

Attributable cases of Cancer and Neurocognitive Disorders in Children in the United States based on Paternal Age

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ABSTRACT

Introduction and Objective: The mean age of fathers in the United States is on the rise. Several reports have suggested that advanced paternal age increases the risk of cancer, psychiatric disease, chromosomal abnormalities, and failing grades in offspring, yet unlike for maternal age, little is known about the quantitative impact of older fathers on these diseases. We thus sought to model the increase in offspring disease between 1972 and 2015 attributable to demographic trends of increasing paternal age within the United States.

Methods: We evaluated all births spanning from 1972 to 2015 using weighted data provided by the Centers for Disease Control's National Vital Statistics System. Births were subsequently categorized into ranges of paternal age. A literature review revealed published offspring disease incidence rates that were utilized to calculate the number of births affected for each respective paternal age category and disease type. All rates were adjusted for maternal age. The number of births affected by each disease was calculated for each year based on the incidence rate of disease for a given paternal age group. Missing incidence rates were estimated using linear approximation using data from published cohort studies. Cases per 4 million annual births are listed.

Results: Between 1972 and 2015, the mean paternal age rose from 27.4 years to 30.9 years. This resulted in a shift in the percentage of fathers with age greater than 40 years, 4.1% to 8.5%. After adjusting for maternal age, the increase in paternal age could lead to an estimated 54,030 additional cases of prostate cancer in their offspring compared to 1972. Achondroplasia due to increasing paternal age was also estimated to increase by 126 cases—an increase of 11.6%. Similarly, an estimated 3,774 additional cases of autism and 68,174 additional cases of bipolar disease are expected in births occurring in 2015 compared to 1972. The percentage of children born in 2015 expected to suffer from substance abuse, failing grades, and low education attainment also increased by 17.2%, 13.9% and 4.8%, respectively, compared to 1972 due to effects associated with increasing paternal age.

Conclusions: As demographic patterns shift in the US and the age of paternity increases, an increasing number of paternal age diseases may affect offspring. A higher percentage of births are expected to suffer from childhood and adult cancers, chromosomal abnormalities, psychiatric comorbidities, and poor educational performance based on the increase in paternal age over the past forty years. The public health impact of increasing paternal age requires further investigation.

BACKGROUND

Mean paternal age has increased from 1972 to 2015 from 27.4 to 30.9 years within the US.

Recent studies have suggested that older fathers may have a higher risk of producing children with cancer, psychiatric disease, chromosomal abnormalities, and neurocognitive deficits.

While the etiology of this trend remains largely unknown, an increased rate of de novo mutations over time as men age is likely contributory. Spermatogenesis is continuous, and aging increases the number of chromosome replication events by primary spermatocytes.

Thus, while paternal age may not be a significant barrier to conception, the effects of older fathers on offspring health are certainly worth considering.

METHODS

All births born in the US in 1972 and 2015 were compiled using a weighted dataset provided by the Centers for Disease Control called the 'National Vital Statistics System.

A comprehensive literature review of cohort studies was subsequently conducted to determine specific prevalence rates for each paternal age group after adjustment for maternal characteristics.

Missing rates were estimated using a linear regression model.

The estimated number of births affected by each disease was calculated for each year and normalized to 4 million births to determine the association of paternal age and the number of affected births for each disease over time.

RESULTS

- In 1972, 3,266,235 weighted births were recorded compared to 3,988,733 in 2015.
 - Using published prevalence rates adjusted for maternal age:
 - 54,030 additional cases of prostate cancer
 - 107,885 additional cases of breast cancer
 - 3,774 additional cases of autism
 - 68,174 additional cases of bipolar disease
 - 35,913 additional cases of substance abuse
- are expected to have occurred by 2015 due to the rise in older fathers

Table 1. Estimate of the increase in number of cancer and congenital disease over time attributable to paternal age.

	All estimates normalized to 4 million births per year*					
	# affected in 1972		# affected in 2015		Total increase	
Total Births	3,266,235		3,988,733			
Childhood Leukemia						
All Fathers	160	0.004%	160	0.004%		
35+ years	53	0.001%	69	0.002%	0	0.0%
Prostate Cancer						
< 27 years	70,060	1.75%	33,342	0.83%		
27 - 31 years	56,873	1.42%	56,318	1.41%		
32 - 37 years	41,743	1.04%	82,380	2.06%		
38+ years	79,218	1.98%	129,885	3.25%	54,030	21.8%
Breast Cancer						
< 30 years	28,908	0.72%	16,597	0.42%		
30 - 40 years	150,283	3.76%	264,849	6.62%		
> 40 years	10,596	0.27%	16,226	0.41%	107,885	56.8%
Achondroplasia						
< 25 years	267	0.007%	116	0.003%		
25 - 29 years	225	0.006%	163	0.004%		
30 - 34 years	152	0.004%	238	0.006%		
35 - 39 years	78	0.002%	170	0.004%		
45 - 49 years	29	0.001%	53	0.001%		
> 50 years	333	0.008%	470	0.012%	126	11.6%

CONCLUSIONS

- Paternal age is on the rise
- The prevalence rates of certain cancers, congenital disorders, and psychiatric illnesses have been shown to directly correlate with advancing paternal age.
- The increasing number of births affected by aging fathers is non-trivial and is likely associated with a significant economic burden that should be further evaluated.

Table 2. Estimate of the increase in number of neurocognitive disease over time attributable to paternal age.

	All estimates normalized to 4 million births per year*					
	# affected in 1972		# affected in 2015		Total increase	
Schizophrenia						
20 - 24 years	54	0.001%	23	0.001%		
25-29 years	72	0.002%	52	0.001%		
30 - 34 years	47	0.001%	72	0.002%		
35-44 years	48	0.001%	100	0.003%		
45+ years	70	0.002%	101	0.003%	59	20.2%
Autism						
20 - 24 years	2,431	0.06%	1,091	0.03%		
25-29 years	3,956	0.10%	2,866	0.07%		
30 - 34 years	2,839	0.07%	4,443	0.11%		
35-44 years	2,653	0.07%	5,568	0.14%		
45+ years	3,754	0.09%	5,438	0.14%	3,774	24.1%
Bipolar						
20 - 24 years	6,129	0.15%	2,751	0.07%		
25 - 29 years	15,456	0.39%	11,198	0.28%		
30 - 34 years	13,186	0.33%	20,640	0.52%		
35 - 44 years	34,937	0.87%	73,325	1.83%		
45+ years	66,816	1.67%	96,786	2.42%	68,174	49.9%
Anorexia nervosa						
< 25 years	4,213	0.11%	1,830	0.05%		
25 - 29 years	4,125	0.10%	2,987	0.07%		
30 - 34 years	2,375	0.06%	3,717	0.09%		
35 - 39 years	1,139	0.03%	2,466	0.06%		
40 - 44 years	620	0.02%	1,210	0.03%		
45+ years	2,143	0.05%	3,106	0.08%	703	4.8%
Failing grades						
20 - 24 years	228,480	5.71%	102,565	2.56%		
25 - 29 years	352,975	8.82%	256,222	6.41%		
30 - 34 years	246,737	6.17%	386,211	9.66%		
35 - 44 years	154,558	3.86%	324,385	8.11%		
45+ years	160,328	4.01%	232,242	5.81%	158,547	13.9%
Low Education (<10 years)						
20 - 24 years	364,912	9.12%	163,809	4.10%		
25 - 29 years	368,076	9.20%	266,665	6.67%		
30 - 34 years	179,445	4.49%	280,880	7.02%		
35 - 44 years	128,373	3.21%	269,429	6.74%		
45+ years	273,781	6.84%	396,583	9.91%	62,780	4.8%
Substance Abuse						
20 - 24 years	41,426	1.04%	18,596	0.46%		
25 - 29 years	55,667	1.39%	40,330	1.01%		
30 - 34 years	35,650	0.89%	55,801	1.40%		
35 - 44	30,870	0.77%	64,788	1.62%		
45+ years	44,609	1.12%	64,619	1.62%	35,913	17.2%