Elevated risks of pregnancy complications and adverse outcomes with increasing maternal age

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BACKGROUND: In the USA, between 1980 and 2004, the proportion of all births increased 2-fold in women aged ≥30, 3-fold in women aged ≥35 and nearly 4-fold in women aged ≥40. The objective of this study was to evaluate the risks of pregnancy complications and adverse outcomes with increasing maternal age using national vital statistics data. METHODS: The study population included 8,079,996 live births of singletons of ≥20 weeks among women aged 30–54 from the 1995–2000 US Birth Cohort Linked Birth/Infant Death Data Set. Outcomes were modelled by maternal age and parity using multinomial logistic regression to calculate adjusted odds ratios (AORs) and 95% confidence intervals. RESULTS: The risks for most outcomes paralleled increasing maternal age including prolonged and dysfunctional labour, excessive labour bleeding, breech and malpresentation and primary Caesarean delivery. The highest AORs among women aged ≥45 versus 30–34 by parity (primiparas and multiparas, respectively) were for chronic hypertension (3.70, 4.89), diabetes (2.19, 2.58), primary Caesarean (3.14, 2.85), excessive labour bleeding (1.54, 1.49), pregnancy hypertension (1.55, 2.13) and birth <32 weeks (2.11, 1.77). CONCLUSIONS: Increasing maternal age is associated with significantly elevated risks for pregnancy complications and adverse outcomes, which vary by parity.

Key words: adverse outcomes/Caesarean birth/maternal age/pregnancy complications

Introduction

In the USA, there has been a long-term trend of child bearing at older ages, with contemporary birth rates for women aged ≥30 at their highest levels since the mid-1960s (Martin et al., 2006). Between 1980 and 2004, the proportion of first births increased 3-fold in women aged ≥30 (from 8.6 to 25.4%), 6-fold in women aged ≥35 (from 1.3 to 8.3%) and 15-fold in women aged ≥40 (from 0.1 to 1.5%) (Martin et al., 2006). A similar pattern has occurred for all births during this same time period, with increases of 2-fold, 3-fold and nearly 4-fold, respectively, in each of the three age groups. Births to women aged ≥50 have been available in national statistics since 1997 and have averaged an annual increase of 14%. This shift in age at childbearing is in part attributed to the increased availability and widespread use of fertility-enhancing therapies. With assisted reproduction technology (ART) and the use of donated oocytes for older women, the upper age boundary for conception and pregnancy has been redefined (Paulson et al., 2002). More than half of all IVF cycles are among women aged ≥35, and between 1998 and 2003 (the most recent year for which data are available), the number of cycles increased by >39% (Centers for Disease Control and Prevention, Society for Assisted Reproductive Technology (SART), 2005). In ART pregnancies, the proportion of women who use donor eggs increases exponentially after years of age 40 (<5% of cycles among women <35 years of age to 77% of cycles among women >45 years of age) (Center for Disease Control and Prevention, SART, 2005). A growing body of literature suggests an excess of adverse outcomes in pregnancies after infertility treatment, but the etiology is unclear—older maternal age is likely a contributing factor, as well as the underlying cause of the infertility (Dhont et al., 1999; Helmerhorst et al., 2004; Jackson et al., 2004; Schieve et al., 2004; Shevell et al., 2005; Wang et al., 2005; Ombelet et al., 2006; Romundstad.
et al., 2006). Older women are disproportionately represented among the population treated for infertility, particularly older primiparas. An increasing proportion of births is the result of ART (ranging from 1.2% in the USA to 4.2% in Denmark) (Andersen et al., 2006), making the health consequences of childbearing at older ages of national and international importance. The objective of this study was to evaluate the risks for pregnancy complications, including Caesarean birth, with advancing maternal age among women pregnant with singletons aged ≥30.

Materials and methods

The data set for this study includes the Birth Cohort Linked Birth/Infant Death Data Set (1995–2000) from the National Center for Health Statistics. For the Linked Birth/Infant Death Data Set, the birth certificates are linked to the infant death certificates if the death occurred before 1 year of age. The methodology takes advantage of two existing data sources: State-linked-files for the identification of linked birth and infant death certificates and National Center for Health Statistics (NCHS) natality and mortality computerized statistical files, the source of computer records for the two linked certificates. All States link infant death certificates to their corresponding birth certificates for legal and statistical purposes. The data have been coded according to uniform coding specifications, have passed rigid quality control standards, have been edited and reviewed and are the basis for official US birth and death statistics. Limitations in vital statistics death data include the change in coding from The International Classification of Diseases, Ninth Revision (ICD-9) to ICD-10 during the study period. For the Linked Birth/Infant Death Data Sets, the ICD-9 coding was used for all infant deaths in the 1995–98 data sets, and the ICD-10 coding was used in the 1999 and 2000 data sets.

The data were limited to liveborn singleton births in women aged ≥30. The characteristics of this data set are given in Table I. Institutional Review Board approval was not sought for this study because we used a public-use, de-identified data set.

Definitions of maternal risks

The maternal risks evaluated in this study, as reported in the birth certificate (Martin et al., 2006), included the following: Risk factors prior to or during pregnancy: diabetes—a metabolic disorder characterized by excessive discharge of urine and persistent thirst, which includes juvenile onset adult onset, and gestational diabetes during pregnancy; chronic hypertension—blood pressure persistently greater than 140/90 diagnosed prior to onset of pregnancy or before the 20th week of gestation. Pregnancy complications and adverse outcomes: pregnancy-associated hypertension—an increase in blood pressure of at least 30 mm Hg systolic or 15 mm Hg diastolic on two measurements taken 6 h apart after the 20th week of gestation; tocolysis—use of medications to inhibit preterm uterine contractions to extend the length of pregnancy and, therefore, avoid a preterm birth; premature rupture of membranes (>12 h)—rupture of the membranes at any time during pregnancy and >12 h before the onset of labour; birth <32 weeks and infant death (death from day 0 to day 364). Labour factors: induction of labour—the initiation of uterine contractions before the spontaneous onset of labour by medical or surgical means for the purpose of delivery; stimulation of labour—augmentation of previously established labour by use of oxytocin; precipitous labour—extremely rapid labour and delivery lasting <3 h; prolonged labour—abnormally slow progress of labour lasting >20 h; dysfunctional labour—failure to progress in a normal pattern of labour; excessive bleeding in labour and delivery—this risk was calculated as including the risk factors of abruptio placenta, placenta previa and other excessive bleeding during labour and delivery; breech or malpresentation—at birth, the presentation of the fetal buttocks rather than the head or other malpresentation. Mode of delivery: vaginal birth, vaginal birth after Caesarean (VBAC) (multiparas only), forceps, vacuum, primary Caesarean and repeat Caesarean (multiparas only). Low-risk pregnancies included those which were full-term (≥37 weeks gestation) and vertex (non-breech or malpresentation), as defined by Healthy People 2010 (US Department of Health and Human Services, 2000), plus the absence of congenital anomalies in the infant, as well as the absence of abruptio placenta, placenta previa or excessive bleeding during labour and delivery.

Causes of infant mortality

The causes of infant mortality are categorized into seven major groups, overall and by the four maternal age groups: (i) certain infectious and parasitic diseases; (ii) neoplasms and other diseases; (iii) congenital anomalies; (iv) conditions originating in the perinatal period; (v) sudden infant death syndrome; (vi) accidents, homicide and neglect; (vii) all other causes.

Statistical analysis

Descriptive statistics of the study population, including univariate analyses comparing across the four maternal age groups using analysis of variance for continuous variables and x² for categorical variables, are given in Table I. Odds ratios and 95% confidence intervals were computed from multinomial logistic regression models and estimated by the unconditional maximum-likelihood method, adjusting for maternal race (white, black and others) and smoking status (smokers, non-smokers and unknown), with women aged 30–34 as the reference group within parity groups for comparison of medical risk factors, pregnancy complications and adverse outcomes. Multinomial logistic regression is a logistic regression (binary outcome) where each level of maternal age group (30–34, 35–39, 40–44 and ≥45 years) was related to the baseline group (women aged 30–34), while controlling for covariates. Adjusting for maternal education, trimester of prenatal care and marital status did not significantly change the results and were not included in the final models. The models of infant death were additionally adjusted for the presence of congenital anomalies, with and without gestational age. Including maternal diabeties, chronic hypertension and excessive bleeding did not change the estimates and were not retained in the final models. The models of labour factors and mode of delivery by parity were additionally adjusted for macrosomia (birthweight >4000 g) and breech or malpresentation, as well as gestational age and the presence of congenital anomalies. Models of mode of delivery by primary Caesarean versus vaginal birth were analysed additionally within each maternal age group, comparing primiparas to multiparas without a prior history of a Caesarean birth, separately for all pregnancies and for low-risk pregnancies. All analyses were performed using the Statistical Package for the Social Sciences (SPSS) software, version 14.0 (SPSS, Chicago, IL, USA, 2006).

Results

The study population included 8 079 996 singleton pregnancies. As shown in Table I, all maternal characteristics differed significantly across age groups, with older mothers less likely to smoke and more likely to be of higher parity. Mean birthweight decreased and the proportion of low birthweight (<2500 g) and very low birthweight (<1500 g) increased
with advancing maternal age. The proportion of term births (≥37 weeks) decreased significantly with advancing maternal age for both primiparas and multiparas. The proportion of macrosomic infants (birthweights >4000 g) also differed across maternal age groups, but not in a consistent pattern. The proportion of low-risk pregnancies declined significantly with advancing maternal age.

The models of medical risk factors, pregnancy complications and adverse outcomes by parity and maternal age group are given in Table II. Among primiparas, the risks for all outcomes increased with advancing age, except for premature rupture of membranes; the highest risks for women ≥45 years compared with ages 30–34 were for chronic hypertension [adjusted odds ratio (AOR) 3.70], diabetes (AOR 2.19), birth <32 weeks (AOR 2.11) and pregnancy-associated hypertension (AOR 1.55). Among multiparas, a similar pattern was observed, with a generally steeper increase in risk with older age for all outcomes. The highest risks for multiparous women ≥45 years compared with women aged 30–34 were for chronic hypertension (AOR 4.89), diabetes (AOR 2.58), pregnancy-associated hypertension (AOR 2.13), birth <32 weeks (AOR 1.77) and infant death (AOR 1.55). When infant death is modelled without adjusting for gestation age, there is a significantly increased risk of death with advancing maternal age for both parity groups; after adjustment for gestational age, this pattern is still evident only among the multiparas.

The causes of infant death by maternal parity and age groups are given in Table III. Deaths due to congenital anomalies increased with advancing maternal age, accounting for more than one-third and one-half of infant deaths, respectively, among the oldest primiparas and oldest multiparas. Deaths due to conditions originating in the perinatal period accounted for more than half of all infant deaths to primiparas and 30–40% of all infant deaths to multiparas, regardless of age group.
Within age groups, the risk of primary Caesarean birth for
birth (AOR 3.15 for primiparas; AOR 2.85 for multiparas).
The models of labour factors by parity and maternal
age groups are given in Table IV. The factors that increased
with advancing maternal age for both parity groups included
induction of labour, prolonged and dysfunctional labour,
excessive bleeding and breech or malpresentation. For both
parity groups, the risk of stimulation of labour decreased
with advancing maternal age; for primiparas, the risk of precipi-
titous labour decreased as well. The highest risks for women
≥45 years compared with ages 30–34 among primiparas
were for excessive bleeding (AOR 1.73) and breech or malpresentation
of primary Caesarean birth increased with maternal
age; for multiparas, the risk of forceps and vacuum also
increased with age, but to a lesser extent. Also for both
parity groups, the risk of vaginal birth decreased with advanc-
ing age; for primiparas, the risk of vacuum also decreased;
for multiparas, the risk of a VBAC decreased. The highest
risk for both parity groups for women ≥45 years compared
with ages 30–34 was of primary Caesarean birth (AOR
3.14 for primiparas; AOR 2.55 for multiparas). The models
based on the low-risk pregnancy study population were
nearly identical to those for all pregnancies, with the
highest risk at the oldest age also for primary Caesarean
birth (AOR 3.15 for primiparas; AOR 2.85 for multiparas).
Within age groups, the risk of primary Caesarean birth for
multiparas compared with multiparas without a history of a
prior Caesarean birth was consistently more than 5-fold
greater at each age (AORs ranging from 5.54 to 5.90).
Among low-risk pregnancies, a similar pattern was seen,
with AORs ranging from 6.62 to 7.06 within each age
group. Because of the very low rate of VBAC, once a primi-
para delivers by Caesarean, it is a strong determinant of the
subsequent mode of delivery for her future pregnancies,
establishing a pattern for continued elevated rates of surgical
delivery.

### Discussion

Our results quantify the increase in pregnancy risk factors with
advancing maternal age, particularly for primary Caesarean
delivery and prolonged and dysfunctional labour. The
Healthy People 2010 targets for Caesarean delivery for
low-risk women (singleton, full-term pregnancy, vertex presen-
tation) are set at 15% for primiparas and 63% for multiparas
with a history of a prior Caesarean. Our results indicate that
contemporary rates are 80 and 17% higher, respectively
(27% for primiparas and 74% for multiparas) than these
national targets. Many factors have resulted in this high Caesarean
rate in the USA, as summarized in a recent editorial by
Resnick (2006), including medical malpractice, fear of birth
trauma and the potential risk of cerebral palsy due to difficult
vaginal deliveries and the perceived lower risk of stress
urinary incontinence and uterine and vaginal prolapse.
Recent analyses indicate that the rise in the primary Caesarean

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**Table II. Comparison of medical risk factors, pregnancy complications and adverse outcomes by maternal parity and age groups**

<table>
<thead>
<tr>
<th>Maternal age groups (years)</th>
<th>%</th>
<th>AOR*</th>
<th>%</th>
<th>AOR</th>
<th>95% CI</th>
<th>%</th>
<th>AOR</th>
<th>95% CI</th>
<th>%</th>
<th>AOR</th>
<th>95% CI</th>
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</tr>
<tr>
<td>Diabetes</td>
<td>3.5</td>
<td>1.00</td>
<td>4.8</td>
<td>1.39</td>
<td>1.37–1.41</td>
<td>6.1</td>
<td>1.81</td>
<td>1.75–1.86</td>
<td>7.2</td>
<td>2.19</td>
<td>1.94–2.47</td>
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<td>1.00</td>
<td>1.6</td>
<td>1.66</td>
<td>1.62–1.71</td>
<td>2.6</td>
<td>2.69</td>
<td>2.57–2.81</td>
<td>3.4</td>
<td>3.70</td>
<td>3.11–4.41</td>
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<td>Complications and outcomes</td>
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<tr>
<td>Pregnancy-associated hyperten(sion</td>
<td>5.0</td>
<td>1.00</td>
<td>5.6</td>
<td>1.13</td>
<td>1.11–1.14</td>
<td>6.2</td>
<td>1.28</td>
<td>1.24–1.31</td>
<td>7.4</td>
<td>1.55</td>
<td>1.37–1.75</td>
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<tr>
<td>Tocolysis</td>
<td>1.9</td>
<td>1.00</td>
<td>2.0</td>
<td>1.04</td>
<td>1.02–1.07</td>
<td>2.1</td>
<td>1.11</td>
<td>1.06–1.16</td>
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<td>1.12</td>
<td>0.91–1.39</td>
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<tr>
<td>Premature rupture of membranes</td>
<td>4.6</td>
<td>1.00</td>
<td>5.1</td>
<td>1.11</td>
<td>1.09–1.12</td>
<td>5.2</td>
<td>1.14</td>
<td>1.10–1.17</td>
<td>4.7</td>
<td>1.02</td>
<td>0.88–1.18</td>
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<tr>
<td>Birth &lt;32 weeks gestation</td>
<td>1.5</td>
<td>1.00</td>
<td>2.0</td>
<td>1.31</td>
<td>1.28–1.34</td>
<td>2.5</td>
<td>1.65</td>
<td>1.58–1.72</td>
<td>3.0</td>
<td>2.11</td>
<td>1.76–2.53</td>
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<td>1.00</td>
<td>0.6</td>
<td>1.27</td>
<td>1.22–1.33</td>
<td>0.7</td>
<td>1.36</td>
<td>1.25–1.48</td>
<td>0.8</td>
<td>1.54</td>
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<td>0.6</td>
<td>1.05</td>
<td>1.00–1.10</td>
<td>0.7</td>
<td>0.96</td>
<td>0.87–1.05</td>
<td>0.8</td>
<td>1.08</td>
<td>0.72–1.62</td>
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<tr>
<td>Diabetes</td>
<td>3.4</td>
<td>1.00</td>
<td>4.7</td>
<td>1.38</td>
<td>1.37–1.39</td>
<td>6.4</td>
<td>1.91</td>
<td>1.88–1.94</td>
<td>8.6</td>
<td>2.58</td>
<td>2.43–2.74</td>
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<td>Chronic hypertension (&lt;20 weeks)</td>
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<td>1.00</td>
<td>1.3</td>
<td>1.65</td>
<td>1.62–1.68</td>
<td>2.3</td>
<td>2.88</td>
<td>2.81–2.96</td>
<td>3.6</td>
<td>4.89</td>
<td>4.47–5.35</td>
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<td>Complications and outcomes</td>
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<tr>
<td>Pregnancy-associated hyperten(sion</td>
<td>2.4</td>
<td>1.00</td>
<td>2.9</td>
<td>1.20</td>
<td>1.19–1.21</td>
<td>3.7</td>
<td>1.59</td>
<td>1.56–1.63</td>
<td>4.7</td>
<td>2.13</td>
<td>1.97–2.30</td>
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<td>Tocolysis</td>
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<td>1.00</td>
<td>1.8</td>
<td>0.99</td>
<td>0.97–1.00</td>
<td>1.9</td>
<td>1.04</td>
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<td>Premature rupture of membranes</td>
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<td>1.00</td>
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<td>1.14–1.17</td>
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<td>Birth &lt;32 weeks gestation</td>
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<td>1.5</td>
<td>1.22</td>
<td>1.20–1.23</td>
<td>1.9</td>
<td>1.56</td>
<td>1.52–1.60</td>
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<td>1.58–1.98</td>
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<td>1.00</td>
<td>0.5</td>
<td>1.14</td>
<td>1.11–1.16</td>
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<td>0.96–1.01</td>
<td>0.7</td>
<td>1.18</td>
<td>1.13–1.23</td>
<td>1.1</td>
<td>1.55</td>
<td>1.29–1.85</td>
</tr>
</tbody>
</table>

Note: AOR, adjusted odds ratio.

*Models adjusted for maternal race and smoking status; women aged 30–34 are the reference group.
*bModels of infant death additionally adjusted for the presence of congenital anomalies.
*cModels of infant death additionally adjusted for the presence of congenital anomalies and gestational age.
The risks of Caesarean delivery, beyond the immediate potential for maternal morbidity during the perinatal period, include a doubling of the neonatal mortality risk (MacDorman et al., 2006), as well as a rise in placental complications in subsequent pregnancies, including placenta previa, abruptio placenta and placenta accreta (Wu et al., 2005; Getahun et al., 2006).

There is a concern that older maternal age may be associated with an increase in obstetric complications secondary to a higher incidence of underlying medical disease, decreased cardiovascular reserve and diminished ability to adapt to physical stress that may accompany ageing. The increased incidence of

Table III. Causes of infant death by maternal parity and age groups

<table>
<thead>
<tr>
<th>Maternal age groups (years)</th>
<th>Total, n</th>
<th>% of live births</th>
<th>% of live births</th>
<th>Causes of infant death (% of total deaths)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>40 718</td>
<td>0.5</td>
<td>0.5</td>
<td>Infectious and parasitic diseases</td>
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<td>30–34</td>
<td>24 312</td>
<td>0.5</td>
<td>0.6</td>
<td>Neoplasms and other diseases</td>
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<td>35–39</td>
<td>13 014</td>
<td>0.5</td>
<td>0.7</td>
<td>Congenital anomalies</td>
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<td>40–44</td>
<td>3 211</td>
<td>0.7</td>
<td>0.7</td>
<td>Sudden infant death syndrome</td>
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<td>≥ 45</td>
<td>181</td>
<td>1.0</td>
<td>1.0</td>
<td>Accidents, homicide and neglect</td>
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<td>All other causes</td>
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Table IV. Labour factors by maternal parity and age groups

<table>
<thead>
<tr>
<th>Labour factors</th>
<th>Maternal age groups (years)</th>
<th>%</th>
<th>AOR</th>
<th>95% CI</th>
<th>%</th>
<th>AOR</th>
<th>95% CI</th>
<th>%</th>
<th>AOR</th>
<th>95% CI</th>
<th>%</th>
<th>AOR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primiparas</td>
<td>Induction of labour</td>
<td>20.9</td>
<td>1.00</td>
<td>21.4</td>
<td>1.06</td>
<td>1.05–1.07</td>
<td>22.6</td>
<td>1.17</td>
<td>1.15–1.19</td>
<td>24.5</td>
<td>1.34</td>
<td>1.25–1.45</td>
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</tr>
<tr>
<td></td>
<td>Stimulation of labour</td>
<td>21.9</td>
<td>1.00</td>
<td>21.0</td>
<td>0.97</td>
<td>0.96–0.98</td>
<td>19.3</td>
<td>0.89</td>
<td>0.87–0.90</td>
<td>15.4</td>
<td>0.68</td>
<td>0.63–0.74</td>
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<td>Precipitous labour (&lt;3 h)</td>
<td>0.7</td>
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<td>0.7</td>
<td>0.97</td>
<td>0.94–1.01</td>
<td>0.7</td>
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<td>1.15</td>
<td>1.12–1.18</td>
<td>2.2</td>
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<td>1.17–1.28</td>
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<tr>
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<td>2.9</td>
<td>1.02</td>
<td>1.01–1.03</td>
<td>2.9</td>
<td>1.01</td>
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<td>2.7</td>
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<td>0.4</td>
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<td>1.08–1.11</td>
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<td>1.8</td>
<td>1.11</td>
<td>1.10–1.13</td>
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<td>1.28</td>
<td>1.25–1.31</td>
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<td>1.34–1.65</td>
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<td>3.4</td>
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<td>4.7</td>
<td>1.54</td>
<td>1.42–1.67</td>
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*Models adjusted for maternal race, smoking status, macrosomia (birthweight >4000 g), gestational age, presence of congenital anomalies and breech or malpresentation; women aged 30–34 are the reference group. Model of breech/malpresentation adjusted for maternal race, smoking status, gestational age, presence of congenital anomalies and macrosomia (birthweight >4000 g).

*Includes abruptio placenta, placenta previa and other excessive bleeding during labour and delivery (L&D); models additionally adjusted for Caesarean delivery.
diabetes and chronic and pregnancy-induced hypertension in our study confirms prior reports (Paulson et al., 2002; Salihu et al., 2003) and most likely reflects these age-related changes. Our findings also demonstrate the substantially increased risk for excessive bleeding with advancing maternal age (AOR 1.54 for primiparas and 1.49 for multiparas at age ≥45 versus 30–34). Clinical studies comparing outcomes of assisted versus spontaneous conceptions have reported a significant excess of placental complications, including placental abruption, placenta previa, and vaginal bleeding in the former group (Jackson et al., 2004; Shevell et al., 2005; Romundstad et al., 2006). Women who are treated for infertility may be different in unknown ways from those who conceive spontaneously, making comparisons between the two groups problematic. To overcome this problem, Romundstad et al. (2006) compared consecutive pregnancies among women who delivered after both an assisted and a spontaneous conception, reducing the chances of confounding due to maternal and environmental factors. These researchers reported a 3-fold higher risk of placenta previa associated with assisted conception, suggesting that a substantial portion of the risk may be due to ART. Because >80% of embryos implant during ART in the area in which they are transferred (Baba et al., 2000), and deposition in the lower uterine cavity may improve the rate of successful implantation (Waterstone et al., 1991; Coroleu et al., 2002), the site of replacement may provide insight into this complication.

Infertility, whether resulting in a spontaneous conception after more than a year waiting time to pregnancy or an assisted conception after IVF or non-IVF treatment, has been associated with an excess of prematurity, low birthweight and perinatal infant mortality (Draper et al., 1999; Basso and Baird, 2003; Helmerhorst et al., 2004; Wang et al., 2005; Ombelet et al., 2006). Although it is challenging to unravel the effects of the underlying cause of infertility from the treatment, several studies have reported an excess of adverse outcomes among women with delayed conception (untreated infertility), implicating the former as a more likely aetiology (Draper et al., 1999; Basso and Baird, 2003). Other important confounding factors include paternal age and congenital anomalies. Older paternal age has been associated with an increase in spontaneous abortions, preterm birth and congenital anomalies, with the highest risks when both partners are older (de la Rochebrochard and Thonneau, 2002; Zhu et al., 2005, 2006; Astolfi et al., 2006; Kleinhaus et al., 2006). One possible reason for the increase in preterm birth with advancing maternal age may be the residual effects of fetal reduction, whether iatrogenic or spontaneous, which are more likely in a pregnancy resulting from infertility treatment (Luke et al., 2004). Older maternal age requires more aggressive therapies to achieve a

### Table V. Mode of delivery by maternal parity and age groups

<table>
<thead>
<tr>
<th>Mode of delivery</th>
<th>Maternal age groups (years)</th>
<th>%</th>
<th>AOR</th>
<th>95% CI</th>
<th>%</th>
<th>AOR</th>
<th>95% CI</th>
<th>%</th>
<th>AOR</th>
<th>95% CI</th>
<th>%</th>
<th>AOR</th>
<th>95% CI</th>
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<tbody>
<tr>
<td></td>
<td>30–34</td>
<td>---</td>
<td>---</td>
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<tr>
<td>Primiparas vs. Multiparas</td>
<td>Primary Caesarean</td>
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<td>17.2</td>
<td>1.16</td>
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<td>Primary Caesarean</td>
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<td>1.17</td>
<td>---</td>
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<td>---</td>
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<td>1.18</td>
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<td>Primary Caesarean</td>
<td>---</td>
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<td>18.7</td>
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<td>Vacuum</td>
<td>Primary Caesarean</td>
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<td>1.19</td>
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<td>19.3</td>
<td>1.20</td>
<td>---</td>
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<td>5.90</td>
<td>5.43–6.42</td>
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</tbody>
</table>

Note: VBAC, vaginal birth after Caesarean

*Models adjusted for maternal race, smoking status, gestational age, presence of congenital anomalies, macrosomia (birthweight >4000 g) and breech or malpresentation; women aged 30–34 are the reference group.

*Study population limited to primiparas and multiparas without a prior Caesarean birth; multiparas are the reference category within each age group.

*Gestations ≥37 weeks, non-anomalous infants, non-breech or malpresentation and absence of abruptio placenta, placenta previa and other excessive bleeding during labour and delivery; models adjusted for maternal race, smoking status, gestational age and macrosomia.
pregnancy, including transferring more embryos. Several researchers have reported an increased risk of preterm and low birthweight in pregnancies after fetal reduction (Schieve et al., 2004b; Luke et al., 2004; Pinborg et al., 2005).

Although it cannot be determined from current vital statistics data, the increasing risk for diabetes and Caesarean delivery with advancing maternal age may be related to maternal obesity, as reported in the literature (Ehrenberg et al., 2004; Sheiner et al., 2004; Dempsey et al., 2005; Dietz et al., 2005; Langer et al., 2005; Robinson et al., 2005; Rosenberg et al., 2005; Vahdatian et al., 2005). Among multiparas, this increase in obesity, as a result of either excessive post-partum weight retention or weight gain between pregnancies, is related to adverse pregnancy outcomes including pre-eclampsia, gestational hypertension, gestational diabetes and Caesarean delivery (Villamor and Cnattingius, 2006). Several studies have confirmed that pregnancy is a trigger for excessive weight retention for many women. Data from the Stockholm Pregnancy and Women’s Nutrition (SPAWN) Study from Sweden (Linné et al., 2003), which followed-up parous women 15 years after pregnancy, reported several factors to be significantly associated with becoming overweight: a higher pre-pregnancy BMI, higher gestational weight gain, more retained weight at 1 year post-partum and a greater weight gain between 1-year and 15-year follow-up. These investigators also reported greater weight retention among parous women who had not breastfed and who had stopped smoking during pregnancy. Data from the Coronary Artery Risk Development In Young Adults (CARDIA) Study, which tracked black and white women 5 years (Smith et al., 1994) and 10 years post-partum (Gunderson et al., 2004), reported similar findings. At the 5 year follow-up, primiparas within both racial groups gained 2–3 kg more than nulliparas and had greater increases in waist-to-hip ratio independent of weight gain. At each level of parity, black women demonstrated greater adverse changes in adiposity than did white women. At the 10-year follow-up, substantial excess weight gain was associated with short pregnancies (recurrent spontaneous abortions, abortions or preterm births) and a first birth in women overweight prior to conception. Increases in waist girth were cumulative with both first and subsequent births among overweight as well as normal weight women. A higher waist circumference in early pregnancy is associated with an increased risk for developing pregnancy-associated hypertension (Sattar et al., 2001), as well as subsequent insulin resistance (Wahrenberg et al., 2005). With the new data items of maternal height and pre-pregnancy weight on the revised birth certificate, it will be possible to calculate pre-pregnancy BMI (weight/height²) and confirm the associations between parity, obesity and adverse pregnancy outcomes.

We found an increased risk of infant death with advancing age for both primiparas and multiparas, even after controlling for the presence of congenital anomalies. This pattern is attenuated with the additional adjustment for gestational age because there is a greater risk of prematurity among the oldest gravidas. In primiparas, this trend became non-significant, in part, because there was a larger increase in prematurity with age and there were fewer women in this group.

Our finding of an increased risk of infant death among multiparas with advancing age even after controlling for the presence of congenital anomalies and gestational age may also be related to the higher prevalence of maternal obesity with older age. In the USA, the prevalence of overweight, obesity and extreme obesity (BMI ≥25, ≥30 and ≥40) among women aged 20–39 is estimated to be 54.5, 29.1, and 5.6%, respectively; among women aged 40–59, it is 64.9, 36.7 and 7.8%, respectively (Hedley et al., 2004). Conversely, the contemporary percentage of US adults at a healthy weight (33%) is about half the Healthy People 2010 target level of 60%. Clinical studies have reported a strong association between maternal overweight and obesity and perinatal mortality (Cnattingius et al., 1998; Froen et al., 2002; Kristensen et al., 2005; Yu et al., 2006).

One of the limitations of this analysis is the inability to differentiate pregnancies which were the result of infertility treatment. With the 2003 revision of the birth certificate, this will be possible, including information on types of treatments (medications and ART). The revision will also include additional measures of maternal morbidity (maternal transfusion, ruptured uterus, unplanned hysterectomy and admission to intensive care). Currently, though, less than half of all States have implemented the 2003 revision of the birth certificate and the release of the data on the new items (including infertility treatments, maternal height and pre-pregnancy weight) has been delayed indefinitely. Known limitations of vital statistics data include the unreliability of selected items (such as maternal weight gain) and the high rate of missing values for other items (such as the age of father) (Martin et al., 2006). In addition, it is known that because of variation in the birth certificate from State to State, a percentage of records in the national data file will have items that are not stated: 0.5% for obstetric procedures, 0.6% for complications of labour and/or delivery, 0.5% for method of delivery, 1.0% for abnormal conditions of the newborn and 0.9% for congenital anomalies of the newborn (Martin et al., 2006). A recent population-based validation study from Washington State (Lydon-Rochelle et al., 2005) compared data on the birth certificate with hospital discharge data. These researchers found that medical conditions and complications were under-reported in birth certificates by ~50%. This suggests that the magnitude of the risks may be even higher than reported in our study. The findings in our study should be duplicated once the vital statistics data are released, and confirmed and refined with clinical studies, particularly the associations between maternal obesity, parity, infertility and adverse pregnancy outcomes. In conclusion, this analysis demonstrates the substantial increased risks of pregnancy complications that accompany advancing maternal age. These risks should be considered when counselling older women during infertility treatment and in their subsequent antenatal management.

Acknowledgement
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Centers for Disease Control and Prevention (2005) 2003 Assisted Reproductive Technology Success Rates: National Summary and Fertility Clinic Reports. US Department of Health and Human Services, Atlanta, GA.


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