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The Association of Paternal Age and Perinatal Outcomes between 2007 and 2016 in the United States

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Abstract

Objective

To evaluate the impact of advanced paternal age (APA) on maternal and perinatal outcomes in the US.

Design

A retrospective, population-based cohort study.

Setting

United States of America.

Subjects

All 40,529,905 documented live births between 2007 and 2016 in the US.

Main outcome measures

Primary perinatal outcomes included were gestational age, birth weight, apgar score, NICU admission, postpartum antibiotics, and seizures. Primary maternal outcomes evaluated were gestational diabetes and pre-eclampsia. Secondary outcome measured was the number of preventable perinatal events.

Results

Increasing paternal age was associated with increased risk of premature births, low birth weights, and low Apgar scores. **After adjusting for maternal age**, infants born to fathers 45 years and older had 14% higher odds of being admitted to the NICU (OR 1.14, 1.13-1.16), independent of gestational age, and 18% higher odds of having seizures (OR: 1.18, .97-1.44) compared to fathers 25 to 34 years. There were 34% higher odds of gestational diabetes (OR 1.34, 1.29-1.38) in mothers with the oldest partners. 13.2% (12.5%-13.9%) of premature births and 18.2% (17.5%-18.9%) of gestational diabetes in births associated with older fathers were estimated to be attributable to APA.

Conclusions

APA is associated with negative effects on both mothers and offspring. Given the relatively low prevalence of APA in the US, population level impacts are currently modest. Nevertheless, as APA has doubled in the US over the past generation, further investigation is warranted on the impact of paternal age on birth outcomes and public health.

Introduction

The age at which parents have children within the United States continues to rise.^{1,2} The number of first births to women older than 35 years has climbed by about 2% annually since the 1970s, and the percentage of all births in the US to fathers over 40 has doubled to 9% over the same time period. While the effects of advanced maternal age on perinatal outcomes have been extensively studied, research on the impact of older fathers on offspring health has been limited mostly to the evaluation of congenital disease risk.³⁻⁸

Indeed, the high number of male germ-cell divisions in aging fathers has been proposed to increase the risk of autism, genetic abnormalities, psychiatric morbidity, and neoplasia in offspring, but recent studies have also suggested a potential paternal effect on perinatal morbidity.^{6,9-14} One common explanation arises from the epigenetic changes that occur within spermatocytes, specifically histone modifications and DNA methylation changes in spermatozoa of older men. These alterations occur in regions of the genome that are responsible for several offspring diseases.¹⁵ Disruption of histone methylation in developing male germ cells may be the precursor to aberrant embryonic and placental development with prior studies suggesting paternal imprinting of aging may affect both fetal growth and maternal health during pregnancy.^{16,17}

Utilizing birth registries, several groups have attempted to characterize the risk of advanced paternal age on risk for adverse birth events such as preterm birth, low birth weight, and pre-eclampsia.¹⁸ However, findings remain inconclusive due to insufficient sample sizes, short study periods, and difficulty obtaining reliable paternal age data.¹⁸⁻²⁰ Thus, the potential association between advanced paternal age and health of the mother and offspring remains poorly defined. The objective of this study was to examine the association of paternal age on maternal and neonatal health and to estimate the impact of advancing paternal age in the United States.

Methods

Data Source

This retrospective cohort analysis draws on data published by the National Vital Statistics System (NVSS), a federal data sharing program provided by the CDC and the National Center for Health Statistics (NCHS). Through contracts with individual vital registration systems within each state, the NCHS compiles live birth data collected from birth certificates and permits distribution of these statistics for medical research purposes. Standard birth certificates contain self-reported parental demographics such as age, race, and education as well as pregnancy and birth outcomes, which are documented by health care providers. All births occurring within the United States since 1985 are captured by this system.²¹ The NCHS ensures completion, accuracy, and standardization of reporting of vital events by providing training modules and guidelines for healthcare practitioners collecting birth data.²² Coding of the data also undergoes rigorous statistical quality checks and is edited for accuracy by the NCHS. If systematic reporting failures are noted, records are returned to the registration site for correction.²⁰ This study was exempt from our Institutional Review Board approval as all data are federally mandated for collection and de-identified prior to being made available for analysis. Thus, no patients were directly involved in the study.

Study Cohort and Demographic Variables

All reported live births between 2007 and 2016 within the United States were included in the analysis. Data files were compiled sequentially by year, and all available demographic variables were extracted including age, race, education, marital status, smoking history, and access to care. Paternal age was categorized into ten year intervals: <25 years, 25 to 34 years, 35 to 44 years, 45 years to 54 years, and 55 years and older.²³ Five year intervals were also analyzed though no significant difference in trends were noted (Supplemental Table 1). Racial categories were defined by the US Office of Management and Budget (OMB), and subjects were categorized based on how they self-identified. Data on paternal education was unavailable until 2009 due to NCHS collection policy. Missing paternal data from birth certificates were accounted for using inverse probability weighting (IPW).²⁴ To account for inconsistent reporting of paternal data across various demographics, a logistic regression model incorporating maternal age, race, birth year, and education was

utilized to model the probability of paternal reporting for each birth. Inverse probability weighting was subsequently applied to all statistical analyses to maximize generalizability to all births. This weighting methodology was described previously.²⁴

Outcomes

The primary outcome of interest was the perinatal risk to child and mother correlated with advanced paternal age. A preliminary literature search was conducted to determine birth outcomes that have previously been associated with advanced paternal ages. Of these variables, those available within the NVSS data files were subsequently included in the analysis. Neonatal outcomes evaluated were premature birth (gestational age <37 weeks), low birth weight (birth weight <2500 grams), low 5-minute Apgar score (<8), requirement of assisted ventilation at birth, admission to the Neonatal Intensive Care Unit (NICU), requirement of postpartum antibiotics, and seizures.^{25,26} A neonatal adverse event was defined as the requirement or occurrence of at least one of the following: assisted ventilation, NICU admission, antibiotics, or seizure. The maternal outcomes evaluated were gestational diabetes, preeclampsia, and eclampsia. All variables were categorized as dichotomous while gestational age, birth weight (LBW), and Apgar score were also presented as continuous variables. The sex-ratio of all births was also evaluated for each paternal age group.

Statistical Analysis

The mean paternal age with standard deviations along with standard demographics of all live births were analyzed from 2007 and 2016 as a pooled cohort. Logistic regression models were created to estimate the adjusted odds ratio (AOR) for each perinatal outcome by paternal age group with fathers between 25 and 34 years as the reference. Given the collinearity between paternal and maternal age, stratified analyses based on maternal age and sensitivity analyses were also performed. Moreover, given the association between adverse birth outcomes and prematurity, separate analyses were conducted while limiting analyses to full term infants (Supplemental Table 2). Other subgroup analyses were conducted to ensure that the paternal age association was not confounded by paternal age grouping, birth order, birth year, or missing paternal data (Supplemental Tables). To test for a systematic change in sex-ratio between paternal age groups, the number and percentage of male and female births to each paternal age group were compared. The Wilcoxon rank-sum test was used to determine whether a significant difference existed among age groups. A regression analysis was also conducted to determine adjusted odds ratios of siring a son for each paternal age group.

The number and percentage of men who fathered children with each morbidity were compared. The number of preventable perinatal events if fathers within the United States were all younger than 45 years of age was also estimated. The population attributable risk was calculated using the standard formula (observed prevalence – predicted prevalence of outcome after shift to new distribution of younger fathers)/(observed prevalence).^{27,28} All statistical analysis was carried out using Stata version 14 (College Station, TX) and the user-written package *punaf* (Population Attributable Risk Fraction).²⁹ Statistical tests were all two-sided and ninety-nine percent confidence intervals were provided for precision of the estimates.

Results

A total of 40,529,905 births occurring within the United States were evaluated between 2007 and 2016. Paternal, maternal and infant demographics were described in Table 1. The mean age of fathers during this time period increased from 30.0 years to 31.2 years.

After adjusting for maternal age, race, education, maternal smoking status, and number of prenatal visits, births sired by the oldest fathers were found to be associated with worse birth outcomes (Table 2). Fathers over 45 years sired children born at earlier gestational ages (on average 0.12 weeks younger, CI: -0.13 to -0.11) and had 14% higher odds of having a premature birth (<37 weeks) compared to younger fathers (AOR: 1.14, CI: 1.13 to 1.16). Infants born to fathers in the second-oldest age group were also born 20.2 grams lighter, CI: -22.5 to -18.0, and had a 14% greater risk of low birth weight (<2500g) than infants born to younger fathers (AOR: 1.14, CI: 1.12 to 1.15). The odds of having a low Apgar score (< 8) was found to be greater for only fathers older than 55 years (AOR: 1.14, CI: 1.08 to 1.20).

1 Infants born to fathers in the oldest age group also had a significantly higher risk of requiring additional
2 medical care after birth. The odds of the child requiring assisted ventilation increased by 10% (AOR: 1.10, CI:
3 1.04 to 1.16) and the odds of requiring NICU admission increased by 28% (AOR: 1.28, CI: 1.24 to 1.33).

4 The secondary sex ratio declined with increasing paternal age as shown in Table 3. Younger fathers (<
5 25 years of age) were more likely to sire a boy than fathers between 25 and 34 years of age after adjustment for
6 other paternal and maternal characteristics including maternal age (AOR: 1.007, CI: [1.003, 1.010]). However,
7 no change in the secondary sex ratio of oldest fathers was noted (AOR: 0.995, CI: [.989, 1.002]). A sub-analysis
8 was additionally conducted excluding births that underwent in vitro fertilization (IVF) (1.53% of all births) with
9 no changes to the conclusions.

10 Pregnancy related outcomes for mothers were also examined. Fathers older than 45 years had 28%
11 increased odds of a pregnancy complicated by gestational diabetes compared to fathers in the reference group
12 (AOR: 1.28, CI: 1.27 to 1.30), though no significant association was found between paternal age and risk of
13 pre-eclampsia or eclampsia (AOR 1.00, CI: 0.96-1.05 and AOR 1.03, CI: 0.84-1.25, respectively).

14 After stratification by maternal age, increasing paternal age remained significantly associated with
15 perinatal outcomes with similar trends across all maternal age strata (Figure 1 and Supplemental Figure 1).
16 Similar findings were noted when limiting the analysis to first births to mothers (Supplemental Table 3). In
17 addition, similar findings were identified during separate time periods (i.e. 2007 vs 2016) indicating that these
18 trends were not influenced by recent changes in medical practice (Supplemental Table 4).

19 The distribution of paternal age groups was recalculated for a scenario in which all fathers were younger
20 than 45 years of age in order to estimate the population attributable risk of advanced paternal age. Table 4
21 demonstrates that over the last decade, 13% (CI: 12.5% to 13.9%) of all premature births and 14.5% (CI: 13.6%
22 to 15.4%) of infants with low birth weight born to older fathers (under the assumption of a causal relation) can
23 be attributed to the increase in number of fathers older than 45 years. 15.1% (CI: 14.2% to 15.9%) of all NICU
24 admissions and 18.2% (CI: 17.5% to 18.9%) of all gestational diabetes diagnoses are also attributable to these
25 older fathers.

32 Discussion

33 Paternal age is rising in the United States with potential implications for maternal and child health.
34 Infants born to fathers over 35 years were found to be at a higher risk of premature birth, low birth weight, and
35 increased morbidity (e.g. assisted ventilation, NICU stay, antibiotic administration) during the perinatal period.
36 A large percentage of cases of premature births, LBW, and NICU admissions in children of older fathers was
37 found to be associated with advanced paternal age. In addition, increased paternal age is negatively associated
38 with maternal health as identified through an elevated risk of gestational diabetes. Though, as the prevalence of
39 advanced paternal age remains modest, the impact of these associations at a population level remains uncertain.
40 **Indeed, the increased odds ratios are <1.5, suggesting the overall risk of these outcomes likely still remains low.**
41 The increased risks associated with father's age appears to be "dose" dependent with a J-shaped association
42 curve. While the youngest fathers tend to have worse perinatal outcomes as men in their twenties, fathers that
43 are 35 years and older appear to have significantly worse perinatal outcomes. This trend continues with
44 increasing age (dose).

45 The initial identification of paternal contribution to birth outcome dates back to Willhelm Weinberg's
46 discovery of a correlation between achondroplasia and birth order in 1912, but it was James Crow's seminal
47 work at the turn of the century that spurred significant interest into paternal age effects on infant health.^{9,30} Still,
48 there is a dearth of published data on the paternal effects on birth outcomes, and the little existing data have
49 been mostly equivocal. Studies evaluating the association between paternal age and risk of preeclampsia, low
50 Apgar scores, and NICU admissions have also been rare.

51 Astolfi and colleagues evaluated 1.5 million Italian births between 1990 and 1998 and observed that
52 fathers 45 to 49 years of age had a higher risk of significantly preterm births (<32 weeks of gestation) compared
53 to fathers 25 to 29 years of age, particularly in first-born children.¹⁹ In contrast, a study of 2.5 million American
54 births to married, nulliparous women between 1995 and 2000 uncovered an association between teenage fathers

1 and preterm births but no association for fathers with advanced age.²⁰ However, in this study only 0.5% of births
2 (13,907 total births) were to fathers over the age of 45. The risk of other perinatal complications such as
3 preeclampsia, low birth weight, and low Apgar scores also remains uncertain given mixed findings from mostly
4 underpowered studies.^{18,25,26,31–36} While Reichman and Teitler initially found that fathers older than 35 years were at
5 increased risk for LBW, their findings were later questioned due to missing paternal ages thought to result in
6 selection bias.^{20,33}

7
8 Recent studies have begun to uncover a potential epigenetic link between the aging paternal genome and
9 offspring health outcomes.³⁷ Age-dependent alterations, such as DNA methylation, have been observed in
10 mammalian somatic and germline cells. Higher rates of methylation were found on ribosomal DNA of older rat
11 spermatozoa compared to younger controls.³⁸ Additionally, genomic imprinting has been suggested to influence
12 placental growth, morphology, and nutrient transfer, which in part explains the paternal influence on birth
13 outcomes.³⁹ For example, the overexpression of a demethylase enzyme (*Kdm1a*) in mice was found to result in
14 loss of methylation of H3K4, an epigenetic mark associated with developmental genes in sperm. The offspring
15 of these mice had increased rates of birth defects and neonatal mortality.^{40,41} Similarly, *IGF2* is a paternally
16 expressed gene susceptible to epigenetic modification that affects growth factors for both the placenta and
17 embryo.^{16,17} This may partially explain the increased placental weight found in pregnancies to older fathers which
18 in turn has been associated with an increased risk for pre-eclampsia and other maternal comorbidities (e.g.
19 gestational diabetes).⁴⁴ It has become increasingly clear that male aging influences germline integrity through
20 other mechanisms as well, such as DNA fragmentation, telomere lengthening, mutations, and overall genomic
21 instability.²³ Investigators have estimated that males develop approximately two additional mutations in their
22 germline DNA throughout life with *de novo* mutations increasing the risk of preterm birth.^{42,43} There certainly
23 exists a need to further elucidate the potential causal relationship between advanced paternal age and maternal
24 and infant outcomes, though it appears that the paternal effect on placental health may play a nontrivial, though
25 speculative, role.

26
27 The current study incorporates all live births over a span of ten years allowing for an unbiased analysis
28 of recent trends. The pooling of all births during this time period minimizes the risk of confounding from yearly
29 fluctuations in perinatal outcomes. Moreover, similar measures of association were identified from separate
30 times periods within the cohort indicating that findings do not reflect a time dependent phenomenon. Given the
31 increased risk of negative birth outcomes in premature births, a subset analysis with only term births was
32 conducted to corroborate the paternal age findings. The addition of IPW further reduces the overrepresentation
33 of certain demographics of fathers: mostly older, college-educated fathers who are more likely to be present at
34 birth.² There are several other advantages of utilizing national birth certificate data provided by the NCHS. This
35 unique system allows for incorporation of important covariates as well as for the formulation of propensity
36 weighting to adjust for missing paternal data. The inclusion of all births within the United States allows for
37 estimation of rates of occurrence and associated attributable risk fractions, which facilitates evaluation of the
38 public health impact of aging fathers.²⁹

39
40 As over 12% of births to fathers 45 years and older with adverse outcomes might have been prevented
41 were the father younger, the significance of these data is most important to parents planning their reproductive
42 future. Preconception counseling guidelines may need to change to incorporate the possibility that delaying
43 parenthood for fathers may not be as inconsequential as previously understood. The cumulative risk over
44 hundreds of thousands of births to older fathers is also likely to be significant both in terms of economic burden
45 and overall public health.

46
47 While this study found an overall positive association between older fathers and declining sex ratio, the
48 oldest group still maintained a similar proportion of male compared to female offspring as the reference group.
49 Thus, there appears to be no meaningful alteration in secondary sex ratio based on paternal age. It remains
50 likely that an altered secondary sex ratio is due to a combination of genetics and environmental exposures,
51 which are more likely to explain the declining ratio than advanced paternal age.⁴⁵

52
53 There are several limitations of using the Vital Statistics System for perinatal research. The natality
54 database uses birth certificate data that are completed by parents and health-care workers and reviewed
55 carefully for errors but remains susceptible to inaccuracies. This database is also limited to live births which

1 prevents the inclusion of stillbirths in the analysis. However, as fetal mortality is known to be associated with
2 advanced paternal age, the inclusion of these data would likely reinforce the findings of this study.⁴⁶ Though
3 inverse probability weighting was used to adjust for missing paternal data, the potential for over-representation
4 of fathers from certain sociodemographic backgrounds remains.² Multiple births to the same father are also not
5 accounted for in this study as all data are collected at the maternal level, allowing for the potential bias of some
6 at-risk fathers disproportionately contributing to estimated effects. Finally, despite attempts to adjust and
7 account for potential maternal confounding using regression analysis and stratification, some residual
8 confounding effects from older fathers being associated with older mothers may remain.
9

10
11 Nevertheless, this is the largest known study to evaluate potential fetal-maternal risks associated with
12 advancing paternal age. While it is important to note that the absolute risk of advancing paternal age on adverse
13 perinatal conditions remains modest, our findings emphasize the need to further investigate the public health
14 implications of the rising paternal age within the US and other developed countries.
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Table 1. Paternal, maternal, and infant demographics by paternal age group. Data described as the number of births and percentage of all births within each paternal age group. Missing paternal age data is presented as the number of birth certificates without paternal age for each category and the percentage of the total number of missing paternal age data.

# (%)	Birth Certificates	Paternal age (years)											
		< 25		25 - 34		35 - 44		45 - 54		55+		Missing Paternal Age	
Paternal Characteristics		6,319,860	15.6%	18,289,776	45.1%	8,476,310	20.9%	1,091,848	2.7%	111,130	0.3%	6,240,981	
Race													
	White	2,675,449	42.3%	10,514,234	57.5%	4,813,626	56.8%	547,388	50.1%	51,299	46.2%	548,536	8.8%
	Black	1,173,282	18.6%	2,004,854	11.0%	957,685	11.3%	197,292	18.1%	25,535	23.0%	179,190	2.9%
	Native American	84,260	1.3%	129,771	0.7%	44,769	0.5%	6,923	0.6%	847	0.8%	13,005	0.2%
	Asian	86,488	1.4%	961,160	5.3%	747,699	8.8%	83,329	7.6%	8,062	7.3%	74,281	1.2%
	Hispanic	2,046,130	32.4%	4,178,787	22.9%	1,667,539	19.7%	215,563	19.7%	20,141	18.1%	244,879	3.9%
	Other/ Unknown	254,251	4.0%	500,970	2.7%	244,992	2.9%	41,353	3.8%	5,246	4.7%	5,181,090	83.0%
Education													
	No High School	1,163,624	18.4%	1,792,661	9.8%	720,306	8.5%	115,949	10.6%	13,986	12.6%	22,930	0.4%
	High School	2,897,740	45.9%	7,152,708	39.1%	2,693,506	31.8%	370,827	34.0%	36,582	32.9%	48,896	0.8%
	College	105,916	1.7%	3,898,117	21.3%	2,555,614	30.2%	281,475	25.8%	28,387	25.5%	5,657	0.1%
	Unknown	2,152,580	34.1%	5,446,290	29.8%	2,506,884	29.6%	323,597	29.6%	32,175	29.0%	6,163,498	98.8%
Maternal Characteristics													
Age (years)													
	< 20	5,475,967	86.7%	3,621,663	19.8%	324,652	3.8%	42,161	3.9%	5,478	4.9%	3,211,653	51.5%
	20 - 29	808,886	12.8%	13,646,776	74.6%	4,407,694	52.0%	382,294	35.0%	41,164	37.0%	2,447,035	39.2%
	30- 39	34,765	0.5%	1,017,567	5.6%	3,720,600	43.9%	629,762	57.7%	58,389	52.5%	572,413	9.2%
	40+	242	0.0%	3,770	0.0%	23,364	0.3%	37,631	3.5%	6,099	5.5%	9,880	0.2%
Maternal Race													
	White	2,947,988	46.7%	10,918,297	59.7%	4,915,885	58.0%	541,681	49.6%	45,072	40.6%	2,407,096	38.6%
	Black	1,038,967	16.4%	1,753,821	9.6%	846,975	10.0%	176,350	16.2%	23,795	21.4%	2,074,983	33.2%
	Native American	89,035	1.4%	135,352	0.7%	45,390	0.5%	7,022	0.6%	816	0.7%	99,588	1.6%
	Asian	131,870	2.1%	1,178,655	6.4%	918,320	10.8%	130,083	11.9%	18,104	16.3%	180,402	2.9%
	Hispanic	2,041,846	32.3%	4,185,812	22.9%	1,704,974	20.1%	230,456	21.1%	22,685	20.4%	1,417,190	22.7%
	Other/ Unknown	70,154	1.1%	117,839	0.6%	44,766	0.5%	6,256	0.6%	658	0.6%	61,722	1.0%
Maternal Education													
	No High School	1,615,314	25.6%	2,142,333	11.7%	888,685	10.5%	157,039	14.4%	19,876	17.9%	1,571,612	25.2%
	High School	3,974,943	62.9%	8,863,877	48.5%	3,222,251	38.0%	455,578	41.7%	48,311	43.5%	2,895,458	46.4%
	College	226,784	3.6%	5,843,718	32.0%	3,666,236	43.3%	384,519	35.2%	33,158	29.8%	216,967	3.5%
	Unknown	502,819	8.0%	1,439,848	7.9%	699,138	8.3%	94,712	8.7%	9,785	8.8%	1,556,944	24.9%
	Median [25%, 75%] # of Prenatal Visits*	11 [9, 13]		12 [10, 13]		12 [10, 14]		12 [9, 14]		11 [9, 13]		10 [8, 13]	
	Married	2,108,222	33.4%	13,229,565	72.3%	6,958,644	82.2%	835,087	76.5%	80,465	72.4%	936,607	15.0%
	Gestational Diabetes	185,717	2.9%	967,204	5.3%	661,093	7.8%	104,321	9.6%	10,746	9.7%	283,818	4.5%
	Pre-eclampsia	297,358	4.7%	832,200	4.6%	385,532	4.6%	54,894	5.0%	5,769	5.2%	307,963	4.9%
	Eclampsia	16,938	0.3%	40,641	0.2%	20,029	0.2%	3,041	0.3%	330	0.3%	21,107	0.3%
Infant Characteristics													
	Mean Birth Weight and 99% CI (grams)*	3220 [3219.4, 3220.6]		3306.6 [3306.3, 3306.9]		3304.6 [3304.1, 3305.2]		3253.2 [3251.6, 3254.8]		3202.4 [3197.4, 3207.4]		3148.4 [3147.7, 3149.0]	
	Mean Gestational Age and 99% CI (weeks)*	38.69 [38.68, 38.69]		38.72 [38.72, 38.72]		38.54 [38.54, 38.54]		38.36 [38.35, 38.37]		38.26 [38.24, 38.28]		38.35 [38.35, 38.36]	
	Premature Birth (< 37 weeks)	745,615	11.8%	1,902,785	10.4%	993,011	11.7%	154,819	14.2%	17,867	16.1%	959,100	15.4%
	Low Birth Weight (< 2500 g)	518,957	8.2%	1,273,508	7.0%	663,742	7.8%	107,612	9.9%	13,031	11.7%	704,080	11.3%
	Low 5 Minute Apgar Score (< 8)	258,283	4.1%	617,300	3.4%	281,172	3.3%	42,269	3.9%	4,928	4.4%	295,878	4.7%
	Assisted Ventilation	200,197	3.2%	547,699	3.0%	259,905	3.7%	37,986	3.5%	4,178	3.8%	193,697	3.1%
	NICU	385,777	6.1%	1,095,543	6.0%	563,784	6.7%	89,329	8.2%	10,648	9.6%	424,343	6.8%
	Antibiotics	116,124	1.8%	302,290	1.7%	134,836	1.6%	19,865	1.8%	2,235	2.0%	114,295	1.8%
	Seizures	1,715	0.0%	4,409	0.0%	2,000	0.0%	300	0.0%	33	0.0%	1,986	0.0%
	Adverse Event	524,725	8.3%	1,449,012	7.9%	720,770	8.5%	110,645	10.1%	12,833	11.6%	543,107	8.7%

Table 2a. Multivariate linear regression models predicting effect of paternal age on birth outcomes before and after adjustment for year, maternal age, race, and education, parental race and education, prenatal visits, tobacco use, and marital status.

		Paternal age (years)									
		< 25		25 - 34		35 - 44		45 - 54		55+	
Gestational Age (weeks)	unadjusted	-0.03	[-.04, -.03]	reference		-0.18	[-.18, -.18]	-0.36	[-.37, -.35]	-0.46	[-.48, -.44]
	adjusted	-0.01	[-.02, -.01]	reference		-0.06	[-.07, -.06]	-0.12	[-.13, -.11]	-0.17	[-.20, -.14]
Birth Weight (g)	unadjusted	-86.6	[-87.3, -85.9]	reference		-1.97	[-2.59, -1.34]	-53.4	[-54.9, -51.9]	-104.2	[-108.7, -99.7]
	adjusted	-22.9	[-24.1, -21.7]	reference		0.95	[-.02, 1.91]	-20.2	[-22.5, -18.0]	-49.2	[-55.9, -42.5]
Apgar (5 minute)	unadjusted	-0.03	[-.04, -.03]	reference		0.01	[0.00, 0.01]	-0.02	[-.03, -.02]	-0.05	[-.06, -.05]
	adjusted	-0.02	[-.02, -.02]	reference		0.01	[.01, .01]	-0.01	[-.01, -.01]	-0.02	[-.03, -.01]

Table 2b. Multivariate logistic regression models predicting effect of paternal age on birth outcomes before and after adjustment for year, maternal age, race, and education, parental race and education, prenatal visits, tobacco use, and marital status. Adverse event is defined as the requirement of assisted ventilation, NICU, antibiotics, or seizure after birth.

		Paternal age (years)									
		< 25		25 - 34		35 - 44		45 - 54		55+	
Premature Birth (< 37 weeks)	unadjusted	1.15	[1.15, 1.16]	reference		1.14	[1.14, 1.15]	1.42	[1.41, 1.43]	1.65	[1.62, 1.69]
	adjusted	1.03	[1.02, 1.04]	reference		1.06	[1.05, 1.06]	1.14	[1.13, 1.15]	1.25	[1.22, 1.29]
Low Birth Weight (< 2500 g)	unadjusted	1.20	[1.19, 1.20]	reference		1.14	[1.13, 1.14]	1.46	[1.45, 1.47]	1.78	[1.73, 1.82]
	adjusted	1.05	[1.04, 1.06]	reference		1.04	[1.04, 1.05]	1.14	[1.12, 1.15]	1.27	[1.22, 1.31]
Low 5 Minute Apgar Score (< 8)	unadjusted	1.23	[1.23, 1.24]	reference		0.98	[.97, .98]	1.15	[1.14, 1.17]	1.34	[1.29, 1.39]
	adjusted	1.11	[1.10, 1.12]	reference		0.97	[.96, .98]	1.04	[1.02, 1.06]	1.14	[1.08, 1.20]
Assisted Ventilation	unadjusted	1.06	[1.05, 1.07]	reference		1.02	[1.02, 1.03]	1.17	[1.15, 1.18]	1.27	[1.21, 1.32]
	adjusted	1.04	[1.02, 1.05]	reference		1.00	[.99, 1.01]	1.06	[1.04, 1.16]	1.10	[1.04, 1.16]
NICU	unadjusted	1.03	[1.03, 1.04]	reference		1.12	[1.11, 1.12]	1.39	[1.38, 1.40]	1.64	[1.59, 1.68]
	adjusted	1.01	[1.00, 1.02]	reference		1.03	[1.03, 1.04]	1.14	[1.13, 1.16]	1.28	[1.24, 1.33]
Antibiotics	unadjusted	1.13	[1.12, 1.14]	reference		0.96	[.95, .97]	1.09	[1.07, 1.11]	1.20	[1.13, 1.26]
	adjusted	1.04	[1.03, 1.06]	reference		0.96	[.95, .97]	1.03	[1.00, 1.05]	1.06	[.99, 1.14]
Seizures	unadjusted	1.14	[1.06, 1.22]	reference		0.98	[.91, 1.05]	1.13	[.97, 1.32]	1.21	[.77, 1.89]
	adjusted	1.06	[.93, 1.20]	reference		1.00	[.91, 1.11]	1.18	[.97, 1.44]	1.30	[.77, 2.20]
Adverse Event	unadjusted	1.05	[1.05, 1.06]	reference		1.08	[1.07, 1.08]	1.31	[1.30, 1.32]	1.52	[1.48, 1.55]
	adjusted	1.03	[1.02, 1.03]	reference		1.02	[1.01, 1.02]	1.12	[1.11, 1.13]	1.24	[1.20, 1.28]

Table 2c. Multivariate logistic regression models predicting effect of paternal age on maternal pregnancy outcomes before and after adjustment for year, maternal age, race, and education, parental race and education, prenatal visits, tobacco use, and marital status.

		Paternal age (years)									
		< 25		25 - 34		35 - 44		45 - 54		55+	
Gestational Diabetes	unadjusted	0.83	[.82, .83]	reference		1.15	[1.15, 1.16]	1.28	[1.27, 1.29]	1.34	[1.30, 1.38]
	adjusted	0.82	[.81, .83]	reference		1.16	[1.15, 1.16]	1.28	[1.27, 1.30]	1.34	[1.29, 1.38]
Pre-eclampsia	unadjusted	1.04	[1.03, 1.04]	reference		1	[.99, 1.00]	1.11	[1.10, 1.12]	1.15	[1.11, 1.19]
	adjusted	1.06	[1.05, 1.07]	reference		0.97	[.96, .97]	0.99	[.98, 1.01]	1.00	[.96, 1.05]
Eclampsia	unadjusted	1.21	[1.18, 1.24]	reference		1.06	[1.04, 1.09]	1.25	[1.20, 1.32]	1.34	[1.16, 1.54]
	adjusted	1.11	[1.06, 1.16]	reference		0.99	[.96, 1.03]	1.02	[.95, 1.10]	1.03	[.84, 1.25]

Table 3. Comparison of sex-ratio by paternal age group. p value was derived from a non-parametric test of trend for the decreasing sex-ratio across the advancing paternal age groups.

	Paternal age (years)									
	< 25		25 - 34		35 - 44		45 - 54		55+	
Female (%)	4,134,050	48.66%	10,351,338	48.78%	4,612,303	48.82%	603,896	48.89%	60,795	48.78%
Male (%)	4,361,018	51.34%	10,870,121	51.22%	4,835,218	51.18%	632,267	51.11%	64,848	51.22%
OR [99% CI]	1.007	[1.003, 1.010]	reference		0.997	[.994, .1.00]	0.995	[.989, 1.002]	1.004	[.985, 1.023]

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Table 4. Total number of affected births (weighted) and births attributable to paternal age 45 years and older for all perinatal outcomes. Attributable births are presented as a percentage of all affected births along with the 95% confidence interval.

	Total Cases	# of Affected Births to:				p value	% of Cases Prevented if Father were < 45	95% CI	
		Fathers < 45	%	Fathers 45+	%				
Premature Birth	4,608,250	4,409,654	11.3%	198,597	14.6%	< 0.001	13.2%	12.5%	13.9%
Low Birth Weight	3,141,068	3,003,266	7.7%	137,802	10.1%	< 0.001	14.5%	13.6%	15.4%
Low Apgar Score	1,629,302	1,568,507	4.0%	60,795	4.5%	< 0.001	5.9%	4.5%	7.2%
Gestational Diabetes	2,225,092	2,095,396	5.3%	129,696	9.5%	< 0.001	18.2%	17.5%	18.9%
Pre-eclampsia	1,876,535	1,807,634	4.6%	68,901	5.1%	< 0.001	3.9%	2.8%	5.0%
Eclampsia	97,069	93,219	0.2%	3,850	0.3%	< 0.001	5.4%	0.1%	11.0%
Assisted Ventilation	1,483,395	1,426,653	3.6%	56,742	4.2%	< 0.001	8.6%	7.2%	9.9%
NICU	3,035,690	2,901,941	7.4%	133,749	9.8%	< 0.001	15.1%	14.2%	15.9%
Antibiotics	816,272	786,280	2.0%	29,992	2.2%	< 0.001	6.2%	4.4%	8.0%
Seizures	11,794	11,348	0.0%	446	0.0%	0.041	19.9%	2.9%	36.7%
Adverse Events	3,351,823	3,209,968	8.2%	141,855	10.4%	< 0.001	12.2%	11.5%	13.0%

Supplemental Table 1. Multivariate linear and logistic regression model replicas of Table 2 with '5 year paternal age intervals'

		Paternal age (years)															
		<20		20-24		25-29		30-34		35-39		40-44		45-50		>50	
Gestational Age (weeks)		-0.10	[-.11, -.09]	-0.02	[-.02, -.01]	reference		-0.05	[-.06, -.05]	-0.08	[-.09, -.08]	-0.13	[-.13, -.12]	-0.15	[-.16, -.14]	-0.18	[-.20, -.16]
Birth Weight (g)		-54.7	[-57.1, -52.2]	-16.3	[-17.6, -15.1]	reference		4.0	[3.0, 4.9]	6.0	[4.8, 7.1]	-3.6	[-5.3, -2.0]	-15.3	[-17.9, -12.7]	-33.8	[-37.5, -30.0]
Apgar (5 minute)		-0.04	[-.05, -.04]	-0.01	[-.01, -.01]	reference		0.01	[0.01, 0.01]	0.01	[.01, .01]	0.00	[.00, .01]	-0.01	[-.01, .00]	-0.01	[-.02, -.01]
		Paternal age (years)															
		<20		20-24		25-29		30-34		35-39		40-44		45-50		>50	
Premature Birth (< 37 weeks)		1.14	[1.13, 1.16]	1.03	[1.02, 1.04]	reference		1.04	[1.03, 1.05]	1.06	[1.06, 1.07]	1.12	[1.11, 1.13]	1.16	[1.15, 1.18]	1.22	[1.20, 1.25]
Low Birth Weight (< 2500 g)		1.15	[1.13, 1.17]	1.05	[1.04, 1.06]	reference		1.03	[1.03, 1.04]	1.05	[1.04, 1.06]	1.10	[1.09, 1.11]	1.15	[1.13, 1.17]	1.23	[1.21, 1.26]
Low 5 Minute Apgar Score (< 8)		1.24	[1.21, 1.27]	1.07	[1.06, 1.08]	reference		0.96	[.95, .97]	0.94	[.93, .95]	0.98	[.97, 1.00]	1.01	[.99, 1.03]	1.06	[1.03, 1.09]
Assisted Ventilation		1.11	[1.09, 1.14]	1.03	[1.01, 1.04]	reference		1.00	[.99, 1.01]	0.99	[.98, 1.00]	1.02	[1.01, 1.04]	1.06	[1.03, 1.08]	1.09	[1.05, 1.12]
NICU		1.08	[1.06, 1.10]	1.01	[1.00, 1.02]	reference		1.03	[1.02, 1.04]	1.03	[1.02, 1.04]	1.10	[1.09, 1.11]	1.16	[1.14, 1.17]	1.23	[1.21, 1.26]
Antibiotics		1.12	[1.09, 1.15]	1.02	[1.01, 1.04]	reference		0.98	[.97, .99]	0.94	[.92, .95]	0.97	[.95, .99]	1.01	[.98, 1.04]	1.04	[1.00, 1.09]
Seizures		0.97	[.75, 1.25]	1.08	[.94, 1.23]	reference		1.02	[.92, 1.13]	1.01	[.89, 1.14]	1.03	[.87, 1.21]	1.23	[.98, 1.55]	1.15	[.83, 1.59]
Adverse Event		1.10	[1.08, 1.11]	1.02	[1.01, 1.03]	reference		1.02	[1.01, 1.02]	1.01	[1.01, 1.02]	1.07	[1.06, 1.08]	1.12	[1.11, 1.14]	1.20	[1.17, 1.22]
		Paternal age (years)															
		<20		20-24		25-29		30-34		35-39		40-44		45-50		>50	
Gestational Diabetes		0.59	[.57, .61]	0.91	[.90, .92]	reference		1.16	[1.15, 1.17]	1.25	[1.24, 1.26]	1.34	[1.32, 1.35]	1.42	[1.40, 1.44]	1.44	[1.41, 1.47]
Pre-eclampsia		1.12	[1.10, 1.15]	1.04	[1.02, 1.05]	reference		0.96	[.96, .97]	0.94	[.93, .95]	0.97	[.96, .99]	0.99	[.95, .99]	0.99	[.96, 1.01]
Eclampsia		1.21	[1.11, 1.32]	1.07	[1.02, 1.13]	reference		0.95	[.92, .99]	0.95	[.91, 1.00]	1.00	[.94, 1.06]	0.99	[.91, 1.08]	1.01	[.90, 1.13]

Supplemental Table 2. Multivariate linear and logistic regression model replicas of Table 2 with only 'term births,' defined as births at least 37 weeks into gestation.

	Paternal age (years)									
	< 25		25 - 34	35 - 44		45 - 54		55+		
Birth Weight (g)	-22.4	[-23.4, -23.4]	reference	5.38	[4.6, 6.2]	-9.3	[-11.2, -7.4]	-30.0	[-35.7, -24.4]	
Apgar (5 minute)	-0.02	[-.02, -.02]	reference	0.01	[.01, .01]	0.00	[-.01, .01]	-0.01	[-.02, -.01]	
	Paternal age (years)									
	< 25		25 - 34	35 - 44		45 - 54		55+		
Low Birth Weight (< 2500 g)	1.07	[1.05, 1.08]	reference	1.04	[1.02, 1.05]	1.18	[1.15, 1.20]	1.36	[1.28, 1.43]	
Low 5 Minute Apgar Score (< 8)	1.15	[1.13, 1.17]	reference	0.95	[.94, .96]	1.01	[.99, 1.04]	1.15	[1.07, 1.23]	
Assisted Ventilation	1.05	[1.04, 1.07]	reference	0.98	[.97, .99]	1.05	[1.02, 1.07]	1.09	[1.02, 1.18]	
NICU	1.02	[1.00, 1.03]	reference	1.01	[1.00, 1.02]	1.16	[1.14, 1.18]	1.37	[1.31, 1.44]	
Antibiotics	1.08	[1.06, 1.10]	reference	0.91	[.90, .93]	1.00	[.97, 1.04]	1.06	[.96, 1.17]	
Seizures	1.08	[.94, 1.25]	reference	0.99	[.88, 1.11]	1.08	[.85, 1.37]	1.18	[.61, 2.27]	
Adverse Event	1.04	[1.03, 1.05]	reference	0.99	[.99, 1.00]	1.11	[1.10, 1.13]	1.27	[1.22, 1.33]	
	Paternal age (years)									
	< 25		25 - 34	35 - 44		45 - 54		55+		
Gestational Diabetes	0.82	[.81, .83]	reference	1.16	[1.15, 1.16]	1.28	[1.27, 1.30]	1.34	[1.29, 1.39]	
Pre-eclampsia	1.06	[1.05, 1.08]	reference	0.96	[.95, .97]	0.97	[.96, .99]	0.97	[.92, 1.02]	
Eclampsia	1.12	[1.06, 1.19]	reference	0.98	[.93, 1.02]	1.00	[.91, 1.10]	1.09	[.83, 1.41]	

Supplemental Table 3. Multivariate linear and logistic regression model replicas of Table 2 with only 'maternal first births'

		Paternal age (years)									
		< 25		25 - 34	35 - 44		45 - 54		55+		
Gestational Age (weeks)		-0.03	[-.03, -.02]	reference	-0.08	[-.09, -.07]	-0.14	[-.16, -.12]	-0.17	[-.23, -.11]	
Birth Weight (g)		-8.5	[-19.4, -6.6]	reference	-17.4	[-19.4, -15.5]	-30.0	[-34.9, -25.0]	-47.2	[-60.8, -33.6]	
Apgar (5 minute)		-0.01	[-.01, .00]	reference	0.00	[.00, .00]	0.00	[-.01, .01]	0.00	[-.02, .02]	
		Paternal age (years)									
		< 25		25 - 34	35 - 44		45 - 54		55+		
Premature Birth (< 37 weeks)		1.02	[1.01, 1.03]	reference	1.10	[1.09, 1.11]	1.16	[1.13, 1.19]	1.23	[1.16, 1.32]	
Low Birth Weight (< 2500 g)		0.99	[.97, 1.00]	reference	1.10	[1.09, 1.12]	1.15	[1.12, 1.19]	1.20	[1.12, 1.29]	
Low 5 Minute Apgar Score (< 8)		1.02	[1.01, 1.04]	reference	0.99	[.97, 1.01]	0.98	[.94, 1.02]	0.98	[.88, 1.09]	
Assisted Ventilation		0.98	[.96, 1.00]	reference	1.01	[.99, 1.02]	1.02	[.98, 1.06]	0.99	[.89, 1.10]	
NICU		0.93	[.92, .95]	reference	1.06	[1.05, 1.07]	1.11	[1.08, 1.14]	1.15	[1.07, 1.23]	
Antibiotics		0.96	[.94, .98]	reference	0.98	[.95, 1.00]	0.97	[.92, 1.02]	1.00	[.88, 1.15]	
Seizures		0.89	[.75, 1.07]	reference	0.92	[.78, 1.10]	1.07	[.73, 1.58]	0.71	[.19, 2.67]	
Adverse Event		0.95	[.94, .96]	reference	1.05	[1.04, 1.06]	1.08	[1.05, 1.11]	1.12	[1.05, 1.19]	
		Paternal age (years)									
		< 25		25 - 34	35 - 44		46 - 54		55+		
Gestational Diabetes		0.80	[.78, .81]	reference	1.12	[1.11, 1.14]	1.21	[1.18, 1.25]	1.38	[1.27, 1.49]	
Pre-eclampsia		0.97	[.95, .98]	reference	0.97	[.96, .98]	0.91	[.88, .94]	0.93	[.85, 1.01]	
Eclampsia		0.98	[.92, 1.05]	reference	1.02	[.96, 1.09]	0.94	[.81, 1.09]	1.10	[.77, 1.57]	

Supplemental Table 4a. Multivariate linear and logistic regression model replicas of Table 2 with 'births from 2007'

	Paternal age (years)									
	< 25		25 - 34	35 - 44		45 - 54		55+		
Gestational Age (weeks)	-0.03	[-.05, -.02]	reference	-0.04	[-.05, -.02]	-0.04	[-.07, -.01]	-0.04	[-.15, .08]	
Birth Weight (g)	-31.4	[-35.3, -27.5]	reference	4.5	[1.2, 7.9]	-14.2	[-16.1, 4.1]	-32.3	[-58.3, -6.3]	
Apgar (5 minute)	-0.01	[-.02, -.01]	reference	0.01	[-.01, .01]	-0.01	[-.02, .00]	-0.02	[-.05, .01]	
	Paternal age (years)									
	< 25		25 - 34	35 - 44		45 - 54		55+		
Premature Birth (< 37 weeks)	1.07	[1.05, 1.09]	reference	1.03	[1.01, 1.05]	1.1	[1.06, 1.15]	1.14	[1.02, 1.28]	
Low Birth Weight (< 2500 g)	1.09	[1.06, 1.11]	reference	1.03	[1.01, 1.06]	1.07	[1.02, 1.12]	1.26	[1.11, 1.43]	
Low 5 Minute Apgar Score (< 8)	1.15	[1.10, 1.20]	reference	0.95	[.91, .99]	1.04	[.96, 1.14]	1.06	[.83, 1.35]	
Assisted Ventilation	1.05	[1.03, 1.07]	reference	1.02	[1.00, 1.04]	1.20	[1.13, 1.19]	1.25	[1.18, 1.26]	
NICU	1.02	[1.00, 1.04]	reference	1.05	[1.03, 1.07]	1.15	[1.12, 1.17]	1.26	[1.22, 1.33]	
Antibiotics	1.03	[.99, 1.04]	reference	0.95	[.91, .99]	1.08	[1.03, 1.15]	1.03	[.91, 1.24]	
Seizures	1.13	[.94, 1.46]	reference	0.96	[.68, 1.14]	1.32	[.95, 1.78]	1.19	[.65, 1.90]	
Adverse Event	1.29	[1.15, 1.44]	reference	1.07	[.97, 1.18]	1.12	[.91, 1.38]	1.16	[.64, 2.12]	
	Paternal age (years)									
	< 25		25 - 34	35 - 44		45 - 54		55+		
Gestational Diabetes	0.81	[.78, .85]	reference	1.15	[1.12, 1.18]	1.33	[1.26, 1.40]	1.34	[1.15, 1.56]	
Pre-eclampsia	1.10	[1.06, 1.14]	reference	0.9	[.87, .93]	0.95	[.88, 1.01]	0.90	[.73, 1.11]	
Eclampsia	1.29	[1.15, 1.44]	reference	1.07	[.97, 1.18]	1.12	[.91, 1.38]	1.16	[.64, 2.12]	

Supplemental Table 4b. Multivariate linear and logistic regression model replicas of Table 2 with 'births from 2016'

	Paternal age (years)									
	< 25		25 - 34	35 - 44		45 - 54		55+		
Gestational Age (weeks)	-0.03	[-.05, -.02]	reference	-0.05	[-.06, -.05]	-0.12	[-.14, -.10]	-0.18	[-.25, -.11]	
Birth Weight (g)	-24.3	[-27.2, -21.4]	reference	2.5	[.26, 4.7]	-17.2	[-22.2, -12.1]	-48.4	[-63.2, -33.6]	
Apgar (5 minute)	-0.02	[-.02, -.01]	reference	0.01	[.01, .01]	-0.01	[-.01, .00]	-0.02	[-.04, -.01]	
	Paternal age (years)									
	< 25		25 - 34	35 - 44		45 - 54		55+		
Premature Birth (< 37 weeks)	1.03	[1.02, 1.05]	reference	1.06	[1.05, 1.07]	1.15	[1.12, 1.18]	1.25	[1.17, 1.33]	
Low Birth Weight (< 2500 g)	1.05	[1.03, 1.07]	reference	1.04	[1.02, 1.05]	1.13	[1.09, 1.16]	1.26	[1.17, 1.35]	
Low 5 Minute Apgar Score (< 8)	1.09	[1.06, 1.12]	reference	0.96	[.94, .98]	1.01	[.96, 1.05]	1.10	[.99, 1.24]	
Assisted Ventilation	1.04	[1.02, 1.06]	reference	1.05	[1.03, 1.05]	1.10	[1.09, 1.13]	1.12	[1.08, 1.15]	
NICU	1.01	[.99, 1.03]	reference	1.03	[1.01, 1.04]	1.14	[1.11, 1.18]	1.28	[1.19, 1.37]	
Antibiotics	1.02	[.98, 1.05]	reference	0.95	[.92, .97]	1.06	[1.01, 1.12]	1.02	[.88, 1.18]	
Seizures	1.17	[.89, 1.55]	reference	0.98	[.79, 1.21]	1.37	[.93, 2.04]	1.29	[.44, 3.77]	
Adverse Event	1.02	[1.00, 1.04]	reference	1.01	[1.00, 1.02]	1.11	[1.09, 1.14]	1.24	[1.16, 1.32]	
	Paternal age (years)									
	< 25		25 - 34	35 - 44		45 - 54		55+		
Gestational Diabetes	0.82	[.80, .84]	reference	1.16	[1.14, 1.17]	1.28	[1.25, 1.32]	1.31	[1.22, 1.42]	
Pre-eclampsia	1.06	[1.04, 1.08]	reference	0.97	[.95, .99]	0.99	[.96, 1.03]	0.96	[.88, 1.06]	
Eclampsia	1.15	[1.04, 1.27]	reference	0.99	[.92, 1.07]	1.11	[.96, 1.29]	0.91	[.59, 1.41]	

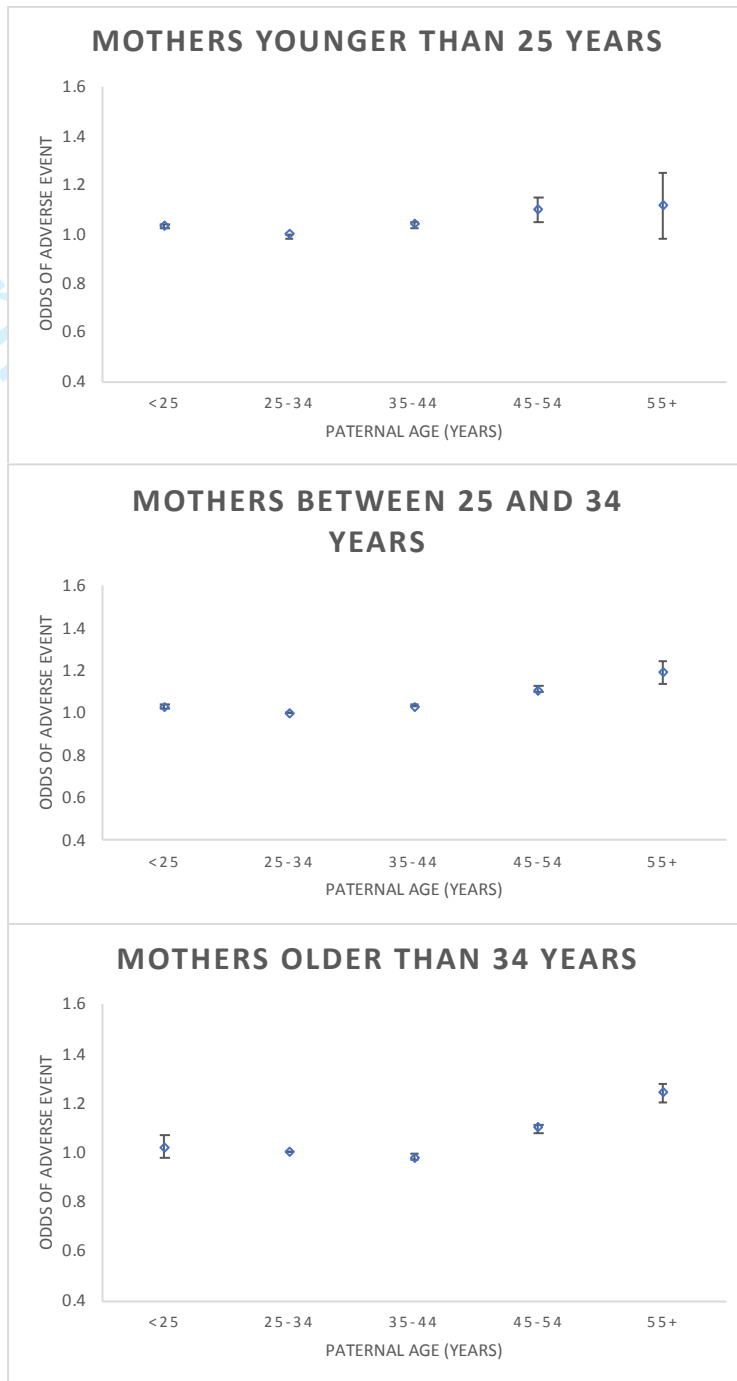
Supplementary Table 5. Multivariate linear and logistic regression model replicas of Table 2 limited to 'births with complete paternal data.'

	Paternal age (years)									
	< 25		25 - 34	35 - 44		45 - 54		55+		
Gestational Age (weeks)	-0.01	[-.01, .00]	reference	-0.06	[-.07, -.06]	-0.12	[-.13, -.12]	-0.18	[-.21, -.16]	
Birth Weight (g)	-21.8	[-23.0, -20.6]	reference	0.56	[-.38, 1.50]	-22.0	[-24.1, -19.9]	-52.0	[-58.0, -46.0]	
Apgar (5 minute)	-0.02	[-.02, -.02]	reference	0.01	[.00, .01]	-0.01	[-.01, .00]	-0.02	[-.03, -.01]	

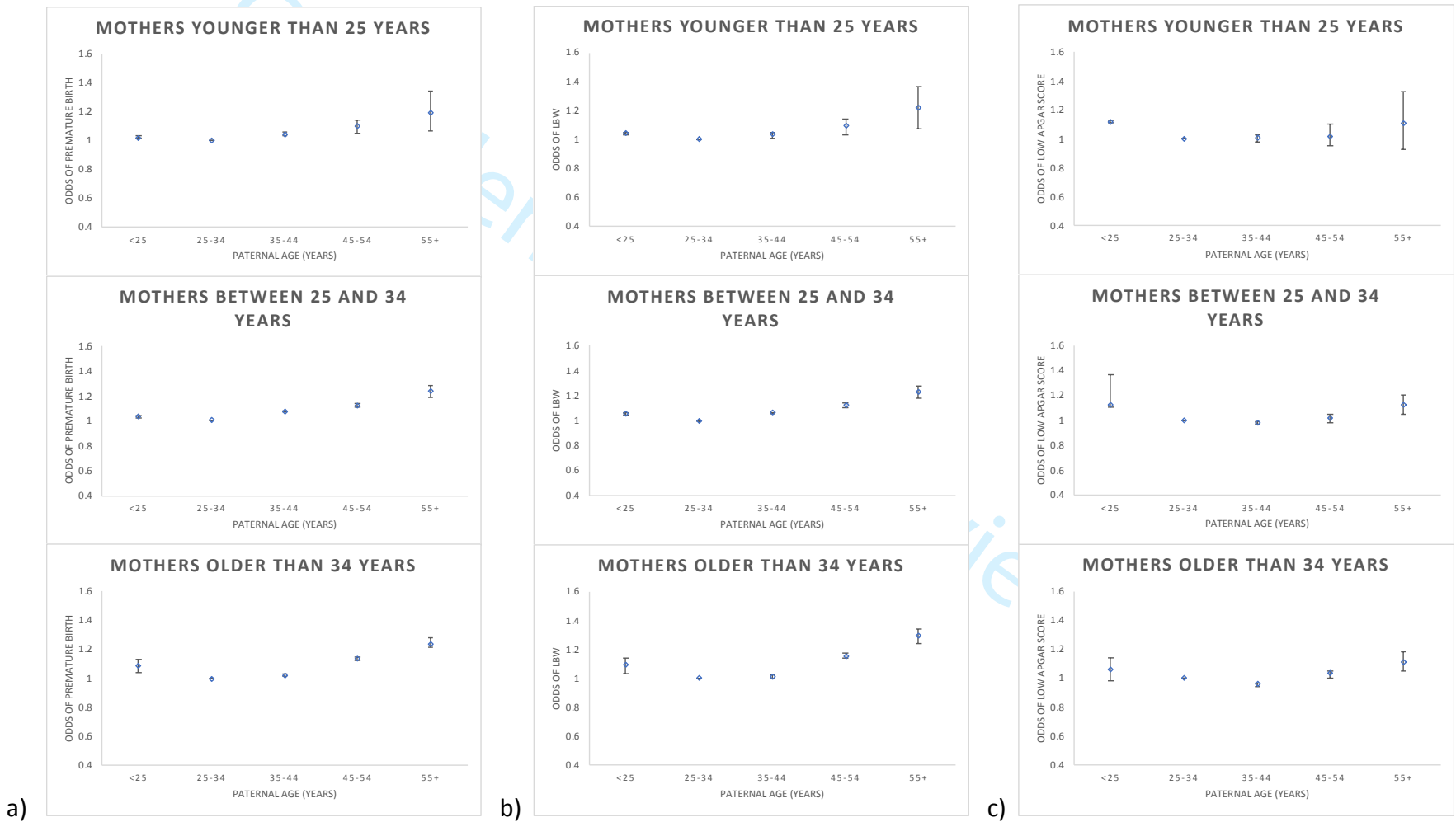
	Paternal age (years)									
	< 25		25 - 34	35 - 44		45 - 54		55+		
Premature Birth (< 37 weeks)	1.03	[1.02, 1.04]	reference	1.06	[1.05, 1.06]	1.15	[1.14, 1.16]	1.27	[1.23, 1.31]	
Low Birth Weight (< 2500 g)	1.05	[1.04, 1.06]	reference	1.05	[1.04, 1.05]	1.15	[1.13, 1.16]	1.28	[1.24, 1.33]	
Low 5 Minute Apgar Score (< 8)	1.11	[1.10, 1.12]	reference	0.97	[.96, .98]	1.03	[1.01, 1.05]	1.13	[1.07, 1.19]	
Assisted Ventilation	1.04	[1.03, 1.05]	reference	0.99	[.98, 1.00]	1.06	[1.04, 1.08]	1.11	[1.05, 1.17]	
NICU	1.00	[.99, 1.02]	reference	1.05	[1.03, 1.08]	1.10	[1.08, 1.12]	1.24	[1.20, 1.30]	
Antibiotics	1.04	[1.03, 1.06]	reference	0.95	[.94, .96]	1.03	[1.00, 1.05]	1.06	[.99, 1.14]	
Seizures	1.07	[.95, 1.21]	reference	1.00	[.90, 1.10]	1.18	[.97, 1.43]	1.27	[.75, 2.17]	
Adverse Event	1.03	[1.02, 1.03]	reference	1.02	[1.01, 1.02]	1.12	[1.11, 1.13]	1.25	[1.21, 1.29]	

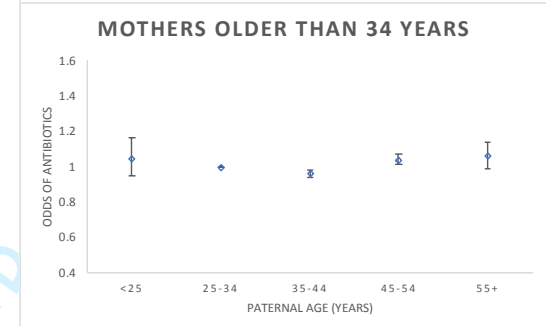
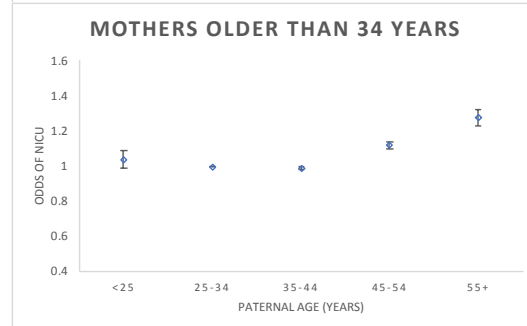
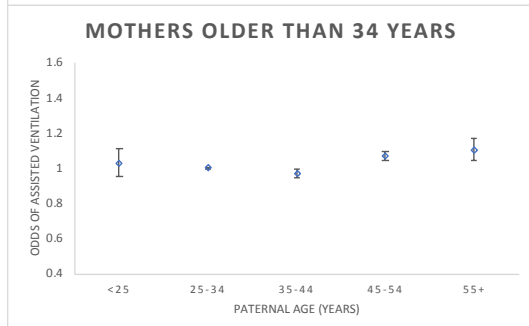
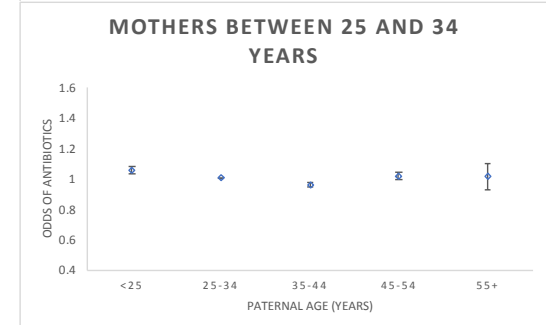
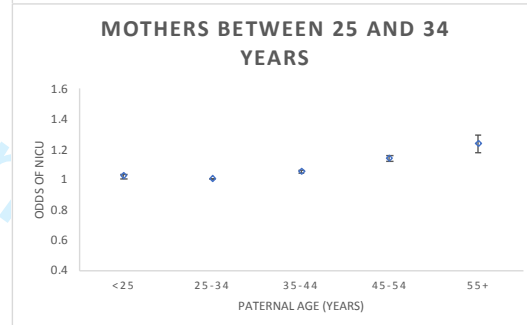
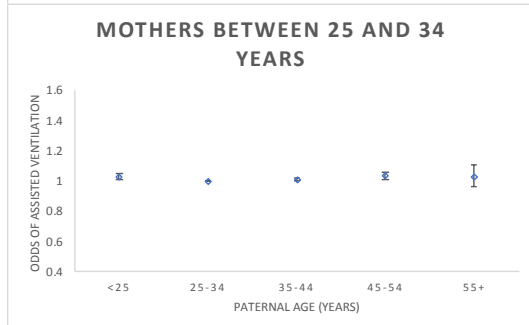
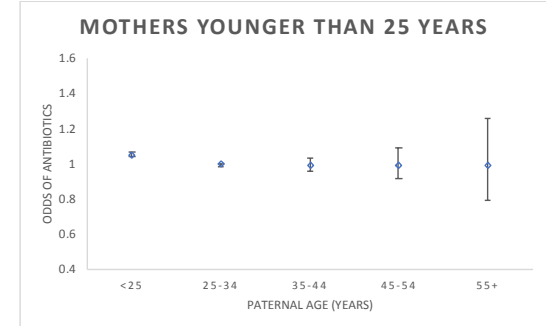
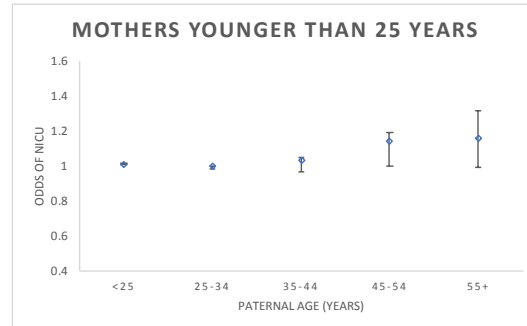
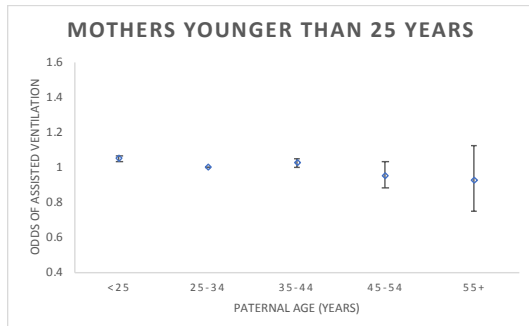
	Paternal age (years)									
	< 25		25 - 34	35 - 44		45 - 54		55+		
Gestational Diabetes	0.83	[.82, .84]	reference	1.15	[1.15, 1.16]	1.28	[1.27, 1.30]	1.34	[1.30, 1.39]	
Pre-eclampsia	1.06	[1.05, 1.07]	reference	0.96	[.96, .97]	0.99	[.98, 1.01]	1.01	[.96, 1.05]	
Eclampsia	1.11	[1.06, 1.16]	reference	0.99	[.96, 1.03]	1.04	[.96, 1.12]	1.06	[.87, 1.30]	

Figure 1. Scatter plots of the odds of an adverse birth event by paternal age stratified by maternal age group. Error bars indicate the 95% confidence intervals based on the distribution of births within each paternal age group.



Supplemental Figure 1. Scatter plots of the odds of all outcomes by paternal age stratified by maternal age group. Error bars indicate the 95% confidence intervals based on the distribution of births within each paternal age group. a) Premature Birth, b) Low Birth Weight, c) Low Apgar Score, d) Assisted Ventilation, e) NICU, f) Antibiotics, g) Seizures, h) Gestational Diabetes, i) Pre-eclampsia, j) Eclampsia





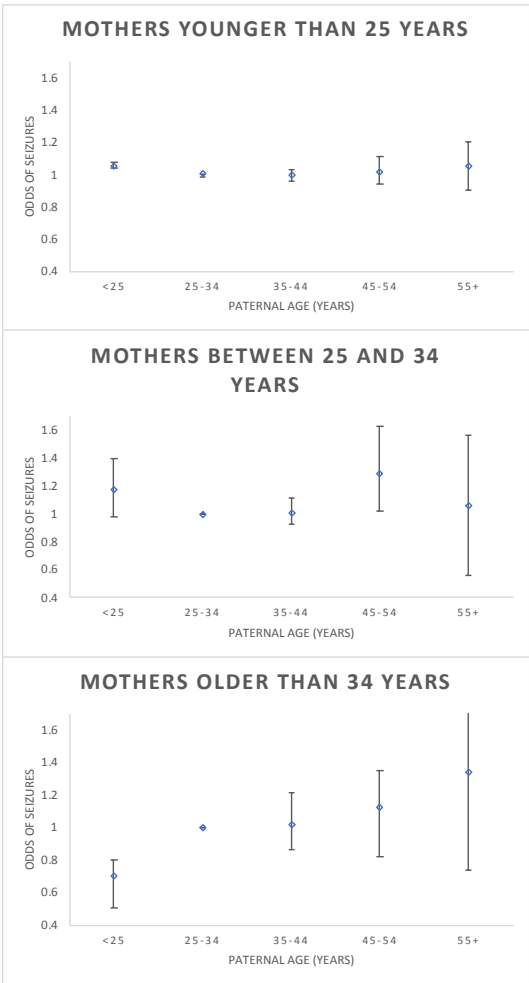
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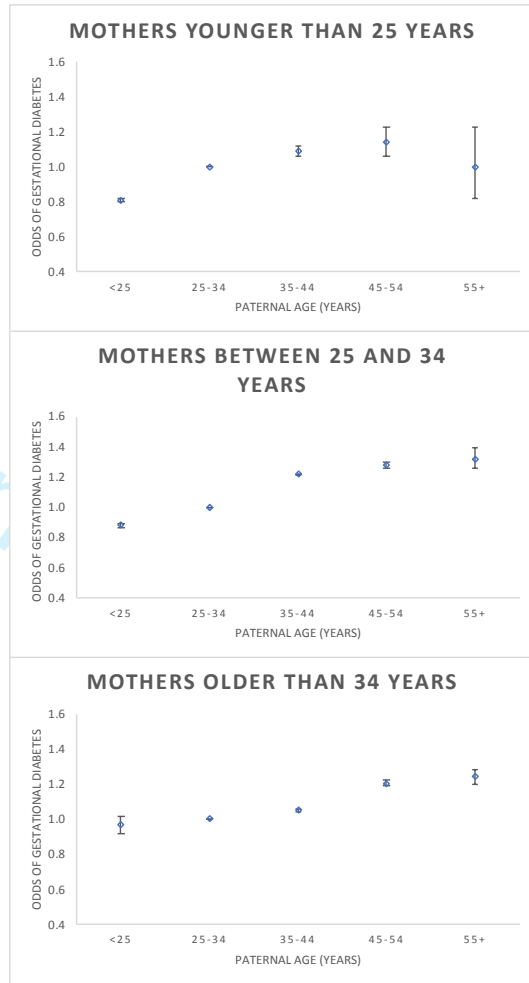
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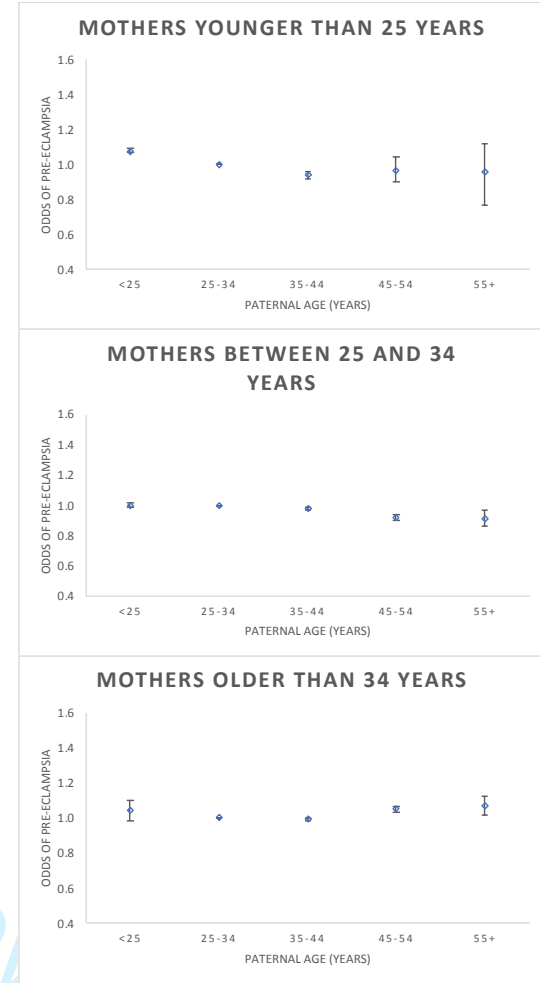
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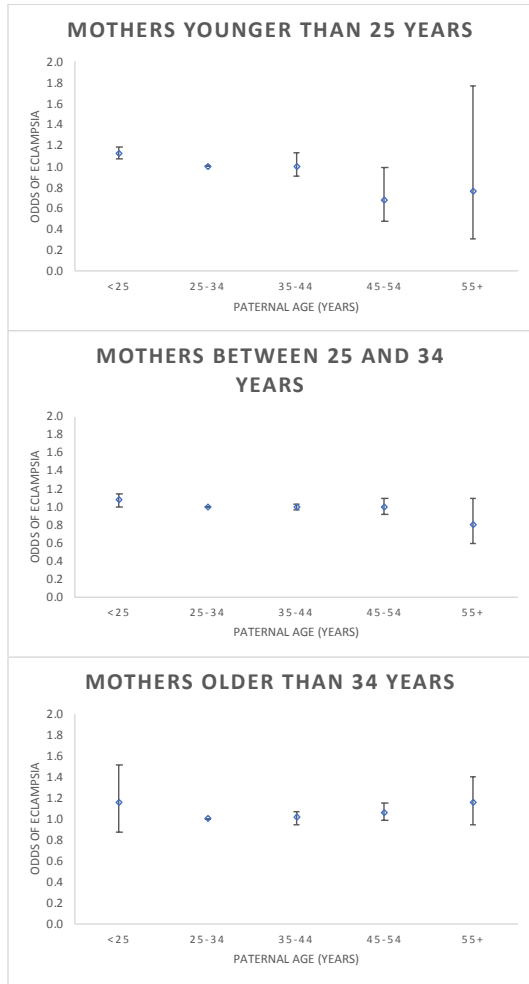


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