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Realizing a desired family size: when should couples start?

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STUDY QUESTION: Until what age can couples wait to start a family without compromising their chances of realizing the desired number of children?

SUMMARY ANSWER: The latest female age at which a couple should start trying to become pregnant strongly depends on the importance attached to achieving a desired family size and on whether or not IVF is an acceptable option in case no natural pregnancy occurs.

WHAT IS KNOWN ALREADY: It is well established that the treatment-independent and treatment-dependent chances of pregnancy decline with female age. However, research on the effect of age has focused on the chance of a first pregnancy and not on realizing more than one child.

STUDY DESIGN, SIZE, DURATION: An established computer simulation model of fertility, updated with recent IVF success rates, was used to simulate a cohort of 10 000 couples in order to assess the chances of realizing a one-, two- or three-child family, for different female ages at which the couple starts trying to conceive.

PARTICIPANTS/MATERIALS, SETTING, METHODS: The model uses treatment-independent pregnancy chances and pregnancy chances after IVF/ICSI. In order to focus the discussion, we single out three levels of importance that couples could attach to realizing a desired family size: (i) Very important (equated with aiming for at least a 90% success chance). (ii) Important but not at all costs (equated with a 75% success chance) (iii) Good to have children, but a life without children is also fine (equated with a 50% success chance).

MAIN RESULTS AND THE ROLE OF CHANCE: In order to have a chance of at least 90% to realize a one-child family, couples should start trying to conceive when the female partner is 35 years of age or younger, in case IVF is an acceptable option. For two children, the latest starting age is 31 years, and for three children 28 years. Without IVF, couples should start no later than age 32 years for a one-child family, at 27 years for a two-child family, and at 23 years for three children. When couples accept 75% or lower chances of family completion, they can start 4–11 years later. The results appeared to be robust for plausible changes in model assumptions.

LIMITATIONS, REASONS FOR CAUTION: Our conclusions would have been more persuasive if derived directly from large-scale prospective studies. An evidence-based simulation study (as we did) is the next best option. We recommend that the simulations should be updated every 5–10 years with new evidence because, owing to improvements in IVF technology, the assumptions on IVF success chances in particular run the risk of becoming outdated.

WIDER IMPLICATIONS OF THE FINDINGS: Information on the chance of family completion at different starting ages is important for prospective parents in planning their family, for preconception counselling, for inclusion in educational courses in human biology, and for increasing public awareness on human reproductive possibilities and limitations.

STUDY FUNDING/COMPETING INTEREST(S): No external funding was either sought or obtained for this study. There are no conflicts of interest to be declared.

Key words: family planning / delay of childbearing / preconception counselling / natural fertility / reproductive failure

Introduction

Although voluntary childlessness has become an accepted way of life in modern western societies, most young people in Europe want to have two or more children, with an average of 2.2 (Testa, 2007). In a recent survey in the Netherlands, 13% of young adults aged 18–22 years did not yet know if they wanted to have children, 4% wanted no children, 18% wanted one child, 46% two children, 15% three children, and only 4% wanted four or more (Kooiman and Stoeldraijer, 2015). During the life course there is often adjustment to a lower number of children or to a 'no-child family' (Testa, 2007; Liefbroer, 2009). The mean difference between the intended and realized family size, also called fertility gap, was estimated to be 0.35 children per woman in the European Union (EU) in 2006, varying from 0.28 in Germany and Austria to 0.71 in Finland (Sobotka and Lutz, 2010). The fertility gap is related to personal or socio-economic factors which delay the start of childbearing, for example not having met a suitable partner, broken relationships, financial constraints, and competing educational, professional or personal ambitions (Mills et al., 2011). Consequently, many couples experience a tension between the desire to have children and reasons to delay childbearing.

In this paper we will focus on the impact of biological barriers on realizing an envisioned family. From a biological point of view, the optimal period for a woman to have children is between ages 18 and 30 years. Thereafter, the ability to conceive and have children declines progressively (Bongaarts, 1975; Wood, 1989) because of depletion and ageing of the pool of oocytes stored in the ovaries during the fetal period (te Velde and Pearson, 2002). The advent of reliable methods of contraception in the 1960s enabled women to postpone childbearing, to prevent the birth of not yet wanted children, and to plan the start of building a family (Goldin, 2006). As a result, since 1970 the mean age at first childbirth has increased by 4–5 years in most EU countries, and the proportion of women having their first child above 30 years of age increased from ~8% to ~40% (Lutz et al., 2003). Trying to have a first baby later inevitably implies that the proportion of couples who failed in doing so has also increased (te Velde et al., 2012). Furthermore, for those couples that do succeed in having a first child, some will fail to have a second one.

The aim of the present paper is to provide evidence-based information for prospective parents about the timing of their first pregnancy, in order to have a sufficiently high chance to realize their desired family size.

Materials and Methods

We simulate a cohort of couples trying for their first child, and follow them over time. Some couples may already be infertile—i.e. unable to have a live birth—at a very young age, but usually infertility occurs later (Menken et al., 1986; Eijkemans et al., 2014). To simulate the age-related decline in fertility in the cohort, we used the micro-simulation model developed by Leridon (2004), which is based on a large set of age-dependent data on monthly pregnancy chances in natural non-contraceptive populations collected by Henry (1965) and Leridon (1977). The model accounts for three age-dependent variables that together determine the chance of having a live birth: the monthly chance of conception (fecundability), the chance of pregnancy loss after conception, and the chance of having reached the stage of permanent sterility when conception can no longer occur. For the chance of the age-dependent pregnancy loss after a conception, data from contemporary populations were used as such data were not available in data from natural fertility populations. For a further description of the

model and the use of historical and contemporary populations see Leridon (2004) (pp. 1550–1551 and references therein). The model assumes an average natural per cycle conception rate (fecundability) of 23% between age 20 and 30 years, which is in line with data of contemporary populations (see discussion in Eijkemans et al., 2014). The chance of achieving a second pregnancy is related to the chance of a first pregnancy because each couple is allocated a specific initial fecundability. Fecundability decreases as age increases but a lower initial fecundability implies a lower fecundability at any age (Leridon, 2004). The fetal loss rate of the model is 12% at age 20 years, 13% at age 25 years, 15% at age 30 years, 18% at age 35 years, 25% at age 40 years and almost 35% at age 45 years. The age-dependent chance of sterility of the model is 1% at age 25 years, increasing to 2% at age 30 years, 5% at age 35 years, 17% at age 40 years and 55% at age 45 years.

The model also has an IVF treatment option (see Habbema et al., 2009). As ICSI is a variant of IVF, we will use the term IVF for both. The model uses IVF success rates and their dependence on the age of the woman, the duration of trying, whether the couple already has a child or not, and on the rank number of the treatment cycle, according to Lintsen et al. (2007). As Lintsen et al. (2007) uses data from 2003, all success rates have been updated to the 2013 IVF results in The Netherlands, which had, for example, a first cycle success rate including frozen embryo results, of 29.5% at age 35 years (compared with 23.5% in 2003), and a twin pregnancy rate of 5.1% (compared with 22.7% in 2003, and 1% in natural pregnancies). The age-dependent first cycle IVF success rates are 32% at age 25 years, 35% at age 30 years, 30% at age 35 years, 15% at age 40 years and 5% at age 45 years. (http://www.nvog.nl//Sites/Files/0000004040_Landelijke%20IVF%20cijfers%201996-2013.pdf).

The model further assumes that a diagnostic work-up is being performed in all couples who failed to become pregnant within 1 year. Couples whose diagnostic results indicate that they have (almost) no chance to succeed when trying for longer (e.g. tubal infertility), and couples of which the woman is 38 years or older, will immediately have IVF treatment, consisting of a course of three IVF cycles with 4-month intervals (Habbema et al., 2009). The couples of which the woman is not yet 38 years old will continue trying for a natural pregnancy. If pregnancy fails to occur, IVF is applied after 2 years if the woman is 33 years or younger (no pregnancy during 3 years since start) and after 1 year if she is between 33 and 38 (no pregnancy during 2 years). We further assume that couples will wait an average of 15 months after the birth of a child before trying for the next pregnancy, and that couples whose first child was conceived by IVF will again have IVF, starting immediately after these 15 months.

The simulation run size is 10 000 couples, which is sufficiently large for obtaining precise model results.

We calculate the chance that a couple succeeds in completing a one-, two- and three-child family, depending on the age of the women at the start of building a family. We derive the maximum age at which the couple should start in order to have a sufficiently high chance to realize the intended family size ('maximum starting age').

What constitutes a sufficiently high chance level will depend on the strength of the desire of the couple to have children. In order to focus the discussion, we single out three chance levels. At the highest level, the couple wants at least a 90% chance of family completion. Having children is extremely important for these couples; they are inclined to do virtually anything to realize this ambition. The second level of 75% corresponds to couples who would like to have children but not at all costs. For example, for them the burden—financially or physically—and risks of IVF may not be acceptable. At the third level of 50%, children are welcome, but a life without children has also advantages and is considered to be equally valuable. To supplement the discussion on the couples with a 90, 75 or 50% chance level, we present graphs from which family completion chances can be read off for every possible starting age.

The probability of realizing a family can be increased by applying IVF in case a naturally achieved pregnancy does not occur within the period specified

above. Because not all couples are willing to use IVF, we calculate the chance of family completion both with and without the use of IVF treatment.

The robustness of our results under other assumptions with regard to pregnancy chances, sterility rates, IVF results, other treatments, discontinuation of IVF treatment, and differential importance attached to first and later children is explored in a series of sensitivity analyses (SA):

SA1 (pregnancy chances)

Pregnancy chances are assumed 20% higher and lower than the baseline value of 23%: 18 and 28%.

SA2 (sterility)

Alternative sterility rates are used, based on the results of Eijkemans et al. (2014), with rates of 3, 6, and 9% at ages 25 years, 30 years and 35 years respectively instead of the 1, 2 and 5% in the baseline model at these ages.

SA3 (IVF results)

Higher per cycle IVF success rates are assumed, for exploring the impact of further improvement of IVF. The baseline per cycle success rate of 29.5% is increased with 25% (relative) to a value of 37%.

SA4 (other treatments)

Other treatments may be applied before IVF, especially intrauterine insemination (IUI). Bensdorp and coauthors recently showed that IUI is a successful first-line treatment (Bensdorp et al., 2015). However, reliable data comparing the female age-dependent success rates of IUI with the female age-dependent effect on the natural chance of conceiving are lacking. We explored the value of other treatments by arbitrarily assuming their added benefit to be equal to the success rate of an additional IVF cycle. Thus, in this SA four instead of three IVF cycles are applied.

SA5 (IVF discontinuation)

Even when couples intend to have three IVF cycles, many drop out before the third attempt, also in fully reimbursed programmes. A recent review concluded that 22% of couples discontinue from three consecutive cycles (Brandes et al., 2009; Gameiro et al., 2013). The possibility that couples discontinue IVF treatment is explored by simulating one or two IVF cycles instead of three.

SA6 (family size preferences)

Differential importance may be attached to first and later children. This is modelled by assuming that couples want a 90% probability for a first child, and 75 or 50% for a second child, or they want a 90% probability for two children, and 75 or 50% for a third child.

Technical details of the sensitivity analyses are presented in Supplementary Data.

Results

The maximum female age at which couples should start unprotected intercourse in order to realize a one-, two- or three-child family is shown in Table I. The starting age strongly depends on the desired success chance. The upper part of the table gives starting ages if IVF is not applied. Couples who would like to have two children and request a high 90% chance level of achieving this should start at female age 27 years at the latest. The 75%- and 50%-level couples can start considerably later, at age 34 years and 38 years, respectively. If a 90% level couple intends to use IVF, the start can be 4 years later, at age 31

Table I Maximum female age (years) at which couples should start building a 1-, 2- or 3-child family, for a 50, 75 and 90% chance of realizing the desired family size, with and without IVF.

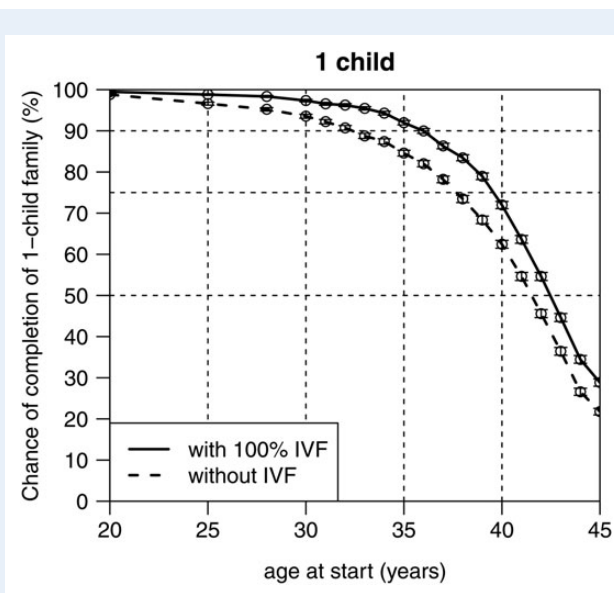| Chance of realization	1-child family	2-child family	3-child family
Without IVF			
50%	41	38	35
75%	37	34	31
90%	32	27	23
With IVF			
50%	42	39	36
75%	39	35	33
90%	35	31	28

Figure 1 Relationship between the female age at which couples start building a family and the chance of realizing a family with one child, with and without use of IVF. The short lines above and below each point in the graph indicate the 95% confidence intervals.

years. The impact of IVF use on starting age is much lower for the 75%-level and the 50%-level couples. When the couple intends to have only one child, the starting age can be 3–5 years later than for a two-child family, while for three children the starting age should be 3 years earlier (see Table I).

In Figs 1–3, the chances for completing a one-, two- and three-child family are given for all possible starting ages. For example, you can read from Fig. 2 that a start age of 35 years will give a couple an 80% chance of realizing a two-child family when IVF is used, and a 70% chance when it is not used.

If robustness is defined as a difference of at most 1 year in earlier or later starting age compared with the baseline, most results of the SA with regard to pregnancy chances, sterility rates, IVF results, other
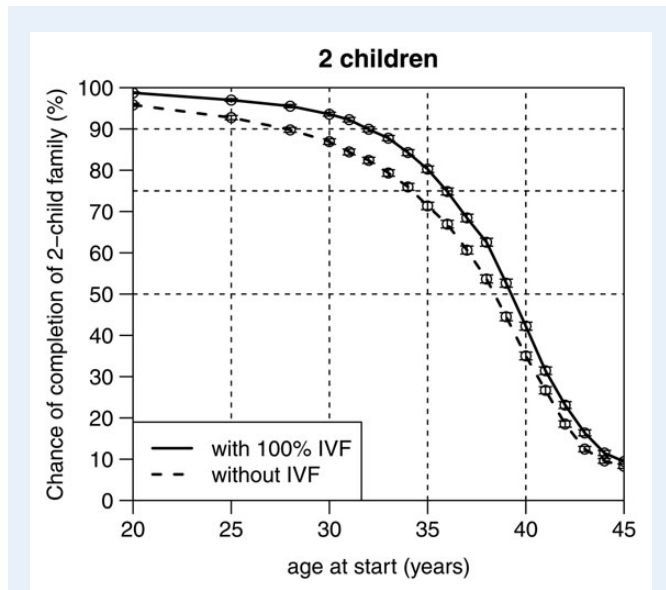
Figure 2 Relationship between the female age at which couples start building a family and the chance of realizing a family with two children, with and without use of IVF. The short lines above and below each point in the graph indicate the 95% confidence intervals.
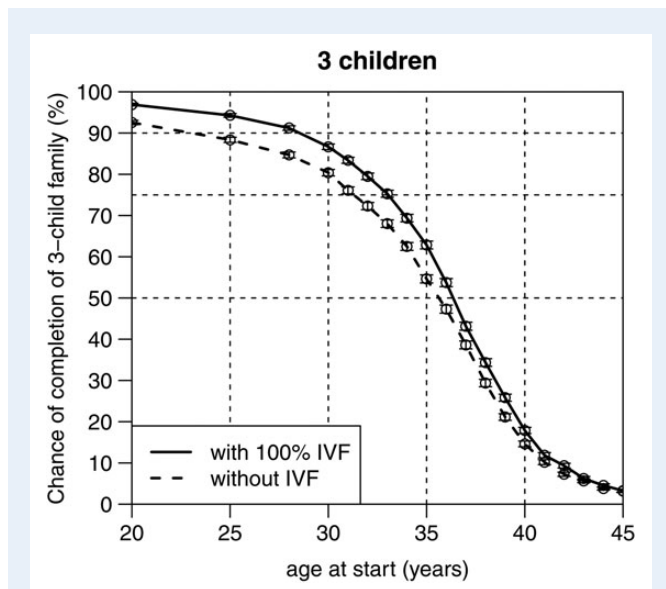

Figure 3 Relationship between the female age at which couples start building a family and the chance of realizing a family with three children, with and without use of IVF. The short lines above and below each point in the graph indicate the 95% confidence intervals.

treatments, and discontinuation of IVF treatment show robustness of the baseline results (see Table II). There are three exceptions, all for couples wanting a 90% family completion chance. First, when high sterility rates at young ages are assumed (SA2), couples who reject IVF should start 3–4 years earlier. Second, if IVF results improve (SA3) or additional treatment is applied (SA4), couples who want a two-child family can start 2 years later. Third, when only one IVF cycle is performed instead of three

(SA5), couples should start 2 or 3 years earlier if wanting a two- or three-child family, respectively. For SA6, which explores the consequences of attaching differential importance to first and later children, the baseline results in Table I show that the starting age which is required for a high 90% chance of the first child(ren), is always sufficiently early to also satisfy the lower 75 or 50% chance levels for having one more child.

Discussion

So far, studies about age-related fertility decline have focused on the delay of bearing of a first child. To our knowledge, this is the first time that the maximum female age for starting a family has been estimated. We focused on three values for the chance of family completion: 50, 75 and 90%. In addition, we provided graphs from which the latest starting age can be read off for any chance level. Couples who want a high (i.e. 90%) chance of having a two-child family may be surprised to find out that they have to start at age 31 years at the latest when accepting IVF, and as early as 27 years of age when they intend not to use IVF. For a three-child family, couples have to start 3–4 years earlier. On the other hand, the results may be reassuring for couples who are content with one child and do not wish a very high chance of success: They can start at age 37 years for a 75%- and at age 41 years for a 50% success chance.

The baseline results are, by and large, endorsed by the sensitivity analysis. The main exception is SA2 with higher sterility rates at young ages, based on the results of Eijkemans *et al.* (2014). The sterility rates in the SA are corroborated by the 3–5% primary infertility rates below age 30 years mentioned by Menken *et al.* (1986) and Greenhall and Vessey (1990). On the other hand, a recent worldwide analysis of Mascarenhas *et al.* (2012) found a 2% primary infertility rate for ages 20–44 years, which is consistent with the low sterility rates used in the baseline.

The results on latest starting age assume that the couples start trying for the next pregnancy 15 months after the birth of a child. If a couple wants a different space after the birth of a child, the latest starting ages should be adapted accordingly. For example, for a period of 9 instead of 15 months, the latest starting age will be half a year later for a two-child family, and one year later for a three-child family.

There are many misunderstandings about the age-related fertility decline in women and the possible role of IVF in influencing this process. From fertility-awareness studies and population surveys, we know that most young people are too optimistic about their chances to conceive spontaneously after age 35 (Heffner, 2004; Leridon, 2004; Schmidt, 2010; Daniluk and Koert, 2012; Daly and Bewley, 2013; Franklin, 2013). In contrast, others think that there is an age deadline of 40 years, above which women are too old to have children (Billari *et al.*, 2011) whereas, in fact, an average 40-year old woman still has a more than 50% chance to spontaneously conceive a live birth pregnancy (Eijkemans *et al.*, 2014). Also, supposedly due to the 'miracle' stories in the media about 60-year old women who became a mother after IVF, young people tend to overestimate the effectiveness of IVF (Maheshwari *et al.*, 2008; Schmidt, 2010; Daniluk and Koert, 2012).

We focused on female age but realize that the age-related decline concerns couple fecundity, which includes the age of the male partner. However, the female contribution is far more important (Minneau and Trussell, 1982; Menken *et al.*, 1986) unless the male is much older, which is currently rather exceptional in western countries.

Table II Results of the sensitivity analysis (SA). Impact of changes in assumptions on the latest starting age (years) for realizing a one-, two- or three-child family with a 90, 75 or 50% chance of success.

Without IVF**		I child 90%	I child 75%	I child 50%	2 child 90%	2 child 75%	2 child 50%	3 child 90%	3 child 75%	3 child 50%
Pregn.Chance High*	SA1	+1***	+1	0	+1	0	0	+1	+1	+1
Pregn.Chance Low	SA1	−1	0	0	0	−1	−1	−1	−1	0
Sterility Rates High	SA2	−3	0	−1	−4	−1	−1	−4	0	0
Baseline age		**32**	**37**	**41**	**27**	**34**	**38**	**23**	**31**	**35**
With IVF		I child 90%	I child 75%	I child 50%	2 child 90%	2 child 75%	2 child 50%	3 child 90%	3 child 75%	3 child 50%
Pregn.Chance High	SA1	+1	0	0	+1	+1	0	+1	0	0
Pregn.Chance Low	SA1	0	0	0	0	0	−1	−1	−1	−1
Sterility Rates High	SA2	0	0	−1	−1	0	−1	−1	−1	−1
IVF Results Improved	SA3	+1	0	0	+2	+1	0	+1	0	0
Other Treatments	SA4	+1	0	0	+2	+1	0	+1	0	0
IVF 1 cycle	SA5	−1	−1	−1	−2	−1	−1	−3	−2	−1
IVF 2 cycles	SA5	0	−1	0	−1	0	−1	−1	−1	0
Baseline age		**35**	**39**	**42**	**31**	**35**	**39**	**28**	**33**	**36**

*Pregn.Chance: chance of pregnancy.

**SA3, SA4 and SA5 only affect starting ages with IVF.

***Positive numbers indicate the number of years that couples can start later than under baseline assumptions, and negative numbers the number of years that couples should start earlier.

From a reproductive perspective, single women and lesbians may need a male donor to have a child. Although most donors have normal sperm, the success chances are probably not higher compared with other couples when using donor insemination with cryopreserved and thawed sperm procedures, which decrease sperm quality. We therefore think that these couples can also use the results presented in Table I.

Couples who are highly motivated to conceive and are well informed of the best period within a cycle to conceive can sometimes reach higher fecundabilities than the 0.23 used in the baseline: see Wang et al. (2003) who studied newly married and highly motivated Chinese couples. It might thus be wise to discuss with couples facing fertility problems if they can improve their chances of conceiving by better timing of intercourse.

The data in Table I show that the eventual use of IVF has the greatest impact on starting ages for the couples wishing a 90% chance of conceiving. This is fortunate because it means that the most motivated couples, who will usually readily accept the burden and risks of IVF, will profit most. The impact of IVF on starting age should not be confused with the effectiveness of IVF in terms of an increase in chance of success. The increase in the chance of realizing a two-child family by using IVF is considerable (6–8%) for starting ages between 30 and 40, but decreases outside this range because of the high natural pregnancy chances under age 30 and because of decreasing IVF success rates over age 40. At older ages, both natural and IVF pregnancy chances deteriorate rapidly, and IVF will therefore influence high maximum starting ages only slightly. At young ages, pregnancy chances deteriorate very gradually, and the small extra chance provided by IVF will therefore increase the maximum starting ages by several years. Altogether, the impact of IVF on starting age is

real but limited. This may be a disappointment for couples who mistakenly think that IVF is a panacea in case a natural pregnancy fails to occur (Maheshwari et al., 2008).

Our results confirm that IVF with fresh oocytes from the patient has limited effectiveness in counteracting the age-related decline of fertility (Leridon, 2004). New techniques have emerged to address this problem. Oocyte donation is already widely used for women above 40 years of age and is quite effective if the oocytes come from young donors. As we had no reliable data on the use of donor oocytes we did not include this in our analyses, and because donor oocytes are not available in most countries or are very costly. The other techniques—freezing of embryos or oocytes—are still more or less experimental but may evolve rapidly.

The results in Table I and Fig. 1 assume either no IVF use at all, or a full treatment of three cycles. Thus, in order to use these results for family planning, young couples should already be rather certain that they will fully accept IVF, or not, many years later. This is not realistic, because the burden of IVF is often underestimated beforehand. Recent studies found that a majority of couples with an indication for IVF will not make use of it (te Velde et al. 2012; Duron et al. 2013). Moreover, many women who started IVF do not complete the full treatment, including in countries where IVF is reimbursed (Brandes et al. 2009; ESHRE Capri Workshop Group 2010). One possibility for the couple is to play safe and use the younger starting ages without IVF. Or they could choose an intermediate value between the maximum starting ages with and without IVF, using the results in Table II of the sensitivity analysis on incomplete IVF use (SA5).

Our study addresses the question of the appropriate age for starting a family. When couples change their mind about the use of IVF, the number

of children, or the importance they attach to realizing the desired family size after they have started, the results of this paper can usually not be applied anymore. Another limitation is that the calculations are based on population data, and therefore apply to couples for which age is the only known fertility-related attribute. This is usually the case when couples start building a family, but not after a fertility investigation has been performed. A more informed prognosis of natural conception is now possible, by taking the results of the fertility investigation into account. The prognosis can vary between no chance at all, when a two-sided tubal blockage or azoospermia has been found, and good pregnancy prospects when all components of the fertility investigation are normal and the woman is relatively young. The chances of a natural pregnancy can be read off from prediction rules for natural pregnancy (Hunault *et al.*, 2004) and for pregnancy after IVF from prediction rules for IVF success rates (Templeton *et al.*, 1996; Lintsen *et al.*, 2007; Nelson and Lawlor, 2011; and a review by Leushuis *et al.*, 2009).

Our conclusions would have been more persuasive if derived directly from large-scale studies in which prospective parents were grouped according to motivation, intended family size and acceptance of IVF, and subsequently followed for many years. Due to logistic and financial constraints, such studies cannot easily be undertaken. A simulation study with assumptions based on the best scientific data, as performed in the present study, is the next best option, and perfectly feasible. In order to be based on the best evidence in the future, we recommend that the calculations and results in this paper should be updated every 5–10 years, taking new primary data into account. In particular, the assumptions on IVF success chances run the risk of becoming outdated.

The strength of our study is that it translates knowledge about human fecundity and effectiveness of IVF into the operational concept of 'chance of family completion' at different starting ages, which is crucial for prospective parents in planning their family. Such information is not yet available. Knowledge about when to start trying to become pregnant is important in preconception counselling, which is increasingly used. If couples would like to wait some time with having children, they have to become aware about how motivated they are to have children, what is their envisioned family size and whether or not they will accept IVF in case natural conception fails. Furthermore, our results can be included in educational courses on human biology, and may help to increase public awareness on human reproductive possibilities and limitations.

In conclusion, the maximum female age at which couples should start a family can be estimated, and depends on the intended family size, the desired chance of realizing the family, and the attitude towards the use of IVF. Information on maximum starting age may be relevant for many couples and can be integrated into counselling and education activities.

Supplementary data

Supplementary data are available at http://humrep.oxfordjournals.org/.

Authors' roles

J.D.F.H. and E.R.t.V. conceived the idea of the study and its design, M.J.C.E. is responsible for the methodology and performed the analyses, and H.L. developed the original simulation model (adapted by M.J.C.E.) and contributed significantly to the interpretation of the results. J.D.F.H. wrote the manuscript. All authors gave detailed comments on all versions, contributed intellectually to the final version of the manuscript, and approved the final version.

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Conflict of interest

None declared.

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