Research paper

Younger or older parental age and risk of suicidality, premature death, psychiatric illness, and criminality in offspring

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A R T I C L E   I N F O

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Maternal age
Paternal age
Suicidality
Psychiatric disorder
Premature mortality
Criminality

A B S T R A C T

Background: Younger or older parental age has been linked with a range of adverse offspring endpoints. We investigated associations between parental age and nine adverse offspring outcomes in three correlated domains: (i) Premature death: suicide, unnatural death, natural death; (ii) Psychiatric morbidity: any mental illness, suicide attempt, substance misuse; (iii) Criminality: violent offending, imprisonment, driving whilst intoxicated.

Methods: Persons born in Denmark 1966–1996 were followed from their 15th until 40th birthday or December 2011 (N=1,793,681). Incidence rate ratios were estimated.

Results: Offspring of teenage mothers had the greatest risks for all nine adverse outcomes, especially for imprisonment, violent offending, substance misuse, and attempted suicide. Teenage fatherhood was also associated with elevated risks for offspring adverse psychiatric and criminality outcomes, but not premature mortality (at ages 15–39 years). For the psychiatric and criminality outcomes there was a U-shape trend linked with paternal age, but risks for premature mortality tended to increase with rising paternal age. On the contrary, maternal age 30 years and over was not linked with raised risks for any of the outcomes examined.

Limitations: Parental links are based on legal and not biological relationships.

Conclusions: The substantially elevated risks linked with teenage motherhood for a variety of poor offspring outcomes is a concern for clinicians and policymakers. The associations observed across such a wide array of adverse outcomes also suggest that multiple causal mechanisms may be implicated.

1. Introduction

With the rise of effective contraception, improving employment opportunities for women, changing gender roles, and advances in assisted reproductive technologies, there has been a trend towards delayed parenthood in western societies (Mills et al., 2011). On the contrary, teenage childbirth rates have fallen markedly since 1990 (WHO, 2014). The associations between parental age and risks of adverse pregnancy and birth outcomes and of childhood diseases have been well-reported. For example, while teenage pregnancy is associated with increased risks for pre-term delivery, low birth weight and neonatal mortality (Chen et al., 2007), advancing paternal age has been linked to elevated risks of miscarriages (Nybo Andersen et al., 2000, 2004), obstetric complications (Cleary-Goldman et al., 2005), and common childhood cancers in offspring (Sergentanis et al., 2015). In addition to early physical health complications, a range of other offspring adverse outcomes have been related to parental age. For example, children born to teenage mothers or fathers have elevated risks for mood, neurotic, and stress-related disorders (McGrath et al., 2014), behavioural and emotional disorders (McGrath et al., 2014), substance use (Coyne et al., 2013; Ekéus, 2006; Fergusson and Woodward, 1999; McGrath et al., 2014), and criminal offending (Coyne et al., 2013; Fergusson and Woodward, 1999; Jaffee et al., 2001), while those born to older fathers have elevated risks for schizophrenia (McGrath et al., 2014, D’Onofrio et al., 2014), and developmental disorders (McGrath et al., 2014, D’Onofrio et al., 2014). On the contrary, increasing maternal age is associated with better language development (Sutcliffe et al., 2012) and a lower risk of adverse externalizing behaviour (Saha et al., 2009).

There is, therefore, evidence that both teenage parenthood and advancing age fatherhood are associated with increased risks for poor psychiatric and psychosocial outcomes in the offspring. On the
contrary, older motherhood may be protective against these risks although investigations with such focus are relatively rare (for example, Sutcliffe et al., 2012). In this study, we aimed to estimate the associations between parental age and risks for a range of adverse events in offspring between mid-adolescence and mid-adulthood in a national Danish cohort so that direct comparisons of these risks can be made without differential inter-cohort biases. Studies investigating multiple adverse events across several outcome domains conducted in the same cohort are also uncommon in the literature. Outcomes were categorized into one of three domains: 1. Premature mortality (suicide, unnatural death, natural death); 2. Psychiatric morbidity (any mental illness, suicide attempt, alcohol or drug use disorder); 3. Criminality (violent offending, receiving a custodial sentence, convicted of driving under the influence of alcohol or drugs). These outcomes are correlated and share similar aetiological pathways (Neelaman et al., 1998; O'Donnell, et al., 2015), with adolescence to mid-adulthood being particularly vulnerable periods for their occurrences (Mok, et al., 2015). We compared risks by maternal and paternal ages for each outcome, as well as across the multiple adverse outcomes.

2. Methods

2.1. Study population

Since 1968 the Danish Civil Registration System has registered all persons living in Denmark (Pedersen, 2011). It captures information such as gender, date and place of birth, continuously updated information on vital status, and parents' identities. The unique personal identification number used in all national registers enables accurate and complete linkage between registers and between relatives. Our study population included all persons born in Denmark between 1st January 1966 and 31st December 1996, who were residing in the country on their 15th birthday, and whose parents were both Danish-born (N=1,793,681).

2.2. Codes of ethics

Approval to conduct this study was granted formally by the Danish Data Protection Agency, and data access was agreed by the State Serum Institute and Statistics Denmark. Since this project was based exclusively on registry data it did not need approval from the Danish National Committee on Health Research Ethics. According to the Danish Act on Processing of Personal Data, Section 10, this also meant that the investigators were not required to obtain informed consent from persons in the study population.

2.3. Measurement of adverse outcomes

Cohort members were linked via their personal identifier to various national registers to obtain the first date of occurrence for each of the nine adverse outcomes examined.

2.3.1. Premature mortality

The study cohort was linked with the Register of Causes of Death (Juel and Helweg-Larsen, 1999) to identify suicides (ICD-8: E950-E959; ICD-10: X60-X84), unnatural deaths (ICD-8: E80-E899; ICD-10: Y01-Y89), and natural deaths (all other ICD mortality codes). This Register contains information for all residents who died in Denmark in 1970 or later.

2.3.2. Psychiatric morbidity

Cohort members were linked via their personal identifier to the Psychiatric Central Research Register (Mors et al., 2011) and the National Patient Register (Lynge et al., 2011) to obtain information on suicide attempts and history of mental illness. The Psychiatric Central Research Register contains data on all admissions to psychiatric inpatient facilities from 1969 onwards. The National Patient Register was established in 1977 and contains data on all admissions to public general hospitals. In both registers, information on outpatients was included from 1995 onwards. Between 1969 and 1993, the diagnostic system used was the Danish modification of the International Classification of Diseases, 8th revision, and from 1994, the International Classification of Diseases, 10th revision, Diagnostic Criteria for Research.

Onset of any psychiatric disorder (ICD10: F00-F99, ICD8: 290-315) and mental and behavioural disorders due to psychoactive substance abuse (ICD10: F10-F19, ICD8: 291.x9, 294.39, 303.x9, 303.20, 303.28, 303.90, 304.x9) was determined as the date of the first diagnosis. Our classification of attempted suicide was identical to that used previously (Nordentoft et al., 2011), using different algorithms for different time periods. From 1977 to 1986, persons who made a suicide attempt were identified using the ICD-8 codes E9500-E9599 in either the National Patient Register or Psychiatric Central Research Register. From 1987 to 1993, these persons were defined as persons admitted with a 'reason for contact code' of 4 in the National Patient Register. After 1994, cases were identified as people fulfilling at least one of the following criteria in either the National Patient Register or the Psychiatric Central Research Register:

1) Reason for contact code =4 (National Patient Register)
2) Any psychiatric diagnosis (ICD-10 chapter F) and a comorbid diagnosis of poisoning with medication and biological compounds (ICD-10 codes T36 through T50) or non-medical compounds, excluding alcohol and poisoning from food (ICD-10 codes T32 through T60)
3) Any psychiatric disorder (ICD-10 Chapter F) and comorbid diagnosis reflecting lesions on forearm, wrist or hand (ICD-10 codes S51, S55, S59, S61, S65, or S69)
4) Any hospital contact due to poisoning with weak or strong analgesics, hypnotics, sedatives psychoactive drugs, anti-epileptics and anti-Parkinson drugs or carbon monoxide (ICD 10 codes T39, T42, T43, and T58)
5) Intentional self-harm: ICD-10 X60-X84 (recorded as a primary or secondary diagnosis in either Register)

2.3.3. Criminality

The National Crime Register became electronic in November 1978, and all judicial verdicts and police decisions relating to criminal charges have been registered on a personal level since. Data have been made available to researchers through Statistics Denmark from 1980 onwards. We defined interpersonal violent offending as encompassing all convictions for homicide, assault, robbery, aggravated burglary or arson, possessing a weapon in a public place, violent threats, extortion, human trafficking, abduction and kidnapping, rioting and other public order offences, terrorism, and sexual offences (except for possessing child pornographic material). We defined a custodial sentence as one imposing mandatory detainment of the convicted individuals, either in prison or in some other closed therapeutic and/or education institution, such as a reformatory, or a forensic psychiatric or drug detoxification unit. We defined driving whilst intoxicated as encompassing all driving offences committed whilst under the influence of alcohol, narcotics, or non-prescribed medicine. For each criminality outcome, we considered the first offence after cohort members’ 15th birthdays, as this is the threshold for adult criminal responsibility in Denmark.

2.4. Maternal and paternal age

Paternal ages at cohort member’s births were categorized as 12–19, 20–24, 25–29, 30–34, 35–39, 40–44, and 45 years and over, and we applied 25–29 years as a generic reference category for relative risk estimation (McGrath et al., 2014). The same categories were also used...
for maternal age except the oldest category included in the analyses was 40–44 years, due to the small number of events for maternal age 45 years and over.

2.5. Other measures

2.5.1. Parental histories of psychiatric illnesses

Maternal and paternal histories of any mental illnesses were obtained from the Psychiatric Central Research Register (Mors et al., 2011) and the National Patient Register (Lyne et al., 2011), as described in the subsection ‘Psychiatric morbidity’ earlier.

2.5.2. Socioeconomic status

Parental socioeconomic status was measured via the highest maternal and paternal educational attainment level (primary school, high school/vocational training, higher education), assessed in the year of cohort members’ 15th birthdays, or in the year when the information was last available before their 15th birthdays. The information was obtained from the Integrated Database for Labour Market Research (Danmarks Statistik, 1991).

2.5.3. Urbanicity of birthplace

This was classified as central area of the capital city (Copenhagen), suburb of the capital city, provincial city, provincial town, or rural, as applied in previous Danish registry studies (for example, Pedersen and Mortensen, 2001).

2.6. Study design and statistical analyses

Cohort members were followed up from their 15th birthday until either the occurrence of outcome of interest, death, emigration from Denmark, 40th birthday, or December 31st, 2011, whichever came first. The cohort was followed up for a total of 25.8 million person-years. Incidence rate ratios (IRRs) for each adverse outcome were estimated by log-linear Poisson regression using the SAS 9.4 GENMOD procedure. IRRs were adjusted for the other parent’s age, offspring age and sex, and calendar year (Model 1). Further adjustments were made for parental histories of psychiatric illnesses, parental socioeconomic status, and urbanicity of birthplace (Model 2). Age, calendar year, and histories of parental mental illnesses were treated as time-dependent variables; all other covariates as time-fixed. Confidence intervals (CIs) at the 95% level were calculated from likelihood ratio tests. Population attributable fractions (PAFs) were calculated from the percentage of cases across the maternal and paternal age ranges and from the IRRs estimated for the other parent’s age, offspring age and sex, calendar year, parental histories of psychiatric illnesses, parental socioeconomic status, and urbanicity of birthplace (as in Model 2) (Benichou, 2001).

3. Results

The number and percentage distributions of cohort members by maternal and paternal age are presented in Table 1. The number of cases and incidence rates for each adverse outcome by maternal and paternal age are shown in Table 2. Due to the small number of events for maternal age 45 years and over, the oldest maternal age category included in our analyses was age 40–44 years. Across all age groups and for all outcomes, incidence rates were highest for those born to teenage mothers or teenage fathers, except for suicide and natural death for which the youngest and oldest paternal age groups were linked with similarly raised incidence rates.

Model 1 in Figs. 1–3 shows incidence rate ratios (IRRs) by maternal age (red lines) and paternal age (blue lines) adjusted for the other parent’s age, offspring age and sex, and calendar year. Estimates additionally adjusted for parental histories of mental illnesses, parental socioeconomic status and urbanicity of birthplace, are shown under Model 2. Tables of these IRRs can be found in eTable 1 (for Model 1) and eTable 2 (for Model 2) in the Online Supplement.

Model 1 shows that offspring of mothers aged 12–19 years had significantly increased risks for all nine adverse outcomes compared to those born to mothers aged 25–29 years. Risks were highest for custodial sentencing (IRR 2.64; 95% CI 2.54-2.74), violent offending (IRR 2.37; 95% CI 2.29-2.45), alcohol or drug use disorders (IRR 2.10; 95% CI 1.99-2.21), and attempted suicide (IRR 1.93; 95% CI 1.85-2.02). Further adjustment (Model 2) indicated that between 13% (for natural death) and 33% (for custodial sentencing) of the elevated risks associated with being born to a teenage mother could be explained by parental histories of mental illnesses, parental socioeconomic status, and urbanicity of birthplace. However, even after such adjustment, risks remained significantly raised for all outcomes except for natural death. Offspring born to teenage fathers also showed significantly elevated risks for adverse psychiatric and criminality outcomes, but not for premature mortality (at ages 15–39 years). The effect sizes were, however, smaller than those linked with teenage mothers.

For each of the psychiatric and criminality outcomes there was a U-shape trend associated with paternal age, with the greatest risks being found in offspring of fathers from the youngest and oldest age groups (Figs. 2 and 3, Model 1). This U-shape pattern for paternal age was not seen for the three mortality outcomes, for which risks tended to increase with rising paternal age and for suicide in particular. After adjusting for all confounders examined, patterns of relative risk associated with paternal age for the psychiatric and criminality outcomes (except for any mental illness) resembled more of an inverted J than a U-shape (Figs. 2 and 3, Model 2). The risks were highest for offspring of teenage fathers while those associated with older fathers were less, though continued to be significantly, elevated. However, older paternal age was no longer associated with significantly raised risks for premature mortality after such adjustment, except for risk of natural death linked with paternal age 45 years and over, which remained raised (IRR 1.28; 95% CI 1.02-1.59).

| Table 1 |
| Number and percentage of cohort members by maternal and paternal age at birth. * |

<table>
<thead>
<tr>
<th>Parental age (years)</th>
<th>12–19</th>
<th>20–24</th>
<th>25–29</th>
<th>30–34</th>
<th>35–39</th>
<th>40–44</th>
<th>45 and over</th>
<th>All ages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mother</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>92,713</td>
<td>527,405</td>
<td>679,557</td>
<td>362,975</td>
<td>112,550</td>
<td>17,654</td>
<td>827</td>
<td>1,793,681</td>
</tr>
<tr>
<td>%</td>
<td>5.2%</td>
<td>29.4%</td>
<td>37.9%</td>
<td>20.2%</td>
<td>6.3%</td>
<td>1.0%</td>
<td>0.05%</td>
<td>100%</td>
</tr>
<tr>
<td>Father</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>23,578</td>
<td>304,795</td>
<td>648,093</td>
<td>492,394</td>
<td>217,785</td>
<td>74,643</td>
<td>32,393</td>
<td>1,793,681</td>
</tr>
<tr>
<td>%</td>
<td>1.3%</td>
<td>17.0%</td>
<td>36.1%</td>
<td>27.5%</td>
<td>12.1%</td>
<td>4.2%</td>
<td>1.8%</td>
<td>100%</td>
</tr>
</tbody>
</table>

* Study population included all persons born in Denmark between 1st January 1966 and 31st December 1996, who were residing in the country on their 15th birthday, and whose parents were both Danish-born.
The U-shape relative risk pattern for paternal age was not seen for maternal age, as risks for all nine outcomes were highest for offspring of teenage mothers and tended to decrease for those born to older mothers. Results from both sets of adjustment revealed that maternal age 30 years and over was not associated with raised risks for any of the nine adverse outcomes. In fact, offspring born to mothers aged 30 years or over had significantly lower risks for violent offending and receiving a custodial sentence, while those born to mothers aged 30–34 years additionally showed significantly lower risks for attempted suicide, alcohol or drug misuse, and driving whilst intoxicated.

As with children of teenage mothers, after adjustment for all confounders examined, offspring of women aged 20–24 years showed elevated risks for all adverse psychiatric and criminality outcomes, suicide and unnatural death, but not for natural death (at age 15–39 years). Similarly, compared to offspring of fathers aged 25–29 years, those born to men aged 20–24 years had higher risks for all adverse psychiatric and criminality outcomes, but not of premature mortality.

Table 2 shows that 26% of all unnatural deaths observed were suicides. IRRs for unnatural deaths excluding suicides are presented in eTable 3 in the Online Supplement for both sets of adjusted estimates (i.e. Models 1 and 2). Comparisons with the IRRs for unnatural deaths reported in eTables 1 and 2 and in Fig. 1(B) show that the magnitudes and patterns of IRRs for these deaths with or without suicides included were very similar. We also investigated associations between maternal and paternal age and risks of offspring adverse outcomes without adjusting for the other parent’s age. These results are presented in eFig. 1–3 in the Online Supplement. Estimates adjusted for offspring age and sex, and calendar year only were shown under Model 3, while those additionally adjusted for parental histories of mental illnesses, parental socioeconomic status and urbanicity of birthplace, are shown under Model 4.

To assess the population impact of these associations, for each adverse outcome, we reported the PAF. The PAF is a measure of the proportion of cases in the population that theoretically would not have occurred if the IRR in the specific parental age category was similar to that of the reference category (i.e. age 25–29 years). PAFs adjusted for the other parent’s age, offspring age and sex, calendar year, parental histories of psychiatric illnesses, parental socioeconomic status, and urbanicity of birthplace are shown in eTable 4 in the Online Supplement. These figures suggest that although teenage motherhood was associated with the highest relative risks of adverse outcomes, the associated PAFs were of similar magnitudes to those of mothers aged 20–24 years for most of the outcomes examined. Overall, the population impact of maternal age on all adverse outcomes investigated in this study was greatest for maternal age under 25 years.

Table 2

<table>
<thead>
<tr>
<th>Number of cases</th>
<th>Incidence rate</th>
<th>Parental age (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>12–19</td>
</tr>
<tr>
<td><strong>Premature mortality</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suicide</td>
<td></td>
<td>177</td>
</tr>
<tr>
<td>Father</td>
<td></td>
<td>10.2</td>
</tr>
<tr>
<td>Mother</td>
<td></td>
<td>43</td>
</tr>
<tr>
<td>Unnatural death</td>
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</tr>
<tr>
<td>Father</td>
<td></td>
<td>4.96</td>
</tr>
<tr>
<td>Mother</td>
<td></td>
<td>208</td>
</tr>
<tr>
<td>Natural death</td>
<td></td>
<td>48.2</td>
</tr>
<tr>
<td>Father</td>
<td></td>
<td>3.28</td>
</tr>
<tr>
<td>Mother</td>
<td></td>
<td>1.42</td>
</tr>
<tr>
<td></td>
<td></td>
<td>32.9</td>
</tr>
<tr>
<td><strong>Psychiatric morbidity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All mental illnesses</td>
<td></td>
<td>10,852</td>
</tr>
<tr>
<td>Father</td>
<td></td>
<td>667.2</td>
</tr>
<tr>
<td>Mother</td>
<td></td>
<td>2,869</td>
</tr>
<tr>
<td>Attempted suicide</td>
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<td>710.3</td>
</tr>
<tr>
<td>Father</td>
<td></td>
<td>4,379</td>
</tr>
<tr>
<td>Mother</td>
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<td>259.6</td>
</tr>
<tr>
<td>Attempted suicide</td>
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<td>1,220</td>
</tr>
<tr>
<td>Father</td>
<td></td>
<td>291.2</td>
</tr>
<tr>
<td>Alcohol or drug use disorders</td>
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</tr>
<tr>
<td>Father</td>
<td></td>
<td>3,046</td>
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<tr>
<td>Mother</td>
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<td>178.2</td>
</tr>
<tr>
<td>Attempted suicide</td>
<td></td>
<td>834</td>
</tr>
<tr>
<td>Father</td>
<td></td>
<td>196.1</td>
</tr>
<tr>
<td><strong>Criminality</strong></td>
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<tr>
<td>Violent criminal offence</td>
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</tr>
<tr>
<td>Father</td>
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<td>412.6</td>
</tr>
<tr>
<td>Mother</td>
<td></td>
<td>1,818</td>
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<td>Custodial sentence</td>
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<td>Father</td>
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<tr>
<td>Mother</td>
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<td>1,736</td>
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<td>Driving under influence of alcohol or drugs</td>
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<td>421.2</td>
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</tr>
<tr>
<td>Custodial sentence</td>
<td></td>
<td>399.8</td>
</tr>
</tbody>
</table>

* Due to the small number of cases of adverse outcomes for maternal age 45 years and over, the oldest maternal age category reported in our study was 40–44 years.
4. Discussion

4.1. Summary of main findings

In a national cohort of individuals followed up from mid-adolescence to middle age, we have estimated incidence rates and IRRs for a range of adverse outcomes according to parental age at birth. Offspring of teenage mothers had the greatest risks for all nine adverse outcomes investigated, especially for custodial sentencing, violent offending, alcohol or drug use disorder, and attempted suicide. With the exception of unnatural death, the IRRs were higher in offspring of mothers who were 15–19 years old at birth compared to those born to mothers aged 30–34 years. For custodial sentencing, the IRRs were highest in offspring of mothers aged 15–19 years at birth. In contrast, for unnatural death, the IRRs were highest in offspring of mothers aged 35–39 years at birth.

Fig. 1. Incidence rate ratios and 95% confidence intervals for premature mortality outcomes: (A) Suicide; (B) Unnatural death; (C) Natural death. Red line - maternal age; Blue line – paternal age. *Model 1: IRRs were adjusted for the other parent’s age, offspring age and sex, and calendar year. †Model 2: as in Model 1, but estimates were additionally adjusted for parental histories of mental illnesses, parental socioeconomic status, and urbanicity of birthplace.
of natural death, risks remained significantly raised even after adjusting for all confounding factors examined. Teenage fatherhood was also associated with elevated risks of psychiatric and criminality outcomes in offspring, but not premature mortality (at ages 15–39 years). For each of the psychiatric and criminality outcomes there was a U-shape trend associated with paternal age. For the mortality outcomes, risks tended to increase with rising paternal age. Maternal age 30 years and over was not associated with raised risks for any of the nine adverse
Fig. 3. Incidence rate ratios and 95% confidence intervals for criminality outcomes: (A) Violent offending; (B) Custodial sentence; (C) Driving whilst under the influence of alcohol or drugs. Red line - maternal age; Blue line – paternal age. *Model 1: adjusted for the other parent’s age, offspring age and sex, and calendar year. †Model 2: as in Model 1, but additionally adjusted for parental histories of mental illnesses, parental socioeconomic status, and urbanicity of birthplace.
outcomes. In fact, older maternal age appears protective against some of the risks for offspring suicidality and adverse psychosocial outcomes.

4.2. Evidence from existing research and interpretation

Our results generally concur with those from previous research (Bjorggaard et al., 2013; Coyne et al., 2013; Ekéus, 2006; Fergusson and Woodward, 1999; Harden et al., 2007; Kuja-Halkola et al., 2012; McGrath et al., 2014; Miller et al., 2010). By examining multiple adverse outcomes in the same population, we were additionally able to make direct comparisons of risks of offspring adverse outcomes across several domains. However, the lack of an association between young fatherhood and suicide risk in offspring that we observed, contrasted with the findings reported from a Swedish case-control study, which showed a small increased odds linked with paternal age 24 years or younger (Niederkrotenthaler et al., 2012). Variations in study designs and populations may contribute to these differences in findings.

The explanations for our findings are likely to include a complex interplay of genetic, psychosocial, and environmental influences. For example, one of the mechanisms postulated as linking advancing paternal age with adverse health outcomes in offspring is increased prevalence of de novo mutations (Kong et al., 2012; Kuja-Halkola et al., 2012; McGrath et al., 2014). Fathers transmit a much higher number of genetic mutations to their offspring than mothers, and paternal age is the dominant factor in determining the number of de novo mutations in the child (Kong et al., 2012). Factors associated with delayed fatherhood are also likely to contribute to the elevated risks of at least some of the adverse outcomes in offspring. Research into schizophrenia, for example, has suggested that most of the association between older paternal age and risk of schizophrenia cannot be explained by paternal age-related de novo mutations, but rather by some unknown factors related to both delayed fatherhood and schizophrenia (Ek et al., 2015; Pedersen et al., 2014; Petersen et al., 2011).

Teens are more likely than older mothers to come from disadvantaged social backgrounds, have low educational attainment and substance use disorders, be living as a lone parent and dependent on social welfare (Ekéus et al., 2006). The increased risks of adverse outcomes in children of teenage parents could therefore at least in part be attributed to the disadvantaged environments these children were raised in (Fergusson and Woodward, 1999; Jaffee et al., 2001). However, both our study and previous research conducted using the Swedish national registers have found that, even after adjusting for various socioeconomic confounders, offspring of teenage mothers remained significantly more likely than those born to mothers aged 25–29 years to attempt suicide or use illicit drugs (Ekéus et al., 2006). Similarly, a study of young adults in New Zealand reported that, after controlling for potential social and contextual factors, there remained a significant link between paternal age and elevated risks of criminality, substance use and mental health problems in offspring (Fergusson and Woodward, 1999). The relationship between teenage motherhood and adverse psychosocial and criminality outcomes in their offspring has been reported to be partially mediated by poor and inconsistent parenting practices, and perhaps also by lower educational attainment among these children (Fergusson and Woodward, 1999; Jaffee et al., 2001). On the contrary, increasing maternal age has been linked with more effective child-rearing skills and the provision of a more nurturing and supportive home environment (Fergusson and Woodward, 1999), which may help to explain the lower risks of adverse outcomes in offspring of older mothers.

Previous research has also reported evidence for a 'social selection' effect. For example, characteristics such as antisocial behaviour in some teenagers are also associated with their propensity of becoming a teenage parent (Jaffee et al., 2001). These characteristics may be transmitted from teenage parents to their offspring both genetically and via the home environment, increasing the risks of adverse outcomes in offspring (Jaffee et al., 2001). However, research conducted on children of female twins has found that the association between teenage motherhood and mental health problems in offspring remained significant after controlling for shared familial factors (Harden et al., 2007). Evidence from sibling studies has also suggested a causal relationship between advancing paternal age and offspring psychiatric morbidity (D’Onofrio et al., 2014) and number of violent offences committed (Kuja-Halkola et al., 2012). The association between advancing paternal age and likelihood of offspring ever committing a violent crime, as well as between adolescent motherhood and violent and non-violent criminality in offspring, may however be confounded by shared familial risk factors (Coyne et al., 2013; Kuja-Halkola et al., 2012).

4.3. Strengths and limitations

One of the main strengths of our study was the use of a complete national cohort, providing abundant statistical power and precision for examining rare adverse events. By examining the same cohort at risk, we were able to compare the risks for multiple outcomes without differential inter-cohort biases, as would be the case if comparisons between single outcomes reported from different studies were made. Furthermore, unlike many previous studies that have focused on the youngest and oldest parental age strata, we have estimated associations across maternal and paternal age distributions, and long-term outcomes in offspring up to mid-adulthood. By using registry data, there were also no issues of recall or selection bias, due to participants' unwillingness to report suicide attempts, mental illnesses, or criminal offences, as in the case of sampled population surveys (for example, Fergusson and Woodward, 1999).

Our study also has its limitations, however. Firstly, in the Danish Civil Registration System, parental links are based on legal and not biological relationships. Secondly, our study has excluded individuals with unknown maternal or paternal links - approximately 0.2% of the population (Pedersen, 2011). The effect of missing parental links on risk of the adverse outcomes is not known, although it is most likely that the estimates would have been biased downwards. Thirdly, milder cases of mental disorders treated in primary care settings are not recorded in the Psychiatric Central Research Register, so our estimates for psychiatric morbidity outcomes relate only to cases at the more severe end of the psychopathological spectrum. Fourthly, as with all other observational studies, residual confounding is a potential issue. Although we adjusted for parental history of mental illness, parental education, and urbanization of birth place, we were unable to adjust for some other key potential confounders such as parental history of criminal offending (Friessl et al., 2011). Data on criminal offending were only available from 1981 onwards. Since our study population included all persons born between 1966 and 1996, much of this information would be missing for cohort members born in the early years, especially for crimes committed when those parents were at a young age. Lastly, our estimates of PAF need to be interpreted with caution as we cannot assume causality in the links observed between parental age and adverse outcomes in offspring (Benichou, 2001).

5. Conclusions

The wide array of adverse outcomes reported in this study suggests that multiple causal mechanisms may be implicated, and the substantially elevated risks linked with teenage motherhood for a variety of poor offspring outcomes is a concern for clinicians and policymakers. Despite the decline in teen birth rates in recent decades, one in nine of all births worldwide are still to teenage girls aged 15–19 years (WHO, 2014). Not only does teenage pregnancy continue to pose significant social and economic challenges for the society (WHO, 2014), offspring of teenage mothers, and to a lesser extent of teenage fathers, are at elevated risks for a range of adverse outcomes occurring between mid-adolescence and mid-adulthood. In addition, offspring of older fathers
not only have elevated risks for childhood physical and developmental disorders (D’Onofrio et al., 2014; McGrath et al., 2014; Sergentanis et al., 2015), but also for suicidality and adverse psychosocial outcomes in adulthood – associations which have been less commonly reported. Advancing maternal age was not associated with risks for any of the offspring outcomes studied here and may even appeared to be protective against some of these risks, but such benefits need to be weighed against the elevated risks for adverse pregnancy and birth outcomes associated with older age pregnancy (Cleary-Goldman et al., 2005; Nybo Andersen et al., 2000).

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Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.jad.2016.10.001.

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