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Supplemental Material

Parental Occupational Exposure to Organic Solvents and Testicular Germ Cell Tumors in Their Offspring (NORD-TEST Study)

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Table of Contents

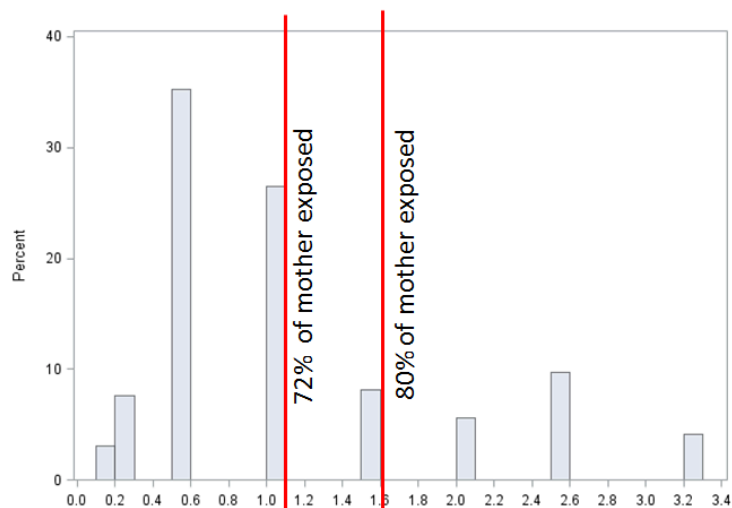
Table S1	The cut-offs of paternal and maternal solvent exposure
Fig. S1	SAS output representing the distribution of methylene chloride level of exposure among mothers exposed, and the distribution of 1,1,1-trichloroethane level of exposure among fathers exposed.
Table S2	Correlation matrix between different solvents for which the parents are occupationally exposed
Table S3	Paternal and maternal exposure to solvents prior to birth and risk to develop testicular cancer unadjusted and adjusted for potential confounders
Table S4	Paternal exposure to solvents prior to the child's birth and testicular germ cell tumour risk in the offspring stratified by country
Table S5	Risk of testicular germ cell tumour stratified by subtypes in relation to maternal and paternal prenatal exposure to solvents.

Table S1: The cut-offs of paternal and maternal solvent exposure

	75th percentiles values for mothers' exposures (in ppm)	90th percentiles values of fathers' exposures (in ppm)
Benzene	0.20	0.30
Toluene	6.00	24.00
Methylene chloride	1.50	1.50
Perchloroethylene	3.00	3.00
Trichloroethylene	1.20	1.20
1,1,1-trichloroethane	0.75	0.80

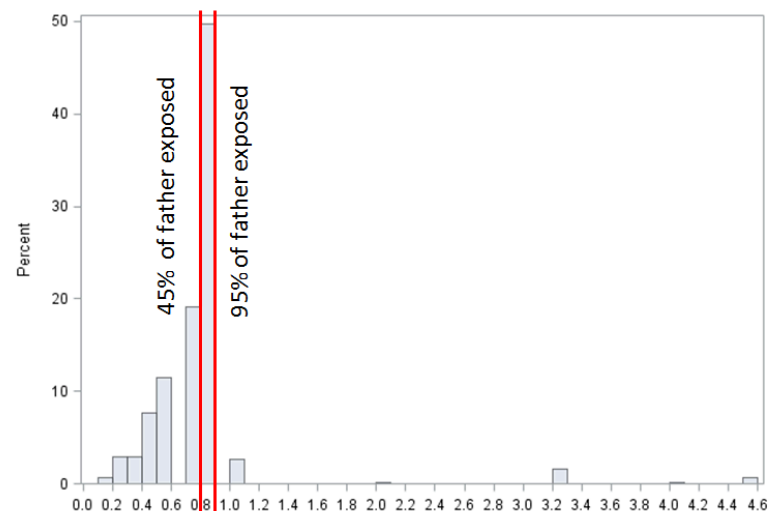
Fig. S1: SAS output representing the distribution of methylene chloride level of exposure among mothers exposed, and the distribution of 1,1,1-trichloroethane level of exposure among fathers exposed.

Distribution of methylene chloride among mother exposed



75th percentiles values for mothers' exposures is not available.
the cut-off was performed at the 72th percentile giving two categories
0.1 to 1, and 1.5 to 3.2

Distribution of 1,1,1-trichloroethane among father exposed



90th percentiles values for fathers' exposures is not available. And the number of father with an exposure level of 0.8 represent half the father's population
the cut-off was performed at the 45th percentile giving two categories
0.1 to 0.75, and 0.8 to 4.5

Table S2: Correlation matrix between different solvents for which the parents are occupationally exposed

	Benzene	Toluene	Methylene chloride	Perchloroethylene	Trichloroethylene	1,1,1-trichloroethane
Maternal exposure						
Benzene	1.00	0.57	0.22	0.12	0.15	0.12
Toluene	0.57	1.00	0.41	0.00	0.08	0.30
Methylene chloride	0.22	0.41	1.00	0.24	0.17	0.53
Perchloroethylene	0.12	0.00	0.24	1.00	0.72	0.55
Trichloroethylene	0.15	0.08	0.17	0.72	1.00	0.73
1,1,1-trichloroethane	0.12	0.30	0.53	0.55	0.73	1.00
Paternal exposure						
Benzene	1.00	0.89	0.81	-0.01	0.03	0.60
Toluene	0.89	1.00	0.85	-0.01	0.02	0.65
Methylene chloride	0.81	0.85	1.00	0.09	0.05	0.73
Perchloroethylene	-0.01	-0.01	0.09	1.00	0.39	0.28
Trichloroethylene	0.03	0.02	0.05	0.39	1.00	0.56
1,1,1-trichloroethane	0.60	0.65	0.73	0.28	0.56	1.00

Binary solvent exposure variables (no, yes) were used to measure the correlation coefficients (Phi).

Table S3: Paternal and maternal exposure to solvents prior to birth and risk to develop testicular cancer unadjusted and adjusted for potential confounders

	Maternal exposure				Paternal exposure			
	Cases	Controls	OR (95% CI) ^a	AOR (95% CI) ^b	Cases	Controls	OR (95% CI) ^a	AOR (95% CI) ^b
	n (%)	n (%)			n (%)	n (%)		
Aromatic hydrocarbon solvents (ARHC)								
Any of ARHC solvents ^c								
	Unexposed	6914 (98.5)	22794 (98.8)		7243 (92.2)	23545 (92.3)		
	Exposed	104 (1.5)	287 (1.2)	1.23 (0.97,1.55)	1.20 (0.94,1.52)	612 (7.8)	1951 (7.7)	1.02 (0.92,1.12) 1.02 (0.93,1.12)
<i>Benzene</i>								
	Unexposed	6932 (98.8)	22840 (99)		7315 (93.1)	23810 (93.4)		
	Exposed	86 (1.2)	241 (1)	1.18 (0.91,1.52)	1.15 (0.89,1.49)	540 (6.9)	1686 (6.6)	1.03 (0.93,1.14) 1.03 (0.93,1.14)
<i>Toluene</i>								
	Unexposed	6963 (99.2)	22921 (99.3)		7274 (92.6)	23644 (92.7)		
	Exposed	55 (0.8)	160 (0.7)	1.22 (0.88,1.68)	1.21 (0.88,1.67)	581 (7.4)	1852 (7.3)	1.02 (0.92,1.12) 1.02 (0.92,1.12)
Chlorinated hydrocarbon solvents (CHC)								
Any of CHC solvents ^d								
	Unexposed	6910 (98.5)	22737 (98.5)		6888 (87.7)	22524 (88.3)		
	Exposed	108 (1.5)	344 (1.5)	1.05 (0.84,1.31)	1.01 (0.80,1.26)	967 (12.3)	2972 (11.7)	1.07 (0.99,1.16) 1.07 (0.99,1.16)
<i>Methylene chloride</i>								
	Unexposed	6964 (99.2)	22939 (99.4)		7322 (93.2)	23848 (93.5)		
	Exposed	54 (0.8)	142 (0.6)	1.34 (0.97,1.85)	1.33 (0.96,1.84)	533 (6.8)	1648 (6.5)	1.05 (0.95,1.16) 1.05 (0.95,1.16)
<i>Perchloroethylene</i>								
	Unexposed	6977 (99.4)	22956 (99.5)		7763 (98.8)	25220 (98.9)		
	Exposed	41 (0.6)	125 (0.5)	1.10 (0.77,1.57)	1.01 (0.68,1.44)	92 (1.2)	276 (1.1)	1.07 (0.84,1.36) 1.07 (0.84,1.37)
<i>Trichloroethylene</i>								
	Unexposed	6958 (99.1)	22866 (99.1)		7396 (94.2)	24073 (94.4)		
	Exposed	60 (0.9)	215 (0.9)	0.92 (0.69,1.24)	0.85 (0.63,1.15)	459 (5.8)	1423 (5.6)	1.09 (0.97,1.21) 1.09 (0.97,1.21)
<i>1,1,1-trichloroethane</i>								
	Unexposed	6937 (98.8)	22815 (98.8)		7017 (89.3)	22937 (90.0)		
	Exposed	81 (1.2)	266 (1.2)	1.03 (0.8,1.32)	1.00 (0.77,1.29)	838 (10.7)	2559 (10.0)	1.08 (1.00,1.18) 1.09 (1.00,1.18)
<i>Any solvent^e</i>								
	Unexposed	6841 (97.5)	22565 (97.8)		6789 (86.4)	22181 (87.0)		
	Exposed	177 (2.5)	516 (2.2)	1.15 (0.96,1.38)	1.12 (0.94,1.35)	1066 (13.6)	3315 (13.0)	1.06 (0.98,1.15) 1.06 (0.99,1.15)

Abbreviations: CI, confidence interval; n, number; OR, odds ratio; AOR, Adjusted odds ratio.

^aORs and its corresponding 95% CI were derived based on logistic regression analysis conditional on year and country of child's birth, the reference category (unexposed) was the parents that were not occupationally exposed to the solvent of interest.

^bModel adjusted for Age of father at birth, age of mother at birth, and family history of testicular cancer (father and/or brother(s)).

^cBenzene and/or toluene.

^dMethylene chloride, perchloroethylene, trichloroethylene, and/or 1,1,1-trichloroethane.

^eAt least one of the following solvents: benzene, toluene, methylene chloride, perchloroethylene, trichloroethylene, 1,1,1-trichloroethane.

Table S4: Paternal exposure to solvents prior to the child's birth and testicular germ cell tumour risk in the offspring stratified by country

	Finland			Norway			Sweden		
	Cases (n)	Controls (n)	OR (95% CI) ^a	Cases (n)	Controls (n)	OR (95% CI) ^a	Cases (n)	Controls (n)	OR (95% CI) ^a
Aromatic hydrocarbon solvents (ARHC)									
Any of ARHC solvents ^b									
Unexposed	950	3739		2770	8011		3523	11795	
Exposed	57	245	0.91 (0.68,1.23)	260	705	1.08 (0.93,1.26)	295	1001	0.99 (0.87,1.14)
<i>Benzene</i>									
Unexposed	968	3,820		2,795	8,090		3,552	11,900	
Exposed	39	164	0.93 (0.65,1.33)	235	626	1.10 (0.94,1.29)	266	896	1.00 (0.87,1.16)
<i>Toluene</i>									
Unexposed	956	3,757		2,783	8,043		3,535	11,844	
Exposed	51	227	0.88 (0.65,1.20)	247	673	1.07 (0.92,1.25)	283	952	1.00 (0.87,1.15)
Chlorinated hydrocarbon solvents (CHC)									
Any of CHC solvents ^c									
Unexposed	912	3672		2712	7848		3264	11004	
Exposed	95	312	1.21 (0.95,1.54)	318	868	1.08 (0.94,1.24)	554	1792	1.05 (0.94,1.16)
<i>Methylene chloride</i>									
Unexposed	958	3,790		2,826	8,173		3,538	11,885	
Exposed	49	194	0.99 (0.72,1.37)	204	543	1.09 (0.92,1.29)	280	911	1.03 (0.90,1.19)
<i>Perchloroethylene</i>									
Unexposed	989	3,956		3,001	8,623		3,773	12,641	
Exposed	18	28	2.42 (1.32,4.41)	29	93	0.90 (0.59,1.37)	45	155	0.95 (0.68,1.34)
<i>Trichloroethylene</i>									
Unexposed	940	3,768		2,924	8,413		3,532	11,892	
Exposed	67	216	1.21 (0.91,1.60)	106	303	1.06 (0.84,1.34)	286	904	1.07 (0.93,1.23)
<i>1,1,1-trichloroethane</i>									
Unexposed	915	3,693		2,773	8,019		3,329	11,225	
Exposed	92	291	1.26 (0.98,1.61)	257	697	1.08 (0.93,1.26)	489	1571	1.05 (0.94,1.18)
<i>Any solvent^d</i>									
Unexposed	898	3602		2661	7698		3230	10881	
Exposed	109	382	1.13 (0.90,1.42)	369	1018	1.08 (0.95,1.23)	588	1915	1.04 (0.94,1.15)

Abbreviations: CI, confidence interval; n, number; OR, odds ratio.

^aORs and its corresponding 95% CI were derived based on logistic regression analysis conditional on year and country of child's birth, the reference category (unexposed) was the parents that were not occupationally exposed to the solvent of interest.

^bBenzene and/or toluene.

^cMethylene chloride, perchloroethylene, trichloroethylene, and/or 1,1,1-trichloroethane.

^dAt least one of the following solvents: benzene, toluene, methylene chloride, perchloroethylene, trichloroethylene, 1,1,1-trichloroethane.

Table S5: Risk of testicular germ cell tumour stratified by subtypes in relation to maternal and paternal prenatal exposure to solvents.

	Non-Seminoma			Seminoma		
	Cases n (%)	Controls n (%)	OR (95% CI) ^a	Cases n (%)	Controls n (%)	OR (95% CI) ^a
Maternal exposure						
Aromatic hydrocarbon solvents (ARHC)						
Any of ARHC solvents ^b						
Unexposed	3854 (98.5)	12732 (98.7)		3060 (98.5)	10062 (98.9)	
Exposed	57 (1.5)	171 (1.3)	1.11 (0.82,1.52)	47 (1.5)	116 (1.1)	1.39 (0.98,1.98)
<i>Benzene</i>						
Unexposed	3,866 (98.8)	12,762 (98.9)		3,066 (98.7)	10,078 (99.0)	
Exposed	45 (1.2)	141 (1.1)	1.03 (0.73,1.46)	41 (1.3)	100 (1.0)	1.39 (0.95,2.04)
<i>Toluene</i>						
Unexposed	3,879 (99.2)	12,804 (99.2)		3,084 (99.3)	10,117 (99.4)	
Exposed	32 (0.8)	99 (0.8)	1.10 (0.73,1.68)	23 (0.7)	61 (0.6)	1.41 (0.86,2.33)
Chlorinated hydrocarbon solvents (CHC)						
Any of CHC solvents ^c						
Unexposed	3851 (98.5)	12701 (98.4)		3059 (98.5)	10036 (98.6)	
Exposed	60 (1.5)	202 (1.6)	1.02 (0.76,1.37)	48 (1.5)	142 (1.4)	1.10 (0.79,1.54)
<i>Methylene chloride</i>						
Unexposed	3,876 (99.1)	12,808 (99.3)		3,088 (99.4)	10,131 (99.5)	
Exposed	35 (0.9)	95 (0.7)	1.34 (0.89,2.00)	19 (0.6)	47 (0.5)	1.35 (0.79,2.33)
<i>Perchloroethylene</i>						
Unexposed	3,886 (99.4)	12,830 (99.4)		3,091 (99.5)	10,126 (99.5)	
Exposed	25 (0.6)	73 (0.6)	1.19 (0.75,1.89)	16 (0.5)	52 (0.5)	0.98 (0.55,1.73)
<i>Trichloroethylene</i>						
Unexposed	3,880 (99.2)	12,785 (99.1)		3,078 (99.1)	10,081 (99.0)	
Exposed	31 (0.8)	118 (0.9)	0.89 (0.59,1.34)	29 (0.9)	97 (1.0)	0.96 (0.63,1.46)
<i>1,1,1, trichloroethane</i>						
Unexposed	3,864 (98.8)	12,742 (98.8)		3,073 (98.9)	10,073 (99.0)	
Exposed	47 (1.2)	161 (1.2)	1.00 (0.72,1.40)	34 (1.1)	105 (1.0)	1.06 (0.72,1.57)
<i>Any solvent</i> ^d						
Unexposed	3811 (97.4)	12604 (97.7)		3030 (97.5)	9961 (97.9)	
Exposed	100 (2.6)	299 (2.3)	1.12 (0.89,1.42)	77 (2.5)	217 (2.1)	1.19 (0.91,1.56)
Paternal exposure						
Aromatic hydrocarbon solvents (ARHC)						
Any of ARHC solvents ^b						
Unexposed	3958 (92.2)	12908 (92.5)		3285 (92.2)	10637 (92.2)	
Exposed	333 (7.8)	1051 (7.5)	1.03 (0.91,1.18)	279 (7.8)	900 (7.8)	1.00 (0.87,1.15)
<i>Benzene</i>						
Unexposed	4,002 (93.3)	13,077 (93.7)		3,313 (93.0)	10,733 (93.0)	
Exposed	289 (6.7)	882 (6.3)	1.06 (0.92,1.22)	251 (7.0)	804 (7.0)	1.00 (0.87,1.17)
<i>Toluene</i>						
Unexposed	3,977 (92.7)	12,953 (92.8)		3,297 (92.5)	10,691 (92.7)	
Exposed	314 (7.3)	1,006 (7.2)	1.01 (0.89,1.16)	267 (7.5)	846 (7.3)	1.02 (0.88,1.18)
Chlorinated hydrocarbon solvents (CHC)						
Any of CHC solvents ^c						
Unexposed	3758 (87.6)	12315 (88.2)		3130 (87.8)	10209 (88.5)	
Exposed	533 (12.4)	1644 (11.8)	1.08 (0.97,1.2)	434 (12.2)	1328 (11.5)	1.06 (0.95,1.20)
<i>Methylene chloride</i>						
Unexposed	3,999 (93.2)	13,024 (93.3)		3,323 (93.2)	10,824 (93.8)	
Exposed	292 (6.8)	935 (6.7)	1.02 (0.89,1.17)	241 (6.8)	713 (6.2)	1.09 (0.94,1.27)

	Non-Seminoma			Seminoma		
	Cases n (%)	Controls n (%)	OR (95% CI) ^a	Cases n (%)	Controls n (%)	OR (95% CI) ^a
<i>Perchloroethylene</i>						
Unexposed	4,239 (98.8)	13,790 (98.8)		3,524 (98.9)	11,430 (99.1)	
Exposed	52 (1.2)	169 (1.2)	1.01 (0.74,1.39)	40 (1.1)	107 (0.9)	1.15 (0.79,1.67)
<i>Trichloroethylene</i>						
Unexposed	4,029 (93.9)	13,175 (94.4)		3,367 (94.5)	10,898 (94.5)	
Exposed	262 (6.1)	784 (5.6)	1.15 (0.99,1.33)	197 (5.5)	639 (5.5)	1.01 (0.86,1.20)
<i>1,1,1-trichloroethane</i>						
Unexposed	3,822 (89.1)	12,541 (89.8)		3,195 (89.6)	10,396 (90.1)	
Exposed	469 (10.9)	1,418 (10.2)	1.11 (0.99,1.24)	369 (10.4)	1,141 (9.9)	1.06 (0.93,1.20)
<i>Any solvent^d</i>						
Unexposed	3704 (86.3)	12153 (87.1)		3085 (86.6)	10028 (86.9)	
Exposed	587 (13.7)	1806 (12.9)	1.09 (0.98,1.20)	479 (13.4)	1509 (13.1)	1.03 (0.92,1.16)

Abbreviations: CI, confidence interval; n, number; OR, odds ratio.

^a ORs and its corresponding 95% CI were derived based on logistic regression analysis conditional on year and country of child's birth, the reference category (unexposed) was the parents that were not occupationally exposed to the solvent of interest.

^b Benzene and/or toluene.

^c Methylene chloride, perchloroethylene, trichloroethylene, and/or 1,1,1-trichloroethane.

^d At least one of the following solvents: benzene, toluene, methylene chloride, perchloroethylene, trichloroethylene, 1,1,1-trichloroethane.