

# Cancer Risk in Children and Young Adults (Offspring) Born after Medically Assisted Reproduction: a Systematic Review and Meta-Analysis.

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**Table S1.** Search Strategy for the Meta-Analysis; up to July 3, 2018.

PubMed	<p>((("Neoplasms/epidemiology"[Mesh] OR "Tumor"[tiab] OR "Tumors"[tiab] OR "Tumour"[tiab] OR "Tumours"[tiab] OR "cancer"[tiab] OR "cancers"[tiab] OR "Neoplasia"[tiab] OR "Neoplastic"[tiab] OR "Neoplasm"[tiab] OR "Neoplasms"[tiab] OR "carcinoma"[tiab] OR "malignancy"[tiab] OR "malignancies"[tiab] OR "malignant"[tiab] OR "Leukemia"[Mesh] OR "Myeloproliferative Disorders"[Mesh] OR "Myelodysplastic-Myeloproliferative Diseases"[Mesh] OR "Lymphoma"[Mesh] OR "Central Nervous System Neoplasms"[Mesh] OR "Glioma"[Mesh] OR "Neuroectodermal Tumors, Primitive"[Mesh] OR "Neuroblastoma"[Mesh] OR "Retinoblastoma"[Mesh] OR "Kidney Neoplasms"[Mesh] OR "Liver Neoplasms"[Mesh] OR "Hepatoblastoma"[Mesh] OR "Bone Neoplasms"[Mesh] OR "Osteosarcoma"[Mesh] OR "Chondrosarcoma"[Mesh] OR "Sarcoma"[Mesh] OR "Adrenocortical Carcinoma"[Mesh] OR "Thyroid Neoplasms"[Mesh] OR "Nasopharyngeal Neoplasms"[Mesh] OR "Melanoma"[Mesh] OR "Neoplasms, Germ Cell and Embryonal"[Mesh] OR "Neoplasms, Gonadal Tissue"[Mesh]) AND ("Risk"[Mesh] OR "Risk Assessment"[Mesh] OR "Risk Factors"[Mesh] OR "Odds Ratio"[Mesh] OR "Incidence"[Mesh] OR "Prevalence"[Mesh] OR "Probability"[Mesh:noexp] OR "Epidemiologic Studies"[Mesh] OR risk[ti] OR odds[ti] OR likelihood[ti] OR incidence[ti] OR prevalence[ti] OR propensit*[ti] OR probabilit*[ti] OR frequen*[ti] OR correlat*[ti] OR connect*[ti] OR epidemiolog*[ti] OR associat*[ti] OR relate*[ti] OR relationship[ti] OR "registries"[MeSH Terms]) NOT ("case report"[Title] OR "case study"[Title] OR "Neoplasms, Experimental"[Mesh])) AND ("Reproductive Techniques, Assisted"[Mesh] OR ART OR IVF OR "in vitro fertilization" OR ICSI OR "intracytoplasmic sperm injection" OR "ovarian stimulation") AND (infant[MeSH] OR child[MeSH] OR adolescent[MeSH] OR pediatric[MeSH] OR paediatric[MeSH] OR children[MeSH] OR childhood) AND English[Filter])</p>
Web of Science	<p>(TS=( Neoplasms/epidemiology OR Tumor OR Tumors OR Tumour OR Tumours OR cancer OR cancers OR Neoplasia OR Neoplastic OR Neoplasm OR Neoplasms OR carcinoma OR malignancy OR malignancies OR malignant OR Leukemia OR Myeloproliferative Disorders OR Myelodysplastic-Myeloproliferative Diseases OR Lymphoma OR Central Nervous System Neoplasms OR Glioma OR Neuroectodermal Tumors, Primitive OR Neuroblastoma OR Retinoblastoma OR Kidney Neoplasms OR Liver Neoplasms OR Hepatoblastoma OR</p>

	Bone Neoplasms OR Osteosarcoma OR Chondrosarcoma OR Sarcoma OR Adrenocortical Carcinoma OR Thyroid Neoplasms OR Nasopharyngeal Neoplasms OR Melanoma OR Neoplasms, Germ Cell and Embryonal OR Neoplasms, Gonadal Tissue) AND (TS=(Risk OR Risk Assessment OR Risk Factors OR Odds Ratio OR Incidence OR Prevalence OR Probability OR Epidemiologic Studies) OR (TI=(risk OR odds OR likelihood OR incidence OR prevalence OR propensit* OR probabilit* OR frequen* OR correlat* OR connect* OR epidemiolog* OR associat* OR relate* OR relationship OR registries)) NOT (TI=(case report OR case study OR Neoplasms, Experimental))) AND (TS=(Assisted Reproductive Techniques OR ART OR IVF OR in vitro fertilization OR ICSI OR intracytoplasmic sperm injection OR ovarian stimulation)) AND (TS=(infant OR child OR adolescent OR pediatric OR paediatric OR children OR childhood))) AND LANGUAGE: (English)
Scopus	TITLE-ABS-KEY (( neoplasms OR tumor OR tumors OR tumour OR tumours OR cancer OR cancers OR neoplasia OR neoplastic OR neoplasm OR neoplasms OR carcinoma OR malignancy OR malignancies OR malignant OR leukemia OR "Myeloproliferative Disorders" OR "Myelodysplastic-Myeloproliferative Diseases" OR lymphoma OR glioma OR neuroblastoma OR retinoblastoma OR hepatoblastoma OR osteosarcoma OR chondrosarcoma OR sarcoma OR melanoma ) AND ( "Assisted Reproductive Techniques" OR art OR ivf OR "in vitro fertilization" OR icsi OR "intracytoplasmic sperm injection" OR "ovarian stimulation" ) AND ( infant OR child OR adolescent OR pediatric OR paediatric OR children OR childhood ) AND ( risk OR "Risk Assessment" OR "Risk Factors" OR "Odds Ratio" OR incidence OR prevalence OR probability OR "Epidemiological Studies" OR epidemiology ) ) AND ( LIMIT-TO ( LANGUAGE , "English " ) )

**Table S2.** Studies characteristics included in the meta-analysis.

Authors, year, location	Study design, population in study	Type of treatment	Outcome	Risk (95% CI)	Adjustment factors	NOS
<b>Michalek et al.<sup>22</sup> (1996), US</b>	Case control 183 cases/372 controls (<15y)	MAR Hormone treatment	Neuroblastoma	OR 10.4 (1.2-90.0)	Unadjusted	5
<b>Roman et al.<sup>23</sup> (1997), UK</b>	Case control 217 cases/368 controls (<30y)	MAR Hormone treatment	HEMATOLOGICAL Leukaemia	OR 2.7 (0.6-11.9)	Unadjusted	6
<b>Doyle et al.<sup>24</sup> (1998), UK</b>	Cohort 2,507 children born after ART (<6y), average follow up 8.6 years	MAR ART	All cancers	SIR 0.57 (0.07-2.06)	Application of cumulative national cancer rates (calendar year and length of follow-up)	7
<b>Schüz et al.<sup>25</sup> (1999), Germany</b>	Case control 2,358 cases/2,588 controls (<16y)	MAR Hormone treatment	HEMATOLOGICAL Leukaemia HEMATOLOGICAL Lymphoma NH NEURAL CNS tumors	OR 1.6 (1.0-2.5) OR 0.9 (0.4-1.9) OR 1.0 (0.6-1.8)	SES SES, age, gender, vicinity to a nuclear installation, year	6

			Neuroblastoma	OR 1.1 (0.5-2.4)	of birth, degree of urbanization			
			RENAL Nefroblastoma	OR 1.3 (0.6-2.7)				
			BONE Bone tumors	OR 0.6 (0.1-2.4)				
			SARCOMAS Soft tissue sarcomas	OR 1.1 (0.5-2.4)				
<b>Olshan et al.<sup>26</sup> (1999), US and Canada</b>	Case control 504 cases/504 controls ( $<19y$ )	MAR Any fertility drug	Neuroblastoma	OR 1.2 (0.7-2.2)	Mother's race, mother's education, household income in the birth year	6		
		MAR Any ovulation-inducing drug		OR 1.5 (0.8-2.7)				
		MAR Clomiphene		OR 1.6 (0.8-3.0)				
<b>Bruinsma et al.<sup>27</sup> (2000), Australia</b>	Cohort 5,249 births ( $<16y$ ) Average follow-up 3y9m	MAR ART	All cancers	SIR 1.39 (0.62-3.09)	Child's year of birth	7		
<b>Klip et al.<sup>28</sup> (2001), Netherlands</b>	Cohort, follow-up 6y 26,428 women, 17,000 children ( $<15y$ ) Average follow-up 6y	MAR Any fertility treatment	All cancers	RR 0.8 (0.3-2.3)	Gender, years of follow up	8		
		MAR ART IVF	All cancers	RR 0.8 (0.2-2.4)				
		MAR Any fertility treatment	HEMATOLOGICAL Leukaemia	SIR 1.3 (0.3-3.7)				
<b>Brinton et al.<sup>29</sup> (2004), Denmark</b>	Cohort 30,364 women, 16,786 children ( $<20y$ ) Average follow-up 10y1m	MAR Any ovulation-inducing drug	All cancers	RR 0.82 (0.4-1.6)	Mother's age at birth	8		
		MAR Clomiphene		RR 0.77 (0.4-1.6)				
		MAR hCG		RR 0.69 (0.3-1.5)				
		MAR hMG		RR 0.59 (0.1-3.1)				
		MAR Any ovulation-inducing drug		HEMATOLOGICAL Hematopoietic			RR 2.30 (0.8-6.6)	
		MAR Clomiphene		RR 1.78 (0.6-4.8)				
		MAR hCG		RR 1.54 (0.5-4.7)				
		MAR Any ovulation-inducing drug		NEURAL CNS tumors			RR 0.26 (0.1-0.9)	
		MAR Clomiphene					RR 0.37 (0.1-1.4)	
		MAR hCG					RR 0.24 (0.1-1.1)	
		MAR Any ovulation-inducing drug		OTHER Other solid cancers			RR 0.67 (0.1-3.3)	
		MAR Clomiphene					RR 0.34 (0.1-2.4)	
		MAR hCG					RR 0.44 (0.0-4.4)	
		MAR Any ovulation-inducing drug		All cancers			RR 0.53 (0.2-1.3)	Mother's age at birth
		MAR Clomiphene					RR 0.50 (0.2-1.3)	

				0-4 years		
		MAR		RR		
		hCG		0.56 (0.2-1.5)		
				0-4 years		
		MAR		RR		
		Any ovulation-inducing drug		1.51 (0.6-4.1)		
				5-20 years		
		MAR		RR		
		Clomiphene		1.22 (0.4-3.3)		
				5-20 years		
		MAR	All cancers	RR		Mother's age at birth
		hCG		0.82 (0.2-3.2)		
				5-20 years		
		MAR		RR		
		hMG		6.24 (1.1-36.0)		
				5-20 years		
<b>McLaughlin et al.<sup>30</sup> (2006), US</b>	Cohort 6,114 live births (<6y) No average follow-up	MAR Any fertility treatment	HEPATIC Hepatoblastoma	RR 9.2 (2.1-31.5)	Child's year of birth, birth weight	8
			HEMATOLOGICAL Leukaemia	OR 1.10 (0.51-2.35)		
		MAR Any fertility drug	HEMATOLOGICAL ALL	OR 0.89 (0.36-2.24)	Mother's age, children's sex, race, education	7
	Case control 158 cases/173 controls (<20y) Down Syndrome		HEMATOLOGICAL AML	OR 1.43 (0.55-3.72)		
		MAR Other treatment, no fertility drug	HEMATOLOGICAL Leukaemia	OR 1.53 (0.44-5.28)		
			HEMATOLOGICAL AML	OR 3.31 (0.81-13.57)		
			NEURAL CNS tumors	OR 1.1 (0.6-2.2)		
			NEURAL Ependymomas	OR 2.6 (0.9-7.8)		
<b>Mallol-Mesnard et al.<sup>32</sup> (2008), France</b>	Case control 209 cases/1,681 controls (<15y)	MAR Any fertility treatment	NEURAL Embryonal tumor	OR 0.6 (0.2-2.1)	Age, gender	7
			NEURAL Astrocytomas	OR 0.8 (0.1-6.3)		
			NEURAL Other gliomas	OR 0.9 (0.2-3.9)		
		MAR Any fertility treatment		OR 0.9 (0.4-2.0)		
		MAR Any ovulation inducing drug		OR 1.0 (0.4-2.9)		
		MAR ART IVF	Neuroblastoma	OR 1.3 (0.4-4.6)	Age, gender	7
<b>Munzer et al.<sup>33</sup> (2008), France</b>	Case control, 191 cases, 1681 controls (0-15y)	MAR Artificial Insemination (AI)		OR 0.8 (0.2-3.9)		
		MAR Any fertility treatment		OR 0.5 (0.1-2.3)		
				<1 year		
		MAR Any fertility treatment		OR 1.2 (0.5-2.7)		
				>=1 year		
<b>Marees et al.<sup>34</sup> (2009), Netherlands</b>	Cohort 40,330 live births (<11y) Average follow-up 6.1y	MAR ART IVF	Retinoblastoma	RR 2.54 (1.02-5.23)	Unadjusted	6
<b>Källén et al.<sup>35</sup> (2010), Sweden</b>	Cohort, 26692 children conceived after IVF (<23y) No average follow-up	MAR ART	All cancers	OR 1.34(1.02-1.76)	Year of birth	8

Puumala et al. <sup>36</sup> (2010), US and Canada	Case control 443 cases/324 controls (<1y)	MAR Any ovulation- inducing drug	HEMATOLOGICAL Leukaemia	OR 1.01 (0.48-2.13)	Year of birth, maternal age, maternal education, maternal race, smoking during pregnancy, household income, gestational age, birth weight	7
			HEMATOLOGICAL ALL	OR 1.42 (0.64-3.15)		
			HEMATOLOGICAL AML	OR 0.44 (0.13-1.44)		
Puumala et al. <sup>37</sup> (2011), US and Canada	Case control 278 cases/422 controls (<15y)	MAR Any ovulation- inducing drug	GERM CELL TUMORS Germ Cell Tumors	OR 0.84 (0.28-2.58)	Children' age, sex, gestational age, maternal age, race, education, household income	6
			GERM CELL TUMORS Gonadal Tumors	OR 1.48 (0.48-4.63)		
		MAR Any ovulation- inducing drug	GERM CELL TUMORS Germ Cell Tumors	OR 0.99 (0.25-3.94) Female only		
			GERM CELL TUMORS Gonadal Tumors	OR 1.79 (0.42-7.66) Female only		
Petridou et al. <sup>38</sup> (2012), Greece and Sweden	a. Case control Sweden: 591 cases/5,910 controls (0-12 years)	MAR ART IVF	HEMATOLOGICAL Leukaemia	OR 1.59 (0.86-2.95)	Birth weight, birth order, maternal age at birth, maternal education, maternal smoking during pregnancy, multiple birth	8
			HEMATOLOGICAL ALL	OR 1.90 (0.96-3.78)		
			HEMATOLOGICAL non-ALL	OR 0.95 (0.21-4.25)		
	b. Case control Greece: 1,091 cases/1,091 controls (0-14 years)	MAR ART IVF	HEMATOLOGICAL Leukaemia	OR 1.66 (0.82-3.37)	Birth weight, birth order, maternal age at birth, maternal education, maternal smoking during pregnancy, multiple birth	5
			HEMATOLOGICAL ALL	OR 1.62 (0.75-3.47)		
			HEMATOLOGICAL non-ALL	OR 2.92 (0.30-28.50)		
Foix-L'Hélias et al. <sup>39</sup> (2012), France	Case control 244 cases/28,170 controls (<6y)	MAR ART IVF	Retinoblastoma	OR 1.37 (0.64-2.95)	Maternal age at birth, smoking	6
Puumala et al. <sup>40</sup> (2012), USA	Case control 383 cases/387 controls (<6y)	MAR Any fertility drug	HEPATIC Hepatoblastoma	OR 1.12 (0.61-2.04)	Birth weight, year of birth, gender, maternal age, maternal education, maternal race, plurality, gestational age	6
				MAR ART		
Rudant et al. <sup>41</sup> (2013), France	Case control 764 cases/1,681 controls (<15y)	MAR Any fertility treatment	HEMATOLOGICAL Leukaemia	OR 1.8 (1.3-2.6)	Age, gender, parental professional category, maternal age at childbirth	7
		MAR ART IVF		OR 1.0 (0.4-2.2)		
		MAR		OR 1.2 (0.4-3.6)		

		Artificial Insemination (AI)		
		MAR		OR
		Any ovulation-inducing drug		2.5 (1.6-4.0)
		MAR		OR
		Any fertility treatment		1.9 (1.3-2.8)
		MAR	HEMATOLOGICAL	OR
		ART		1.0 (0.4-2.3)
		IVF		
		MAR	ALL	OR
		Artificial Insemination (AI)		1.3 (0.5-3.9)
		MAR		OR
		Any ovulation-inducing drug		2.6 (1.6-4.3)
		MAR	HEMATOLOGICAL	OR
		Any fertility treatment		1.4 (0.6-3.3)
		MAR		OR
		Any ovulation-inducing drug	AML	2.3 (0.9-6.1)
		MAR		SIR
		All cancers		0.98 (0.81-1.19)
		MAR	HEMATOLOGICAL	SIR
		Leukaemia		0.91 (0.63-1.27)
		MAR	NEURAL	SIR
		CNS tumors		0.85 (0.54-1.29)
		MAR	NEURAL	SIR
		Neuroblastoma		0.88 (0.40-1.68)
		MAR	NEURAL	SIR
		Retinoblastoma		0.59 (0.12-1.73)
		MAR	RENAL	SIR
		Renal tumors		0.94 (0.41-1.86)
		MAR	HEPATIC	SIR
		Hepatic tumors		3.27 (1.20-7.12)
		MAR	SARCOMAS	SIR
		Bone tumors and extraosseus sarcomas		2.34 (1.43-3.61)
		MAR	BONE	SIR
		Osteosarcoma		2.95 (0.61-8.62)
		MAR	BONE	SIR
		Ewing's sarcoma		2.47 (0.67-6.32)
		MAR	SARCOMAS	SIR
		Rhabdomyosarcoma		2.62 (1.26-4.82)
		MAR	SARCOMAS	SIR
		Other sarcomas		1.42 (0.29-4.15)
		MAR	GERM CELL TUMORS	SIR
		Germ-cell tumors		0.56 (0.07-2.03)
		MAR	HEPATIC	SIR
		Hepatoblastoma		5.18 (1.68-12.08)
		MAR	SARCOMAS	SIR
		Rhabdomyosarcoma		2.01 (0.65-4.70)
		MAR	HEPATIC	SIR
		Hepatoblastoma		1.56 (0.04-8.71)
		MAR	SARCOMAS	SIR
		Rhabdomyosarcoma		3.94 (1.28-9.19)
		MAR	HEPATIC	SIR
		Hepatoblastoma		0 (0-85.57)
		MAR	SARCOMAS	SIR
		Rhabdomyosarcoma		0 (0-46.67)

Williams et al.<sup>42</sup> Cohort  
 (2013), UK 106,013 children conceived  
 by ART (<15y)  
 Average follow-up 6.6y

Unadjusted 8

<p><b>Hargreave et al.<sup>43</sup> (2013), Denmark</b></p>	<p>Cohort 2,830,054 children (&lt;19y) 125,844 children conceived by women with infertility problems Average follow-up 20.0y</p>	<p>MAR Any fertility treatment</p>	<p>All cancers</p>	<p>HR 1.18 (1.05-1.32) 0-19 years</p>	<p>Maternal age at birth, birth order</p>			
			<p>HEMATOLOGICAL Leukaemia</p>	<p>HR 1.30 (1.06-1.60) 0-19 years</p>				
			<p>HEMATOLOGICAL Lymphomas</p>	<p>HR 1.04 (0.72-1.51) 0-19 years</p>				
			<p>NEURAL CNS tumors</p>	<p>HR 1.19 (0.95-1.49) 0-19 years</p>				
			<p>NEURAL SNS (sympathetic nervous system) tumors</p>	<p>HR 1.34 (0.85-2.10) 0-19 years</p>				
			<p>Retinoblastoma</p>	<p>HR 0.97 (0.45-2.10) 0-19 years</p>				
			<p>RENAL Renal tumors</p>	<p>HR 0.96 (0.53-1.73) 0-19 years</p>				
			<p>HEPATIC Hepatic tumors</p>	<p>HR 1.79 (0.76-4.25) 0-19 years</p>				
			<p>BONE Bone tumors</p>	<p>HR 1.07 (0.59-1.91) 0-19 years</p>				
			<p>SARCOMAS Soft tissue sarcomas</p>	<p>HR 1.08 (0.66-1.78) 0-19 years</p>				
			<p>GERM CELL TUMORS Gonadal Tumors</p>	<p>HR 1.20 (0.71-2.02) 0-19 years</p>				
			<p>OTHER Malignant epithelial tumors</p>	<p>HR 0.88 (0.52-1.48) 0-19 years</p>				
			<p>OTHER Unspecified cancers</p>	<p>HR 1.53 (0.69-3.40) 0-19 years</p>				
			<p>913,379 young adults (20- 35y) 29,479 individuals conceived by women with infertility problems Average follow-up 8.4y</p>	<p>MAR Any fertility treatment</p>		<p>All cancers</p>	<p>HR 1.22 (1.04-1.43) 20-35 years</p>	<p>Maternal age at birth, birth order</p>
						<p>OTHER Buccal cavity and pharynx</p>	<p>HR 1.82 (0.44-7.58) 20-35 years</p>	
<p>OTHER Digestive organs</p>	<p>HR 0.32 (0.04-2.27) 20-35 years</p>							
<p>BONE Bones, joints and articular cartilage</p>	<p>HR 1.35 (0.42-4.31) 20-35 years</p>							
<p>OTHER Skin</p>	<p>HR 1.22 (0.94-1.60) 20-35 years</p>							
<p>SARCOMAS Mesothelium and connective tissue</p>	<p>HR 1.71 (0.69-4.21) 20-35 years</p>							
<p>OTHER Breast</p>	<p>HR 1.18 (0.46-2.87) 20-35 years</p>							
<p>OTHER Female genital organs incl. Skin</p>	<p>HR 0.78 (0.39-1.57) 20-35 years</p>							

		OTHER Male genital organs incl. Skin	HR 1.21 (0.82-1.80) 20-35 years	
		OTHER Urinary tract	HR 2.12 (0.66-6.82) 20-35 years	
		NEURAL Eye, brain and other parts of CNS	HR 1.10 (0.67-1.81) 20-35 years	
		OTHER Endocrine glands	HR 2.67 (1.35-5.29) 20-35 years	
		HEMATOLOGICAL Lymphatic and hematopoietic tissue	HR 1.34 (0.84-2.15) 20-35 years	
		OTHER Unspecified cancers	HR 1.09 (0.15-8.03) 20-35 years	
		MAR Any fertility treatment	OR 0.8 (0.5-0.11)	
		MAR ART IVF	OR 0.6 (0.3-1.5)	
		MAR Artificial Insemination (AI)	OR 0.5 (0.2-1.4)	
		MAR Clomiphene	OR 0.6 (0.3-1.3)	
		MAR Gonadotropins	OR 0.7 (0.4-1.3)	
		MAR Dopamine agonists	OR 0.9 (0.2-4.8)	
		MAR Other treatments	OR 0.7 (0.2-2.9)	
		MAR Treatment with unknown drug	OR 0.6 (0.2-1.4)	
		MAR Any fertility treatment	OR 0.7 (0.5-0.11)	
		MAR ART IVF	OR 0.6 (0.2-1.6)	
		MAR Artificial Insemination (AI)	OR 0.4 (0.1-1.4)	
		MAR Clomiphene	OR 0.5 (0.2-1.2)	
		MAR Gonadotropins	OR 0.6 (0.3-1.2)	
		MAR Dopamine agonists	OR 0.5 (0.1-4.6)	
		MAR Other treatments	OR 0.8 (0.2-3.2)	
		MAR Treatment with unknown drug	OR 0.6 (0.2-1.5)	
		MAR Any fertility treatment	OR 1.1 (0.5-2.4)	
Ajrouche et al. <sup>44</sup> (2014), France	Case control 747 cases/1,421 controls (<15y)	HEMATOLOGICAL Leukaemia		Age, gender, last professional category, maternal age at child's birth
		HEMATOLOGICAL ALL		
		HEMATOLOGICAL AML		



			MAR Artificial Insemination (AI)	OR 0.9 (0.1-6.7)		
			MAR Clomiphene	OR 1.1 (0.2-4.6)		
			MAR Gonadotropins	OR 1.2 (0.4-3.6)		
			MAR Dopamine agonists	OR 3.1 (0.3-28.5)		
			MAR Treatment with unknown drug	OR 0.5 (0.1-3.7)		
<b>Wennerholm et al.<sup>45</sup> (2014), Denmark, Sweden, Norway and Finland</b>	Cohort, 92'809 children conceived by ART, 373'196 non-ART, no years or follow up	MAR ART	All cancers	HR 1.15 (0.97-1.35)	Country, maternal age, parity, gestational age, gender	8
			NEURAL CNS tumors	HR 1.49 (1.05-2.13)		
			All cancers	RR 0.95 (0.73-1.24)		
			HEMATOLOGICAL ALL	RR 1.20 (0.72-2.02)	Sex, plurality, gestational age, birth weight z- score, mother's race, age, years of education	7
<b>Spector et al.<sup>46</sup> (2014), US</b>	Cohort 612,361 children (66,782 conceived by ART) (<9y) Average follow-up 4.2y	MAR ART	NEURAL Astrocytomas	RR 0.93 (0.40-2.16)		
			Neuroblastoma	RR 1.07 (0.53-2.16)		
			RENAL Wilms tumor	RR 1.48 (0.61-3.60)		
			Retinoblastoma	RR 1.32 (0.54-3.21)		
			All cancers	HR 1.08 (0.91-1.27)		
			HEMATOLOGICAL Leukaemia	HR 1.06 (0.80-1.41)		
			HEMATOLOGICAL Lymphoma	HR 0.91 (0.45-1.81)		
			NEURAL CNS tumors	HR 1.44 (1.01-2.05)		
			Neuroblastoma	HR 0.87 (0.42-1.80)		
			Retinoblastoma	HR 0.48 (0.17-1.36)	Country, maternal age, parity, gestational age, gender, birth defects, chromosomal aberrations	8
<b>Sundh et al.<sup>47</sup> (2014), Sweden, Denmark, Finland and Norway</b>	Cohort 450,215 children (<15y) (91,796 conceived by ART) Average follow-up 9.5y	MAR ART	RENAL Renal tumors	HR 0.51 (0.22-1.19)		
			HEPATIC Hepatic tumors	HR 2.61 (0.74-9.26)		
			BONE Bone tumors	HR 0.35 (0.11-1.15)		
			SARCOMAS Soft tissue sarcomas	HR 1.22 (0.58-2.59)		
			GERM CELL TUMORS Germ-cell tumors	HR 1.19 (0.44-3.25)		
			OTHER Malignant epithelial tumors	HR 2.03 (1.06-3.89)		
			OTHER Other cancers	HR 1.26 (0.69-2.31)		
<b>Spaan et al.<sup>48</sup> (2015), Netherlands</b>	Cohort 44,000 children (26,000 conceived by ART) (<30y) Average follow-up	MAR ART	All cancers	HR 1.45 (0.69-3.07)	Maternal age, birth weight	8
<b>Hargreave et al.<sup>49</sup> (2015), Denmark</b>	Cohort	MAR Any fertility drug	All cancers	HR 0.94 (0.60-1.46) 0-19 years	Unadjusted	8

	90,888 children (<30y) conceived by women with infertility evaluation Long follow-up, at maximum 42y No average follow-up	MAR Clomiphene	HR 0.77 (0.50-1.19) 0-19 years	Unadjusted							
		MAR Gonadotropins	HR 1.29 (0.71-2.33) 0-19 years								
		MAR GnRH	HR 0.87 (0.49-1.56) 0-19 years								
		MAR hCG	HR 0.92 (0.60-1.40) 0-19 years								
		MAR Progesterone	HR 1.46 (0.75-2.85) 0-19 years								
		MAR Other or unspecified drugs	HR 0.78 (0.48-1.27) 0-19 years								
		MAR Any fertility drug	HR 0.89 (0.36-2.24) 20-29 years								
		MAR Clomiphene	HR 1.43 (0.53-3.88) 20-29 years								
		MAR Gonadotropins	HR 1.60 (0.24-10.82) 20-29 years								
		MAR hCG	HR 1.31 (0.52-3.33) 20-29 years								
MAR Other or unspecified drugs	HR 0.42 (0.06-3.15) 20-29 years										
<b>Lerner-Geva et al.<sup>51</sup> (2016), Israel</b>	Cohort 220,805 children (<15y) (9,042 conceived by ART) Average follow-up 10.6y (ART group) and 9.3y (non-ART group)	MAR ART	All cancers	RR 1.42 (0.85-2.37)	Maternal age, maternal education, ethnicity, plurality, gender, birth weight, congenital malformations	8					
			HEMATOLOGICAL Leukaemia	RR 0.69 (0.26-1.66)							
			HEMATOLOGICAL Lymphomas	RR 2.20 (0.78-6.19)							
			NEURAL CNS tumors	RR 0.45 (0.10-1.99)							
			Neuroblastoma	RR 1.62 (0.72-3.64)							
			Retinoblastoma	RR 7.80 (2.87-21.20)							
			RENAL Renal tumors	RR 4.44 (1.78-11.10)							
			BONE Bone tumors	RR 3.11 (1.05-9.18)							
			SARCOMAS Soft tissue sarcomas	RR 0.94 (0.03-30.90)							
			<b>Reigstad et al.<sup>50</sup> (2016), Norway</b>	Cohort 1,628,658 children (25,782 conceived by ART) (<27y) Average follow-up 6.9y (ART group) and 13.7y (non-ART group)			MAR ART	All cancers	HR 1.21 (0.90-1.63)	Birth year, birth order, maternal age at delivery, place of birth, gender, birthweight, gestational age	8
								HEMATOLOGICAL Leukaemia	HR 1.67 (1.02-2.73)		
								HEMATOLOGICAL ALL	HR 1.16 (0.60-2.27)		
HEMATOLOGICAL AML	HR 2.63 (1.04-6.64)										
HEMATOLOGICAL Other leukaemia	HR 5.13 (1.50-7.60)										

			HEMATOLOGICAL	HR	
			Lymphomas	1.79 (0.66-4.90)	
			HEMATOLOGICAL	HR	
			Hodgkins	3.63 (1.12-11.72)	
			HEMATOLOGICAL	HR	
			Non-Hodgkins	0.99 (0.14-7.28)	
			NEURAL	HR	
			CNS tumors	0.92 (0.47-1.79)	
			NEURAL	HR	
			Astrocytomas	1.45 (0.63-3.29)	
			NEURAL	HR	
			Embryonal CNS tumors	1.70 (0.62-4.69)	
			NEURAL	HR	
			Other gliomas	1.19 (0.16-8.80)	
			NEURAL	HR	
			Other CNS tumors	0.50 (0.07-3.59)	
			Neuroblastoma	1.79 (0.64-4.99)	
			RENAL	HR	
			Renal tumors	1.40 (0.44-4.48)	
			HEPATIC	HR	
			Hepatic tumors	1.76 (0.41-7.46)	
			SARCOMAS	HR	
			Soft tissue sarcomas	1.33 (0.54-3.30)	
			OTHER	HR	
			Other cancers	1.21 (0.38-3.82)	
Wainstock et al. <sup>52</sup> (2017), Israel	Cohort, 242,187 children, 2603 conceived by IVF and 1172 by Ovarian Induction (<18y) Average follow-up 10.5y	MAR ART IVF		HR 1.89 (0.89-4.02)	Maternal age, birthweight, preterm birth, pregnancy- related hypertensive disorders, pregestational and gestational diabetes mellitus
		MAR Any ovulation inducing drug	All cancers	HR 2.03 (0.96-4.30)	
		MAR Any fertility treatment		HR 1.96 (1.14-3.36)	
Williams et al. <sup>53</sup> (2018), UK	Cohort 12,186 children conceived by ART (<15y) Average follow-up 7.9y	MAR ART IVF	All cancers	SIR 0.89 (0.44-1.58)	Unadjusted
		MAR ART ICSI and others micromanipulation	All cancers	SIR 0 (0-1.76)	
		MAR ART Not recorded	All cancers	SIR 3.26 (0.08-18.2)	
			All cancers	SIR 0.83 (0.43-1.45)	
			HEMATOLOGICAL	SIR	
			Leukaemia	0.61 (0.13-1.78)	
			NEURAL	SIR	
			CNS tumors	1.17 (0.32-2.99)	
			Neuroblastoma	0 (0-2.03)	
		MAR ART	Retinoblastoma	SIR 3.29 (0.40-11.87)	
			RENAL	SIR	
			Renal tumors	0.94 (0.02-5.25)	
			HEPATIC	SIR	
	Hepatic tumors	9.12 (1.11-32.95)			
	HEPATIC	SIR			
	Hepatoblastoma	SIR			

8

7

	10.28 (1.25-37.14)
SARCOMAS	SIR
Bone tumors and extraosseus sarcomas	0 (0-2.50)
BONE	SIR
Osteosarcoma	0 (0-18.38)
BONE	SIR
Ewing's sarcoma	0 (0-12.41)
SARCOMAS	SIR
Rhabdomyosarcoma	0 (0-5.91)
SARCOMAS	SIR
Other sarcomas	0 (0-10.45)
GERM CELL TUMORS	SIR
Germ cell tumors	0 (0-6.59)

**Table S3.** Description of MAR Exposure and Types of Cancer in the Selected Studies.

Exposure	N° studies	References
<b>MAR</b>		
Any fertility treatment	8	28,30,32,33,41,43,44,52
Any fertility drug	4	26,31,40,49
Any ovulation inducing drug	7	26,29,33,36,37,41,52
Clomiphene	4	26,29,44,49
Dopamine agonist	1	44
GnRH	1	49
Gonatotropin	2	44,49
Hormone treatment	3	22,23,25
Progesterone	1	49
Treatment with unknow drug	1	44
hCG	2	29,49
hMG	1	29
Any ovulation inducing drug or Insemination	1	39
Artificial insemination	3	33,41,44
Other treatment	2	44,49
Other treatment (no fertility drug)	1	31
<b>ART</b>		
ART	13	24,27,35,40,42,45-48,50,51,53
ICSI or other micromanipulation	1	42
Not recorded	1	53
IVF	11	28,33,34,38a,38b,39,41,42,44,52,53
<b>Outcome</b>		
<b>All cancers site</b>	<b>N° studies</b>	<b>References</b>
<b>All cancers</b>	32	22-53 (38a,38b)
<b>Hematological tumors</b>	16	24, 27-29, 35, 42, 43, 45-53
Hematopoietic	1	29
Lymphatic and hematopoietic tissue	1	43
<b>Leukemias (ICCC-3 I)</b>		
Leukaemia	15	23,25,28,31,36,38a,38b,41-44,47,50,51,53
Other leukaemia	1	51
non-ALL	2	38a,38b
ALL	8	31,36,38a,38b,41,44,46,51





Case-control	1	2	---						
Cohort	6	9	3.59 (2.31-5.57)	<0.0001	9.11	12.19	0.333	0.434	0.404
<b>Age</b>									
<6 years	2	3	2.10 (0.74-5.95)	0.161	7.78	74.31	0.020	0.236	0.117
<15 years	5	9	3.20 (1.76-5.80)	0.0001	19.27	58.49	0.013	0.050	0.211
All others	2	2	1.78 (0.85-3.74)	0.126	0.00	0.00	0.984	---	---
<b>Bone Tumors (ICCC-3 VIII)</b>	5	8	1.50 (0.92-2.46)	0.105	15.20	53.94	0.034	0.508	0.216
<b>Study design</b>									
Case-control	1	1	---						
Cohort	4	7	1.61 (0.97-2.68)	0.066	13.62	55.94	0.034	0.742	0.293
<b>Age</b>									
<6 years	0	0	---						
<15 years	4	6	1.63 (0.84-3.17)	0.146	12.20	59.00	0.032	0.400	0.091
All others	1	2	---						
<b>Sarcomas (ICCC-3 IX)</b>	6	10	1.54 (1.18-2.02)	0.002	9.46	4.90	0.396	0.523	0.325
<b>Study design</b>									
Case-control	1	1	---						
Cohort	5	9	1.61 (1.20-2.17)	0.001	8.71	8.13	0.367	0.524	0.532
<b>Age</b>									
<6 years	0	0	---						
<15 years	4	7	1.81 (1.26-2.61)	0.001	6.48	7.47	0.371	0.847	0.881
All others	2	3	1.22 (0.83-1.81)	0.312	0.80	0.00	0.670	0.284	0.602
<b>Germ Cell Tumors (ICCC-3 X)</b>	4	5	1.13 (0.76-1.67)	0.541	1.22	0.00	0.875	0.329	0.327
<b>Study design</b>									
Case-control	1	2	---						
Cohort	3	3	1.14 (0.73-1.77)	0.577	0.73	0.00	0.695	0.377	0.117
<b>Age</b>									
<6 years	0	0	---						
<15 years	3	4	1.05 (0.58-1.87)	0.879	1.10	0.00	0.776	0.289	0.497
All others	1	1	---						
<b>ART</b>									
<b>Neural Tumors (ICCC-3 III)</b>	7	11	1.21 (1.01-1.46)	0.040	8.88	0.00	0.543	0.188	0.312
<b>Study design</b>									
Case-control	0	0	---						
Cohort	7	11	1.21 (1.01-1.46)	0.040	8.88	0.00	0.543	0.188	0.312
<b>Age</b>									
<6 years	0	0	---						
<15 years	5	5	1.07 (0.78-1.47)	0.666	5.10	21.53	0.277	0.331	0.624
All others	2	6	1.35 (1.02-1.77)	0.034	2.78	0.00	0.733	0.336	0.573
<b>Neuroblastoma (ICCC-3 IV)</b>	6	6	1.13 (0.81-1.58)	0.477	2.57	0.00	0.766	0.193	0.573
<b>Study design</b>									
Case-control	1	1	---						





<6 years	0	0							
<15 years	3	6	2.05 (1.39-3.02)	0.0003	4.54	0.00	0.475	0.723	0.573
All others	1	1	---						