The impact of a decline in fecundity and of pregnancy postponement on final number of children and demand for assisted reproduction technology

H. Leridon\textsuperscript{1,2,3,5} and R. Slama\textsuperscript{2,3,4}

\textsuperscript{1}INED, Paris F-75020, France; \textsuperscript{2}INSERM, U822 ‘Épidémiologie, Démographie et Sciences Sociales’, IFR 69, Le Kremlin-Bicêtre F-94276, France; \textsuperscript{3}UMR 822, Univ Paris-Sud, Le Kremlin-Bicêtre F-94276, France; \textsuperscript{4}Helmholtz Center Munich, German Research Center for Environmental Health, Institute of Epidemiology, 85764 Neuherberg, Germany

\textsuperscript{5}Correspondence address. Ined, 133 boulevard Davout, 75980 Paris Cedex 20, France. E-mail: leridon@ined.fr

BACKGROUND: Over the past decades, the proportion of couples who resort to infertility treatment has tremendously increased, and fertility (the final number of children) sharply declined. We explored the roles of two potential causes of these trends: a temporal decline in the couples’ fecundability and a postponement of age at initiation of pregnancy attempts. METHODS: We conducted a Monte–Carlo simulation for the reproductive history of 100,000 women based on the fertility and socio-demographic characteristics of the 1968 birth cohort in France. Declines in fecundability of various amplitudes have been implemented, as well as increases in the distribution of age at initiation of pregnancy attempts. RESULTS: A decline in fecundability by 15\% implied a decrease in fertility by 4\%, and an increase in the proportion of couples eligible for infertility treatments by 73\%. An increase in the mean age at initiation of first pregnancy attempt by 2.5 years from 25 years entailed a decrease by 5\% in fertility and an increase by 32\% in the proportion of couples eligible for infertility treatments. CONCLUSION: A relatively important decrease in fecundability and an increase by 2.5 years in age at first pregnancy attempt are likely to have only a limited impact on fertility. However, they may have a large impact on the proportion of involuntarily infertile couples, likely to resort to assisted reproduction techniques.

\textit{Keywords}: fecundity; postponing pregnancy; assisted reproduction technology; infertility; fecundability

Introduction

The average number of children born per woman has been declining sharply in most developed countries during the last decades. This was mainly due to the changes in behavior of couples: having children is now seen as competing with many other aspirations of the woman, the man and the couple (Van De Kaa, 1987; Lesthaeghe and Surkyn, 1988). Another major behavioral change in many countries is the postponement of childbearing. Contemporary couples are not only wishing fewer children than their forerunners, they also want to start having them later in their life. The mean age at first birth rose by 2–4 years in many countries over the last 20–30 years (Sobotka, 2004) and the mean age at childbearing (all parities) is now exceeding 30 years in Denmark, Finland, Italy, Netherlands, Sweden or Switzerland (Council of Europe, 2005). Such averages are still in the best ages of the reproductive period, but their increases mean that some couples are trying to have children at older and older ages. Some of them could fail to procreate. Berrington (2004) suggested to call such couples ‘perpetual postponers’: they still want one (more) child but can never decide when it is appropriate to start trying to have it. They can thus end their reproductive life with fewer children than wished.

In this paper, we will use the word ‘fertility’ as a synonym for the actual number of children for a woman or a group of women. This is in agreement with the demographic usage, but more restrictive than the medical usage (see Habbema \textit{et al}., 2004). The word ‘fecundity’ will refer to the ability of men and women to bear children. This ability depends on fecundability (the monthly probability of pregnancy among sexually active non-contraceptive couples), on the rate of fetal mortality (the probability that a pregnancy does not result in a live birth) and on the probability of being permanently sterile (i.e. unable to conceive).

In addition to the above-mentioned trends of fertility, a decline in fecundity can be suspected. Several reports indicated a possible decline in semen parameters over the last decades in developed countries (Carlsen \textit{et al}., 1992; Auger \textit{et al}., 1995; Swan \textit{et al}., 2000). This possible decline has been accompanied by clear increases in the incidence of testis cancer, a pathology...
associated to decreased fertility before and after the onset of the disease (Moller and Skakkebaek, 1999; Jacobsen et al., 2000), and led to the hypothesis of an increased incidence of testicular dysgenesis syndrome (Skakkebaek et al., 2001). How such adverse temporal trends in male reproductive health may translate at the level of the couple is unclear. Sperm concentration and morphology are clearly associated with fecundability (Bonde et al., 1998a,b; Slama et al., 2002), however, their ability to predict 1-year involuntary infertility is limited (Guzick et al., 2001). Moreover, since only the changes in sperm concentration values in the range from 0 to 50 million sperm/ml are associated with the probability of pregnancy at the population level (Boné et al., 1998a,b; Slama et al., 2002), important variations in sperm concentrations may have a limited effect on the probability of pregnancy. Indeed, a decline by 21% in median sperm concentration, which corresponds to the decline observed among French semen donors extrapolated over a 15-year period, would only translate into a relative decline by 7% in fecundability (Slama et al., 2004). Similarly, a decline by 47% in sperm concentration (as extrapolated for French semen donors over a 45 years period) would reduce fecundability by 15% (Slama et al., 2004). From the point of view of public health, however, the relevant endpoint is the occurrence of a live birth (fertility) or the occurrence of involuntary infertility for 12 months or more, a duration above which expensive and painful fertility treatments may be initiated.

Our aim is to assess the potential impact on fertility (the final number of children) and on the demand for assisted reproduction technologies (ART) of the following biological and demographic trends: a decline in fecundability with an amplitude coherent with what is expected because of a temporal deterioration of male reproductive health, and a further postponement of births in line with current demographic trends. We will also estimate the possible impact of the recourse to ART on fertility.

Materials and Methods

A simulation model of reproduction for 100 000 women

The demographic effects of such changes are not easy to forecast because fertility depends on a large number of factors. A first set of parameters is biological. We have already mentioned a key one: fecundability, the monthly risk of conception. In addition, we must take into account the age at onset of permanent sterility, the risk of fetal wastage, the duration of pregnancy (for a live birth and for a spontaneous abortion) and the duration of amenorrhea following the end of pregnancy. A second set of parameters depends on the behavior of the women. This list must include the age at entry into a stable union, the number of children wanted, the spacing desired before each birth and the effectiveness of contraception used during the periods when a pregnancy is not wished. Taking into account all these parameters in formal models of reproduction would be very challenging. Simulation models, based on the Monte Carlo technique, offer a practical alternative that has been used in demography for several decades (Jacquard, 1967; Larsen and Menken, 1989; Leridon, 2004).

In such models the full reproductive biographies of a set of women are simulated by a series of random drawings and tests of comparison. The age at marriage (or at entry in first union) is taken at random from a distribution of observed ages at first union in a reference population. A newly married woman is not supposed to want a child immediately: she will use contraception during a given period (e.g. 2 years) and then we assume that she will be fully exposed to the risk of conceiving. The occurrence of a conception will depend on her fecundability (see below). When a conception has occurred the outcome of the pregnancy depends of the probability of a fetal death at that specific age. After delivery, the woman then enters into a ‘non susceptible period’ whose duration varies according to the outcome of the pregnancy. If she still wants another child we assume that she is exposed again to the risk of pregnancy after some delay, depending on the minimum spacing between births that she wishes. The process continues until the woman reaches the age of 55 years, but in practice no more events occur when the age of permanent sterility is reached (this age is taken at random in a distribution of such ages; see below). Some births may occur after the desired number of children has been achieved or during the spacing periods because contraceptive methods are not 100% effective. These failures are estimated, as well as the proportion of women who do not reach the desired number of children because of an early age at permanent sterility, a low fecundability or repeated spontaneous abortions.

There are several sources of random variations between women. The ages at first union and at onset of permanent sterility are drawn from given distributions. The occurrence of a conception during a given month results from a drawing where the chance of success is equal to the value of fecundability during that month. Fecundability has a biological basis but is also modulated by the effectiveness of contraception, when it is used. The outcome of the pregnancy is also a random event.

Due to these random variations each biography differs from the previous one. We computed averages and distributions for the whole set of women. For the same reason, if we run a new simulation with the same parameters the results will differ slightly, exactly as in a random sampling of an actual population. However, in practice our results are based on cohorts of 100 000 women, resulting in a very low variance. As an example, ten successive runs for the ‘initial population’ (see next section) resulted in a mean number of children ranging from 2.000 to 2.007, a proportion of couples involuntarily childless ranging from 9.7 to 10.0%, and a proportion of couples eligible for ART varying from 11.5 to 11.8%.

Hypotheses and calibration of the model

For the present study, the calibration of the model has been done in two steps. First the biological ingredients were adjusted by comparison with populations where there was no birth control, a context of ‘natural fertility’. Fecundability was assumed to depend on age, with a maximum at 20–24 years followed by a decline to zero at the age of onset of permanent sterility. The maximum value also varied between couples: the average value was set to 0.23 and its distribution was assumed to follow a Beta function of parameters 3 and 10 (Leridon, 1977; Wood, 1994). Such a function includes low values for fecundability, but strictly speaking no couple is assigned a value equal to zero. This is why we added a proportion of totally sterile couples, which increased with age. The proportion of couples permanently sterile by age of woman, sterility referring here to the inability to conceive (i.e. to start a pregnancy which will be known by the woman), was estimated by matching the age distribution at last birth resulting from the model to the one observed in a natural fertility population (Leridon, 2008). The proportions are 2% when the woman is aged 30 years, 5% at age 35, 17% at age 40 and 55% at age 45. Finally, the maternal age dependence of the rate of fetal wastage has been estimated from contemporary populations, as an average of twelve series (Leridon, 1977). The risk of a fetal death
thus strictly depends on the age of the woman: it amounts to 13.5% at age 25–29, 16.0% at 30–34, 20.0% at 35–40, 27.0% at 40–44 and 37.0% at 45–49 years. An important result shown in Leridon (2008) is that the rise of the risk of being unable to have a live birth with age is mainly due to the increasing risk of a pregnancy resulting in a miscarriage or a still birth, more than to the inability to conceive—at least up to age 40–45.

For behavioral factors, we have selected the case of the French population around year 2000, as experienced by the generation born in 1968, and the key assumptions are given in column 2 of Table I. For women aged 25–34 years, the mean number of children desired was 2.11, with 25.5% of couples wishing 0, 20.0% wishing 1, 51% wishing 2, 17.5% wishing 3 and 4% wishing 4 children (adapted from (Toulemon and Leridon 1999)). Couples are not looking for a pregnancy the soon: they use contraception to avoid a pregnancy during 18 months after a birth, and then they start being exposed to a new conception attempt: an increase by two and half years in our simulation, but the mean age for all parities is identical.

For behavioral factors, we have selected the case of the French population around year 2000, as experienced by the generation born in 1968, and the key assumptions are given in column 2 of Table I. For women aged 25–34 years, the mean number of children desired was 2.11, with 25.5% of couples wishing 0, 20.0% wishing 1, 51% wishing 2, 17.5% wishing 3 and 4% wishing 4 children (adapted from (Toulemon and Leridon 1999)). Couples are not looking for a pregnancy the soon: they use contraception to avoid a pregnancy during 18 months after a birth, and then they start being exposed to a new conception attempt: an increase by two and half years in our simulation, but the mean age for all parities is identical.

The detailed results of the simulation for this ‘initial population’ are shown in column 2 of Table II. We then allowed the fecundity parameter of the model to vary, to measure the resulting changes on overall fertility. The reproductive history of 100,000 women is simulated, so that the variance is minimized as explained above.

### Compulation of a decline in fecundity

We simulated declines in fecundity by 7 and 15%, which correspond to the estimated effect of the reported decline among French semen donors over a 15 and 45-year period, respectively (Slama & et al., 1996; Belaisch-Allart et al., 1997), 3 years at age 35, 2 years at age 40 and 1 year at age 45. Finally, we generated proportions of unwanted births and of mistimed births (pregnancies starting during a spacing period but not ended by an abortion) very close to those observed in France.

The impact of a decline in fecundability was also estimated using a second hypothesis of a heterogeneous fecundability decline, corresponding to a situation in which variations in fecundability were driven by an external factor affecting only the values of fecundability below some threshold. This is what would happen if the decline in fecundability was mediated by a decrease in sperm concentration, which is only related to fecundability below 40–50 millions spermatozoa/ml. One way to take this into account is to assume that the reduction in fecundability is effective only below some value \( S \). We did so by setting all initial fecundability values below \( S \) to \( (w \times K \times S) \), with \( 0 < w < 1 \) such that the resulting mean fecundability equals the one obtained in the homogeneous approach. The heterogeneous hypothesis is not relevant for a halving of fecundability because such an overall reduction cannot be reached if only a part of the population is affected. Results appear in Tables II and III.

### Postponement of maternal age at childbearing

We then assumed that the individuals decide to postpone their first birth by entering into a first union at the same age, but starting their first pregnancy attempt later after entry into union than the above-described initial situation. We explored two hypotheses for postponement of the first pregnancy attempt: an increase by two and half years and an increase by almost 6 years. The first hypothesis matches the changes in mean age at maternity observed in Italy or The Netherlands.
Table II. Effect of a reduction in fecundability (initial fertility rate: 2.0 children).

<table>
<thead>
<tr>
<th>Initial population</th>
<th>Relative change in fecundability:</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Decrease by 7%</td>
<td>Decrease by 15%</td>
<td>Decrease by 50%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Homogeneous decrease*</td>
<td>Heterogeneous decrease</td>
<td>Homogeneous decrease*</td>
<td>Heterogeneous decrease</td>
</tr>
<tr>
<td></td>
<td>Change‡</td>
<td>Change‡</td>
<td>Change‡</td>
<td>Change‡</td>
</tr>
<tr>
<td>Mean fecundability</td>
<td>0.231</td>
<td>0.215 – 6.9%</td>
<td>0.214 – 7.4%</td>
<td>0.197 – 14.7%</td>
</tr>
<tr>
<td>Mean age at maternity</td>
<td>29.2</td>
<td>29.2 – 0.0%</td>
<td>29.3 – 0.3%</td>
<td>29.2 – 0.0%</td>
</tr>
<tr>
<td>Mean final number of children</td>
<td>2.00</td>
<td>1.98 – 0.8%</td>
<td>1.98 – 0.8%</td>
<td>1.96 – 2.9%</td>
</tr>
<tr>
<td>Mean time to 1st conception (months)</td>
<td>9.6</td>
<td>10.0 – 4.2%</td>
<td>10.5 – 9.4%</td>
<td>10.7 – 11.5%</td>
</tr>
<tr>
<td>TTC1 ≥ 1 year (per 100 1st births)</td>
<td>20.5</td>
<td>21.8 – 6.3%</td>
<td>24.0 – 17.1%</td>
<td>23.9 – 16.6%</td>
</tr>
<tr>
<td>Infertile after 5 years (per 100 married)</td>
<td>6.7</td>
<td>7.1 – 6.0%</td>
<td>7.1 – 6.0%</td>
<td>7.5 – 16.9%</td>
</tr>
<tr>
<td>Childless couples (%)</td>
<td>11.7</td>
<td>11.9 – 1.7%</td>
<td>11.9 – 1.7%</td>
<td>12.2 – 4.3%</td>
</tr>
<tr>
<td>Couples involuntarily childless (%)</td>
<td>9.9</td>
<td>10.0 – 1.0%</td>
<td>10.0 – 1.0%</td>
<td>10.2 – 3.0%</td>
</tr>
<tr>
<td>Couples with fewer births than wanted (%)</td>
<td>14.9</td>
<td>15.1 – 1.3%</td>
<td>15.1 – 1.3%</td>
<td>15.7 – 5.4%</td>
</tr>
<tr>
<td>Couples eligible for ART (%)</td>
<td>11.6</td>
<td>12.2 – 5.2%</td>
<td>12.6 – 8.6%</td>
<td>13.2 – 13.8%</td>
</tr>
<tr>
<td>Couples with more births than wanted (%)</td>
<td>15.8</td>
<td>14.5 – 8.2%</td>
<td>14.5 – 8.2%</td>
<td>13.5 – 14.6%</td>
</tr>
<tr>
<td>Unplanned births (per 100 births)</td>
<td>15.5</td>
<td>14.4 – 7.1%</td>
<td>14.4 – 7.1%</td>
<td>13.3 – 14.2%</td>
</tr>
</tbody>
</table>

*Fecundability level multiplied by a given factor (K = 0.93 and 0.85, respectively) for all the population, compared to the distribution in the initial population.
†Fecundability unchanged for all couples of the initial population above a given fecundability threshold (S = 0.2), and set to a given value below the threshold for the rest of the population (K = 0.7 and 0.4, respectively). K has been chosen to give a mean fecundability similar to the homogeneous case. Relative change compared to the initial population. §Time to conception. ART, assisted reproduction technology. Fecundability: the monthly probability of pregnancy among sexually active non-contraceptive couples.

Table III. Effect of a reduction in fecundability (initial fertility rate: 1.5 child).

<table>
<thead>
<tr>
<th>Initial population</th>
<th>Relative change in fecundability:</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Decrease by 7%</td>
<td>Decrease by 15%</td>
<td>Decrease by 50%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Homogeneous decrease*</td>
<td>Heterogeneous decrease</td>
<td>Homogeneous decrease*</td>
<td>Heterogeneous decrease</td>
</tr>
<tr>
<td></td>
<td>Change‡</td>
<td>Change‡</td>
<td>Change‡</td>
<td>Change‡</td>
</tr>
<tr>
<td>Mean fecundability</td>
<td>0.231</td>
<td>0.215 – 6.9%</td>
<td>0.213 – 7.8%</td>
<td>0.195 – 15.6%</td>
</tr>
<tr>
<td>Mean age at maternity</td>
<td>29.0</td>
<td>29.0 – 0.0%</td>
<td>29.0 – 0.0%</td>
<td>29.0 – 0.0%</td>
</tr>
<tr>
<td>Mean final number of children</td>
<td>1.50</td>
<td>1.48 – 1.4%</td>
<td>1.47 – 2.3%</td>
<td>1.46 – 3.0%</td>
</tr>
<tr>
<td>Mean time to first conception (months)</td>
<td>11.7</td>
<td>12.1 – 3.4%</td>
<td>13.4 – 14.5%</td>
<td>12.5 – 6.8%</td>
</tr>
<tr>
<td>TTC1 ≥ 1 year (per 100 1st births)</td>
<td>22.0</td>
<td>23.7 – 7.7%</td>
<td>26.5 – 20.5%</td>
<td>25.3 – 15.0%</td>
</tr>
<tr>
<td>Infertile after 5 years (per 100 married)</td>
<td>14.6</td>
<td>15.0 – 2.7%</td>
<td>15.9 – 8.9%</td>
<td>15.2 – 4.1%</td>
</tr>
<tr>
<td>Childless couples (%)</td>
<td>17.9</td>
<td>18.3 – 2.2%</td>
<td>18.6 – 3.9%</td>
<td>18.7 – 4.5%</td>
</tr>
<tr>
<td>Couples involuntarily childless (%)</td>
<td>11.3</td>
<td>11.6 – 2.7%</td>
<td>13.9 – 23.0%</td>
<td>12.1 – 7.1%</td>
</tr>
<tr>
<td>Couples with fewer births than wanted (%)</td>
<td>7.7</td>
<td>8.4 – 9.1%</td>
<td>10.1 – 31.2%</td>
<td>9.0 – 16.9%</td>
</tr>
<tr>
<td>Couples with more births than wanted (%)</td>
<td>18.2</td>
<td>17.0 – 6.6%</td>
<td>16.7 – 8.2%</td>
<td>15.7 – 13.7%</td>
</tr>
<tr>
<td>Unplanned births (per 100 births)</td>
<td>20.7</td>
<td>19.3 – 6.8%</td>
<td>19.4 – 6.3%</td>
<td>18.1 – 12.6%</td>
</tr>
</tbody>
</table>

*Fecundability level multiplied by a given factor (K = 0.93 and 0.85, respectively) for all the population, compared to the distribution in the initial population.
†Fecundability unchanged for all couples of the initial population above a given fecundability threshold (S = 0.2), and set to a given value below the threshold for the rest of the population (K = 0.7 and 0.4, respectively). K has been chosen to give a mean fecundability similar to the homogeneous case. Relative change compared to the initial population. §Time to conception. ART, assisted reproduction technology. Fecundability: the monthly probability of pregnancy among sexually active non-contraceptive couples.

over the last two decades and the second one would reflect more drastic changes in couples' behavior. Results are shown in Table IV.

Impact of ART on fertility rate

Our model identifies couples eligible for ART but does not assume that these eligible couples indeed resort to ART. Since ART could impact on the fertility rate, we combined our estimates of the number of couples eligible for ART with previously published age-specific estimates of success rates of ART (Leridon, 2005). We used the net success rates of ART as estimated in our previous work (Leridon, 2004), to take into account the fact that a fraction of couples undergoing ART would have had a child even in the absence of ART. The number of additional births that could be expected if all eligible couples were using ART (two IVF or ICSI attempts on average) is equal to the proportion eligible, times the rate of success, times 1.26 to account for multiple births (Andersen et al., 2006). We also assumed that in case of failure of the inseminations, 50% of the couples would make a second attempt 2 years later.
Results

The initial characteristics of the simulated population are given Table I.

Effects of a decline in fecundability

In Table II, we show the impact of three homogeneous reductions in fecundability, when the initial fertility is 2.0 children: fertility was reduced by <1 and 2%, when fecundability decreased by 7 and 15%, respectively. The mean age at maternity did not vary when fecundability decreased by 7 or 15%; this is because the mean time to conception is only lengthened by 1 month, and the (small) reduction in final fertility is concentrated on births of higher orders. The increase in the proportion of couples with fewer children than wanted corresponded to 1 and 5%, respectively. The last and extreme assumption, based on a halving of fecundability, had greater impacts: fertility was reduced by 8%; 19% of couples had fewer children than wanted (compared with 15% in the initial population), and 38% of couples waited more than 1 year to get their first conception (compared with 20% in the initial population, hence a doubling in frequency).

When the reduction in fecundability affected only the couples already below a given threshold (heterogeneous hypothesis), the effects were somewhat higher than in the homogeneous case, especially when the average reduction was 15%: starting from a fertility of 2.0, fertility was reduced by 4%, the proportion of couples with fewer children than wanted was increased by 23% and the frequency of 5 year involuntary infertility was increased by 54% (Table II).

The effects of the same changes in fecundability, when the initial fertility level was 1.5 child per woman, are shown in Table III. They are often greater than in the previous cases, but not substantially. Total fertility was, e.g. decreased by 10% in the worst case (fecundability reduced by 50%), as compared with 8% when the initial fertility was 2.0 children.

The proportion of couples eligible for ART was 11.6% in the initial population when fecundity was 2.0 (Table II) and rose to 20.1% when fecundability decreased by 15% (in the heterogeneous case), a relative increase by 73%. Therefore, the relative impact of a decline in fecundability is much higher on the proportion of couples eligible for ART than on the fertility rate. When the initial fertility rate was 1.5, the relative increase in the proportion of couples eligible for ART was 100% (Table III).

Effects of the postponement of childbearing

When mean age at first pregnancy attempt increased from 25.1 to 27.6 years fertility was reduced by 5.2%; a further 3 years reduced fertility by 11.9% compared with the initial population (Table IV). The proportion of couples remaining childless increased substantially when childbearing attempts were postponed by 6 years (from 11.7 to 17.7%, an increase by 51%), as well as the proportion of couples ending with fewer children than wanted (from 14.8 to 24.0%, an increase by 62%). The proportion of couples suffering from 5 year involuntary childlessness increased also dramatically (by 46% in the first hypothesis and 86% in the second); the proportion of couples eligible for ART rose also quite significantly (by, respectively, 32 and 79%): more than one couple out of five would be eligible for ART in the second hypothesis.

Finally, Fig. 1 allows for some comparison between the consequences of a decline in fecundability and of a postponement of the first birth. The effects of a decline in fecundability and of a postponement of the first birth on fertility are both limited. In rough numbers, a decline by 30% in fecundability is equivalent to an increase by 2.5 years in the spacing between marriage and age at first attempt to conceive, and a decline in fecundability of 50% to a spacing increased by 5 years.

Taking ART into account

When we assumed that all couples who were eligible for ART resorted to it, the fertility rate in the initial population was 2.04 (Table V). A decline in fecundability by 15% (heterogeneous situation) resulted in a fertility rate equal to 1.99, which corresponds to a relative decline by 2.5%, smaller than our previous
estimate of 4.0% in a situation without resort to ART. If only half of eligible couples resort to ART, the relative decline due to the same reduction in fecundability would be 3.5%.

Similarly, when we assumed that all couples eligible to ART resorted to it, a postponement by 30 months in the delay between marriage and start of a pregnancy attempt induced a decrease from a value of 2.04 to 1.95 in the fertility level, or a relative decrease by 4.4%, close to the decrease by 5.0% observed when no couple was supposed to resort to ART (Table V). If 50% of the eligible couples resort to ART, then the postponement by 30 months in the delay between marriage and start of a pregnancy attempt induced a relative decrease by 5.0% in the fertility level, a relative change very close to what is observed in the absence of ART (Table V).

**Discussion**

Using a Monte–Carlo simulation approach based on a detailed population model taking into account the age dependence of biological fecundity, rate of fetal loss and sterility as well as the distribution of age at entry in union observed in France for the 1968 birth cohort (or approximately in year 2000), we estimated the consequences of a decline in fecundability and of a postponement of age at childbearing.

**Assumptions concerning the decline in fecundability**

Our results concerning the effect on fertility of a decline in fecundability were relatively robust to the shape of the decline in fecundability. This was not the case for variations in the proportions of couples with fewer children than planned or eligible for ART, which were greater when fecundability was assumed to decline only for couples, who initially had a fecundability level below a given threshold (heterogeneous decline) than when fecundability declined homogeneously within the population.

The heterogeneous shape of decline may be more coherent with the decline in fecundability being due to a decline in sperm concentration, since sperm concentration influences fecundability only below a threshold of 40–50 millions spermatozoa/ml. Declines in fecundability may also be caused by other seminal characteristics or by female-mediated factors. Some recent behaviors or emerging epidemics might be detrimental to a man or a couple’s fecundity, such as male overweight (Jensen et al., 2004a,b; Sallmen et al., 2006) or smoking. Indeed, the effect of maternal smoking during pregnancy, a behavior that became more frequent in many countries since the middle of the 20th century, appears to be a potential major threat to the future fecundity of the son (Storgaard et al., 2003; Jensen et al., 2004a,b) or the daughter (Jensen et al., 1998). The potentially negative effects on fecundity of some pollutants affecting the general population have also been documented. This is the case for chemical compounds acting as endocrine disruptors, such as phthalate esters (Jonsson et al., 2005; Hauser et al., 2006, 2007), pesticides (Cohn et al., 2003; Swan et al., 2003; Meeker et al., 2004), polychlorinated biphenyls (Cooper et al., 2005; Windham et al., 2005) and maybe also of drinking water (Fenster et al., 2003) and air pollutants (Selevan et al., 2000; Rubes et al., 2005).

**The effectiveness of ART**

We also reported the estimated effects of a decline in the couples’ fecundity and of a postponement of age at the start of a pregnancy attempt assuming that 50 or 100% of couples eligible for ART resorted to ART (Table V). When ART is

<table>
<thead>
<tr>
<th>Initial population (before change)</th>
<th>Reduction in fecundability:</th>
<th>Additional postponement:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>15%, homog.</td>
<td>15%, heterog.</td>
</tr>
<tr>
<td>TFR without ART</td>
<td>2.00</td>
<td>1.96</td>
</tr>
<tr>
<td>TFR if all eligible use ART</td>
<td>2.04</td>
<td>2.00</td>
</tr>
<tr>
<td>TFR if 50% eligible use ART</td>
<td>2.02</td>
<td>1.98</td>
</tr>
</tbody>
</table>

**Figure 1:** Effects on total fertility, the proportion of couples infertile after 5 years and on the proportion of couples eligible for assisted reproduction technologies (ART) of (A) a reduction in fecundability and (B) an increased spacing of first birth (initial fertility: 2.0 children).
taken into account, the increase in fertility (TFR, total fertility rate) is too limited to compensate for the births ‘lost’ by the decline in fecundity or the postponement of pregnancies. Use of ART by 50% of the couples, who were eligible—a rather high rate for a real population—would make up for only about one-fifth of the births lost by an additional postponement of 30 months for pregnancy attempts in the French population: \((1.92 \rightarrow 1.90)/(2.00 \rightarrow 1.90)\), or one-third of births lost by a 15% reduction in fecundability ((1.95 \rightarrow 1.92)/(2.00 \rightarrow 1.92)). This is less than estimated by Hoorens et al. (2007) with a different approach, partly because these authors assumed that if a couple undergoes ART, the probability of conceiving naturally would be permanently zero. We believe that such an assumption is inaccurate.

In conclusion, relatively important declines in fecundability entailed modest changes in the mean number of children, but could imply rather strong relative variations in the proportion of couples suffering from 5 year involuntary infertility as well as in the proportion of couples eligible for ART. A postponement by 2.5 years in the mean age at start of a pregnancy entailed modest changes in the mean number of children, but that such an assumption is inaccurate.

1.92)). This is less than estimated by Hoorens et al. (2007) with a different approach, partly because these authors assumed that if a couple undergoes ART, the probability of conceiving naturally would be permanently zero. We believe that such an assumption is inaccurate.

In conclusion, relatively important declines in fecundability entailed modest changes in the mean number of children, but could imply rather strong relative variations in the proportion of couples suffering from 5 year involuntary infertility as well as in the proportion of couples eligible for ART. A postponement by 2.5 years in the mean age at start of a pregnancy attempt had, similarly, a limited effect on fertility, and a strong influence on the proportion of couples suffering from 5 year involuntary infertility as well as in the proportion of couples eligible for ART. A wide use of ART would make up for only a small part of the reduction in fertility.

**Funding**

R. Slama benefited of a joint grant from INSERM (Paris, France) and Helmholtz Center Munich, Institute of Epidemiology (Neuherberg, Germany) during part of the project.

**References**


Rubes J, Selevan SG, Evenson DP, Zudova D, Vozdova M, Zudova Z, Robbins WA, Perreault SD. Episodic air pollution is associated with increased DNA


Skakkebaek NE, Rajpert-De Meyts E, Main KM. Testicular dysgenesis syndrome: an increasingly common developmental disorder with environmental aspects. *Hum Reprod* 2001;16:972–978.


Submitted on December 18, 2007; resubmitted on February 22, 2008; accepted on March 10, 2008