# Advanced maternal age

Tracey A Mills Tina Lavender

# Abstract

Delayed childbearing is a growing trend in developed countries. Between 1982 and 2012, the number of live births to UK women over 40 more than quadrupled. This accelerating demographic shift is of major clinical and public health concern, because advanced maternal age has consistently been associated with adverse pregnancy outcomes. Current evidence suggests increased risk of miscarriage, ectopic pregnancy and stillbirth. Most studies also report elevated maternal morbidity resulting from hypertensive disorders and gestational diabetes. Many questions remain unanswered regarding the underlying mechanisms. The contribution of age per se versus co-morbidities is unclear, as is the age threshold at which increased risks become significant. Despite the increased risks, there are potential psychological and social advantages to delaying childbirth and absolute numbers of complications are small. Further studies are required to develop effective strategies to reduce poor outcomes and provide optimal care for pregnant women of advanced age.

Keywords maternal age; pregnancy complications; pregnancy outcome; stillbirth

# Background

The UK Office of National Statistics (ONS) recently reported that the mean age for women giving birth in England and Wales had risen to 29.8 years in 2012, a continuation of the increase in maternal age reported since 1976. Fertility rates for women aged less than 25 years are falling, with the largest percentage decline observed in women under 20. In contrast, fertility rates amongst women aged 35–39 and 40 and over continue to increase, by 53% and 66% respectively, between 2001 and 2011. These data reflect an accelerating demographic shift; over the past three decades the number of live births to women over 40 years in England and Wales more than quadrupled from 6519 in 1982 to 29994 in 2012 (Figure 1).

Advanced maternal age, usually defined as pregnancy at the age of 35 years and over, has also become increasingly common in other developed countries. Despite declining fertility overall in the USA, births to women over 40 continue to rise and the age first birth has increased from 21.4 in 1970 to 25.4 in 2010. In Australia, of women having their first birth, 42% were over 30 and 15% over 35 in 2008. Changes in gender roles, especially the increased focus on educational and career goals for women, are

**Tracey A Mills PhD MA BSC RM** is a Lecturer in Midwifery at the School of Nursing, Midwifery and Social Work, University of Manchester, UK. Conflicts of interest: none.

**Tina Lavender PhD MSC RM** is Professor of Midwifery at the School of Nursing, Midwifery and Social Work, University of Manchester, UK. Conflicts of interest: none.

often cited as important factors underlying this phenomenon. However, there have been few detailed examinations of the reasons for the increase in delayed childbirth; effective contraception, assisted reproductive technologies and changing patterns of family building, including increased divorce and remarriage are also likely to contribute.

# Introduction

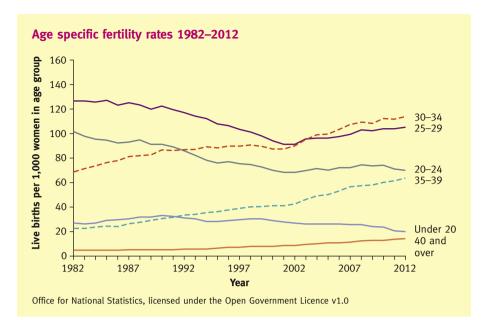
The demographic shift towards later childbearing has become a major clinical and public health concern because advanced maternal age has been associated with poor pregnancy outcomes. The UK Confidential Enquiry report for 2006–2008 confirmed the findings of the previous triennium, of significantly increased maternal mortality from all causes amongst older women. There were 9.7 maternal deaths per 100,000 maternities among women aged 25–29, rising to 18.8 in women aged 35–39 and 29.2 in women over 40. There are also consistent reports that the risk of fetal loss due to miscarriage, ectopic pregnancy and stillbirth increases significantly after the age of 35 (Figure 2).

Provision of appropriate support and care to the increasing number of older women becoming pregnant relies on a clear understanding of the risks. Although numerous studies have investigated the association between advanced maternal age and pregnancy complications, the data is conflicting. There is limited consensus regarding the magnitude and relative importance of particular risks and several important questions remain unanswered; it is not clear whether increased risks relate to age per se or the presence of co-morbidities. Secondly, evidence concerning the age threshold at which adverse outcomes become significant is limited. Some studies have suggested this occurs after 35 years, while others contend that the association is only clinically important at age 40. Kenyon and Bewley assert that the literature surrounding advanced maternal age should be interpreted cautiously because of important limitations in existing studies. Despite the considerable increase in births, older women account for a small percentage of the overall maternity population; around 10-20% of women are over 35 and 2-4% are over 40. Therefore, large sample sizes are needed to assess the effect of age on adverse outcomes which are infrequent, such as stillbirth. However, the largest studies are retrospective examinations of national birth registers which collect limited data. It is therefore often impossible to control adequately for variables which are likely to influence outcome, for example the children of older women may be fathered by older men. The age range of the control groups used for comparison varies considerably between studies (examples include 20-30, 25-29, under 35 years). In addition to the increased incidence of co existing medical conditions, women of advanced age are more likely to be primiparous, use assisted reproductive technologies (ART) including ovarian stimulation and in vitro fertilisation, and have multiple pregnancies. All of these are independent risk factors for poor pregnancy outcomes.

#### Antenatal risks

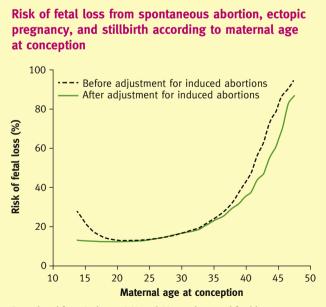
# Early pregnancy

Around the age of 35, female fertility begins to decline sharply due to a progressive decrease in the numbers and quality of oocytes. Older women take longer to conceive and are therefore





more likely to seek ART. Unfortunately, ART (including IVF) are significantly less successful than in younger women without recourse to donor eggs. If pregnancy is achieved, advanced maternal age is strongly associated with an increased risk of miscarriage. In a study of the Danish National Birth Registers, Nybo-Andersen et al. reported that the risk of miscarriage in recognised pregnancies for women aged 35–39 was 24.6%, rising to 51% in women aged 40–44 and 93.4% in women aged 45 or older, compared to 11.1% for women aged 20–24. The risk was unrelated to parity or previous reproductive history,



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Figure 2

suggesting an independent effect of age. The high rate of miscarriage in older women is thought to result predominantly from impaired oocyte quality, defective chromosome segregation and aneuploidy. There is also an increase in euploid losses, suggesting that uterine factors might also contribute. The incidence of ectopic pregnancy also increases with maternal age; Nybo-Andersen et al. reported rates of 1.4% at age 21, rising to 6.9% at 44 years or older. This is likely to relate to an increased frequency of tubal pathologies in older women and the greater use of ART, which has an independent effect in increasing the risk of ectopic pregnancy.

An increased incidence of chromosomal disorders including trisomies 13 (Patau syndrome), 18 (Edwards' syndrome) and 21 (Down syndrome) is the most well recognised risk of advanced maternal age amongst health professionals and women themselves. The likelihood of Down syndrome, the most common trisomy, rises from around 1:1300 at maternal age 25 to 1:100 at 40 and 1:30 at age 45. However, 80% of Down syndrome children are born to women under 35 and therefore the UK National Screening Committee advises that all pregnant women are offered Down syndrome screening, irrespective of age. The first trimester combined test (nuchal translucency,  $\beta$  human chorionic gonadotrophins ( $\beta$ hCG) and pregnancy associated protein-A (PAPP-A)), which is performed between 11 + 0 and 13 + 6 weeks, is the preferred screening test.

# Hypertensive disorders

The incidence of hypertension in non-pregnant women increases with age, notably after the age of 40. Therefore, older women are more likely to enter pregnancy with pre-existing hypertension. Mild to moderate chronic hypertension usually has only limited impact on maternal wellbeing during pregnancy, although it is associated with significant perinatal mortality resulting from fetal growth restriction (FGR) and placental abruption. Severe and longstanding hypertensive disease (especially when complicated by renal and vascular impairment) can lead to significant Download English Version:

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