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ORIGINAL RESEARCH

A Nation-Wide Swedish Cohort Study on Early Maternal Age at First Childbirth and Risk for Offspring Deaths, Accidents, and Suicide Attempts

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Abstract

In a sample of over one million Swedish first-born offspring, we examined associations between early maternal age at first childbirth (MAFC; i.e., < 20 and 20–24 vs 25–29 years) and offspring non-accidental deaths, accidental deaths, deaths by suicide, non-fatal accidents, and suicide attempts. We included year of birth and several maternal and paternal characteristics as covariates and conducted maternal cousin comparisons to adjust for unmeasured confounding. Early MAFC (e.g., teenage childbearing) was associated with all outcomes, with the most pronounced risk elevation for accidental deaths [Hazard Ratio (HR) < 20 2.50, 95% confidence interval (CI) 2.23, 2.80], suicides (HR < 20 2.08, 95% CI 1.79, 2.41), and suicide attempts (HR < 20 2.85, 95% CI 2.71, 3.00). Adjusting for covariates and comparing cousins greatly attenuated associations (e.g., accidental deaths HR < 20 1.61, 95% CI 1.22, 2.11; suicides HR < 20 1.01, 95% CI 0.69, 1.47; and suicide attempts HR < 20 1.35, 95% CI 1.19, 1.52). A similar pattern emerged for non-accidental deaths and non-fatal accidents. Therefore, results indicated maternal background factors may be largely responsible for observed associations.

Keywords Maternal age at childbearing · Teenage childbearing · Offspring outcomes · Deaths · Suicides · Accidents

Introduction

Early maternal age at childbearing is associated with increased risk of adverse offspring outcomes (e.g., mortality, mental health problems, substance use, and criminal convictions) in youth and young adulthood (Coyne and D'Onofrio 2012; Furstenberg 2003). Research has proposed specific mechanisms of action, such as maternal–fetal competition for nutrients (King 2003), adverse birth outcomes (e.g., preterm birth; D'Onofrio et al. 2013a, b; Fall et al. 2015; Vaughan et al. 2014; Weng et al. 2014), parenting problems, or financial and educational ramifications of early maternal age at childbearing (Coyne and D'Onofrio 2012).

However, observed associations with early maternal age at childbearing could be due to background factors (e.g., lower educational achievement, predisposition to or pre-existing psychopathology, or socioeconomic deprivation) that differ among women bearing children earlier versus later in life rather than causal mechanisms linking maternal age at childbearing and outcomes across development (Jaffee et al. 2001). Research also suggests that age at first childbearing (Rodgers et al. 2007) and adverse outcomes (e.g., suicide;

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Brent and Melhem 2008) are heritable, indicating that shared genetic factors could explain associations between early maternal age at childbearing and adverse offspring outcomes (Coyne and D'Onofrio 2012).

Given that background factors could partially or fully confound observed associations with early maternal age at childbearing and experimental methods cannot be used to study maternal age at childbearing, researchers must use observational methods that rigorously adjust for confounding in order to evaluate the consequences of early maternal age at childbearing. The majority of research on early maternal age at childbearing has relied on measured covariates (e.g., maternal educational attainment and socioeconomic status) to account for confounding (e.g., Ekeus et al. 2006; Myrskylä and Fenelon 2012; Niederkrotenthaler et al. 2012; Taylor et al. 1983). However, this approach is greatly limited by (a) the inability to measure all potential confounders and (b) measurement error of the covariates that are included (Academy of Medical Sciences Working Group 2007; Rutter 2007). Family-based designs are well suited to study the potential effects of early maternal age at childbearing (Coyne and D'Onofrio 2012; Myrskylä and Fenelon 2012), as these designs can account for unmeasured genetic and environmental factors and, thereby, improve the conditions for causal inference.

Previous research that has used family-based designs to study the consequences of early maternal age at childbearing on various offspring behavioral health outcomes, including internalizing problems (Harden et al. 2007), behavior/conduct problems (D'Onofrio et al. 2009), substance use problems (Harden et al. 2007), and criminality (Coyne et al. 2013), has primarily supported a causal interpretation of early maternal age at childbearing. On the other hand, the few reports on offspring mortality have shown mixed results. Two previous studies used sibling comparisons and the same data source as the present study (Swedish registry data) to evaluate associations between maternal age at childbearing and offspring mortality. While the first study found no support for an independent association between early maternal age at childbearing and all-cause mortality (Barclay and Myrskyla 2018), the second study found a linear association between increasing maternal age at childbearing and reduced risk of offspring all-cause mortality and death by suicide (Carslake et al., 2019). Of note, the second study did not evaluate mortality before age 18 as follow-up did not begin until offspring were age 18. Consistent with the second Swedish study, another sibling comparison using Norwegian registry data reported that increasing maternal age at childbirth was associated with reduced risk of offspring death by suicide (Bjørngaard et al. 2013).

To address the limitations of previous research, we conducted a population-based study with data obtained from Swedish registers to investigate the magnitude of the associations between early maternal age at first childbirth (MAFC) and death, accident, and suicide attempt outcomes in first-born offspring after accounting for confounding factors. We focused on age at first childbirth to reduce potential bias from birth order and carry over effects (i.e., MAFC affecting subsequent pregnancies). For our outcomes we focused on offspring deaths not due to older age rather than age-related physical diseases. Specifically, we studied associations with non-accidental/non-suicidal deaths (referred throughout as non-accidental deaths), accidental deaths, suicides, non-fatal accidents, and suicide attempts.

We included year of birth and several maternal and paternal characteristics as covariates and conducted cousin comparisons to additionally adjust for unmeasured confounding. Specifically, we examined children of maternal siblings, thereby including half and full cousins. Cousin comparisons account for all environmental factors shared by cousins that make them similar, including any confounding that extends to family background characteristics on their maternal side. Additionally, cousin comparisons help account for some genetic selection because, on average, offspring of full siblings share 12.5% of their genetic variants. Cousin comparisons cannot rule out confounding by factors that are not shared by extended-family members, as well as differences due to paternal characteristics. Therefore, cousin comparisons rule out less confounding than sibling comparisons. The advantage of cousin over sibling comparisons is that cousin comparisons can answer questions about risks that tend to be shared by siblings, including maternal age at first childbirth. Cousin comparisons are also not biased by potential carryover effects. Studying maternal age at childbirth with sibling comparisons is also problematic because differences in year of birth and birth order are highly correlated with differences in maternal age at childbirth within nuclear families. (See D'Onofrio et al. 2013a, b for a review on family-based, quasi-experimental designs.)

Therefore, we expand upon previous studies, including Swedish-registry-based research, by (a) restricting the sample to first-born offspring and utilizing cousin comparisons to reduce bias from carryover effects, cohort effects, and birth order, (b) adjusting for year of birth and studying a more recent cohort (offspring born 1973 to 2012) to further reduce bias from cohort effects, and (c) examining additional outcomes, including accidental deaths and suicide attempts.

Methods

This population-based, cohort study used data recorded in national Swedish registries to create a target sample of all first-born, singleton pregnancies without missing data occurring to women under the age of 30 years resulting in live births between 1973 and 2012. This study was approved

by the institutional review board at Indiana University and the regional ethical review board in Stockholm, Sweden. A STROBE checklist (Table S1) documents that the necessary items were included in this report.

We obtained data by linking information from seven Swedish registers. The Medical Birth Register includes information on 96–99% of births and pregnancy characteristics since 1973 (Cnattingius et al. 1990; National Board of Health and Welfare, 2003, 2013). The Cause of Death Register includes information on principal and contributing causes of death since 1958 (Brooke et al. 2017). The National Patient Register began recording information on public hospital admissions in 1964, and from 1987 it covers diagnostic codes from all hospital admissions in Sweden. Since 2001 it additionally includes 80% of diagnostic codes from specialist outpatient care (Ludvigsson et al. 2011; National Board of Health and Welfare 2009, 2019; WHO 1992). The Education Register includes highest level of completed formal education (Statistics Sweden 2009). The National Crime Register includes criminal convictions since 1973 (BRÅ 2011; Fazel and Grann 2006). The Register of the Total Population contains information on all migrations since 1901 (Statistics Sweden 2013). The Multi-Generation Register links all individuals born since 1932 and residing in Sweden since 1961 to their adoptive and biological parents (Statistics Sweden 2010).

Measures

Exposure

MAFC categories included < 20, 20–24, and 25–29 years. Note that we also examined MAFC as continuous in a sensitivity analyses (see below).

Outcomes

We used either death records or inpatient and outpatient diagnoses made using the International Classification of Diseases (ICD) eighth, ninth, and tenth editions criteria to define all binary outcomes (Table S2 includes specific ICD codes). We included all selected ICD codes if they were present in the hospital or mortality records, regardless of whether they were primary. We assessed offspring mortality before age 40 due to non-accidental deaths (Anderson et al. 2001), accidents (i.e., accidental poisoning, accidental overdose, transport accidents, and all other accidents; Anderson et al. 2001; Chang et al. 2017; Rockett et al. 2010), and suicides (i.e., intentional and undetermined intent self-injurious behavior; e.g., Runeson et al. 2010). Mortality outcomes were coded as ever present (1) or absent (0). To assess non-fatal behavioral health outcomes, we captured accidents or suicide attempts. Given the possibility of repeated accidents or suicide attempts, we coded the first instance of a non-fatal event as present (1); otherwise, absence of a non-fatal event was coded as 0. Given the rarity of suicidal behavior in young childhood (Borges et al. 2008; Kosky 1983), we defined suicidal behavior as occurring at or after age 9 years. While suicide and suicide attempt were derived from ICD codes indexing behavior due to intent to injure and not intent to die, research has suggested that these measures are valid and epidemiological research has widely used them to index suicidal behavior (Tøllefsen et al. 2015).

Covariates

We included offspring year of birth as a covariate (categorized into 8 groups). We also controlled for several maternal and paternal characteristics. These characteristics included inpatient and outpatient ICD diagnoses made prior to conception of substance use disorder, schizophrenia, bipolar disorder, intentional or undetermined intent suicide attempts; any criminal convictions before conception; maternal and paternal country of origin (Sweden versus other); and paternal age at childbearing. Previous research has validated the ICD-coded psychiatric diagnoses (D'Onofrio et al. 2012; Kendler et al. 2012; Lichtenstein et al. 2009; Tidemalm et al. 2008) and shown high predictive validity for the criminality measure (D'Onofrio et al. 2010; Frisell et al. 2011).

Analyses

We conducted analyses in SAS 9.4 and STATA 16.0.

Descriptive Statistics

We assessed the occurrence of the outcomes and the covariates stratified by MAFC categories in the target sample.

Associations Between Maternal Age at Childbearing and Offspring Outcomes

For all models, we fit Cox proportional hazard regression models to account for right censoring. Offspring were censored at date of first event, emigration, death, or end of the study follow up. We fit three models to predict the outcomes from MAFC < 20 years and MAFC 20–25 years. Model 1 was the baseline population-wide model that only accounted for year of birth. Model 2 was the adjusted population-wide model that included all measured covariates as predictors. Model 3 compared exposure-discordant cousin pairs (i.e., cousin pairs who were discordant on MAFC category) while adjusting for measured covariates. We defined cousin pairs as pairs of offspring who shared a maternal grandmother identifier but differed on maternal identifier. For cousin comparisons, we used fixed effects models and stratified

Cox regression to make within-family comparisons (Allison 2009).

We fit all models in the entire analytic sample except models predicting suicide and suicide attempt. Because we defined suicide and suicide attempt as occurring after age 9 years, we fit these models in the subsample of offspring born between 1973 and 2004 to allow adequate follow-up time.

Sensitivity Analyses

First, to determine the potential impact of excluding later-born offspring, we fit the adjusted models in a sample that included second- and later-born offspring. Second, given that the reasons for non-accidental death likely differ in infancy and later in life (Chen et al. 2008; Coyne and D'Onofrio 2012; Olausson et al. 1999; Restrepo-Méndez et al. 2011), we used logistic regression to assess baseline and adjusted population-wide associations between MAFC and non-accidental death occurring before age one. Third, in order to assess whether the associations with offspring accidental deaths and non-fatal accidents were driven by specific types of accidents, we estimated associations between MAFC and specific types of fatal and non-fatal accidents (i.e., accidental poising related to alcohol use, other accidental poising, accidental overdose, motor vehicle accidents, other transport accidents, and other accidents). Fourth, in order to examine cohort effects, including cohort effects that may have been due to the National Patient Register covering less information for earlier born offspring, we estimated unadjusted associations stratified by year of birth (i.e., 1973–1982, 1983–1992, 1993–2002, 2003–2012). Fifth, we re-estimated all main analyses models using continuous MAFC as a linear predictor to examine whether our decision to categorize MAFC into a few, discrete groups influenced our findings.

Results

Sample

The target sample included 4,070,974 offspring born January 1st 1973 to December 31st 2012 and followed through December 31st 2013 and sequentially excluded offspring who were part of multiple births (99,569), stillborn (13,601), second- or later-born (2,263,620), with missing MAFC (4), or born to women who were 30 years or older (443,980). We excluded offspring born to women 30 years or older because of our focus on early age at first childbearing, and previous research has indicated there is a different pattern of associations with advancing age at childbearing (e.g., Myrskylä and Fenelon 2012; Sujan et al. 2016). After applying the exclusions, the resulting target sample included 1,250,200 singleton, live, first-born offspring born to women under the age of 30 years in Sweden between 1973 and 2012.

To create the analytic sample, we started with the target sample and excluded offspring with missing maternal identifiers (3240), missing paternal identifiers (16,046), fathers with missing paternal age (14,397), mothers with missing country of origin (106), and fathers with missing country of origin (203). The resulting analytic sample of 1,216,208 offspring represents 97.3% of the target sample. For two of our outcomes (i.e., suicide and suicide attempt), we conducted the analyses on a subsample of the analytic sample comprising 1,004,815 offspring born between January 1st 1973 and December 31st 2004 in order to have adequate follow-up time. Otherwise, the risk period started at birth.

Descriptive Statistics

Table 1 provides the prevalence of the covariates and estimated cumulative incidence of the outcomes by age 25 years stratified by MAFC category in the target sample. Table S3 provides information on the number of exposure discordant cousins stratified by exposure status. Table S4 provides information on the number of cousins who were doubly discordant (i.e., discordant on both the MAFC category and the outcome).

Associations with Offspring Outcomes

Non-accidental Deaths

Compared to MAFC 25–29, MAFC < 20 was associated with an elevated risk of non-accidental death in the baseline model [Hazard Ratio (HR) 1.23, 95% confidence interval (CI) 1.14, 1.32; Table 2] and adjusted model (HR 1.14, 95% CI 1.04, 1.24). Among cousins, the association was minimal and could not be distinguished from the null (HR 1.06, 95% CI 0.90, 1.25). Across all models, the relationship between MAFC and non-accidental death showed an inverse linear trend, such that the magnitude of associations between MAFC 20–24 and non-accidental death was smaller compared to MAFC < 20 (Table 2).

Accidental Deaths

Compared to MAFC 25–29, early MAFC was associated with increased risk of accidental death in the baseline model (MAFC < 20 HR 2.50, 95% CI 2.23, 2.80; MAFC 20–24 HR 1.42, 95% CI 1.30, 1.56). This association was attenuated in adjusted (MAFC < 20 HR 1.96, 95% CI 1.71, 2.25; MAFC 20–24 HR 1.31, 95% CI 1.19, 1.45) and cousin comparison models (MAFC < 20 HR 1.61, 95% CI 1.22, 2.11; MAFC 20–24 HR 0.99, 95% CI 0.81, 1.21).

Table 1 Demographics in target sample

	Maternal age at first childbirth (years)		
	< 20	20–24	25–29
	n = 114,006 (9.1%)	n = 525,330 (42.0%)	n = 610,864 (48.9%)
Offspring Outcomes			
Non-accidental deaths[a]	1092 (1.1)	3658 (0.8)	3173 (1.0)
Accidental deaths[a]	357 (0.4)	865 (0.2)	566 (0.2)
Non-alcohol related accidental poisoning[a]	2 (0.0)	9 (0.0)	5 (0.0)
Alcohol related accidental poisoning[a]	14 (0.0)	20 (0.0)	12 (0.0)
Accidental overdose[a]	44 (0.1)	97 (0.0)	51 (0.0)
Motor vehicle accidents[a]	216 (0.3)	520 (0.1)	334 (0.1)
Other transport accidents[a]	125 (0.2)	341 (0.1)	213 (0.0)
Other accidents[a]	222 (0.3)	549 (0.2)	397 (0.1)
Suicides[a]	158 (0.2)	396 (0.1)	242 (0.1)
Non-fatal accidents[a]	9930 (10.7)	43,128 (10.6)	45,079 (10.7)
Non-alcohol related accidental poisoning[a]	158 (0.2)	547 (0.1)	556 (0.1)
Alcohol related accidental poisoning[a]	57 (0.1)	145 (0.0)	96 (0.0)
Accidental overdose[a]	264 (0.3)	805 (0.2)	642 (0.2)
Motor vehicle accidents[a]	4642 (5.6)	19,016 (5.2)	17,216 (4.8)
Other transport accidents[a]	4757 (5.7)	1923 (5.3)	17,640 (4.8)
Other accidents[a]	9423 (10.8)	41,648 (10.8)	43,792 (10.9)
Suicide attempts[a]	1790 (2.2)	4719 (1.4)	3173 (1.0)
Year of birth			
1973 to 1977	32,323 (28.4)	96,550 (18.4)	69,479 (11.4)
1978 to 1982	19,749 (17.3)	76,775 (14.6)	63,948 (10.5)
1983 to 1987	14,251 (12.5)	74,191 (14.1)	71,333 (11.7)
1988 to 1992	15,412 (13.5)	87,945 (16.7)	91,562 (15)
1993 to 1997 (reference)	9789 (8.6)	58,351 (11.1)	80,347 (13.2)
1998 to 2002	7402 (6.5)	40,477 (7.7)	72,497 (11.9)
2003 to 2007	7451 (6.5)	41,329 (7.9)	78,112 (12.8)
2008 to 2012	7629 (6.7)	49,712 (9.5)	83,586 (13.7)
Maternal characteristics			
Substance use disorder diagnosis before conception	1307 (1.1)	5030 (1)	3999 (0.7)
Schizophrenia or bipolar disorder before conception	23 (0)	335 (0.1)	659 (0.1)
Definite or uncertain suicide attempt before conception	2323 (2)	8149 (1.6)	6790 (1.1)
Any criminal convictions before conception	8201 (7.2)	34,894 (6.6)	34,654 (5.7)
Country of origin			
Sweden	93,770 (82.3)	444,646 (84.6)	529,577 (86.7)
Missing	433 (0.4)	1446 (0.3)	1511 (0.2)
Paternal characteristics			
Age at year of birth			
< 20 years	12,925 (11.3)	3619 (0.7)	244 (0)
20 to 24 years	64,178 (56.3)	164,771 (31.4)	26,009 (4.3)
25 to 29 years (reference)	24,109 (21.1)	246,125 (46.9)	265,145 (43.4)
30 and older	8073 (7.1)	96,404 (18.4)	305,253 (50)
Missing	4721 (4.1)	14,411 (2.7)	14,213 (2.3)
Substance use disorder diagnosis before conception	2291 (2)	7592 (1.4)	6116 (1)
Schizophrenia or bipolar disorder before conception	89 (0.1)	432 (0.1)	539 (0.1)
Definite or uncertain suicide attempt before conception	1317 (1.2)	4769 (0.9)	3999 (0.7)
Any criminal convictions before conception	40,293 (35.3)	153,465 (29.2)	146,342 (24)
Country of origin			

Table 1 (continued)

	Maternal age at first childbirth (years)		
	< 20	20–24	25–29
	n = 114,006 (9.1%)	n = 525,330 (42.0%)	n = 610,864 (48.9%)
Sweden	87,547 (76.8)	429,743 (81.8)	522,555 (85.5)
Missing	3514 (3.1)	8552 (1.6)	7146 (1.2)

[a]Age 25 Kaplan Meier estimate

Table 2 Associations between maternal age at first childbirth and offspring mortality and morbidity

	Baseline HR (95% CI)	Adjusted HR (95% CI)	Cousin comparison HR (95% CI)
Non-accidental deaths			
MAFC < 20 years	1.23 (1.14, 1.32)	1.14 (1.04, 1.24)	1.06 (0.90, 1.25)
MAFC 20–24 years	1.08 (1.02, 1.13)	1.05 (1.00, 1.11)	1.04 (0.93, 1.15)
Accidental deaths			
MAFC < 20 years	2.50 (2.23, 2.80)	1.96 (1.71, 2.25)	1.61 (1.22, 2.11)
MAFC 20–24 years	1.42 (1.30, 1.56)	1.31 (1.19, 1.45)	0.99 (0.81, 1.21)
Suicides[a]			
MAFC < 20 years	2.08 (1.79, 2.41)	1.57 (1.31, 1.89)	1.01 (0.69, 1.47)
MAFC 20–24 years	1.36 (1.21, 1.53)	1.25 (1.10, 1.43)	0.98 (0.74, 1.30)
Non-fatal accidents			
MAFC < 20 years	1.41 (1.38, 1.44)	1.30 (1.27, 1.33)	1.14 (1.08, 1.19)
MAFC 20–24 years	1.16 (1.14, 1.17)	1.11 (1.10, 1.13)	1.04 (1.01, 1.07)
Suicide attempts[a]			
MAFC < 20 years	2.85 (2.71, 3.00)	2.16 (2.03, 2.29)	1.35 (1.19, 1.52)
MAFC 20–24 years	1.48 (1.42, 1.54)	1.34 (1.28, 1.39)	1.09 (1.00, 1.19)

HR hazard ratio, *CI* confidence interval, *MAFC* maternal age at first childbirth. Reference group is MAFC of 25 to 29 years

[a]Suicide and suicide attempt analyses conducted in a subsample of offspring born 1973 through 2004 in order to have an adequate follow up period

Death by Suicide

In baseline models, early MAFC was associated with an elevated risk of suicide (MAFC < 20 HR 2.08, 95% CI 1.79, 2.41; MAFC < 20–24 HR 1.36, 95% CI 1.21, 1.53). The association was attenuated after covariate adjustment (MAFC < 20 HR 1.57, 95% CI 1.31, 1.89; MAFC < 20–24 HR 1.25, 95% CI 1.10, 1.43). Moreover, early MAFC was not associated with increased risk of suicide in the cousin comparison models (MAFC < 20 HR 1.01, 95% CI 0.69, 1.47; MAFC 20–24 HR 0.98, 95% CI 0.74, 1.30).

Non-fatal Accidents

MAFC < 20 was associated with increased risk for non-fatal accidents (baseline HR 1.41, 95% CI 1.38, 1.44), which remained largely unchanged when including measured covariates (adjusted HR 1.30, 95% CI 1.27, 1.33). The results were similar, albeit smaller in magnitude, for MAFC 20–24 (baseline HR 1.16, 95% CI 1.14, 1.17; adjusted HR 1.11, 95% CI 1.10, 1.13). When comparing cousins, the associations with non-fatal accidents were substantially attenuated (MAFC < 20 HR 1.14, 95% CI 1.08, 1.19; MAFC 20–24 HR 1.04, 95% CI 1.01, 1.07).

Suicide Attempts

In baseline and adjusted population-wide models, earlier MAFC was associated with increased risk of suicide attempt. Associations with MAFC < 20 (baseline HR 2.85, 95% CI 2.71, 3.00; adjusted HR 2.16, 95% CI 2.03, 2.29) were stronger than associations with MAFC 20–24 (baseline HR 1.48, 95% CI 1.42, 1.54; adjusted HR 1.34, 95% CI 1.28, 1.39). Associations with early MAFC were attenuated in the cousin comparisons (MAFC < 20 HR 1.35, 95% CI 1.19, 1.52; MAFC 20–24 HR 1.09, 95% CI 1.00, 1.19).

Sensitivity Analyses

Sensitivity analyses suggested that the main findings were commensurate in a sample that did not exclude second- and later-born offspring, though the magnitude of the associations were somewhat smaller than in the sample restricted to first-born offspring (Table S5). Early MAFC was also not associated with infant non-accidental death before age one in population-wide models, suggesting that observed associations with non-accidental death in main analyses models were not driven by infant mortality (Table S6). Baseline associations were also generally similar across the different types of accidents (though substance-related accidents were slightly higher), suggesting that observed associations with fatal and non-fatal accidents were not driven by a specific type of accident (Table S7). Though we lacked statistical power to precisely estimate associations stratified by year of birth, unadjusted associations were also generally similar across years of birth, reducing concerns that cohort effects and selective outcome missingness among earlier born offspring influenced our results (Table S8). Additionally, we found the same patterns of results for all the outcomes across all three models when we used continuous MAFC. The crude associations with continuous MAFC were largest for accidental deaths, suicides, and suicide attempts, and adjusting for measured covariates and comparing cousins greatly reduced the magnitude of the associations (Table S9).

Discussion

In a sample of over one million Swedish first-born offspring, we examined associations between early MAFC (i.e., < 20 and 20–24 compared to 25–29 years) and offspring non-accidental deaths, accidental deaths, deaths by suicide, non-fatal accidents, and suicide attempts in offspring. Consistent with previous studies (Ekeus et al. 2006; Myrskylä and Fenelon 2012; Niederkrotenthaler et al. 2012; Taylor et al. 1983), our results showed that early MAFC was associated with all assessed outcomes in population-wide models. However, given that MAFC is associated with other risk factors for adverse offspring outcomes, the observed population-wide associations could have been due to confounding factors, such as variance in paternal characteristics. Therefore, we compared cousins born to women of different ages while also adjusting for year of birth and maternal and paternal characteristics. Consistent with a previous sibling-comparison study that did not support an independent association between early MAFC and offspring mortality (Barclay and Myrskyla 2018), our cousin comparison suggested that early MAFC was not associated with a substantial increased risk of offspring non-accidental deaths and deaths by suicide. However, we did find independent associations between MAFC before age 20 and accidental deaths, non-fatal accidents, and suicide attempt in cousin comparison models.

Our findings should be interpreted in light of several limitations. First, the remaining independent associations could be due to unmeasured confounding as cousin comparisons cannot rule out confounding by factors that are not shared by extended-family members or differences due to paternal characteristics. Unlike some previous studies, we did not conduct sibling comparisons, which could have ruled out additional confounding from factors shared within nuclear families. We did not include sibling comparisons due to their inability to differentiate carryover effects, birth order, and year of birth from the associations with maternal age at childbearing. Second, we could not rule out the possibility that observed associations may have been influenced by differential observation time, as offspring born in early years had longer follow-up than offspring born in subsequent years. While our use of Cox proportional hazard regression models and adjustment for year of birth likely limit the influence of differential follow-up on the observed associations, we cannot rule it out as a possibility. Third, despite our large sample size, we lacked statistical power to precisely estimate associations with death by suicide in the cousin comparison model, as well as in some sensitivity analyses. Fourth, we conducted analyses on a Swedish population-based sample and do not know if findings will generalize to other populations. Therefore, future studies will need to evaluate whether our findings replicate across other populations, especially those in which early MAFC is more common (e.g., the United States; Kearney and Levine 2012).

Despite these limitations, our results have important implications. The results suggest that background factors associated with early MAFC, such as low socioeconomic status and/or genetic factors, rather than MAFC itself may be largely responsible for the observed associations between early MAFC and adverse offspring outcomes, primarily non-accidental deaths and suicide. This finding is consistent with prior literature examining the role of education and cognitive ability in relation to MAFC, which supported the role of between-family variance, compared to within-family variance, in examining differences in MAFC (Rodgers et al. 2008). One potential genetic pathway may be that of risky decision-making. Teenage childbearing is associated with conduct disorder and externalizing and self-control problems (Coyne and D'Onofrio 2012), which are partly attributed to genetic contributions (Hicks et al. 2004), and may, in turn, be associated with genetic vulnerabilities and risk for adverse outcomes in the offspring. However, similar to previous studies, different outcomes displayed different associations with early MAFC (Shaw et al. 2006). Notably, offspring accidental deaths and suicide attempts remain relatively elevated in

the cousin comparisons, and to a smaller degree, non-fatal accidents. Results for accidents and suicide attempts are mixed in previous literature and our contribution of a cousin comparison aids in the nuances of differential associations with various outcomes. Our findings suggest that rather than intervening to prevent early MAFC, at-risk families and, in particular, young mothers may benefit more from intervention efforts focused on changing other modifiable risk factors that impact offspring development (Jaffee et al. 2001). For example, previous research has suggested that potential mechanisms of the associations between maternal age at childbearing and offspring outcomes may be low maternal supervision, maternal anxiety and depression, and maternal smoking (Shaw et al. 2006; Taylor et al. 1983), which may be indicative of maternal stress and low socioeconomic status. Bolstering individual-level interventions with population-level interventions targeted at poverty may provide a more holistic approach of supporting teenage mothers and addressing adverse offspring outcomes.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10519-021-10091-7.

Author Contributions ACS, LMO, and BMD conceptualized and designed the study. ACS analyzed the data. ACS and LMO drafted the manuscript. All authors provided critical revisions. ACS and LMO obtained funding for the study. BMD and ASA provided supervision.

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Data Availability The data used in this study are national register information. The authors had no special privileges in accessing the data. Dissemination of personal information is regulated by the Swedish Secrecy Act. In accordance with Swedish law, researchers seeking access to individual-level data must apply for permission through a Research Ethics Board (etikprovningsmyndigheten.se) and from the primary owners, Statistics Sweden (https://www.scb.se/en/services/guidance-for-researchers-and-universities), and the National Board of Health and Welfare (https://www.socialstyrelsen.se/en/statistics-and-data/statistics/).

Code Availability We conducted analyses in SAS 9.4 and STATA 16.0.

Declarations

Conflict of interest Ayesha C. Sujan, Lauren M. O'Reilly, Martin E. Rickert, Henrik Larsson, Paul Lichtenstein, A. Sara Oberg and Brian M. D'Onofrio declare that they have no conflict of interest.

Ethical Approval The institutional review board at Indiana University and the regional ethical review board in Stockholm, Sweden, approved this study.

Informed Consent According to Swedish law, informed consent was not necessary because the study used data available from national Swedish registries.

Human and Animal Rights All data made available to the investigators were done so without identifying information, and the dataset did not involve "intervention or interaction" with subjects for the proposed research. Analysis of the dataset is exempt under Exemption 45 CFR 46.101(b)(4). It involves the study of "existing data … recorded by the investigator in such a manner that subjects cannot be identified." These designations have been confirmed with Institutional Review Boards at the IU (#1404771406A003).

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