Infertility in NZ: impact of delaying starting a family

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This brief paper summarises a talk given at the workshop entitled 'Sub-replacement fertility: is this an issue for New Zealand?' held by the Institute of Policy Studies, Victoria University of Wellington, 26 October 2006.

Data from infertility treatment provides lessons on biological constraints to fertility and the consequence of these biological constraints on social trends in delaying starting a family.

It is useful to check the terms for discussion. Here 'fertility rate' is the number of women having a child per year; 'fecundability' the chance of pregnancy per month or treatment cycle, and 'infertility' the condition of not being pregnant after at least a year of trying to do so. This use of 'infertility' could more properly be called 'infecundity'.

Jane Menken and her colleagues (1986) sought to uncover the maximum potential fertility of women according to age by looking at populations with little or no family limitation. In ten populations taken from the 17th, 18th and 19th century and Hutterites and Iran villagers in the early 20th century, the fertility rate ranged between 400 and 550 per 1000 women aged 20-25 years (Figure 1). On average these women would have spent 2-4 months falling pregnant, 9 months carrying the child and around a year breast feeding before starting again.

Figure 1. Children per 1000 women per year by age

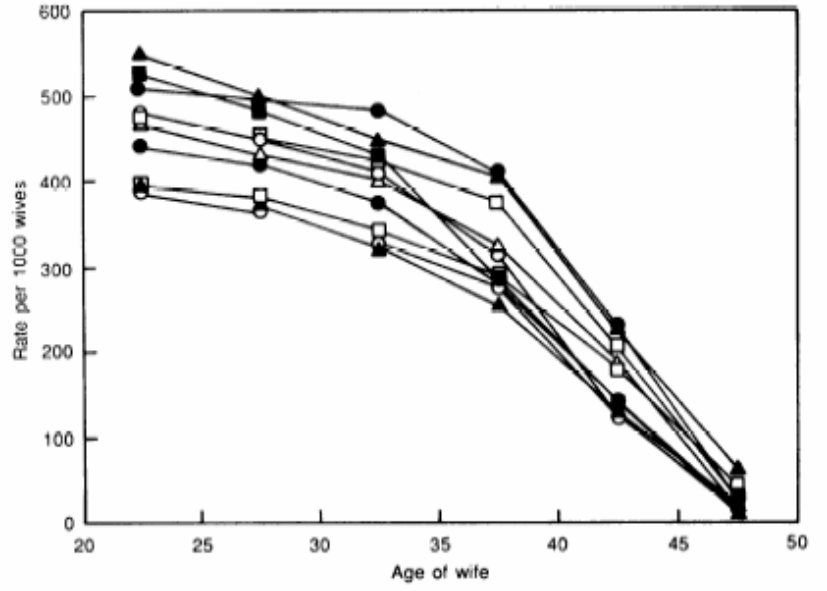


Fig. 1. Marital fertility rates by 5-year age groups (5). The ten populations (in descending order at age 20 to 24) are Hutterites, marriages 1921–30 (▲); Geneva bourgeoisie, husbands born 1600–49 (■); Canada, marriages 1700–30 (●); Normandy, marriages 1760–90 (○); Hutterites, marriages before 1921 (□); Tunis, marriages of Europeans 1840–59 (△); Normandy, marriages 1674–1742 (●); Norway, marriages 1874–76 (□); Iran, village marriages, 1940–50 (▲); Geneva bourgeoisie, husbands born before 1600 (○).

By the age of 40-45, the fertility rate had fallen to a little less than half that experienced by 20-25 year olds. To rule out a contribution from progressive loss of fertility due to complications of pregnancy, Menken et al also looked at the proportion of women having at least one child by woman's age at marriage – again the proportion at 40-44 was a little less than a half that at 20-25 (Figure 2).

Figure 2. Woman having at least one child by age at marriage

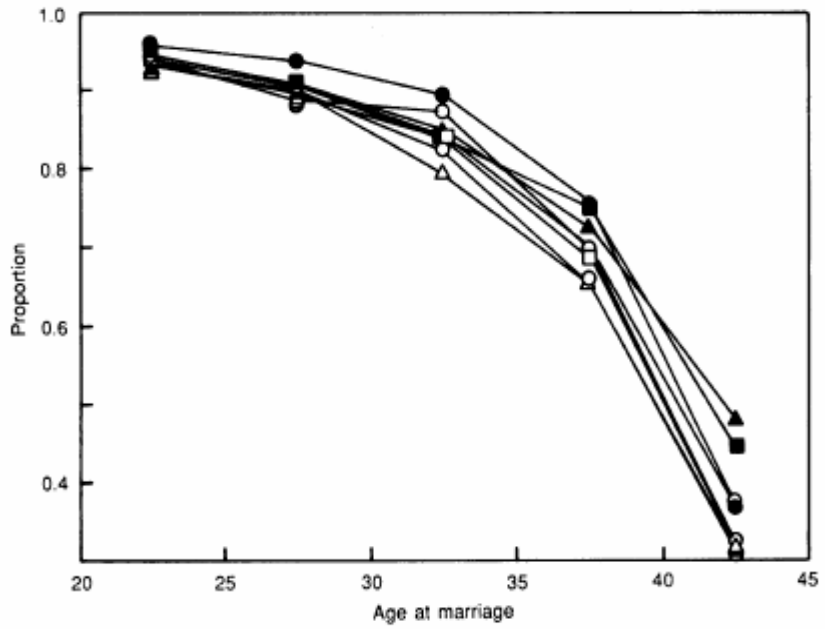
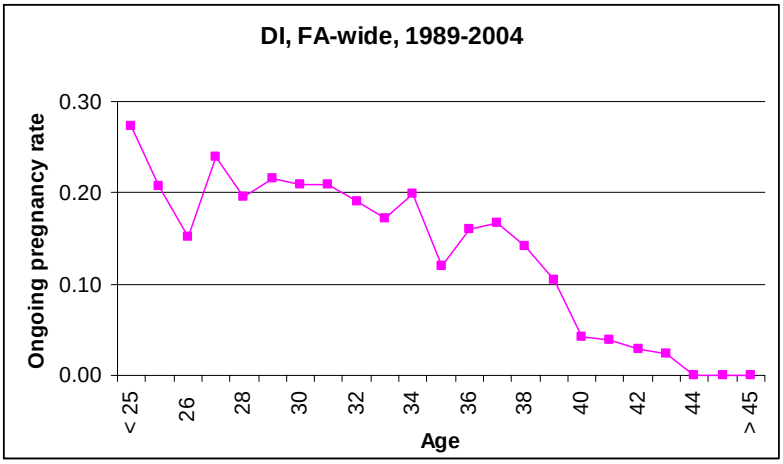


Fig. 2. Proportions having at least one child by 5-year age group at marriage and estimated typical pattern (5). The populations (in descending order at age 35 to 39) are Germany, 14 village genealogies, marriages 1750–1899 (●); England, family reconstitution of 16 rural parishes (mid-16th to early 19th centuries) by the Cambridge Group for the History of Population and Social Structure (■); Ireland, 1911 census (▲); typical pattern (—); England, family reconstitution for Quakers (○); Quebec, rural women born before 1876 (□); Scotland, 1911 census (○); and Quebec, 1946 census, rural women born 1876–85 (△).

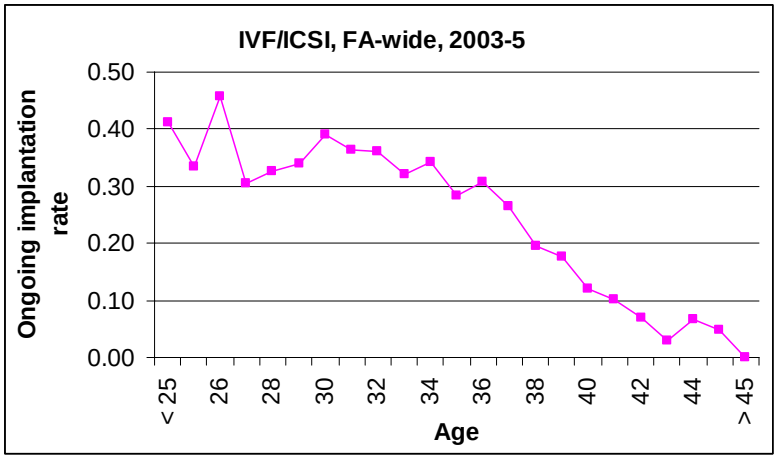
Donor insemination (DI) provides the closest parallel to a normal population within fertility treatment, as it treats putatively normal women whose partners have no or almost no sperm or single women or women in lesbian relationships. Since 1989, age-specific DI pregnancy rates at Fertility Associates clinics have been stable through the use of intrauterine insemination of washed sperm to increase efficiency and algorithms to ensure insemination within 12 hours or so of ovulation. The results of over 6000 DI cycles shown in Figure 3 demonstrate a relatively constant birth rate until age 35, then a drop to virtually zero by age 45. The data in this figure excludes DI cycles using any ovarian stimulation hormones.

Figure 3. Ongoing pregnancy rate (birth rate) in DI treatment by woman's age



IVF treatment is more complex than DI, treating a variety of causes of infertility. Treatment includes ovarian stimulation to produce several eggs in the cycle of treatment, with the best one or two embryos being transferred, and any extra good quality embryos being frozen for later use. Figure 4 shows ongoing implantation rate per fresh embryo transferred at Fertility Associates clinics for IVF undertaken between 2003 and 2005, when pregnancy rates were stable following a period of rapid improvement.

Figure 4. Ongoing implantation rate (birth per embryo transferred) in IVF by woman's age



Again, rates are relatively constant until around 35 (allowing for noise due to few cycles in women younger than 27), and then fall to zero by 45. Absolute rates are higher at 35% per embryo for woman until their mid-30's compared to 20% per cycle in DI because IVF allows choice of the best embryo, whereas in natural menstrual cycles only one egg is ovulated. Adjusting for scale, the fall in IVF and DI rates with woman's age are virtually identical. The birth rate of 20% per cycle in DI in younger women is typical of estimates of fecundability in modern populations.

The fertility clinic data and the Menken data are entirely compatible. For instance, with a pregnancy rate of 20% per month, almost all women aged 20-30 without sterility would be expected to become pregnant within the next 3 years. Using fecundability (monthly pregnancy rates) of 3%, 2%, 1% and 0% for women aged 42, 43, 44 and 45, around 50% of women starting for a pregnancy at 42 would have become pregnant before their time ran out at 45.

Of course reality is more complicated than this – fecundability at a particular age will follow an underlying distribution rather than being a constant, and some women will have profound infertility or even sterility. Nevertheless, the principle and approximation holds.

The fall in fecundability with age, especially after 35, has a strong biological basis. Women have a maximum number of eggs before birth. By birth the number has fallen to around 300,000, by puberty to some 100,000, by 35 to 30,000, and at menopause to around 1000 (Faddy et al, 1992). Loss of fertility precedes menopause by about a decade. Figure 5 shows egg number by age from autopsy data.

Figure 5. Egg number in women by age

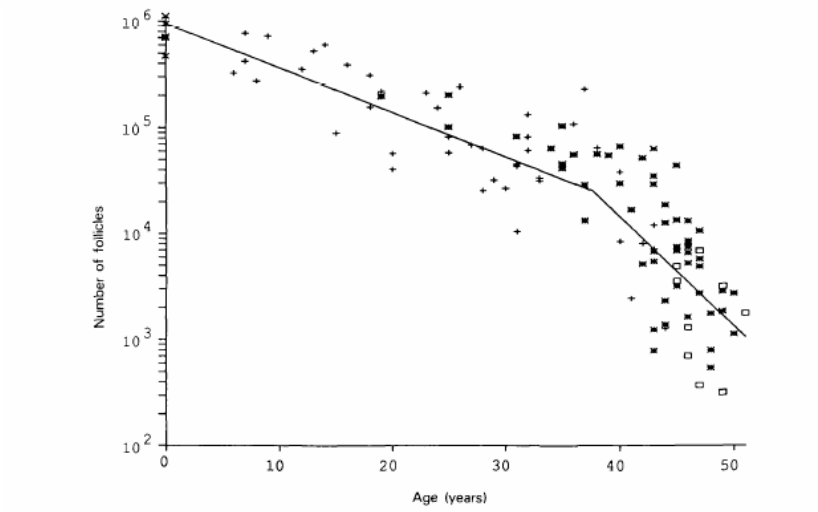


Fig. 1. Bi-exponential model of declining follicle numbers in pairs of human ovaries from neonatal age to 51 years old. Data were obtained from the studies of Block (1952, 1953) (×, $n = 6$; +, $n = 43$), Richardson *et al.* (1987) (□, $n = 9$) and Gougeon (unpublished) (*, $n = 52$).

About 10% of women enter menopause a decade earlier than average, and 1% two decades earlier. There are diagnostic tests, though imperfect, that attempt to predict who might have a lower ovarian reserve than average.

Study of human eggs obtained during IVF suggests that even in younger women 50-75% of eggs are chromosomally abnormal (Wilton, 2004). The incidence of abnormalities increases greatly beyond age 35, resulting in lower pregnancy rates, higher miscarriage rates and an exponential rise in the chance of a child having a chromosomal disorder, particularly Down Syndrome. It is not yet known how the number of eggs in the ovary and chromosome abnormally in individual eggs are causally related with age.

Even though IVF treatment restores (or through embryo selection even improves) fecundability, the fall after 35 has a profound impact for infertile couples. For potentially fertile couples, a lower fecundability means needing to try on average longer to achieve pregnancy, which is ‘fun and free’. For couples who need treatment to restore their fecundability, treatment is invasive and expensive, and needing more treatment because of advanced age is an extra burden. The cost of a single IVF treatment cycle ranges between NZ$ 7000 and 10,000 depending on the techniques used and the amount of drugs required. Public funding of infertility treatment in New Zealand is severely restricted with a maximum of two cycles in a couple’s lifetime, and then only if stringent eligibility criteria are met. Criteria include the woman being 39 or younger, not being overweight, and not smoking. Having children aged 12 or younger reduces points for eligibility, as does a shorter duration of infertility. Couples with ‘unexplained’ infertility need to wait 5 years to become eligible.

The major decision facing infertile couples without an absolute cause of infertility is for how long to try themselves before seeking treatment. Among younger women, about 90% will become pregnant within 12 months, and about 55% of the rest will become pregnant within the following 3 years; whereas thereafter conceptions are sporadic (Gnoth etal, 2005). For those starting in their mid-30's, there is insufficient time to try for up to four years without eroding their chance of success on treatment if they do not become pregnant by themselves.

This would not be too much a problem if most people presented with infertility in their late 20's or early 30's. However, the average age at first medical consultations for infertility is now 35-36 in Auckland and Wellington, and has increased by 12 months over the past 6 years. The average age of private IVF treatment has been increasing in parallel with the average age of birth in New Zealand, but about 6 years later. Thus as the average age of women giving birth has increased from 27 to 31 between 1987 and 2005 in New Zealand, the average age at private IVF treatment has climbed to 37. Age trends among those having publicly funded treatment have been blurred by reductions in the waiting lists, the advent of a second treatment cycle for those not pregnant after the first, and an upper age of 39, but the average age at treatment is around 35.

In summary, the trend to delay the onset of starting a family now means at least half those seeking fertility treatment have their chances eroded due to the woman's age.

Donor insemination treatment is likely to offer a reasonable approximation of fecundability by woman's age, and both DI and IVF data can be used to calculate how fecundability falls with age. These data could be used to estimate key parameters to model the impact of age shifts in starting a family and shifts in birth interval on the number of children born annually in a population, and hence how changes in these are other factors could encourage or inhibit population replacement.

References

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