): This work was funded by a Chief Scientist Office Postdoctoral Training Fellowship in Health Services Research and Health of the Public Research (Ref PDF/12/06). The views expressed here are those of the authors and not necessarily those of the Chief Scientist Office. The authors have no competing interests.

Trial registration number: N/A

Key words: IVF/ICSI outcome, treatment independent live birth, infertility, live birth rate, duration of infertility, female age

Introduction

Infertility affects around one in six couples in the UK (Oakley et al. 2008). Conventional in-vitro insemination (IVF), as well as intracytoplasmic sperm injection (ICSI), are the recommended treatments for women with prolonged unresolved infertility (National Institute for Health and Clinical Excellence 2013). The number of cycles and embryo transfers of IVF or ICSI treatment in the UK has increased almost three-fold over 20 years from 18,304 in 1994 to 52,288 in 2014 (Human Fertilisation and Embryology Authority 2016, Human Fertilisation and Embryology Authority 2007). While initially used to treat women with tubal disease, the scope of IVF has expanded in the last two decades to embrace a wider range of indications, including unexplained and mild male factor infertility where there is no identified barrier to pregnancy (Kamphuis et al. 2014).

Although the success rate per cycle of IVF in the UK has doubled from 14% in 1994 to around 27% in 2014 (Human Fertilisation and Embryology Authority 2007, Human Fertilisation and Embryology Authority 2016), these figures show that the majority of women still do not become pregnant after their first IVF or ICSI cycle (de Mouzon et al. 2010, Human Fertilisation and Embryology Authority 2016, McLernon et al. 2016). Most discontinue treatment after their first attempt due to the psychological and physical burden of treatment as well as financial constraints (Deka and Sarma 2010, Gautam 2010, Nandi et al. 2014, McLernon et al. 2016). Although women who have no absolute barrier to conception retain the ability to conceive on their own, many equate unsuccessful treatment with the end of any hope of having a baby (Throsby 2002).

Few studies have reported treatment-independent live birth rates after IVF treatment and explored factors associated with them. In a recent record-linkage cohort study of women starting treatment with assisted reproductive technology (ART) and followed for up to 5

years, the rate of treatment-independent live births was 11% (Malchau et al. 2017). In a French survey, about 17% and 24% of women achieved a spontaneous pregnancy following either successful or unsuccessful IVF (Troude et al. 2012). Younger female age and shorter infertility duration have been shown to be associated with treatment-independent live birth (Shimizu et al. 1999, Hennelly et al. 2000, Osmanagaoglu et al. 2002, Brandes et al. 2010, Khalili et al. 2012, Troude et al. 2012). Women with unexplained infertility had better prognosis in comparison with those with other causes of infertility (Eijkemans et al. 2008, Donckers et al. 2011). Many of these studies have relatively small sample sizes, a short duration of follow-up or, in the case of surveys, poor response rates (Shimizu et al. 1999, Osmanagaoglu et al. 2002, Cahill et al. 2005, Troude et al. 2016). As a result, it is difficult to determine with any degree of accuracy, the chance of a treatment-independent pregnancy or the clinical factors which affect this.

We conducted a population-based cohort study to determine the incidence of women who had a treatment-independent live birth following: a) IVF or ICSI treatment which resulted in a live birth (successful group) or b) IVF or ICSI treatment which did not result in a live birth (unsuccessful group). We also aimed to identify factors in each group that were associated with treatment-independent live birth.

Methods

Study population

This population-based cohort study included all women residing in the North-East of Scotland who were referred to Aberdeen Fertility Clinic for investigation and subsequently received IVF (including ICSI) treatment at the Aberdeen Assisted Reproduction Unit between January 1998 and December 2011. Aberdeen Assisted Reproduction Unit is the only centre

that provides private and NHS funded IVF treatment in the North-East Scotland region (Grampian, Highlands, Orkney, and Shetland regions) (Pandey et al. 2014).

The following exclusion criteria were applied: a) women aged less than 18 or over 50 at the beginning of their IVF treatment; b) women who underwent their first treatment before January 1998 or after December 2011; c) women residing in the Orkney and Shetland regions; and d) women who were treated using donor sperm, donor oocytes or surrogacy. Of the 3091 women who underwent IVF or ICSI treatment in the Aberdeen Assisted Reproduction Unit during the chosen time period, 2,133 were included in our study after applying the exclusion criteria (see Figure 1).

Study groups and follow up

The cohort of 2,133 women were divided into two groups: a "successfully treated group" of 1,060 women who had a live birth resulting from IVF treatment and an "unsuccessfully treated group" of 1,073 women whose treatment did not result in a live birth. Women in the first group were followed from treatment-dependent live birth until: treatment-independent live birth, they returned to the clinic with a different male partner or 31st December 2012, whichever came first. Women in the second group were followed from the first menstrual cycle after unsuccessful IVF treatment until: treatment-independent live birth, they returned to the clinic with a different male partner or 31st December 2012, whichever came first.

Databases

Aberdeen Fertility Centre database holds registration and demographic data of all infertile women referred to the Aberdeen Assisted Reproduction Unit (Pandey et al. 2014). The

Assisted Reproduction Unit database, which contains treatment details, was record-linked to the Aberdeen Fertility Centre database (Maheshwari et al. 2009). Diagnostic and treatment data from both databases were also record-linked to the national Scottish maternity admission database (SMR02). SMR02 stores maternity admission records which provided the pregnancy outcomes for women in this study (Administrative Data Liaison Service 2017). Live birth data was available until December 2012 meaning that all women were followed for at least one year after their last embryo transfer. The final linked anonymised data was stored on the dedicated secure Data Safe Haven (DaSH) University of Aberdeen server with access restricted to named and approved researchers only.

Baseline characteristics

Baseline characteristics of women at treatment dependent live birth (for the successful group) or after their final IVF cycle (for the unsuccessful group) included female age (years), the cause of infertility (categorised as male factor, unexplained infertility, tubal factor, ovulatory disorder, more than one cause or other), number of fresh or frozen embryo transfers conducted, duration of infertility (years), infertility type (primary versus secondary) and treatment type (IVF or ICSI).

Outcome

The primary outcome was the treatment-independent live birth rate at one, two and a half, five and ten years of follow up. The final linked dataset enabled us to identify all treatment-dependent and treatment-independent live births from the same woman. Gestational age at birth, which was recorded in the national Scottish maternity admission database

(SMR02), was used to identify and code live births as treatment independent or treatment dependent by comparing the estimated pregnancy dates to dates of embryo transfer.

Statistical analysis

Descriptive statistics of women and treatment characteristics were calculated at the time of treatment-dependent live birth (successful group) or after the last IVF cycle (unsuccessful group). The frequency and percentage were used for categorical data and means and standard deviations for normally distributed data. For skewed data, median and the 25th and 75th percentiles were presented.

Treatment independent live birth

We estimated the treatment independent live birth rate at one, two and a half, five and ten years of follow up in both the "successful" and "unsuccessful" groups by fitting a Kaplan-Meier curve for time to pregnancy and calculated the median follow up in both groups.

Factors associated with treatment independent live birth

A multivariable Cox regression model was used per "successful" and "unsuccessful" group to examine the association between baseline characteristics and time-to-treatment-independent live birth. In addition to the baseline characteristics, the year of IVF treatment was included to account for changes in policy and practice.

A backward stepwise selection technique was used with a decrease in Akaike's Information Criterion (AIC) when a variable was removed representing a better fit (Akaike, 1974). Statistical software IBM SPSS statistics version 24 was used for data management and R 3.4.3 was used for data analysis.

Missing data

Approximately 3% of data on patient and/or treatment characteristics was missing. We applied single imputation to account for this, including all mentioned baseline characteristics and the cumulative hazard for pregnancy in the imputation model to account for the time aspect in the data (White and Royston, 2009).

Ethical approval

The study was approved by the North of Scotland Research Ethics Committee (12/NS/0120). Consent was not required from study participants as the final database did not contain identifiable information.

Results

Characteristics of the study population

Clinical characteristics of all women at the time of their last IVF cycle (unsuccessful group) or after giving birth (successful group) are presented in Table I. Women whose treatment was unsuccessful were older (mean of 35.7 versus 33.9 years) compared to women whose IVF treatment was successful. The cause of infertility, number of embryo transfers and duration of infertility (median of 5.1 years for the successful group and 5.3 years for the unsuccessful group) were comparable across the two groups.

Treatment-independent live birth

Of the 1,073 unsuccessfully treated women, 185 had at least one subsequent treatment-independent live birth over the maximum follow-up period of 15 years (Figure 2). The

median follow-up period was 6 years (2.16-10.5). Of the 1,060 successfully treated women, 151 had at least one treatment-independent live birth over the maximum follow-up period of 15 years (Figure 2). The median follow-up time was 5.9 years (2.6-10).

The one-year Kaplan-Meier treatment-independent live birth rate was 10% (95% CI, 8%-12%) among unsuccessfully treated women and 4% (95% CI, 3%-5%) among successfully treated women (Figure 3). At two and a half years, these rates increased to 15% (95% CI, 12%-17%) and 11% (95% CI, 9%-13%) respectively. The five-year rates were 17% (95% CI, 15%-19%) and 15% (95% CI, 12%-17%), and the ten-year rates were 19% (95% CI, 16%-22%) and 17% (95% CI, 14%-19%), respectively.

Predictive factors

Factors associated with a treatment-independent live birth among successfully treated women are shown in Table II as hazard ratios (HR) and 95% confidence intervals (CIs). The multivariable analysis showed that the factors of an increased female age, increased duration of infertility, two or three or more embryo transfers compared to one embryo transfer and ICSI versus IVF treatment (HR: 0.62, 95%CI 0.44 to 0.88) were all associated with a decrease in the chance of treatment-independent pregnancy.

Factors associated with a treatment-independent live birth among unsuccessfully treated women are shown in Table III. The factors of an increased female age, increased duration of infertility and ICSI versus IVF treatment (HR: 0.70, 95%CI 0.47 to 1.05) were associated with a decrease in the chance of pregnancy. The cause of infertility was associated with the chance of pregnancy with tubal factor having the worst prognosis (HR: 0.31. 95%CI 0.17 to 0.55) and ovulatory disorder having the best prognosis (HR: 1.11, 95%CI 0.64 to 1.94) compared to male factor infertility as reference.

Discussion

Principal findings

Following unsuccessful IVF or ICSI treatment, approximately 15% (one in seven) women had a treatment-independent pregnancy leading to live birth over two and a half years, rising to 17% (one in six) over five years. The corresponding figures in women who had an IVF or ICSI live birth were slightly lower at 11% (one in nine) and 15% (one in seven) respectively. After ten years, the percentage is very little more than that at five years. The Kaplan-Meier curve indicated that for the group in which IVF was successful, the time to treatment independent live birth was longer compared to women who were unsuccessful. This difference could be explained by the fact that women who had the desired child through fertility treatment may be less likely to try to get pregnant again soon after having a live birth and may have used contraception for a period of time (Troude et al. 2012).

Increasing female age and duration of infertility were associated with a decreased chance of treatment-independent live birth in both groups. Having more than one embryo transfer and having received ICSI instead of IVF treatment lowered the chance of a treatment-independent live birth among successfully treated women. Among unsuccessfully treated women, the chance of post-IVF live birth was reduced in those with tubal factor infertility and those who received ICSI treatment.

Strengths and limitations

At 2,133, the sample size for this population-based retrospective cohort study was reasonably large compared to most studies which have examined treatment-independent live birth after IVF and the follow up was long (Shimizu et al. 1999, Hennelly et al. 2000,

Osmanagaoglu et al. 2002, Cahill et al. 2005, Ludwig et al. 2008, Donckers et al. 2011, Khalili et al. 2012, Pandey et al. 2014). Our sample is representative of the entire population as there is only one IVF clinic in the region. Data used in this record-linkage study were extracted from high quality and validated databases that have been successfully used in previous studies (Maheshwari et al. 2009, Pandey et al. 2014, Rukuni et al. 2016). A further strength of this study was the fact that our study was not reliant on telephone interviews or postal questionnaires, minimising recall bias and overcoming problems relating to poor response rates reported in some earlier studies (Shimizu et al. 1999, Hennelly et al. 2000, Osmanagaoglu et al. 2002, Cahill et al. 2005, Khalili et al. 2012). Our population-based study design allowed us to avoid the situation reported in a Danish study (Pinborg et al. 2009) where non-response by women who failed to become pregnant led to overestimation of the treatment-independent live birth rate by 5.3%.

The study has a number of limitations. A key drawback is the single-centre retrospective design, which raises questions about generalisability. Although the majority of fertility clinics in the UK have access to the same guidelines (NICE guidelines), the selection of candidates and number of cycles could have been influenced by clinical judgment and patient preferences (Kim et al. 2015). In addition, a multicentre study design with a higher number of participants would have increased the sample size in the different subgroups which would have allowed us to draw more accurate comparisons between causes of infertility. Another factor which could limit the generalisability of our study to other populations is that the population of the North East of Scotland is ethnically relatively homogeneous; the majority of residents are Caucasians (Scottish Gov 2014).

A natural drawback associated with data from clinical databases is the fact that not all desired covariates were available. For instance, data were unavailable on use of

286 contraception or active plans to get pregnant. A questionnaire-based study found that
287 10.9% of women following ICSI treatment had used contraception (Ludwig et al. 2008).
288 Exclusion of women who used active contraception following IVF, leaving a cohort of
289 women who remained actively trying for a second baby, might increase the proportion of
290 treatment-independent live births over the observation period. It is difficult to define a
291 timepoint such as the 'completion of IVF treatment' with certainty as we were unable to
292 distinguish between a treatment-independent conception that occurred between planned
293 IVF cycles and a conception that occurred after the couple decided not to have further IVF.
294 In addition, we lacked information on any pregnancy outcomes which may have occurred
295 outside Scotland and any IVF treatments which may have occurred outside the Grampian
296 region. It is possible that some women could have undergone treatment outside the region
297 and then returned to give birth. This would have been counted as a natural conception using
298 our databases. Finally, although we censored women if they came back with a different
299 partner during treatment cycles, we were not able to detect a change in partnership after
300 IVF treatment. We were also unable to account for dropout factors such as stress due to
301 failed IVF treatment.
302
303 ***Related literature***
304 Our treatment-independent live birth rate of 17% (one in six) over five years in
305 unsuccessfully treated women was higher than the 11.5% reported in a five-year follow-up
306 study in Belgium (Osmanagaoglu et al. 2002), 10% in a five-year cohort study in the
307 Netherlands (Brandes et al 2010), and the 12% observed by Troude et al (2016) in a French
308 cohort followed up for eight years. However, Troude et al (2012) reported a treatment
309 independent live birth rate of 24% among women unsuccessfully treated by IVF over an

average follow-up period of seven years which was longer than our median follow-up period (Troude et al. 2012). Approximately 15% of successfully treated women in our study had a treatment-independent live birth over five years. This figure is slightly lower than the 17% to 21% reported in the literature from France, Ireland and Japan (Shimizu et al. 1999, Hennelly et al 2010, Troude et al. 2012) but higher than the 11.7% observed in a five-year follow-up Danish study (Pinborg et al. 2009).

Recent publications have reported higher rates of treatment-independent live birth after IVF treatment compared to older studies (Shimizu et al. 1999, Hennelly et al 2010, Troude et al. 2012). This is despite the increase in success rate of IVF treatment over the last few years (Human Fertilisation and Embryology Authority 2007, Human Fertilisation and Embryology Authority 2016). Increased availability of IVF and early access for women who have a reasonably good chance of spontaneous pregnancy has been noted to lead to overtreatment (Kamphuis et al. 2014, Marcus et al. 2016). A Danish study found that 9.1% of patients on the waiting list for IVF had a treatment-independent live birth within one year (Eijkemans et al. 2008). The median IVF cycle number in our study was two for unsuccessfully treated women which was higher than the average number in the UK (McLernon et al. 2016). This is probably due to the fact that during the study period, the Scottish Government supported up to two complete cycles of IVF (before increasing it to three rounds in 2017) (Fertility Fairness 2017).

Our study showed that the chance of having a treatment-independent live birth among both successfully and unsuccessfully treated women decreased with increasing female age and duration of infertility. Both of these factors have been identified as being associated with treatment-independent live birth in previous studies (de La Rochebrochard et al. 2009, Khalili et al. 2012, Walschaerts et al. 2012, Troude et al. 2016). In successfully treated

334 women, we observed a lower chance of treatment independent live birth in women who
335 received more than one cycle, in particular in women who received three cycles (or more), a
336 finding also previously demonstrated in a Danish prospective cohort study (Pinborg *et al*.,
337 2009).
338 In those who had unsuccessful IVF, women with ovulatory disorder had an increased chance
339 of treatment-independent live birth whilst those with tubal factor infertility had a decreased
340 chance of treatment-independent live birth. This has been previously reported in a
341 prospective cohort study (Donckers et al, 2011) and is indicative of sporadic ovulation in
342 women with this diagnosis. ICSI was associated with a decreased chance of treatment-
343 independent live birth for both the successful and unsuccessful groups even after
344 accounting for cause of infertility. This finding could be due to the clinician choosing ICSI for
345 couples who have a relatively poor prognosis based on predictors unknown to us.
346
347 ***Wider implications of the findings***
348 This study provides a better understanding of the long-term prognosis of treatment-
349 independent live birth and associated factors of such an outcome. The results can provide
350 an indication to women, who remain childless after fertility treatment or who wish to have
351 another baby after successful IVF treatment, of their prognosis based on their
352 characteristics. Those counselling infertile women should include information about their
353 chance of natural conception at the end of fertility treatment, which starts to peak in the
354 first few years.
355
356 ***Conclusion***

We found that treatment-independent live birth after either successful or failed IVF or ICSI treatment occurs in approximately one in six couples. This is more likely to occur in younger women treated with IVF and who have been trying to conceive for a relatively short duration. Our results will help clinicians to counsel infertile couples on the characteristics associated with a live birth after a failed or successful IVF outcome.

Acknowledgements

We acknowledge the data management support of the Grampian Data Safe Haven (DaSH) and the associated financial support of NHS Research Scotland, through NHS Grampian investment in the Grampian DaSH. For more information, visit the DaSH website http://www.abdn.ac.uk/iahs/facilities/grampian-data-safe-haven.php. We would like to thank all the staff at Aberdeen Fertility Clinic for their help with database queries and case note searching.

Authors' roles

DJM, SB and YE designed the study. YE and RVE conducted the statistical analysis and theliterature search and wrote the article. All authors contributed intellectually to the writing or revising of the manuscript and approved the final version.

Funding

This work was funded by a Chief Scientist Office Postdoctoral Training Fellowship in Health Services Research and Health of the Public Research (Ref PDF/12/06). The views expressed here are those of the authors and not necessarily those of the Chief Scientist Office. The funder did not have any role in the study design, in the collection, analysis, and

interpretation of data, in the writing of the report nor in the decision to submit the paper for publication.

Conflict of interest

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that there was no support from any organisation for the submitted work, no financial relationships with any organisations that might have an interest in the submitted work in the previous three years and no other relationships or activities that could appear to have influenced the submitted work.

Figures

Figure 1. Flow chart showing inclusion and exclusions before data analysis

Figure 2. Flow chart showing the number of women per group and resulting treatment independent live births over the maximum follow-up period of 15 years

Figure 3. Cumulative treatment independent live birth rates over follow up from last IVF cycle or live birth

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Table 1 Characteristics of the women after treatment dependent live birth (successfully treated group) or after their last IVF cycle (unsuccessfully treated group)

Characteristics	Successfully treated group n = 1060	Unsuccessfully treated group n = 1073
Mean (SD) female age (years)	33.9 (4.0)	35.7 (4.7)
Infertility type (primary versus secondary), n (%)	0 (0)	663 (61.8)
Cause of infertility, n (%)		
Male	383 (36.1)	329 (30.7))
Ovulatory	70 (6.6)	85 (7.9)
Unexplained	284 (26.8)	259 (24.1)
Tubal	179 (16.9)	228 (21.1)
Other/unknown	41 (3.9)	59 (5.5)
More than one cause	103 (9.7)	113 (10.5)
Infertility duration (median, 25th-75th)	5.1 (3.9-6.7)	5.3 (3.7-7.2)
Infertility duration, n (%)		
<3	99 (9.3)	140 (13.0)
3-6	607 (57.3)	512 (47.7)
>6	354 (33.4)	421 (39.2)
No. of embryo transfer episodes(median, 25th-75th)	2 (1-3)	2 (1-3)
No. of embryo transfer episodes, n (%)		
1	398 (37.5)	398 (37.1)
2	261 (24.3)	277 (25.8)
3	172 (16.0)	181 (16.9)
>3	229 (21.3)	217 (20.2)
Treatment type		
IVF (in vitro fertilization)	652 (61.5)	708 (65.4)
ICSI (intracytoplasmic sperm injection)	408 (38.5)	371 (34.6)

544 **Table 2 Factors associated with treatment independent live birth over time in successfully treated**
545 **women (n=1060)**

	Multivariable analysis with backward selection based on AIC		
	HR	**95% CI**	**P value**
Female age (per year ≤31)	0.92	0.84 to 1.01	0.10
Female age (per year >31)	0.89	0.77 to 1.02	0.09
Duration of infertility (per year)	0.89	0.83 to 0.97	0.006
Number of embryo transfer episodes			
1 [a]	1		
2	0.74	0.51 to 1.09	0.13
3	0.31	0.17 to 0.59	<0.001
>3	0.52	0.32 to 0.84	0.007
Type of treatment			
IVF [a]	1		
ICSI	0.62	0.44 to 0.88	0.007

546 [a] Used as a reference variable.

547 HR = hazard ratio; CI = confidence interval; BMI = body mass index; IVF = in vitro fertilisation; ICSI =
548 intracytoplasmic sperm injection

549 Note: Female age was included in the model as two continuous linear terms, one for age up to 31
550 and one for age over 31 years

551

552 **Table 3 Factors associated with treatment independent live birth over time in unsuccessfully**
553 **treated women (n=1073)**

	Multivariable analysis with backward selection based on AIC		
	HR	**95% CI**	**P value**
Female age (per year ≤31)	1.04	0.94 to 1.15	0.48
Female age (per year >31)	0.85	0.74 to 0.97	0.02
Duration of infertility (per year)	0.86	0.81 to 0.92	<0.001
Cause of infertility			
Male [a]	1		
Anovulation	1.11	0.64 to 1.94	0.71
Unexplained	1.08	0.70 to 1.67	0.74
Tubal	0.31	0.17 to 0.55	<0.001
Other	0.61	0.30 to 1.22	0.16
More than one cause	0.48	0.26 to 0.87	0.02
Type of treatment			
IVF [a]	1		
ICSI	0.70	0.47 to 1.05	0.08

554 [a] Used as a reference category.

555 HR = hazard ratio; CI = confidence interval; BMI = body mass index; IVF = in vitro fertilisation; ICSI =
556 intracytoplasmic sperm injection

557 Note: Female age was included in the model as two continuous linear terms, one for age up to 31
558 and one for age over 31 years

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Figure 1 Flow chart showing inclusion and exclusions before data analysis

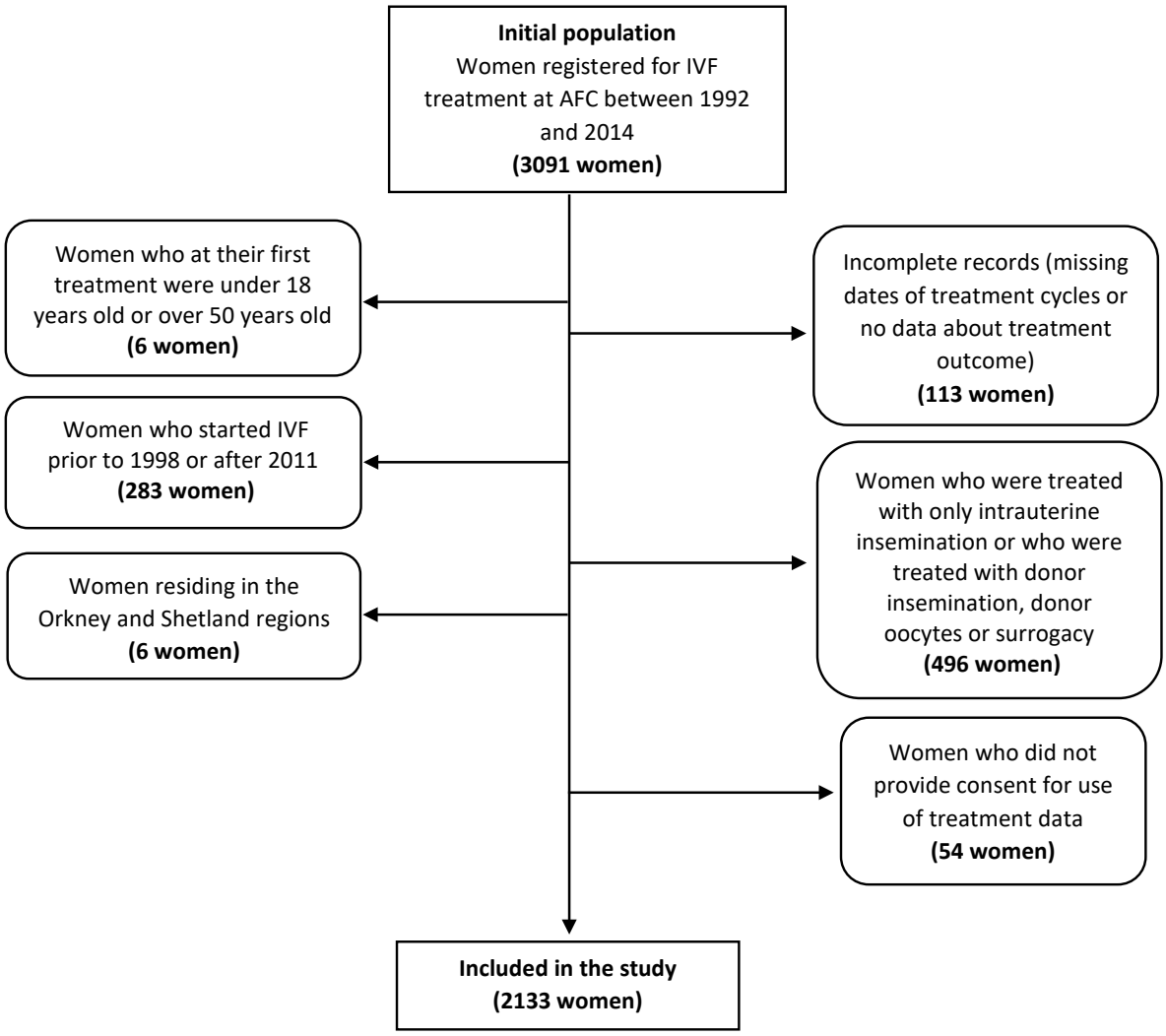
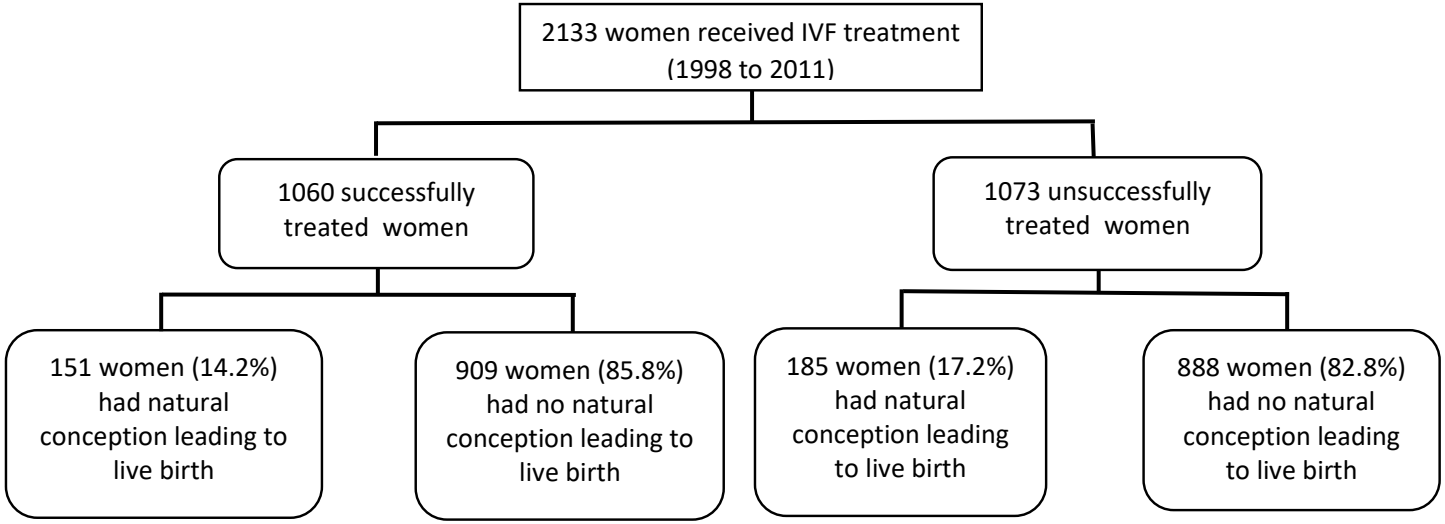


Figure 2 Flow chart showing the number of women per group and resulting treatment independent live births over the maximum follow-up period of 15 years



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Cumulative treatment independent live birth rate
0.4
0.3
0.2
0.1
0.0
Unsuccessfully treated couples
Successfully treated couples
0
2
4
6
8
10
Follow up (years)

576