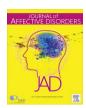
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#### Research paper

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



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#### ABSTRACT

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 parental 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

Abbreviations: CI, Confidence interval; IRR, Incidence rate ratio; PAF, Population attributable fraction

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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 (Neeleman 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 Danishborn (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: E800-E999; ICD-10: V01-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 T52 through T60)
- Any psychiatric disorder (ICD-10 Chapter F) and comorbid diagnosis reflecting lesions on forearm, wrist or hand (ICD-10 codes \$51, \$55; \$59, \$61, \$65, or \$69)
- 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)
- 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

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