Supplementary Online Content

Sandin S, Nygren K-G, Iliadou A, Hultman C, Reichenberg. Autism and Mental Retardation Among Offspring Born After In Vitro Fertilization. *JAMA*. doi:10.1001/jama.2013.7222.

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Description of Swedish population based registers

Register	Description
Medical birth register#	The Medical Birth Register was established in 1973. It contains data on pregnancy and birth for all births in Sweden. More than 95% of the Swedish pregnant population attend antenatal care before the 15th gestational week and the register covers over 99% of all births. This register includes information collected prospectively, starting with the first antenatal visit through the time when mother and child are discharged from the hospital after delivery. Antenatal care routines are standardized and the information is provided through antenatal, obstetrical, and neonatal records, and classified according to the International Classification of Diseases (ICD) version 8 until 1986, version 9 from 1987 to 1996, and version 10 subsequently. Virtually all pregnant women attend an antenatal clinic. During the first visit, usually during pregnancy week 8-13, the woman is asked about the number of years of involuntary infertility. The information is recorded in the Medical Birth Register.
Swedish IVF registers#	Frequencies of all IVF/ICSI treatment in Sweden from 1982 to 2007. From 2007 data are stored in a separate Swedish "quality register". Since 2003 data on embryos transferred are registered as well. The 16 clinics for IVF/ICSI Sweden are required by law to report all treatments. IVF/ICSI treatments are offered to women in the range 25-42 years of age. There are no strict age restrictions for males. Eligibility requires a medically documented fertility problem. In Sweden, almost exclusively, IVF is used to treat female infertility while ICSI is used for male infertility. For IVF without ICSI, sperm is introduced to the egg in a dish or in a test-tube where fertilization takes place, in vitro, usually within 24 hours. The fertilized egg develops into an embryo, which is further cultivated for a total of 2-3 days, to the "cleavage stage", or for 5-6 days to a "blastocyst". One or, occasionally, two (in previous years even more than two) embryos are then transferred to the uterus in a "fresh embryo transfer". Excess embryos can be frozen and later thawed for a second, now frozen-and-thawed, embryo transfer. When ICSI treatments are applied, one single sperm is injected directly into the cytoplasm of the egg where fertilization later takes place. For more serious cases of male infertility when no, or very few, sperm are found in the ejaculate they can be surgically extracted from either the testis or the epididymitis and used in the ICSI procedure.
Statistics Sweden Multigeneration register	The Multigeneration register contains information about the entire Swedish population. Children born from 1932 and alive 1961 are linked to their biological parents. The register comprises 9 million children (index persons), and 11 million unique individuals. Importantly the register includes family information (e.g., identification of parents, siblings and offspring)allowing linkage to other population based registers, which include information on health (e.g. psychiatric hospitalizations), demographic variables (e.g., date of birth, death and emigration).

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eTable 1 Cont

National patient register#	Sweden has universal and publicly financed health insurance coverage that guarantees equal access to health services, regardless of employment status, socio-economic status or regional residency. The register has a nationwide coverage of patient treatment facilities and includes care in psychiatric as well as somatic hospitals. There are no private psychiatric hospitals in Sweden. The Swedish National Patient Register contains details on virtually all psychiatric hospitalizations since 1973. Before 1973 there is data for selected counties only. The register include data on admission and discharge dates and the discharge diagnosis made by the treating physician. Outpatient visits are included since 1999. Diagnostic information is coded using the ICD codes. The standard procedure dictates that diagnosis will be given by a consultant (equivalent of an attending) psychiatrist at the time of discharge from hospital. The diagnostic assessment is then forwarded on a computer medium to the National Patient Register. These routines are standardized across Sweden. All infants and preschool children are regularly seen at well-child care clinics and undergo routine medical and developmental screening. All children aged 4 undergo routine general health screening, that includes mandatory developmental assessment (motor, language, cognitive and social development) conducted by a nurse and pediatrician. Children with any suspected developmental disorder (including autistic disorder and mental retardation) are referred for further assessment by a specialized team in a child psychiatry unit or habilitation service. During the study period diagnoses were made by diagnostic teams with a psychiatrist, clinical psychologist, and speech pathologist or occupational therapist, depending on clinical manifestations. The instruments include parental interviews, cognitive testing of the child, and observations in naturalistic settings, including the home or the unit. The Patient Register contains the diagnostic information. The Patient-Register has shown high reliability for somatic and psychiatric diagnoses. Also, for 130 cases of autistic disorder, we earlier compared registry diagnosis to diagnosis according to the Diagnostic and Statistical Manual 4th Edition (DSM-IV) confirming reliability (methods and results are available from the authors on request). For a diagnosis of mental retardation the evaluation is made by a psychologist and according to standardized tests with high reliability.
Statistics Sweden vital statistics	Individual vital statistics data including date of birth, emigration, immigration and death is maintained by Statistics Sweden (Total Population Register, Emigration and immigration register).

#: Register owned and monitored by the Swedish National Board of Health and Welfare. More detailed documentations at www.socialstyrelsen.se/en/

Note: Data from all registers are joined by the register owner(s)by the unique Swedish personal identification number.

eTable 2. ICD codes for autistic disorder, mental retardation, genetic diseases and parental psychiatric history

Variable	Disease/disorder	ICD codes
Severe development disorder	Autistic disorder #	ICD-9: 299/299B/W/X ICD-10: F84.0
	Mental retardation	ICD-9: 317, 318 or 319 including all sub-codes or 318A, 318B or 318C ICD-10: F70-F73, F78, F79 including all sub-codes
Parental psychiatric history	Affective disorder (mood disorder)	ICD-7: 301 and 302 ICD-8: 296, 298 and 3004.1 ICD-9: 296, 311, 298A, 298B, 300E ICD-10: F30-F34, F38, F39
	Non affective psychosis	ICD-7: 300 or 309 ICD-8: 295, 297, 299, 298.2, 298.3, 298.9 ICD-9: 295, 297, 298, 298C, 298E, 298W, 298X ICD-10: F20-F25, F28, F29, F230-F233, F238, F239
Genetic disease##		**Fragile-X** ICD-9 759,83 or ICD19 Q992, **Angelman** ICD-9 759,89 or ICD-10 Q935, **Prader-Willi** ICD-9 759,81 or ICD-10 Q871, **Zellweger** ICD-9 277,86 or ICD-10 Q878, **William** ICD-9 758,9 or ICD-10 Q938, **Tuberous Sclerosis** ICD-9 259,5 or ICD-10 Q851, **Tourette** ICD-9 307,23 or ICD-10 F952, **Neuofibromatosis** ICD-9 237,7 or ICD-10 Q850, **Duchennes muscular dystrophy** ICD-9 359,1 or ICD-10 QG710, **Cornelia de Lange** ICD-9 759,89 or ICD-10 Q871, **DeGeorge** ICD-9 279,11 or 758,32 or ICD-10 Q821, **Smith-Lemli-Opitz** ICD-9 759.84 or ICD-10 Q871, **Klinfelter** ICD-9 758,7 or ICD-10 Q980, Q981, Q982, Q983 or Q984. There is an overlap where ICD-10 Q871 can be both de Lange and Smith-Lemli-Opitz.

#: Codes used from 1987, ##: Source: Hollander E, Kolevzon A, Coyle JT. *Textbook of Autism Spectrum Disorders*. American Psychiatric Pub; 2010.

eTable 3 Autistic Disorder. Comparing Any IVF vs Spontaneously conceived offspring

Dataset	Sub-Group	Spontaneous or Any IVF	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
All Children		Spontaneous	6,856	33,994,678	15.6	reference group		
All Children		Any IVF	103	231,118	19.0	Crude	1.22 (1.01-1.49)	0.04
All Children						Adj	1.14 (0.94-1.39)	0.18
All Children						*AdjC*	*1.22 (1.01-1.49)*	*0.04*
All Children						*AdjI*	*1.15 (0.93-1.43)*	*0.19*
All Children	*>1998*	*Spontaneous*	*2,123*	*4,708,440*	*36.0*	*reference group*		
All Children	*>1998*	*Any IVF*	*68*	*112,209*	*48.4*	*Adj*	*1.25 (0.98-1.60)*	*0.07*
All Children	*Boys*	*Spontaneous*	*5,067*	*17,453,631*	*25.3*	*reference group*		
All Children	*Boys*	*Any IVF*	*76*	*119,364*	*29.7*	*Adj*	*1.14 (0.91-1.43)*	*0.26*
All Children	*Girls*	*Spontaneous*	*1,789*	*16,541,047*	*9.6*	*reference group*		
All Children	*Girls*	*Any IVF*	*27*	*111,754*	*13.1*	*Adj*	*1.16 (0.79-1.69)*	*0.45*
All Children	*Pre-Term*	*Spontaneous*	*665*	*1,959,075*	*25.6*	*reference group*		
All Children	*Pre-Term*	*Any IVF*	*35*	*53,629*	*29.4*	*Adj*	*1.10 (0.78-1.54)*	*0.59*
All Children	*Term*	*Spontaneous*	*6,191*	*32,035,603*	*15.1*	*reference group*		
All Children	*Term*	*Any IVF*	*68*	*177,489*	*16.2*	*Adj*	*1.00 (0.79-1.28)*	*0.97*

eTable 3 (cont.)

Dataset	Sub-Group	Spontaneous or Any IVF	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
Singletons		Spontaneous	6,683	33,285,383	15.0	reference group		
Singletons		Any IVF	54	149,932	14.4	Crude	0.96 (0.74-1.26)	0.78
Singletons						Adj	0.89 (0.68-1.17)	0.41
Singletons						*AdjC*	*0.96 (0.73-1.26)*	*0.77*
Singletons						*AdjI*	*0.89 (0.67-1.18)*	*0.42*
Singletons	*>1998*	*Spontaneous*	*2,068*	*4,599,526*	*36.0*	*reference group*		
Singletons	*>1998*	*Any IVF*	*36*	*79,704*	*36.1*	*Adj*	*0.92 (0.66-1.29)*	*0.64*
Singletons	*Boys*	*Spontaneous*	*4,939*	*17,095,982*	*24.3*	*reference group*		
Singletons	*Boys*	*Any IVF*	*42*	*77,261*	*23.7*	*Adj*	*0.94 (0.69-1.27)*	*0.68*
Singletons	*Girls*	*Spontaneous*	*1,744*	*16,189,401*	*9.1*	*reference group*		
Singletons	*Girls*	*Any IVF*	*12*	*72,671*	*8.4*	*Adj*	*0.77 (0.43-1.35)*	*0.36*
Singletons	*Pre-Term*	*Spontaneous*	*596*	*1,663,935*	*25.0*	*reference group*		
Singletons	*Pre-Term*	*Any IVF*	*7*	*14,139*	*19.0*	*Adj*	*0.71 (0.34-1.50)*	*0.37*
Singletons	*Term*	*Spontaneous*	*6,087*	*31,621,448*	*14.7*	*reference group*		
Singletons	*Term*	*Any IVF*	*47*	*135,793*	*14.1*	*Adj*	*0.89 (0.67-1.19)*	*0.45*

Note: x indicate cells not estimable since too few cases.
Crude model denotes model adjusting for birth year, age and sex only; Adj model denotes adjusting for birth year, age and sex and additionally adjusting for paternal psychiatric history, maternal psychiatric history and paternal and maternal age; AdjC model denotes adjusting for birth year, age and sex, and additionally for calendar time; AdjI model denotes adjusting for birth year, age and sex, paternal psychiatric history, maternal psychiatric history and paternal and maternal age, and additionally for years of infertility. Relative risk (RR) and two-sided 95% confidence intervals (CI). RR presented for crude models (adjusting for age, sex and birth year only) and adjusted models (additionally adjusting for confounding). RR presented also for the supplementary analyses adjusting for calendar time (AdjC), adjusting for years of infertility (Adj I) and for subgroups of male and female children; subgroups of preterm and term born children; subgroup of children born after 1998. All calculations presented for multiple birth and singletons separately. Supplementary results in italic.

eTable 4 Mental Retardation. Comparing Any IVF vs Spontaneously conceived offspring

Dataset	Sub-Group	Spontaneous or Any IVF	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
All Children		Spontaneous	15,647	33,947,960	39.8		reference group	
All Children		Any IVF	180	230,710	46.3	Crude	1.16 (1.00-1.35)	0.04
All Children						Adj	1.18 (1.01-1.36)	0.03
All Children						*AdjC*	*1.16 (1.00-1.35)*	*0.05*
All Children						*AdjI*	*1.13 (0.96-1.32)*	*0.14*
All Children	*>1998*	*Spontaneous*	*3,408*	*4,703,484*	*70.3*		*reference group*	
All Children	*>1998*	*Any IVF*	*98*	*112,101*	*85.5*	*Adj*	*1.20 (0.98-1.47)*	*0.08*
All Children	*Boys*	*Spontaneous*	*9,429*	*17,430,939*	*47.5*		*reference group*	
All Children	*Boys*	*Any IVF*	*123*	*119,121*	*60.8*	*Adj*	*1.33 (1.11-1.59)*	*<.01*
All Children	*Girls*	*Spontaneous*	*6,218*	*16,517,022*	*33.3*		*reference group*	
All Children	*Girls*	*Any IVF*	*57*	*111,589*	*32.4*	*Adj*	*0.94 (0.73-1.22)*	*0.66*
All Children	*Pre-Term*	*Spontaneous*	*2,127*	*1,950,931*	*96.7*		*reference group*	
All Children	*Pre-Term*	*Any IVF*	*70*	*53,427*	*79.2*	*Adj*	*0.87 (0.69-1.11)*	*0.27*
All Children	*Term*	*Spontaneous*	*13,520*	*31,997,029*	*36.4*		*reference group*	
All Children	*Term*	*Any IVF*	*110*	*177,283*	*36.9*	*Adj*	*1.01 (0.84-1.22)*	*0.90*

eTable 4 (cont.)

Dataset	Sub-Group	Spontaneous or Any IVF	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
Singletons		Spontaneous	15,178	33,240,234	38.5		reference group	
Singletons		Any IVF	101	149,677	38.8	Crude	1.01 (0.83-1.23)	0.93
Singletons						Adj	1.01 (0.83-1.24)	0.89
Singletons						*AdjC*	*1.01 (0.83-1.23)*	*0.94*
Singletons						*AdjI*	*0.95 (0.78-1.17)*	*0.64*
Singletons	*>1998*	*Spontaneous*	*3,306*	*4,594,778*	*69.8*		*reference group*	
Singletons	*>1998*	*Any IVF*	*60*	*79,605*	*74.0*	*Adj*	*1.03 (0.80-1.33)*	*0.81*
Singletons	*Boys*	*Spontaneous*	*9,136*	*17,074,246*	*45.8*		*reference group*	
Singletons	*Boys*	*Any IVF*	*68*	*77,117*	*50.1*	*Adj*	*1.13 (0.89-1.44)*	*0.31*
Singletons	*Girls*	*Spontaneous*	*6,042*	*16,165,988*	*32.3*		*reference group*	
Singletons	*Girls*	*Any IVF*	*33*	*72,561*	*28.1*	*Adj*	*0.84 (0.59-1.18)*	*0.31*
Singletons	*Pre-Term*	*Spontaneous*	*1,875*	*1,656,758*	*95.8*		*reference group*	
Singletons	*Pre-Term*	*Any IVF*	*17*	*14,068*	*66.2*	*Adj*	*0.74 (0.46-1.20)*	*0.22*
Singletons	*Term*	*Spontaneous*	*13,303*	*31,583,476*	*35.8*		*reference group*	
Singletons	*Term*	*Any IVF*	*84*	*135,610*	*36.2*	*Adj*	*1.01 (0.81-1.25)*	*0.94*

Note: x indicate cells not estimable since too few cases.

Crude model denotes model adjusting for birth year, age and sex only; Adj model denotes adjusting for birth year, age and sex and additionally adjusting for paternal psychiatric history, maternal psychiatric history and paternal and maternal age; AdjC model denotes adjusting for birth year, age and sex, and additionally for calendar time; AdjI model denotes adjusting for birth year, age and sex, paternal psychiatric history, maternal psychiatric history and paternal and maternal age, and additionally for years of infertility. Relative risk (RR) and two-sided 95% confidence intervals (CI). RR presented for crude models (adjusting for age, sex and birth year only) and adjusted models (additionally adjusting for confounding). RR presented also for the supplementary analyses adjusting for calendar time (AdjC), adjusting for years of infertility (Adj I) and for subgroups of male and female children; subgroups of preterm and term born children; subgroup of children born after 1998. All calculations presented for multiple birth and singletons separately. Supplementary results in italic.

eTable 5 **Autistic disorder.** Comparing specific IVF procedures vs IVF without ICSI, fresh embryo.

Dataset	Sub-Group	IVF procedure	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
All Children		IVF without ICSI, fresh	53	144,207	29.3	reference group		
All Children		IVF without ICSI, frozen	10	17,121	42.3	Crude	1.44 (0.73-2.85)	0.29
All Children						Adj	1.46 (0.74-2.89)	0.27
All Children						*AdjC*	*1.45 (0.74-2.87)*	*0.28*
All Children						*AdjI*	*1.46 (0.74-2.89)*	*0.27*
All Children						*AdjG*	*1.46 (0.74-2.89)*	*0.27*
All Children		ICSI, fresh	31	58,262	34.0	Crude	1.16 (0.73-1.85)	0.52
All Children						Adj	1.20 (0.75-1.91)	0.45
All Children						*AdjC*	*1.15 (0.73-1.83)*	*0.55*
All Children						*AdjI*	*1.19 (0.75-1.90)*	*0.46*
All Children						*AdjG*	*1.20 (0.75-1.91)*	*0.45*
All Children		ICSI, frozen	1	7,022	9.4	Crude	0.32 (0.04-2.34)	0.26
All Children						Adj	0.33 (0.05-2.40)	0.27
All Children						*AdjC*	*0.32 (0.04-2.33)*	*0.26*
All Children						*AdjI*	*0.33 (0.05-2.40)*	*0.27*
All Children						*AdjG*	*0.33 (0.05-2.40)*	*0.27*

eTable 5 (cont.)

Dataset	Sub-Group	IVF procedure	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
All Children		ICSI, fresh, surgery	8	3,720	135.7	Crude	4.64 (2.17-9.92)	<.01
All Children						Adj	4.60 (2.14-9.88)	<.01
All Children						*AdjC*	*4.57 (2.14-9.77)*	*<.01*
All Children						*AdjI*	*4.60 (2.14-9.89)*	*<.01*
All Children						*AdjG*	*4.60 (2.14-9.88)*	*<.01*
All Children		ICSI, frozen, surgery	0	787	0.0	Crude	x	x
All Children						Adj	x	x
All Children						*AdjC*	*x*	*x*
All Children						*AdjI*	*x*	*x*
All Children						*AdjG*	*x*	*x*
All Children	*Pre-Term*	*IVF without ICSI, fresh*	*17*	*36,927*	*38.4*	*reference group*		
All Children	*Pre-Term*	*IVF without ICSI, frozen*	*3*	*3,297*	*67.9*	*Adj*	*1.69 (0.49-5.79)*	*0.40*
All Children	*Pre-Term*	*ICSI, fresh*	*10*	*11,508*	*51.6*	*Adj*	*1.47 (0.66-3.26)*	*0.35*
All Children	*Pre-Term*	*ICSI, frozen*	*0*	*1,055*	*0.0*	*Adj*	*x*	*x*
All Children	*Pre-Term*	*ICSI, fresh, surgery*	*5*	*764*	*364.5*	*Adj*	*9.54 (3.43-26.57)*	*<.01*
All Children	*Pre-Term*	*ICSI, frozen, surgery*	*0*	*78*	*0.0*	*Adj*	*x*	*x*

eTable 5 (cont.)

Dataset	Sub-Group	IVF procedure	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
All Children	*Term*	*IVF without ICSI, fresh*	*36*	*107,280*	*26.6*		*reference group*	
All Children	*Term*	*IVF, without ICSI, frozen*	*7*	*13,824*	*36.4*	*Adj*	*1.39 (0.62-3.14)*	*0.42*
All Children	*Term*	*ICSI, fresh*	*21*	*46,753*	*29.0*	*Adj*	*1.11 (0.64-1.93)*	*0.72*
All Children	*Term*	*ICSI, frozen*	*1*	*5,967*	*10.9*	*Adj*	*0.42 (0.06-3.09)*	*0.40*
All Children	*Term*	*ICSI, fresh, surgery*	*3*	*2,957*	*65.0*	*Adj*	*2.42 (0.74-7.97)*	*0.14*
All Children	*Term*	*ICSI, frozen, surgery*	*0*	*708*	*0.0*	*Adj*	*x*	*x*
All Children	*Boys*	*IVF without ICSI, fresh*	*42*	*76,420*	*48.4*		*reference group*	
All Children	*Boys*	*IVF without ICSI, frozen*	*6*	*8,788*	*52.6*	*Adj*	*1.13 (0.48-2.68)*	*0.77*
All Children	*Boys*	*ICSI, fresh*	*22*	*28,635*	*49.5*	*Adj*	*1.11 (0.65-1.90)*	*0.69*
All Children	*Boys*	*ICSI, frozen*	*1*	*3,271*	*19.8*	*Adj*	*0.44 (0.06-3.24)*	*0.42*
All Children	*Boys*	*ICSI, fresh, surgery*	*5*	*1,806*	*174.0*	*Adj*	*3.80 (1.48-9.79)*	*<.01*
All Children	*Boys*	*ICSI, frozen, surgery*	*0*	*445*	*0.0*	*Adj*	*x*	*x*
All Children	*Girls*	*IVF, without ICSI, fresh*	*11*	*67,787*	*15.6*		*reference group*	
All Children	*Girls*	*IVF without ICSI, frozen*	*4*	*8,333*	*44.9*	*Adj*	*2.63 (0.84-8.29)*	*0.10*
All Children	*Girls*	*ICSI, fresh*	*9*	*29,627*	*26.7*	*Adj*	*1.50 (0.61-3.66)*	*0.37*
All Children	*Girls*	*ICSI, frozen*	*0*	*3,751*	*0.0*	*Adj*	*x*	*x*
All Children	*Girls*	*ICSI, fresh, surgery*	*3*	*1,915*	*137.7*	*Adj*	*7.31 (2.01-26.59)*	*<.01*
All Children	*Girls*	*ICSI, frozen, surgery*	*0*	*342*	*0.0*	*Adj*	*x*	*x*

eTable 5 (cont.)

Dataset	Sub-Group	IVF procedure	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
All Children	*>1998*	*IVF without ICSI, fresh*	*30*	*52,992*	*43.0*		*reference group*	
All Children	*>1998*	*IVF without ICSI, frozen*	*5*	*8,131*	*55.0*	*Adj*	*1.32 (0.51-3.42)*	*0.57*
All Children	*>1998*	*ICSI, fresh*	*25*	*41,682*	*47.0*	*Adj*	*1.12 (0.65-1.90)*	*0.69*
All Children	*>1998*	*ICSI, frozen*	*1*	*5,637*	*15.9*	*Adj*	*0.38 (0.05-2.80)*	*0.34*
All Children	*>1998*	*ICSI, fresh, surgery*	*7*	*3,127*	*174.9*	*Adj*	*4.16 (1.81-9.55)*	*<.01*
All Children	*>1998*	*ICSI, frozen, surgery*	*0*	*639*	*0.0*	*Adj*	*x*	*x*
Singletons		IVF without ICSI, fresh	30	89,038	23.9		reference group	
Singletons		IVF without ICSI, frozen	5	12,309	25.9	Crude	1.09 (0.42-2.82)	0.86
Singletons						Adj	1.14 (0.44-2.95)	0.79
Singletons						*AdjC*	*1.10 (0.42-2.84)*	*0.85*
Singletons						*AdjI*	*1.13 (0.44-2.94)*	*0.80*
Singletons						*AdjG*	*1.14 (0.44-2.95)*	*0.79*
Singletons		ICSI, fresh	18	39,931	26.0	Crude	1.09 (0.60-2.00)	0.78
Singletons						Adj	1.17 (0.63-2.15)	0.62
Singletons						*AdjC*	*1.07 (0.59-1.97)*	*0.82*
Singletons						*AdjI*	*1.15 (0.63-2.13)*	*0.65*
Singletons						*AdjG*	*1.17 (0.63-2.15)*	*0.62*

eTable 5 (cont.)

Dataset	Sub-Group	IVF procedure	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
Singletons		ICSI, frozen	0	5,519	0.0	Crude	x	x
Singletons						Adj	x	x
Singletons						*AdjC*	*x*	*x*
Singletons						*AdjI*	*x*	*x*
Singletons						*AdjG*	*x*	*x*
Singletons		ICSI, fresh, surgery	1	2,569	21.9	Crude	0.92 (0.12-6.79)	0.93
Singletons						Adj	0.95 (0.13-7.09)	0.96
Singletons						*AdjC*	*0.90 (0.12-6.62)*	*0.91*
Singletons						*AdjI*	*0.94 (0.13-6.98)*	*0.95*
Singletons						*AdjG*	*0.95 (0.13-7.09)*	*0.96*
Singletons		ICSI, frozen, surgery	0	566	0.0	Crude	x	x
Singletons						Adj	x	x
Singletons						*AdjC*	*x*	*x*
Singletons						*AdjI*	*x*	*x*
Singletons						*AdjG*	*x*	*x*

eTable 5 (cont.)

Dataset	Sub-Group	IVF procedure	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
Singletons	*Pre-Term*	*IVF without ICSI, fresh*	*6*	*9,105*	*35.9*		*reference group*	
Singletons	*Pre-Term*	*IVF without ICSI, frozen*	*0*	*944*	*0.0*	*Adj*	*x*	*x*
Singletons	*Pre-Term*	*ICSI, fresh*	*1*	*3,400*	*14.0*	*Adj*	*0.37 (0.04-3.11)*	*0.36*
Singletons	*Pre-Term*	*ICSI, frozen*	*0*	*443*	*0.0*	*Adj*	*x*	*x*
Singletons	*Pre-Term*	*ICSI, fresh, surgery*	*0*	*215*	*0.0*	*Adj*	*x*	*x*
Singletons	*Pre-Term*	*ICSI, frozen, surgery*	*0*	*30*	*0.0*	*Adj*	*x*	*x*
Singletons	*Term*	*IVF without ICSI, fresh*	*24*	*79,932*	*19.9*		*reference group*	
Singletons	*Term*	*IVF without ICSI, frozen*	*5*	*11,365*	*26.3*	*Adj*	*1.41 (0.53-3.71)*	*0.49*
Singletons	*Term*	*ICSI, fresh*	*17*	*36,531*	*24.2*	*Adj*	*1.35 (0.71-2.57)*	*0.37*
Singletons	*Term*	*ICSI, frozen*	*0*	*5,076*	*0.0*	*Adj*	*x*	*x*
Singletons	*Term*	*ICSI, fresh, surgery*	*1*	*2,353*	*21.5*	*Adj*	*1.19 (0.16-8.89)*	*0.87*
Singletons	*Term*	*ICSI, frozen, surgery*	*0*	*535*	*0.0*	*Adj*	*x*	*x*
Singletons	*Boys*	*IVF without ICSI, fresh*	*25*	*47,109*	*47.8*		*reference group*	
Singletons	*Boys*	*IVF without ICSI, frozen*	*3*	*6,365*	*37.1*	*Adj*	*0.84 (0.25-2.80)*	*0.78*
Singletons	*Boys*	*ICSI, fresh*	*13*	*19,618*	*46.6*	*Adj*	*1.05 (0.53-2.11)*	*0.88*
Singletons	*Boys*	*ICSI, frozen*	*0*	*2,583*	*0.0*	*Adj*	*x*	*x*
Singletons	*Boys*	*ICSI, fresh, surgery*	*1*	*1,275*	*53.7*	*Adj*	*1.16 (0.16-8.72)*	*0.88*
Singletons	*Boys*	*ICSI, frozen, surgery*	*0*	*310*	*0.0*	*Adj*	*x*	*x*

eTable 5 (cont.)

Dataset	Sub-Group	IVF procedure	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
Singletons	*Girls*	*IVF without ICSI, fresh*	*5*	*41,928*	*6.0*		*reference group*	
Singletons	*Girls*	*IVF without ICSI, frozen*	*2*	*5,944*	*16.1*	*Adj*	*2.46 (0.48-12.71)*	*0.28*
Singletons	*Girls*	*ICSI, fresh*	*5*	*20,313*	*9.2*	*Adj*	*1.67 (0.48-5.82)*	*0.42*
Singletons	*Girls*	*ICSI, frozen*	*0*	*2,936*	*0.0*	*Adj*	*x*	*x*
Singletons	*Girls*	*ICSI, fresh, surgery*	*0*	*1,294*	*0.0*	*Adj*	*x*	*x*
Singletons	*Girls*	*ICSI, frozen, surgery*	*0*	*256*	*0.0*	*Adj*	*x*	*x*
Singletons	*>1998*	*IVF without ICSI, fresh*	*19*	*36,536*	*37.5*		*reference group*	
Singletons	*>1998*	*IVF without ICSI, frozen*	*3*	*6,413*	*37.3*	*Adj*	*1.04 (0.31-3.55)*	*0.95*
Singletons	*>1998*	*ICSI, fresh*	*13*	*29,649*	*33.4*	*Adj*	*0.92 (0.45-1.87)*	*0.81*
Singletons	*>1998*	*ICSI, frozen*	*0*	*4,446*	*0.0*	*Adj*	*x*	*x*
Singletons	*>1998*	*ICSI, fresh, surgery*	*1*	*2,220*	*33.7*	*Adj*	*0.94 (0.12-7.09)*	*0.95*
Singletons	*>1998*	*ICSI, frozen, surgery*	*0*	*440*	*0.0*	*Adj*	*x*	*x*

Note: x indicate cells not estimable since too few cases.
Crude model denotes model adjusting for birth year, age and sex only; Adj model denotes adjusting for birth year, age and sex and additionally adjusting for paternal psychiatric history, maternal psychiatric history and paternal and maternal age; AdjC model denotes adjusting for birth year, age and sex, and additionally for calendar time; AdjI model denotes adjusting for birth year, age and sex, paternal psychiatric history, maternal psychiatric history and paternal and maternal age, and additionally for years of infertility; AdjG model denotes adjusting for birth year, age and sex and paternal psychiatric history, maternal psychiatric history and paternal and maternal age, and additionally adjusting for presence of genetic diseases. Relative risk (RR) and two-sided 95% confidence intervals (CI). RR presented for crude models (adjusting for age, sex and birth year only) and adjusted models (additionally adjusting for confounding). RR presented also for the supplementary analyses adjusting for calendar time (AdjC), adjusting for years of infertility (Adj I) and adjusting for diagnosis of genetic disease (Adj G) and for subgroups of male and female children; subgroups of preterm and term born children; subgroup of children born after 1998. All calculations presented for multiple birth and singletons separately. Supplementary results in italic.

eTable 6 Mental Retardation. Comparing specific IVF procedures vs IVF without ICSI, fresh embryo

Dataset	Sub-Group	IVF procedure	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
All Children		IVF without ICSI, fresh	94	143,924	60.8	reference group		
All Children		IVF without ICSI, frozen	13	17,095	69.0	Crude	1.14 (0.63-2.04)	0.67
All Children						Adj	1.16 (0.64-2.07)	0.63
All Children						*AdjC*	*1.14 (0.63-2.04)*	*0.67*
All Children						*AdjI*	*1.16 (0.64-2.07)*	*0.63*
All Children						*AdjG*	*1.17 (0.65-2.09)*	*0.60*
All Children		ICSI, fresh	59	58,177	90.6	Crude	1.49 (1.05-2.11)	0.03
All Children						Adj	1.47 (1.03-2.09)	0.03
All Children						*AdjC*	*1.49 (1.05-2.11)*	*0.03*
All Children						*AdjI*	*1.47 (1.03-2.08)*	*0.03*
All Children						*AdjG*	*1.48 (1.04-2.11)*	*0.03*
All Children		ICSI, frozen	8	7,005	103.9	Crude	1.71 (0.82-3.58)	0.16
All Children						Adj	1.70 (0.81-3.56)	0.16
All Children						*AdjC*	*1.71 (0.82-3.58)*	*0.16*
All Children						*AdjI*	*1.70 (0.81-3.57)*	*0.16*
All Children						*AdjG*	*1.72 (0.82-3.60)*	*0.15*

eTable 6 (cont.)

Dataset	Sub-Group	IVF procedure	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
All Children		ICSI, fresh, surgery	6	3,722	144.1	Crude	2.37 (1.03-5.48)	0.04
All Children						Adj	2.35 (1.01-5.45)	0.05
All Children						*AdjC*	*2.37 (1.02-5.47)*	*0.04*
All Children						*AdjI*	*2.35 (1.01-5.46)*	*0.05*
All Children						*AdjG*	*2.37 (1.02-5.51)*	*0.04*
All Children		ICSI, frozen, surgery	0	787	0.0	Crude	x	x
All Children						Adj	x	x
All Children						*AdjC*	*x*	*x*
All Children						*AdjI*	*x*	*x*
All Children						*AdjG*	*x*	*x*
All Children	*Pre-Term*	*IVF without ICSI, fresh*	*38*	*36,788*	*92.2*	*reference group*		
All Children	*Pre-Term*	*IVF without ICSI, frozen*	*5*	*3,285*	*131.0*	*Adj*	*1.44 (0.56-3.66)*	*0.45*
All Children	*Pre-Term*	*ICSI, fresh*	*19*	*11,472*	*136.1*	*Adj*	*1.46 (0.83-2.59)*	*0.19*
All Children	*Pre-Term*	*ICSI, frozen*	*4*	*1,035*	*363.0*	*Adj*	*3.47 (1.22-9.90)*	*0.02*
All Children	*Pre-Term*	*ICSI, fresh, surgery*	*4*	*768*	*413.9*	*Adj*	*4.38 (1.53-12.48)*	*<.01*
All Children	*Pre-Term*	*ICSI, frozen, surgery*	*0*	*78*	*0.0*	*Adj*	*x*	*x*

eTable 6 (cont.)

Dataset	Sub-Group	IVF procedure	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
All Children	*Term*	*IVF without ICSI, fresh*	*56*	*107,136*	*49.5*	*reference group*		
All Children	*Term*	*IVF without ICSI, frozen*	*8*	*13,810*	*51.3*	*Adj*	*1.07 (0.51-2.25)*	*0.86*
All Children	*Term*	*ICSI, fresh*	*40*	*46,706*	*73.8*	*Adj*	*1.51 (0.99-2.31)*	*0.06*
All Children	*Term*	*ICSI, frozen*	*4*	*5,969*	*55.3*	*Adj*	*1.19 (0.43-3.30)*	*0.74*
All Children	*Term*	*ICSI, fresh, surgery*	*2*	*2,954*	*57.2*	*Adj*	*1.21 (0.29-4.99)*	*0.79*
All Children	*Term*	*ICSI, frozen, surgery*	*0*	*708*	*0.0*	*Adj*	*x*	*x*
All Children	*Boys*	*IVF without ICSI, fresh*	*67*	*76,251*	*89.0*	*reference group*		
All Children	*Boys*	*IVF without ICSI, frozen*	*7*	*8,785*	*75.9*	*Adj*	*0.90 (0.41-1.96)*	*0.78*
All Children	*Boys*	*ICSI, fresh*	*41*	*28,570*	*128.7*	*Adj*	*1.50 (1.00-2.26)*	*0.05*
All Children	*Boys*	*ICSI, frozen*	*5*	*3,262*	*137.3*	*Adj*	*1.61 (0.64-4.06)*	*0.31*
All Children	*Boys*	*ICSI, fresh, surgery*	*3*	*1,807*	*147.7*	*Adj*	*1.73 (0.54-5.57)*	*0.36*
All Children	*Boys*	*ICSI, frozen, surgery*	*0*	*445*	*0.0*	*Adj*	*x*	*x*
All Children	*Girls*	*IVF without ICSI, fresh*	*27*	*67,673*	*39.3*	*reference group*		
All Children	*Girls*	*IVF without ICSI, frozen*	*6*	*8,310*	*72.9*	*Adj*	*1.75 (0.72-4.25)*	*0.22*
All Children	*Girls*	*ICSI, fresh*	*18*	*29,607*	*63.0*	*Adj*	*1.41 (0.76-2.59)*	*0.28*
All Children	*Girls*	*ICSI, frozen*	*3*	*3,743*	*83.2*	*Adj*	*1.89 (0.57-6.30)*	*0.30*
All Children	*Girls*	*ICSI, fresh, surgery*	*3*	*1,915*	*163.5*	*Adj*	*3.69 (1.11-12.29)*	*0.03*
All Children	*Girls*	*ICSI, frozen, surgery*	*0*	*342*	*0.0*	*Adj*	*x*	*x*

eTable 6 (cont.)

Dataset	Sub-Group	IVF procedure	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
All Children	*>1998*	*IVF without ICSI, fresh*	*36*	*52,945*	*61.2*	*reference group*		
All Children	*>1998*	*IVF without ICSI, frozen*	*4*	*8,127*	*44.7*	*Adj*	*0.74 (0.26-2.10)*	*0.57*
All Children	*>1998*	*ICSI, fresh*	*48*	*41,626*	*106.9*	*Adj*	*1.78 (1.15-2.75)*	*<.01*
All Children	*>1998*	*ICSI, frozen*	*6*	*5,629*	*98.9*	*Adj*	*1.64 (0.69-3.92)*	*0.26*
All Children	*>1998*	*ICSI, fresh, surgery*	*4*	*3,135*	*119.3*	*Adj*	*2.08 (0.74-5.89)*	*0.17*
All Children	*>1998*	*ICSI, frozen, surgery*	*0*	*639*	*0.0*	*Adj*	*x*	*x*

eTable 6 (cont.)

Dataset	Sub-Group	IVF procedure	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
Singletons		IVF without ICSI, fresh	48	88,895	50.6	reference group		
Singletons		IVF without ICSI, frozen	11	12,271	83.6	Crude	1.65 (0.85-3.21)	0.14
Singletons						Adj	1.67 (0.86-3.24)	0.13
Singletons						*AdjC*	*1.66 (0.85-3.21)*	*0.14*
Singletons						*AdjI*	*1.66 (0.85-3.23)*	*0.14*
Singletons						*AdjG*	*1.70 (0.87-3.31)*	*0.12*
Singletons		ICSI, fresh	34	39,883	80.0	Crude	1.58 (0.99-2.53)	0.06
Singletons						Adj	1.60 (1.00-2.57)	0.05
Singletons						*AdjC*	*1.58 (0.98-2.52)*	*0.06*
Singletons						*AdjI*	*1.59 (0.99-2.55)*	*0.06*
Singletons						*AdjG*	*1.63 (1.01-2.62)*	*0.04*
Singletons		ICSI, frozen	7	5,499	118.4	Crude	2.34 (1.03-5.31)	0.04
Singletons		ICSI, frozen	7	5,499	118.4	Adj	2.36 (1.04-5.36)	0.04
Singletons						*AdjC*	*2.33 (1.03-5.29)*	*0.04*
Singletons						*AdjI*	*2.37 (1.04-5.38)*	*0.04*
Singletons						*AdjG*	*2.40 (1.06-5.46)*	*0.04*

eTable 6 (cont.)

Dataset	Sub-Group	IVF procedure	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
Singletons		ICSI, fresh, surgery	1	2,564	36.1	Crude	0.71 (0.10-5.22)	0.74
Singletons						Adj	0.70 (0.10-5.16)	0.73
Singletons						*AdjC*	*0.71 (0.10-5.18)*	*0.73*
Singletons						*AdjI*	*0.70 (0.10-5.14)*	*0.73*
Singletons						*AdjG*	*0.72 (0.10-5.26)*	*0.74*
Singletons		ICSI, frozen, surgery	0	566	0.0	Crude	x	x
Singletons						Adj	x	x
Singletons						*AdjC*	*x*	*x*
Singletons						*AdjI*	*x*	*x*
Singletons						*AdjG*	*x*	*x*
Singletons	*Pre-Term*	*IVF without ICSI, fresh*	*7*	*9,082*	*61.5*	*reference group*		
Singletons	*Pre-Term*	*IVF without ICSI, frozen*	*4*	*918*	*417.5*	*Adj*	*5.47 (1.58-18.96)*	*<.01*
Singletons	*Pre-Term*	*ICSI, fresh*	*3*	*3,392*	*85.3*	*Adj*	*1.18 (0.30-4.65)*	*0.81*
Singletons	*Pre-Term*	*ICSI, frozen*	*3*	*429*	*737.0*	*Adj*	*9.26 (2.35-36.56)*	*<.01*
Singletons	*Pre-Term*	*ICSI, fresh, surgery*	*0*	*215*	*0.0*	*Adj*	*x*	*x*
Singletons	*Pre-Term*	*ICSI, frozen, surgery*	*0*	*30*	*0.0*	*Adj*	*x*	*x*

eTable 6 (cont.)

Dataset	Sub-Group	IVF procedure	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
Singletons	*Term*	*IVF without ICSI, fresh*	*41*	*79,813*	*48.3*	*reference group*		
Singletons	*Term*	*IVF without ICSI, frozen*	*7*	*11,353*	*55.4*	*Adj*	*1.20 (0.53-2.70)*	*0.66*
Singletons	*Term*	*ICSI, fresh*	*31*	*36,491*	*75.7*	*Adj*	*1.66 (1.01-2.73)*	*0.05*
Singletons	*Term*	*ICSI, frozen*	*4*	*5,070*	*68.7*	*Adj*	*1.52 (0.53-4.33)*	*0.43*
Singletons	*Term*	*ICSI, fresh, surgery*	*1*	*2,348*	*37.0*	*Adj*	*0.81 (0.11-5.96)*	*0.84*
Singletons	*Term*	*ICSI, frozen, surgery*	*0*	*535*	*0.0*	*Adj*	*x*	*x*
Singletons	*Boys*	*IVF without ICSI, fresh*	*34*	*47,029*	*74.0*	*reference group*		
Singletons	*Boys*	*IVF without ICSI, frozen*	*7*	*6,352*	*106.2*	*Adj*	*1.55 (0.68-3.53)*	*0.30*
Singletons	*Boys*	*ICSI, fresh*	*22*	*19,584*	*104.8*	*Adj*	*1.54 (0.88-2.71)*	*0.13*
Singletons	*Boys*	*ICSI, frozen*	*4*	*2,571*	*136.6*	*Adj*	*2.06 (0.71-5.94)*	*0.18*
Singletons	*Boys*	*ICSI, fresh, surgery*	*1*	*1,270*	*71.6*	*Adj*	*1.02 (0.14-7.57)*	*0.98*
Singletons	*Boys*	*ICSI, frozen, surgery*	*0*	*310*	*0.0*	*Adj*	*x*	*x*
Singletons	*Girls*	*IVF without ICSI, fresh*	*14*	*41,865*	*31.2*	*reference group*		
Singletons	*Girls*	*IVF without ICSI, frozen*	*4*	*5,919*	*68.9*	*Adj*	*1.93 (0.63-5.90)*	*0.25*
Singletons	*Girls*	*ICSI, fresh*	*12*	*20,299*	*64.2*	*Adj*	*1.72 (0.78-3.80)*	*0.18*
Singletons	*Girls*	*ICSI, frozen*	*3*	*2,928*	*113.0*	*Adj*	*2.96 (0.84-10.46)*	*0.09*
Singletons	*Girls*	*ICSI, fresh, surgery*	*0*	*1,294*	*0.0*	*Adj*	*x*	*x*
Singletons	*Girls*	*ICSI, frozen, surgery*	*0*	*256*	*0.0*	*Adj*	*x*	*x*

eTable 6 (cont.)

Dataset	Sub-Group	IVF procedure	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
Singletons	*>1998*	*IVF without ICSI, fresh*	*20*	*36,516*	*47.2*	*reference group*		
Singletons	*>1998*	*IVF without ICSI, frozen*	*4*	*6,405*	*51.9*	*Adj*	*1.07 (0.36-3.17)*	*0.90*
Singletons	*>1998*	*ICSI, fresh*	*29*	*29,601*	*87.8*	*Adj*	*1.94 (1.09-3.45)*	*0.02*
Singletons	*>1998*	*ICSI, frozen*	*6*	*4,428*	*117.4*	*Adj*	*2.58 (1.03-6.47)*	*0.04*
Singletons	*>1998*	*ICSI, fresh, surgery*	*1*	*2,214*	*41.5*	*Adj*	*0.94 (0.13-7.06)*	*0.95*
Singletons	*>1998*	*ICSI, frozen, surgery*	*0*	*440*	*0*	*Adj*	*x*	*X*

Note: x indicate cells not estimable since too few cases.

Crude model denotes model adjusting for birth year, age and sex only; Adj model denotes adjusting for birth year, age and sex and additionally adjusting for paternal psychiatric history, maternal psychiatric history and paternal and maternal age; AdjC model denotes adjusting for birth year, age and sex, and additionally for calendar time; AdjI model denotes adjusting for birth year, age and sex, paternal psychiatric history, maternal psychiatric history and paternal and maternal age, and additionally for years of infertility; AdjG model denotes adjusting for birth year, age and sex and paternal psychiatric history, maternal psychiatric history and paternal and maternal age, and additionally adjusting for presence of genetic diseases.Relative risk (RR) and two-sided 95% confidence intervals (CI). RR presented for crude models (adjusting for age, sex and birth year only) and adjusted models (additionally adjusting for confounding). RR presented also for the supplementary analyses adjusting for calendar time (AdjC), adjusting for years of infertility (Adj I) and adjusting for diagnosis of genetic disease (Adj G) and for subgroups of male and female children; subgroups of preterm and term born children; subgroup of children born after 1998. All calculations presented for multiple birth and singletons separately. Supplementary results in italic.

eTable 7 Autistic disorder. Comparing IVF techniques.

Dataset	Technique	Sub-Group	Group of children	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
All Children	*Blastocyst*		*<5 days culture*	*101*	*227,184*	*32.3*	*reference group*		
All Children	*Blastocyst*		*Blastocyst*	*2*	*3,934*	*31.0*	*Crude*	*1.24 (0.29-5.31)*	*0.77*
All Children	*Blastocyst*						*Adj*	*1.40 (0.32-6.13)*	*0.66*
All Children	*Blastocyst*						*AdjI*	*1.39 (0.32-6.08)*	*0.67*
All Children	*Blastocyst*						*AdjG*	*1.40 (0.32-6.13)*	*0.66*
All Children	*Blastocyst*	*Boys*	*<5 days culture*	*75*	*117,333*	*50.2*	*reference group*		
All Children	*Blastocyst*	*Boys*	*Blastocyst*	*1*	*2,031*	*31.5*	*Adj*	*0.92 (0.12-7.08)*	*0.94*
All Children	*Blastocyst*	*Girls*	*<5 days culture*	*26*	*109,851*	*21.4*	*reference group*		
All Children	*Blastocyst*	*Girls*	*Blastocyst*	*1*	*1,902*	*46.3*	*Adj*	*2.90 (0.33-25.23)*	*0.34*
All Children	*Blastocyst*	*PreTerm*	*<5 days culture*	*35*	*52,893*	*47.1*	*reference group*		
All Children	*Blastocyst*	*PreTerm*	*Blastocyst*	*0*	*736*	*0.0*	*Adj*	*x*	*x*
All Children	*Blastocyst*	*Term*	*<5 days culture*	*66*	*174,291*	*27.8*	*reference group*		
All Children	*Blastocyst*	*Term*	*Blastocyst*	*2*	*3,198*	*37.7*	*Adj*	*2.06 (0.46-9.24)*	*0.35*

eTable 7 (cont.)

Dataset	Technique	Sub-Group	Group of children	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
All Children	*Frozen embryo*		*Fresh*	*92*	*206,189*	*32.5*	*reference group*		
All Children	*Frozen embryo*		*Frozen*	*11*	*24,929*	*30.1*	*Crude*	*0.93 (0.49-1.74)*	*0.81*
All Children	*Frozen embryo*					*30.1*	*Adj*	*0.93 (0.50-1.75)*	*0.82*
All Children	*Frozen embryo*					*30.1*	*AdjI*	*0.93 (0.50-1.75)*	*0.83*
All Children	*Frozen embryo*					*30.1*	*AdjG*	*0.93 (0.50-1.75)*	*0.82*
All Children	*Frozen embryo*	*Boys*	*Fresh*	*69*	*106,861*	*51.0*	*reference group*		
All Children	*Frozen embryo*	*Boys*	*Frozen*	*7*	*12,504*	*40.3*	*Adj*	*0.80 (0.37-1.76)*	*0.59*
All Children	*Frozen embryo*	*Girls*	*Fresh*	*23*	*99,328*	*21.0*	*reference group*		
All Children	*Frozen embryo*	*Girls*	*Frozen*	*4*	*12,426*	*28.1*	*Adj*	*1.28 (0.44-3.72)*	*0.64*
All Children	*Frozen embryo*	*PreTerm*	*Fresh*	*32*	*49,199*	*46.2*	*reference group*		
All Children	*Frozen embryo*	*PreTerm*	*Frozen*	*3*	*4,430*	*44.7*	*Adj*	*0.91 (0.28-2.97)*	*0.87*
All Children	*Frozen embryo*	*Term*	*Fresh*	*60*	*156,990*	*28.2*	*reference group*		
All Children	*Frozen embryo*	*Term*	*Frozen*	*8*	*20,499*	*26.9*	*Adj*	*0.97 (0.46-2.03)*	*0.93*
All Children	*ICSI*		*IVF*	*63*	*161,328*	*30.7*	*reference group*		
All Children	*ICSI*		*ICSI*	*40*	*69,790*	*36.4*	*Crude*	*1.19 (0.78-1.80)*	*0.42*
All Children	*ICSI*						*Adj*	*1.21 (0.80-1.85)*	*0.37*
All Children	*ICSI*						*AdjI*	*1.21 (0.80-1.85)*	*0.37*
All Children	*ICSI*						*AdjG*	*1.21 (0.80-1.85)*	*0.37*

eTable 7 (cont.)

Dataset	Technique	Sub-Group	Group of children	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
All Children	*ICSI*	*Boys*	*IVF*	*48*	*85,208*	*48.8*		*reference group*	
All Children	*ICSI*	*Boys*	*ICSI*	*28*	*34,156*	*52.6*	*Adj*	*1.16 (0.71-1.88)*	*0.55*
All Children	*ICSI*	*Girls*	*IVF*	*15*	*76,120*	*18.9*		*reference group*	
All Children	*ICSI*	*Girls*	*ICSI*	*12*	*35,634*	*28.8*	*Adj*	*1.37 (0.64-2.97)*	*0.42*
All Children	*ICSI*	*PreTerm*	*IVF*	*20*	*40,224*	*40.5*		*reference group*	
All Children	*ICSI*	*PreTerm*	*ICSI*	*15*	*13,405*	*64.6*	*Adj*	*1.73 (0.87-3.45)*	*0.12*
All Children	*ICSI*	*Term*	*IVF*	*43*	*121,104*	*27.8*		*reference group*	
All Children	*ICSI*	*Term*	*ICSI*	*25*	*56,385*	*28.5*	*Adj*	*1.04 (0.62-1.73)*	*0.89*
All Children	*Surgically extracted*		*Ejaculated*	*95*	*226,611*	*30.9*		*reference group*	
All Children	*Surgically extracted*		*Surgical*	*8*	*4,507*	*110.1*	*Crude*	*3.29 (1.59-6.84)*	*<.01*
All Children	*Surgically extracted*						*Adj*	*3.29 (1.58-6.87)*	*<.01*
All Children	*Surgically extracted*						*AdjI*	*3.30 (1.58-6.88)*	*<.01*
All Children	*Surgically extracted*						*AdjG*	*3.29 (1.58-6.87)*	*<.01*
All Children	*Surgically extracted*	*Boys*	*Ejaculated*	*71*	*117,114*	*48.3*		*reference group*	
All Children	*Surgically extracted*	*Boys*	*Surgical*	*5*	*2,251*	*141.1*	*Adj*	*2.78 (1.11-6.99)*	*0.03*
All Children	*Surgically extracted*	*Girls*	*Ejaculated*	*24*	*109,497*	*20.1*		*reference group*	
All Children	*Surgically extracted*	*Girls*	*Surgical*	*3*	*2,256*	*111.4*	*Adj*	*4.72 (1.39-16.04)*	*0.01*
All Children	*Surgically extracted*	*PreTerm*	*Ejaculated*	*30*	*52,787*	*42.3*		*reference group*	
All Children	*Surgically extracted*	*PreTerm*	*Surgical*	*5*	*842*	*319.8*	*Adj*	*8.06 (2.97-21.85)*	*<.01*
All Children	*Surgically extracted*	*Term*	*Ejaculated*	*65*	*173,824*	*27.6*		*reference group*	
All Children	*Surgically extracted*	*Term*	*Surgical*	*3*	*3,665*	*51.6*	*Adj*	*1.65 (0.52-5.31)*	*0.40*

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eTable 7 (cont.)

Dataset	Technique	Sub-Group	Group of children	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
Singletons	*Blastocyst*		*<5 days culture*	*52*	*146,799*	*23.8*	*reference group*		
Singletons	*Blastocyst*		*Blastocyst*	*2*	*3,133*	*38.6*	*Crude*	*1.79 (0.41-7.92)*	*0.44*
Singletons	*Blastocyst*						*Adj*	*1.82 (0.40-8.22)*	*0.44*
Singletons	*Blastocyst*						*AdjI*	*1.84 (0.40-8.32)*	*0.43*
Singletons	*Blastocyst*						*AdjG*	*1.82 (0.40-8.22)*	*0.44*
Singletons	*Blastocyst*	*Boys*	*<5 days culture*	*41*	*75,629*	*46.0*	*reference group*		
Singletons	*Blastocyst*	*Boys*	*Blastocyst*	*1*	*1,632*	*42.0*	*Adj*	*1.04 (0.13-8.17)*	*0.97*
Singletons	*Blastocyst*	*Girls*	*<5 days culture*	*11*	*71,169*	*6.6*	*reference group*		
Singletons	*Blastocyst*	*Girls*	*Blastocyst*	*1*	*1,501*	*51.1*	*Adj*	*6.89 (0.61-77.37)*	*0.12*
Singletons	*Blastocyst*	*PreTerm*	*<5 days culture*	*7*	*13,835*	*26.9*	*reference group*		
Singletons	*Blastocyst*	*PreTerm*	*Blastocyst*	*0*	*304*	*0.0*	*Adj*	*x*	*x*
Singletons	*Blastocyst*	*Term*	*<5 days culture*	*45*	*132,964*	*20.9*	*reference group*		
Singletons	*Blastocyst*	*Term*	*Blastocyst*	*2*	*2,829*	*41.2*	*Adj*	*2.09 (0.46-9.52)*	*0.34*
Singletons	*Frozen embryo*		*Fresh*	*49*	*131,538*	*25.1*	*reference group*		
Singletons	*Frozen embryo*		*Frozen*	*5*	*18,394*	*17.3*	*Crude*	*0.69 (0.27-1.73)*	*0.43*
Singletons	*Frozen embryo*						*Adj*	*0.71 (0.28-1.78)*	*0.46*
Singletons	*Frozen embryo*						*AdjI*	*0.71 (0.28-1.79)*	*0.47*
Singletons	*Frozen embryo*						*AdjG*	*0.71 (0.28-1.78)*	*0.46*

eTable 7 (cont.)

Dataset	Technique	Sub-Group	Group of children	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
Singletons	*Frozen embryo*	*Boys*	*Fresh*	*39*	*68,002*	*48.8*		*reference group*	
Singletons	*Frozen embryo*	*Boys*	*Frozen*	*3*	*9,259*	*25.1*	*Adj*	*0.54 (0.17-1.76)*	*0.31*
Singletons	*Frozen embryo*	*Girls*	*Fresh*	*10*	*63,535*	*7.4*		*reference group*	
Singletons	*Frozen embryo*	*Girls*	*Frozen*	*2*	*9,135*	*10.3*	*Adj*	*1.30 (0.28-5.93)*	*0.74*
Singletons	*Frozen embryo*	*PreTerm*	*Fresh*	*7*	*12,721*	*29.3*		*reference group*	
Singletons	*Frozen embryo*	*PreTerm*	*Frozen*	*0*	*1,418*	*0.0*	*Adj*	*x*	*x*
Singletons	*Frozen embryo*	*Term*	*Fresh*	*42*	*118,817*	*22.0*		*reference group*	
Singletons	*Frozen embryo*	*Term*	*Frozen*	*5*	*16,977*	*17.4*	*Adj*	*0.82 (0.32-2.08)*	*0.68*
Singletons	*ICSI*		*IVF*	*35*	*101,347*	*24.6*		*reference group*	
Singletons	*ICSI*		*ICSI*	*19*	*48,585*	*23.1*	*Crude*	*0.94 (0.53-1.67)*	*0.83*
Singletons	*ICSI*						*Adj*	*1.01 (0.56-1.81)*	*0.98*
Singletons	*ICSI*						*AdjI*	*1.00 (0.56-1.79)*	*1.00*
Singletons	*ICSI*						*AdjG*	*1.01 (0.56-1.81)*	*0.98*
Singletons	*ICSI*	*Boys*	*IVF*	*28*	*53,475*	*47.3*		*reference group*	
Singletons	*ICSI*	*Boys*	*ICSI*	*14*	*23,786*	*42.3*	*Adj*	*0.97 (0.50-1.88)*	*0.92*
Singletons	*ICSI*	*Girls*	*IVF*	*7*	*47,872*	*7.7*		*reference group*	
Singletons	*ICSI*	*Girls*	*ICSI*	*5*	*24,798*	*8.0*	*Adj*	*1.15 (0.36-3.68)*	*0.81*
Singletons	*ICSI*	*PreTerm*	*IVF*	*6*	*10,050*	*32.5*		*reference group*	
Singletons	*ICSI*	*PreTerm*	*ICSI*	*1*	*4,089*	*12.0*	*Adj*	*0.35 (0.04-2.91)*	*0.33*

eTable 7 (cont.)

Dataset	Technique	Sub-Group	Group of children	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
Singletons	*ICSI*	*Term*	*IVF*	*29*	*91,297*	*21.3*	*reference group*		
Singletons	*ICSI*	*Term*	*ICSI*	*18*	*44,496*	*21.7*	*Adj*	*1.13 (0.62-2.09)*	*0.69*
Singletons	*Surgically extracted*		*Ejaculated*	*53*	*146,797*	*24.3*	*reference group*		
Singletons	*Surgically extracted*		*Surgical*	*1*	*3,135*	*18.3*	*Crude*	*0.68 (0.09-4.94)*	*0.70*
Singletons	*Surgically extracted*		*Surgical*	*1*	*3,135*	*18.3*	*Adj*	*0.73 (0.10-5.30)*	*0.75*
Singletons	*Surgically extracted*						*AdjI*	*0.72 (0.10-5.25)*	*0.75*
Singletons	*Surgically extracted*						*AdjG*	*0.73 (0.10-5.30)*	*0.75*
Singletons	*Surgically extracted*	*Boys*	*Ejaculated*	*41*	*75,676*	*45.9*	*reference group*		
Singletons	*Surgically extracted*	*Boys*	*Surgical*	*1*	*1,585*	*45.0*	*Adj*	*0.96 (0.13-7.02)*	*0.97*
Singletons	*Surgically extracted*	*Girls*	*Ejaculated*	*12*	*71,121*	*7.9*	*reference group*		
Singletons	*Surgically extracted*	*Girls*	*Surgical*	*0*	*1,550*	*0.0*	*Adj*	*x*	*x*
Singletons	*Surgically extracted*	*PreTerm*	*Ejaculated*	*7*	*13,893*	*26.8*	*reference group*		
Singletons	*Surgically extracted*	*PreTerm*	*Surgical*	*0*	*246*	*0.0*	*Adj*	*x*	*x*
Singletons	*Surgically extracted*	*Term*	*Ejaculated*	*46*	*132,904*	*21.5*	*reference group*		
Singletons	*Surgically extracted*	*Term*	*Surgical*	*1*	*2,889*	*17.8*	*Adj*	*0.83 (0.11-6.03)*	*0.85*

Note: x indicate cells not estimable since too few cases.

Crude model denotes model adjusting for birth year, age and sex only; Adj model denotes adjusting for birth year, age and sex and additionally adjusting for paternal psychiatric history, maternal psychiatric history and paternal and maternal age; AdjC model denotes adjusting for birth year, age and sex, and additionally for calendar time; AdjI model denotes adjusting for birth year, age and sex, paternal psychiatric history, maternal psychiatric history and paternal and maternal age, and additionally for years of infertility; AdjG model denotes adjusting for birth year, age and sex and paternal psychiatric history, maternal psychiatric history and paternal and maternal age, and additionally adjusting for presence of genetic diseases. Relative risk (RR) and two-sided 95% confidence intervals (CI). RR presented for crude models (adjusting for age, sex and birth year only) and adjusted models (additionally adjusting for confounding). RR presented also for the supplementary analyses adjusting for calendar time (AdjC), adjusting for years of infertility (Adj I) and adjusting for diagnosis of genetic disease (Adj G) and for subgroups of male and female children; subgroups of preterm and term born children; subgroup of children born after 1998. All calculations presented for multiple birth and singletons separately. Supplementary results in italic.

eTable 8 Mental Retardation. Comparing IVF techniques.

Dataset	Technique	Sub-Group	Group of children	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
All Children	*Blastocyst*		*<5 days culture*	*179*	*226,774*	*71.9*	*reference group*		
All Children	*Blastocyst*		*Blastocyst*	*1*	*3,936*	*19.5*	*Crude*	*0.27 (0.04-1.94)*	*0.19*
All Children	*Blastocyst*						*Adj*	*0.28 (0.04-2.01)*	*0.20*
All Children	*Blastocyst*						*AdjI*	*0.27 (0.04-2.00)*	*0.20*
All Children	*Blastocyst*						*AdjG*	*0.28 (0.04-2.01)*	*0.20*
All Children	*Blastocyst*	*Boys*	*<5 days culture*	*122*	*117,089*	*100.0*	*reference group*		
All Children	*Blastocyst*	*Boys*	*Blastocyst*	*1*	*2,031*	*39.6*	*Adj*	*0.42 (0.06-3.11)*	*0.40*
All Children	*Blastocyst*	*Girls*	*<5 days culture*	*57*	*109,685*	*52.0*	*reference group*		
All Children	*Blastocyst*	*Girls*	*Blastocyst*	*0*	*1,904*	*0.0*	*Adj*	*x*	*x*
All Children	*Blastocyst*	*PreTerm*	*<5 days culture*	*70*	*52,691*	*115.4*	*reference group*		
All Children	*Blastocyst*	*PreTerm*	*Blastocyst*	*0*	*736*	*0.0*	*Adj*	*x*	*x*
All Children	*Blastocyst*	*Term*	*<5 days culture*	*109*	*174,083*	*56.7*	*reference group*		
All Children	*Blastocyst*	*Term*	*Blastocyst*	*1*	*3,200*	*19.7*	*Adj*	*0.36 (0.05-2.67)*	*0.32*
All Children	*Frozen embryo*		*Fresh*	*159*	*205,824*	*70.5*	*reference group*		
All Children	*Frozen embryo*		*Frozen*	*21*	*24,886*	*74.2*	*Crude*	*1.05 (0.67-1.66)*	*0.83*
All Children	*Frozen embryo*						*Adj*	*1.07 (0.68-1.69)*	*0.77*
All Children	*Frozen embryo*						*AdjI*	*1.07 (0.68-1.70)*	*0.77*
All Children	*Frozen embryo*						*AdjG*	*1.08 (0.68-1.70)*	*0.75*

eTable 8 (cont.)

Dataset	Technique	Sub-Group	Group of children	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
All Children	*Frozen embryo*	*Boys*	*Fresh*	*111*	*106,629*	*100.3*	*reference group*		
All Children	*Frozen embryo*	*Boys*	*Frozen*	*12*	*12,492*	*86.9*	*Adj*	*0.90 (0.49-1.63)*	*0.72*
All Children	*Frozen embryo*	*Girls*	*Fresh*	*48*	*99,195*	*48.5*	*reference group*		
All Children	*Frozen embryo*	*Girls*	*Frozen*	*9*	*12,394*	*71.7*	*Adj*	*1.45 (0.71-2.97)*	*0.30*
All Children	*Frozen embryo*	*PreTerm*	*Fresh*	*61*	*49,028*	*107.6*	*reference group*		
All Children	*Frozen embryo*	*PreTerm*	*Frozen*	*9*	*4,399*	*174.7*	*Adj*	*1.56 (0.77-3.15)*	*0.22*
All Children	*Frozen embryo*	*Term*	*Fresh*	*98*	*156,795*	*56.9*	*reference group*		
All Children	*Frozen embryo*	*Term*	*Frozen*	*12*	*20,488*	*49.2*	*Adj*	*0.90 (0.49-1.64)*	*0.73*
All Children	*ICSI*		*IVF*	*107*	*161,019*	*61.8*	*reference group*		
All Children	*ICSI*		*ICSI*	*73*	*69,691*	*93.5*	*Crude*	*1.51 (1.10-2.09)*	*0.01*
All Children	*ICSI*						*Adj*	*1.51 (1.09-2.09)*	*0.01*
All Children	*ICSI*						*AdjI*	*1.51 (1.09-2.08)*	*0.01*
All Children	*ICSI*						*AdjG*	*1.52 (1.10-2.11)*	*0.01*
All Children	*ICSI*	*Boys*	*IVF*	*74*	*85,036*	*87.6*	*reference group*		
All Children	*ICSI*	*Boys*	*ICSI*	*49*	*34,084*	*129.4*	*Adj*	*1.54 (1.05-2.25)*	*0.03*
All Children	*ICSI*	*Girls*	*IVF*	*33*	*75,982*	*43.2*	*reference group*		
All Children	*ICSI*	*Girls*	*ICSI*	*24*	*35,607*	*68.8*	*Adj*	*1.45 (0.85-2.49)*	*0.18*
All Children	*ICSI*	*PreTerm*	*IVF*	*43*	*40,073*	*96.0*	*reference group*		
All Children	*ICSI*	*PreTerm*	*ICSI*	*27*	*13,354*	*166.7*	*Adj*	*1.73 (1.05-2.86)*	*0.03*

eTable 8 (cont.)

Dataset	Technique	Sub-Group	Group of children	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
All Children	*ICSI*	*Term*	*IVF*	*64*	*120,946*	*49.8*	*reference group*		
All Children	*ICSI*	*Term*	*ICSI*	*46*	*56,337*	*70.1*	*Adj*	*1.44 (0.97-2.15)*	*0.07*
All Children	*Surgically extracted*		*Ejaculated*	*174*	*226,201*	*70.1*	*reference group*		
All Children	*Surgically extracted*		*Surgical*	*6*	*4,508*	*112.1*	*Crude*	*1.56 (0.69-3.54)*	*0.29*
All Children	*Surgically extracted*						*Adj*	*1.67 (0.73-3.79)*	*0.22*
All Children	*Surgically extracted*						*AdjI*	*1.67 (0.73-3.79)*	*0.22*
All Children	*Surgically extracted*						*AdjG*	*1.68 (0.74-3.83)*	*0.22*
All Children	*Surgically extracted*	*Boys*	*Ejaculated*	*120*	*116,869*	*98.6*	*reference group*		
All Children	*Surgically extracted*	*Boys*	*Surgical*	*3*	*2,252*	*112.9*	*Adj*	*1.19 (0.38-3.78)*	*0.76*
All Children	*Surgically extracted*	*Girls*	*Ejaculated*	*54*	*109,333*	*49.4*	*reference group*		
All Children	*Surgically extracted*	*Girls*	*Surgical*	*3*	*2,256*	*130.2*	*Adj*	*2.77 (0.85-9.02)*	*0.09*
All Children	*Surgically extracted*	*PreTerm*	*Ejaculated*	*66*	*52,580*	*109.4*	*reference group*		
All Children	*Surgically extracted*	*PreTerm*	*Surgical*	*4*	*846*	*356.7*	*Adj*	*3.31 (1.18-9.31)*	*0.02*
All Children	*Surgically extracted*	*Term*	*Ejaculated*	*108*	*173,621*	*56.2*	*reference group*		
All Children	*Surgically extracted*	*Term*	*Surgical*	*2*	*3,662*	*43.5*	*Adj*	*0.83 (0.20-3.40)*	*0.80*

eTable 8 (cont.)

Dataset	Technique	Sub-Group	Group of children	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
Singletons	*Blastocyst*		*<5 days culture*	*100*	*146,542*	*63.7*	*reference group*		
Singletons	*Blastocyst*		*Blastocyst*	*1*	*3,135*	*23.7*	*Crude*	*0.39 (0.05-2.85)*	*0.35*
Singletons	*Blastocyst*						*Adj*	*0.35 (0.05-2.61)*	*0.31*
Singletons	*Blastocyst*						*AdjI*	*0.36 (0.05-2.65)*	*0.31*
Singletons	*Blastocyst*						*AdjG*	*0.35 (0.05-2.61)*	*0.31*
Singletons	*Blastocyst*	*Boys*	*<5 days culture*	*67*	*75,485*	*86.9*	*reference group*		
Singletons	*Blastocyst*	*Boys*	*Blastocyst*	*1*	*1,632*	*43.2*	*Adj*	*0.46 (0.06-3.42)*	*0.45*
Singletons	*Blastocyst*	*Girls*	*<5 days culture*	*33*	*71,057*	*46.4*	*reference group*		
Singletons	*Blastocyst*	*Girls*	*Blastocyst*	*0*	*1,503*	*0.0*	*Adj*	*x*	*x*
Singletons	*Blastocyst*	*PreTerm*	*<5 days culture*	*17*	*13,764*	*111.3*	*reference group*		
Singletons	*Blastocyst*	*PreTerm*	*Blastocyst*	*0*	*304*	*0.0*	*Adj*	*x*	*x*
Singletons	*Blastocyst*	*Term*	*<5 days culture*	*83*	*132,779*	*57.1*	*reference group*		
Singletons	*Blastocyst*	*Term*	*Blastocyst*	*1*	*2,831*	*24.4*	*Adj*	*0.39 (0.05-2.86)*	*0.35*
Singletons	*Frozen embryo*		*Fresh*	*83*	*131,341*	*59.1*	*reference group*		
Singletons	*Frozen embryo*		*Frozen*	*18*	*18,336*	*89.1*	*Crude*	*1.51 (0.90-2.52)*	*0.12*
Singletons	*Frozen embryo*						*Adj*	*1.52 (0.91-2.55)*	*0.11*
Singletons	*Frozen embryo*						*AdjI*	*1.52 (0.91-2.55)*	*0.11*
Singletons	*Frozen embryo*						*AdjG*	*1.53 (0.92-2.57)*	*0.10*
Singletons	*Frozen embryo*	*Boys*	*Fresh*	*57*	*67,883*	*82.8*	*reference group*		
Singletons	*Frozen embryo*	*Boys*	*Frozen*	*11*	*9,233*	*108.8*	*Adj*	*1.38 (0.72-2.66)*	*0.33*

eTable 8 (cont.)

Dataset	Technique	Sub-Group	Group of children	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
Singletons	*Frozen embryo*	*Girls*	*Fresh*	*26*	*63,458*	*40.7*	*reference group*		
Singletons	*Frozen embryo*	*Girls*	*Frozen*	*7*	*9,102*	*78.5*	*Adj*	*1.80 (0.78-4.16)*	*0.17*
Singletons	*Frozen embryo*	*PreTerm*	*Fresh*	*10*	*12,690*	*66.9*	*reference group*		
Singletons	*Frozen embryo*	*PreTerm*	*Frozen*	*7*	*1,378*	*498.0*	*Adj*	*6.02 (2.27-15.96)*	*<.01*
Singletons	*Frozen embryo*	*Term*	*Fresh*	*73*	*118,652*	*56.4*	*reference group*		
Singletons	*Frozen embryo*	*Term*	*Frozen*	*11*	*16,958*	*56.1*	*Adj*	*1.03 (0.54-1.95)*	*0.92*
Singletons	*ICSI*		*IVF*	*59*	*101,166*	*54.8*	*reference group*		
Singletons	*ICSI*		*ICSI*	*42*	*48,511*	*80.2*	*Crude*	*1.46 (0.96-2.23)*	*0.08*
Singletons	*ICSI*						*Adj*	*1.50 (0.98-2.29)*	*0.06*
Singletons	*ICSI*						*AdjI*	*1.49 (0.97-2.28)*	*0.07*
Singletons	*ICSI*						*AdjG*	*1.52 (0.99-2.33)*	*0.06*
Singletons	*ICSI*	*Boys*	*IVF*	*41*	*53,381*	*78.2*	*reference group*		
Singletons	*ICSI*	*Boys*	*ICSI*	*27*	*23,735*	*104.3*	*Adj*	*1.46 (0.88-2.44)*	*0.15*
Singletons	*ICSI*	*Girls*	*IVF*	*18*	*47,784*	*35.9*	*reference group*		
Singletons	*ICSI*	*Girls*	*ICSI*	*15*	*24,776*	*64.9*	*Adj*	*1.57 (0.78-3.17)*	*0.21*
Singletons	*ICSI*	*PreTerm*	*IVF*	*11*	*10,000*	*97.4*	*reference group*		
Singletons	*ICSI*	*PreTerm*	*ICSI*	*6*	*4,067*	*136.2*	*Adj*	*1.36 (0.49-3.75)*	*0.55*
Singletons	*ICSI*	*Term*	*IVF*	*48*	*91,165*	*49.3*	*reference group*		
Singletons	*ICSI*	*Term*	*ICSI*	*36*	*44,444*	*71.8*	*Adj*	*1.53 (0.97-2.42)*	*0.07*

eTable 8 (cont.)

Dataset	Technique	Sub-Group	Group of children	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
Singletons	*Surgically extracted*		*Ejaculated*	*100*	*146,548*	*63.5*	*reference group*		
Singletons	*Surgically extracted*		*Surgical*	*1*	*3,129*	*27.6*	*Crude*	*0.42 (0.06-3.06)*	*0.40*
Singletons	*Surgically extracted*						*Adj*	*0.45 (0.06-3.22)*	*0.42*
Singletons	*Surgically extracted*						*AdjI*	*0.45 (0.06-3.22)*	*0.42*
Singletons	*Surgically extracted*						*AdjG*	*0.45 (0.06-3.27)*	*0.43*
Singletons	*Surgically extracted*	*Boys*	*Ejaculated*	*67*	*75,537*	*86.5*	*reference group*		
Singletons	*Surgically extracted*	*Boys*	*Surgical*	*1*	*1,580*	*54.5*	*Adj*	*0.64 (0.09-4.65)*	*0.66*
Singletons	*Surgically extracted*	*Girls*	*Ejaculated*	*33*	*71,011*	*46.4*	*reference group*		
Singletons	*Surgically extracted*	*Girls*	*Surgical*	*0*	*1,550*	*0.0*	*Adj*	*x*	*x*
Singletons	*Surgically extracted*	*PreTerm*	*Ejaculated*	*17*	*13,822*	*110.5*	*reference group*		
Singletons	*Surgically extracted*	*PreTerm*	*Surgical*	*0*	*246*	*0.0*	*Adj*	*x*	*x*
Singletons	*Surgically extracted*	*Term*	*Ejaculated*	*83*	*132,726*	*57.0*	*reference group*		
Singletons	*Surgically extracted*	*Term*	*Surgical*	*1*	*2,884*	*28.4*	*Adj*	*0.53 (0.07-3.85)*	*0.53*

Note: x indicate cells not estimable since too few cases.
Crude model denotes model adjusting for birth year, age and sex only; Adj model denotes adjusting for birth year, age and sex and additionally adjusting for paternal psychiatric history, maternal psychiatric history and paternal and maternal age; AdjC model denotes adjusting for birth year, age and sex, and additionally for calendar time; AdjI model denotes adjusting for birth year, age and sex, paternal psychiatric history, maternal psychiatric history and paternal and maternal age, and additionally for years of infertility; AdjG model denotes adjusting for birth year, age and sex and paternal psychiatric history, maternal psychiatric history and paternal and maternal age, and additionally adjusting for presence of genetic diseases. Relative risk (RR) and two-sided 95% confidence intervals (CI). RR presented for crude models (adjusting for age, sex and birth year only) and adjusted models (additionally adjusting for confounding). RR presented also for the supplementary analyses adjusting for calendar time (AdjC), adjusting for years of infertility (Adj I) and adjusting for diagnosis of genetic disease (Adj G) and for subgroups of male and female children; subgroups of preterm and term born children; subgroup of children born after 1998. All calculations presented for multiple birth and singletons separately. Supplementary results in italic.

eTable 9 Hormones. Comparing offspring born following hormone treatment as only fertility treatment vs offspring spontaneous conceived without use of hormones.

Dataset	Hormones or No Hormones	Number of Cases	Person Years	Rate per 100,000	Model	RR (95% CI)	p-value
Autistic Disorder							
All Children	*No Hormones*	*6,933*	*34,155,462*	*15.6*	*reference group*		
All Children	*Hormone treated*	*26*	*70,333*	*14.1*	*Crude*	*0.90 (0.61-1.33)*	*0.61*
All Children					*Adj*	*0.91 (0.62-1.34)*	*0.64*
Singletons	*No Hormones*	*6,713*	*33,372,926*	*15.0*	*reference group*		
Singletons	*Hormone treated*	*24*	*62,389*	*14.2*	*Crude*	*0.95 (0.63-1.42)*	*0.79*
Singletons					*Adj*	*0.96 (0.64-1.43)*	*0.84*
Mental Retardation							
All Children	*No Hormones*	*15,784*	*34,108,394*	*39.8*	*reference group*		
All Children	*Hormone treated*	*43*	*70,277*	*34.4*	*Crude*	*0.86 (0.64-1.16)*	*0.34*
All Children					*Adj*	*0.89 (0.66-1.21)*	*0.46*
Singletons	*No Hormones*	*15,241*	*33,327,569*	*38.5*	*reference group*		
Singletons	*Hormone treated*	*38*	*62,342*	*33.4*	*Crude*	*0.87 (0.63-1.19)*	*0.39*
Singletons					*Adj*	*0.90 (0.65-1.24)*	*0.52*

Note: x indicate cells not estimable since too few cases.

Crude model denotes model adjusting for birth year, age and sex only; Adj model denotes adjusting for birth year, age and sex and additionally adjusting for paternal psychiatric history, maternal psychiatric history and paternal and maternal age. Relative risk (RR) and two-sided 95% confidence intervals (CI) for autistic disorder and for mental retardation for. For All children and for singletons. All RR from adjusted models.

eTable 10 **Comparisons of offspring born following specific IVF procedures vs offspring born after spontaneous conception.**

Dataset	IVF Procedure	Sub-Group	Autistic Disorder RR (95% CI)#	Autistic Disorder p-value	Mental Retardation RR (95% CI)#	Mental Retardation p-value
All Children	IVF without ICSI, fresh		1.01 (0.77 - 1.32)	0.96	1.01 (0.83 - 1.24)	0.91
All Children	*IVF without ICSI, fresh*	*>1998##*	*1.14 (0.79 - 1.63)*	*0.49*	*0.92 (0.66 - 1.28)*	*0.64*
All Children	*IVF without ICSI, fresh*	*Boys*	*1.07 (0.79 - 1.45)*	*0.66*	*1.14 (0.90 - 1.45)*	*0.28*
All Children	*IVF without ICSI, fresh*	*Girls*	*0.85 (0.47 - 1.54)*	*0.60*	*0.75 (0.51 - 1.09)*	*0.13*
All Children	*IVF without ICSI, fresh*	*Pre-Term*	*0.82 (0.51 - 1.33)*	*0.42*	*0.69 (0.50 - 0.95)*	*0.02*
All Children	*IVF without ICSI, fresh*	*Term*	*0.95 (0.68 - 1.32)*	*0.75*	*0.86 (0.66 - 1.12)*	*0.25*
All Children	IVF without ICSI, frozen		1.43 (0.77- 2.66)	0.26	1.12 (0.65- 1.93)	0.68
All Children	*IVF without ICSI, frozen*	*>1998##*	*1.25 (0.52- 3.00)*	*0.62*	*0.67 (0.25- 1.79)*	*0.42*
All Children	*IVF without ICSI, frozen*	*Boys*	*1.19 (0.54- 2.66)*	*0.67*	*1.00 (0.48- 2.10)*	*1.00*
All Children	*IVF without ICSI, frozen*	*Girls*	*2.17 (0.81- 5.80)*	*0.12*	*1.26 (0.56- 2.80)*	*0.58*
All Children	*IVF without ICSI, frozen*	*Pre-Term*	*1.45 (0.47- 4.51)*	*0.52*	*0.96 (0.40- 2.30)*	*0.92*
All Children	*IVF without ICSI, frozen*	*Term*	*1.30 (0.62- 2.73)*	*0.49*	*0.91 (0.46- 1.83)*	*0.80*

eTable 10 (cont.)

Dataset	IVF Procedure	Sub-Group	Autistic Disorder RR (95% CI)#	Autistic Disorder p-value	Mental Retardation RR (95% CI)#	Mental Retardation p-value
All Children	ICSI, fresh		1.23 (0.86- 1.75)	0.25	1.45 (1.12- 1.87)	<.01
All Children	*ICSI, fresh*	*>1998##*	*1.27 (0.85- 1.88)*	*0.24*	*1.57 (1.18- 2.09)*	*<.01*
All Children	*ICSI, fresh*	*Boys*	*1.21 (0.79- 1.84)*	*0.38*	*1.70 (1.25- 2.31)*	*<.01*
All Children	*ICSI, fresh*	*Girls*	*1.30 (0.67- 2.50)*	*0.44*	*1.04 (0.66- 1.66)*	*0.86*
All Children	*ICSI, fresh*	*Pre-Term*	*1.28 (0.68- 2.38)*	*0.45*	*1.01 (0.64- 1.59)*	*0.96*
All Children	*ICSI, fresh*	*Term*	*1.07 (0.70- 1.65)*	*0.75*	*1.31 (0.96- 1.78)*	*0.09*
All Children	ICSI, frozen		0.32 (0.04- 2.24)	0.25	1.65 (0.82- 3.30)	0.16
All Children	*ICSI, frozen*	*>1998##*	*0.37 (0.05- 2.65)*	*0.32*	*1.48 (0.66- 3.29)*	*0.34*
All Children	*ICSI, frozen*	*Boys*	*0.45 (0.06- 3.17)*	*0.42*	*1.81 (0.75- 4.36)*	*0.18*
All Children	*ICSI, frozen*	*Girls*	*x*	*x*	*1.39 (0.45- 4.30)*	*0.57*
All Children	*ICSI, frozen*	*Pre-Term*	*x*	*x*	*2.39 (0.89- 6.37)*	*0.08*
All Children	*ICSI, frozen*	*Term*	*0.39 (0.05- 2.75)*	*0.34*	*1.03 (0.39- 2.76)*	*0.95*

eTable 10 (cont.)

Dataset	IVF Procedure	Sub-Group	Autistic Disorder RR (95% CI)#	Autistic Disorder p-value	Mental Retardation RR (95% CI)#	Mental Retardation p-value
All Children	ICSI, fresh, surgery		4.56 (2.28- 9.13)	<.01	2.18 (0.98- 4.86)	0.06
All Children	*ICSI, fresh, surgery*	*>1998##*	*4.47 (2.13- 9.40)*	*<.01*	*1.67 (0.63- 4.45)*	*0.31*
All Children	*ICSI, fresh, surgery*	*Boys*	*3.92 (1.63- 9.44)*	*<.01*	*1.85 (0.59- 5.73)*	*0.29*
All Children	*ICSI, fresh, surgery*	*Girls*	*6.18 (1.99-19.18)*	*<.01*	*2.59 (0.83- 8.02)*	*0.10*
All Children	*ICSI, fresh, surgery*	*Pre-Term*	*8.08 (3.35-19.49)*	*<.01*	*2.80 (1.05- 7.48)*	*0.04*
All Children	*ICSI, fresh, surgery*	*Term*	*2.26 (0.73- 7.01)*	*0.16*	*1.00 (0.25- 4.01)*	*1.00*
All Children	ICSI, frozen, surgery		*Not estimable - Too few cases*			

eTable 10 (cont.)

Dataset	IVF Procedure	Sub-Group	Autistic Disorder RR (95% CI)#	Autistic Disorder p-value	Mental Retardation RR (95% CI)#	Mental Retardation p-value
Singletons	*IVF without ICSI, fresh*		*0.89 (0.62 - 1.27)*	*0.52*	*0.83 (0.63 - 1.11)*	*0.21*
Singletons	*IVF without ICSI, fresh*	*>1998##*	*1.02 (0.65 - 1.61)*	*0.92*	*0.74 (0.48 - 1.15)*	*0.18*
Singletons	*IVF without ICSI, fresh*	*Boys*	*1.00 (0.67 - 1.48)*	*0.98*	*0.94 (0.67 - 1.31)*	*0.70*
Singletons	*IVF without ICSI, fresh*	*Girls*	*0.61 (0.25 - 1.46)*	*0.27*	*0.62 (0.37 - 1.05)*	*0.08*
Singletons	*IVF without ICSI, fresh*	*Pre-Term*	*1.01 (0.45 - 2.26)*	*0.98*	*0.47 (0.23 - 0.99)*	*0.05*
Singletons	*IVF without ICSI, fresh*	*Term*	*0.83 (0.56 - 1.25)*	*0.38*	*0.84 (0.62 - 1.14)*	*0.27*
Singletons	*IVF without ICSI, frozen*		*0.96 (0.40- 2.31)*	*0.93*	*1.32 (0.73- 2.38)*	*0.36*
Singletons	*IVF without ICSI, frozen*	*>1998##*	*0.92 (0.30- 2.88)*	*0.89*	*0.84 (0.31- 2.24)*	*0.72*
Singletons	*IVF without ICSI, frozen*	*Boys*	*0.80 (0.26- 2.48)*	*0.70*	*1.39 (0.66- 2.92)*	*0.38*
Singletons	*IVF without ICSI, frozen*	*Girls*	*1.48 (0.37- 5.93)*	*0.58*	*1.17 (0.44- 3.11)*	*0.76*
Singletons	*IVF without ICSI, frozen*	*Pre-Term*	*x*	*x*	*2.46 (0.92- 6.58)*	*0.07*
Singletons	*IVF without ICSI, frozen*	*Term*	*1.11 (0.46- 2.67)*	*0.81*	*0.97 (0.46- 2.03)*	*0.93*

eTable 10 (cont.)

Dataset	IVF Procedure	Sub-Group	Autistic Disorder RR (95% CI)#	Autistic Disorder p-value	Mental Retardation RR (95% CI)#	Mental Retardation p-value
Singletons	*ICSI, fresh*		*1.03 (0.65- 1.64)*	*0.90*	*1.23 (0.87- 1.72)*	*0.24*
Singletons	*ICSI, fresh*	*>1998##*	*0.93 (0.54- 1.60)*	*0.79*	*1.35 (0.93- 1.94)*	*0.11*
Singletons	*ICSI, fresh*	*Boys*	*1.04 (0.60- 1.79)*	*0.90*	*1.35 (0.88- 2.05)*	*0.17*
Singletons	*ICSI, fresh*	*Girls*	*1.04 (0.43- 2.50)*	*0.94*	*1.02 (0.58- 1.80)*	*0.95*
Singletons	*ICSI, fresh*	*Pre-Term*	*0.38 (0.05- 2.73)*	*0.34*	*0.50 (0.16- 1.56)*	*0.23*
Singletons	*ICSI, fresh*	*Term*	*1.11 (0.69- 1.79)*	*0.66*	*1.30 (0.92- 1.85)*	*0.14*
Singletons	*ICSI, frozen*		*x*	*x*	*1.84 (0.88- 3.86)*	*0.11*
Singletons	*ICSI, frozen*	*>1998##*	*x*	*x*	*1.88 (0.84- 4.19)*	*0.12*
Singletons	*ICSI, frozen*	*Boys*	*x*	*x*	*1.85 (0.69- 4.93)*	*0.22*
Singletons	*ICSI, frozen*	*Girls*	*x*	*x*	*1.78 (0.57- 5.51)*	*0.32*
Singletons	*ICSI, frozen*	*Pre-Term*	*x*	*x*	*4.00 (1.29-12.43)*	*0.02*
Singletons	*ICSI, frozen*	*Term*	*x*	*x*	*1.22 (0.46- 3.25)*	*0.69*

eTable 10 (cont.)

Dataset	IVF Procedure	Sub-Group	Autistic Disorder RR (95% CI)#	Autistic Disorder p-value	Mental Retardation RR (95% CI)#	Mental Retardation p-value
Singletons	*ICSI, fresh, surgery*		*0.81 (0.11- 5.75)*	*0.83*	*0.53 (0.07- 3.75)*	*0.52*
Singletons	*ICSI, fresh, surgery*	*>1998##*	*0.88 (0.12- 6.27)*	*0.90*	*0.59 (0.08- 4.20)*	*0.60*
Singletons	*ICSI, fresh, surgery*	*Boys*	*1.09 (0.15- 7.78)*	*0.93*	*0.88 (0.12- 6.22)*	*0.89*
Singletons	*ICSI, fresh, surgery*	*Girls*	*x*	*x*	*x*	*x*
Singletons	*ICSI, fresh, surgery*	*Pre-Term*	*x*	*x*	*x*	*x*
Singletons	*ICSI, fresh, surgery*	*Term*	*0.92 (0.13- 6.54)*	*0.93*	*0.62 (0.09- 4.39)*	*0.63*
Singletons	*ICSI, frozen, surgery*		*Not estimable - Too few cases*			

Note: x indicate cells not estimable since too few cases.
Adj model denotes adjusting for birth year, age and sex and additionally adjusting for paternal psychiatric history, maternal psychiatric history and paternal and maternal age;
>1998 Only include children born between 1st January 1999 and 31st December 2007.
Relative risk (RR) and two-sided 95% confidence intervals (CI) for autistic disorder and for mental retardation for. For All children and for singletons. All RR from adjusted models.

eTable 11 Comparing the risk for autistic disorder and mental retardation multiples vs singletons.

Exposure	Singletons/ Multiples#	Cases	Person Years	Adj Rate## per 100,000	Model###	RR (95% CI)	p-value
Autistic Disorder							
Any IVF	Singletons	54	149,932	24.9	reference group		
	Multiples	49	81,186	46.0	Crude	1.66 (1.13-2.44)	0.010
				46.0	Adj	1.88 (1.28-2.77)	0.001
Spontaneous	Singletons	6,683	33,285,383	13.8	reference group		
	Multiples	173	709,295	15.9	Crude	1.22 (1.05-1.42)	0.010
				15.9	Adj	1.15 (0.99-1.34)	0.068
Relative risk ratio for any IVF vs Spontaneous					Adj	1.63 (1.08-2.47)	0.021

eTable 11 (cont.)

Exposure	Singletons/ Multiples#	Cases	Person Years	Adj Rate## per 100,000	Model###	RR (95% CI)	p-value
Mental Retardation							
Any IVF	Singletons	101	149,677	60.0	reference group		
	Multiples	79	81,033	91.4	Crude	1.36 (1.01-1.83)	0.041
					Adj	1.49 (1.11-2.00)	0.008
Spontaneous	Singletons	15,178	33,240,234	36.4	reference group		
	Multiples	469	707,727	51.1	Crude	1.46 (1.33-1.60)	<0.001
				51.1	Adj	1.42 (1.29-1.56)	<0.001
Relative risk ratio for any IVF vs Spontaneous					Adj	1.05 (0.77-1.43)	0.747

RR: Relative risk
Multiple include twins and any higher order birth
Rate adjusted for sex, age and birth year,
Crude: Model adjusting for birth year, age and sex only, Adj: Model adjusting for birth year, age and sex, and additionally adjusting for paternal psychiatric history, maternal psychiatric history and paternal and maternal age.
Results are presented separately for children following any IVF treatment and spontaneous conception. Multiples include any birth with > 1 live born child. Singletons include birth with one live born child.

eTable 12 **All children**. Distribution of confounders and children characteristics for spontaneuos conceived with and without hormone treatment. Hormone treatment being the only treatment for fertility.

Variable (N: Number of Children)		Spontaneously conceived without hormone treatment	Spontaneously conceived with hormone treatment as the only fertility treatment
Number of Children (% boys)		2,499,096 (51.4)	11,070 (50.7)
Father Psych. History, N (%)		36,255 (1.5)	39 (1.4)
Mother Psych. History, N (%)		46,186 (1.8)	51 (1.8)
Pre-term (before week 37), N (%)		142,402 (5.7)	435 (15.7)
Multiple Birth, N (%)		53,434 (2.14)	606 (21.8)
Birth year, Median (Min-Max)		1994 (1982-07)	2004 (1990-07)
Maternal age distribution, N (%)	<25	531,397 (21.3)	744 (6.7)
	25-29	885,827 (35.4)	3,744 (33.8)
	30-34	730,243 (29.2)	4,311 (38.9)
	>34	351,629 (14.1)	2,271 (20.5)
Paternal age distribution, N (%)	<30	967,423 (38.7)	2,492 (22.5)
	30-39	1,283,183 (51.3)	7,179 (64.9)
	40-49	226,426 (9.1)	1,297 (11.7)
	≥50	22,064 (0.9)	102 (0.9)
Years of involuntary infertility, Median (10th-90th percentiles)		0 (0-0)	2 (0-7)

Hormone treatment being the only treatment for fertility.