Supplementary Table 1. Associations Between Paternal Age and Birth Defect Categories
Without Paternal and Maternal Age Interaction Terms, Adjusted For Maternal Age Only,
National Birth Defects Prevention Study 1997-2004.

Defect category	Adjusted odds ratio per year increase in paternal age*	95% confidence interval	P
Cleft palate	1.02	1.00, 1.04	.015
Diaphragmatic hernia[†]	1.04	1.02, 1.06	<.001
PVS	1.02	1.00, 1.04	.028
RVOTO	1.02	1.01, 1.04	.007
Multiple and complex defects (overall)	1.02	1.01, 1.03	<.001

PVS, pulmonary valve stenosis; RVOTO, right ventricular outflow tract
obstruction

*Adjusted for maternal age and maternal age^2

[†]Cases categorized as complex (mostly Pentalogy of Cantrell) were excluded
from analysis of diaphragmatic hernia

Supplementary Table 2. Associations Between Paternal Age and Birth Defect Categories

With Quadratic Paternal Age Terms, Adjusted For Maternal Age Only, National Birth

Defects Prevention Study 1997-2004.

Defect category	Paternal age	Adjusted odds ratio per year increase in paternal age*	95% confidence interval	P
APVR	20	1.11	1.01, 1.21	0.02
	30	1.03	0.99, 1.07	0.20
	40	0.95	0.88, 1.02	0.18
Cataract[†]	20	1.10	1.00, 1.20	0.04
	30	1.03	0.99, 1.08	0.11
	40	0.97	0.91, 1.04	0.44
Coarctation of the aorta	20	1.05	1.00, 1.11	0.05
	30	1.02	0.99, 1.04	0.14
	40	0.98	0.95, 1.02	0.37
Encephalocele	20	1.10	0.99, 1.23	0.08
	30	1.02	0.97, 1.07	0.51
	40	0.94	0.85, 1.03	0.18
Esophageal atresia	20	1.08	1.01, 1.15	0.02
	30	1.04	1.01, 1.07	0.02
	40	0.99	0.96, 1.03	0.72

APVR, anomalous pulmonary venous return; VATER/VACTERL, Vertebral, Anal,

Cardiac, Tracheo-Esophageal, Renal, and Limb anomalies

*Adjusted for maternal age and maternal age^2

†Cases categorized as syndromic (due to a strong family history of congenital

cataracts) were excluded from analysis of cataracts

Supplementary Table 3. Associations Between Paternal Age and Birth Defect Categories
With Quadratic Paternal Age Terms, Isolated Defects Only, National Birth Defects
Prevention Study 1997-2004.

Defect category	Paternal age	Adjusted odds ratio per year increase in paternal age*	95% confidence interval	P
APVR	20	1.12	1.01, 1.23	0.03
	30	1.03	0.98, 1.07	0.26
	40	0.94	0.87, 1.03	0.17
Cataract[†]	20	1.11	1.00, 1.23	0.06
	30	1.03	0.98, 1.08	0.19
	40	0.96	0.89, 1.04	0.32
Coarctation of the aorta	20	1.07	1.01, 1.14	0.02
	30	1.03	1.00, 1.06	0.03
	40	0.99	0.95, 1.03	0.59
Encephalocele	20	1.17	1.01, 1.36	0.04
	30	1.03	0.96, 1.09	0.43
	40	0.90	0.80, 1.01	0.08
Esophageal atresia	20	1.16	1.04, 1.29	0.01
	30	1.06	1.01, 1.11	0.02
	40	0.97	0.91, 1.04	0.40

APVR, anomalous pulmonary venous return; VATER/VACTERL, Vertebral, Anal, Cardiac, Tracheo-Esophageal, Renal, and Limb anomalies

*Adjusted for maternal age, maternal age^2, gravidity, periconceptional folic acid use, maternal body mass index, paternal birthplace, paternal education, paternal race and ethnicity, singleton/multiple birth, maternal smoking, maternal alcohol use, paternal drug use, use of assisted reproductive technology, and previous stillbirth or miscarriage

†Cases categorized as syndromic (due to a strong family history of congenital cataracts) were excluded from analysis of cataracts

Supplementary Table 4. Estimated Odds Ratios and 95% Confidence Intervals at
Different Paternal and Maternal Ages for Defect Categories With Paternal and Maternal
Age Interaction Terms, Adjusted For Maternal Age Only, National Birth Defects
Prevention Study 1997-2004.

Defect category	Paternal age (years)*	Maternal age (years)	Adjusted odds ratio[†]	95% confidence interval
Gastroschisis[‡]	20	20	1.06	0.79, 1.42
	40	20	0.80	0.48, 1.35
	20	28	2.88	1.78, 4.68
	40	28	0.82	0.57, 1.19
	20	35	3.50	1.04, 11.71
	40	35	0.39	0.18, 0.82
Omphalocele[‡§]	20	20	0.51	0.29, 0.92
	40	20	1.35	0.78, 2.34
	20	28	1.18	0.69, 2.02
	40	28	0.99	0.72, 1.36
	20	35	2.46	1.07, 5.67
	40	35	0.76	0.51, 1.12
Spina bifida[‡§]	20	20	0.74	0.55, 0.99
	40	20	1.36	1.01, 1.82
	20	28	0.97	0.79, 1.19
	40	28	1.03	0.84, 1.27
	20	35	0.96	0.72, 1.29

	40	35	1.04	0.77, 1.39
All orofacial	20	20	0.77	0.62, 0.95
clefts[‡]	40	20	1.03	0.81, 1.32
	20	28	0.90	0.72 1.13
	40	28	1.09	0.96, 1.24
	20	35	1.04	0.71, 1.52
	40	35	1.15	0.96, 1.37
Septal defect[‡]	20	20	0.86	0.72, 1.02
	40	20	1.17	0.98, 1.39
	20	28	1.00	0.90, 1.12
	40	28	1.00	0.89, 1.12
	20	35	1.01	0.87, 1.16
	40	35	0.99	0.86, 1.14

*Referent paternal age was 30 years

[†]Adjusted for maternal age and maternal age^2

[‡]The following maternal and paternal age interaction terms were included in the logistic regression models for each of the defects listed: maternal age x paternal age (gastroschisis, spina bifida, omphalocele, all orofacial clefts, and all septal defects); maternal age^2 x paternal age (gastroschisis, spina bifida, and all septal defects); maternal age x paternal age^2 (gastroschisis, omphalocele, and all orofacial clefts) and maternal age^2 x paternal age^2 (gastroschisis)

§Cases categorized as complex (mostly Pentalogy of Cantrell or OEIS

(Omphalocele, Exstrophy, Imperforate anus, Spinal defects)) were excluded from

analyses of omphalocele and spina bifida

Supplementary Table 5. Estimated Odds Ratios and 95% Confidence Intervals at Different Paternal and Maternal Ages for Defect Categories With Paternal and Maternal Age Interaction Terms, Isolated Defects Only, National Birth Defects Prevention Study 1997-2004.

Defect category	Paternal age (years)*	Maternal age (years)	Adjusted odds ratio[†]	95% confidence interval
Gastroschisis[‡]	20	20	0.86	0.61, 1.20
	40	20	0.77	0.39, 1.49
	20	28	2.73	1.63, 4.56
	40	28	0.80	0.53, 1.22
	20	35	3.86	1.13, 13.17
	40	35	0.33	0.14, 0.77
Omphalocele[‡§]	20	20	0.71	0.31, 1.64
	40	20	1.36	0.66, 2.79
	20	28	1.71	0.85, 3.42
	40	28	0.94	0.63, 1.41
	20	35	3.66	1.28, 10.46
	40	35	0.68	0.42, 1.12
Spina bifida[‡§]	20	20	0.73	0.52, 1.02
	40	20	1.37	0.98, 1.92
	20	28	0.94	0.75, 1.18
	40	28	1.06	0.84, 1.34
	20	35	1.02	0.74, 1.41

	40	35	0.98	0.71, 1.35
All orofacial	20	20	0.71	0.55, 0.91
clefts[‡]	40	20	1.11	0.85, 1.44
	20	28	0.90	0.70 1.16
	40	28	1.11	0.97, 1.28
	20	35	1.11	0.73, 1.69
	40	35	1.12	0.91, 1.36
Septal defect[‡]	20	20	0.76	0.39, 1.49
	40	20	1.31	0.67, 2.55
	20	28	1.05	0.67, 1.64
	40	28	0.96	0.61, 1.50
	20	35	1.12	0.65, 1.94
	40	35	0.89	0.52, 1.53

*Referent paternal age was 30 years

[†]Adjusted for maternal age, maternal age^2, gravidity, periconceptional folic acid use, maternal body mass index, paternal birthplace, paternal education, paternal race and ethnicity, singleton/multiple birth, maternal smoking, maternal alcohol use, paternal drug use, use of assisted reproductive technology, and previous stillbirth or miscarriage

[‡]The following maternal and paternal age interaction terms were included in the logistic regression models for each of the defects listed: maternal age x paternal age (gastroschisis, spina bifida, omphalocele, all orofacial clefts, and all septal defects); maternal age^2 x paternal age (gastroschisis, spina bifida, and all septal

defects); maternal age x paternal age^2 (gastroschisis, omphalocele, and all

orofacial clefts) and maternal age^2 x paternal age^2 (gastroschisis)

§Cases categorized as complex (mostly Pentalogy of Cantrell or OEIS

(Omphalocele, Exstrophy, Imperforate anus, Spinal defects)) were excluded from

analyses of omphalocele and spina bifida

Supplementary Table 5. Number and Percentage of Paternal Age, Categorized by

Paternal Race and Ethnicity, National Birth Defects Prevention Study 1997-2004.

Paternal Race and Ethnicity		*Paternal age*				*Total*
		24 and under	25-34	35 and over	Missing	
NonHispanic White	N	1,959	6,716	3,691	143	12,509
	%	15.7%	53.7%	29.5%	1.1%	100.0%
NonHispanic Black	N	795	1,099	555	159	2,608
	%	30.5%	42.1%	21.3%	6.1%	100.0%
Hispanic	N	1,675	2,216	839	290	5,020
	%	33.4%	44.1%	16.7%	5.8%	100.0%
Asian/Pacific Islander	N	67	263	184	17	531
	%	12.6%	49.5%	34.7%	3.2%	100.0%
Native American/Alaskan Native	N	33	46	25	2	106
	%	31.1%	43.4%	23.6%	1.9%	100.0%
All other races and ethnicities*	N	2,736	3,884	1,740	485	8,845
	%	30.9%	43.9%	19.7%	5.5%	100.0%

*All other races and ethnicities includes all races and ethnicities other than

NonHispanic White, as contained in the dichotomous variable for paternal race

and ethnicity