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High birth weight and other risk factors for Wilms tumour: results of a population-based case-control study

Received: 31 July 2000 and in revised form 9 October 2000 and 14 November 2000 / Accepted: 5 September 2000

Abstract Wilms tumour, or nephroblastoma, is one of the childhood cancers included in two recent population-based case-control studies in West Germany. Altogether, 177 children under the age of 10 years with Wilms tumour diagnosed between 1988 and 1994 and 2006 control children sampled from population registration files participated. Information on potential risk factors was obtained from the parents using a questionnaire and by subsequent telephone interview. We found an association with a high birth weight >4000 g (odds ratio 1.58; 95% confidence interval 1.01–2.48), which was somewhat stronger for children aged 2 years or older. Findings for young maternal age at birth and certain parental occupationally related exposures were not reported by previous studies and thus may be chance findings. As opposed to previous studies, we failed to confirm associations with high parental age at birth, maternal coffee and tea consumption during pregnancy, and exposure to pesticides.

Conclusion Based on this large population-based case-control study, high birth weight may play a role in the aetiology of Wilms tumour, but many risk factors previously suggested are of less importance.

Key words Case-control study · Child · Nephroblastoma · Risk factors · Wilms tumour

Abbreviations *CI* confidence interval · *GCCR* German Childhood Cancer Registry · *LSS* case-control study in Lower Saxony · *NWS* nationwide case-control study · *OR* odds ratio

Introduction

Wilms tumour, or nephroblastoma, is an embryonal malignancy which arises from remnants of immature kidney [1]. In Germany, Wilms tumour accounts for 6.6% of all cancers diagnosed in children [13]. The German Childhood Cancer Registry (GCCR) reports an annual incidence rate of 8.9 per million in children, the highest rates (24.4 per million) are experienced by infants.

The rarity of Wilms tumour has made epidemiological studies difficult to carry out. Therefore, little is known about risk factors for Wilms tumour. The frequency of Wilms tumour varies with ethnicity; the incidence is two to three times higher in blacks than in Asians and that in whites is between both extremes [3, 37, 38]. A subset of cases of Wilms tumour is known to be of genetic aetiology. Wilms tumour has been shown to be associated with congenital anomalies, the most common being anomalies of the genitourinary tract, hemihypertrophy and sporadic aniridia, and with

specific uncommon syndromes including Denys-Drash, Beckwith-Wiedemann, Perlman and Wilms tumour with congenital aniridia, genitourinary abnormalities and mental retardation syndromes [41]. Sharpe and Franco [29] and Little [18] have reviewed the results of epidemiological studies carried out before 1995 and 1997, respectively. Since then, seven papers on this topic have been published [9, 14, 32, 33, 34, 35, 40]. High birth weight, exposure to pesticides, and paternal occupational exposure to pesticides or metals are so far the only factors associated with Wilms tumour with some degree of consistency. Factors for which the evidence is inconsistent include parental age at birth, risk of cancer in relatives of Wilms tumour patients, maternal exposure during pregnancy to cigarettes, tea or coffee, oral contraceptives or anaesthesia, birth order, previous fetal loss, pregnancy hypertension, and paternal occupational exposure to hydrocarbons or lead.

Subjects and methods

From 1993 to 1997, the GCCR conducted two comprehensive case-control studies on risk factors for childhood cancer [11, 12, 27]. The selected diagnostic groups were leukaemia, lymphoma, brain tumour, neuroblastoma, soft tissue sarcoma, bone tumour, and Wilms tumour. The first case-control study was restricted to the state of Lower Saxony (LSS), an area with about 7.7 million inhabitants in the Northwestern part of Germany [11]. Cases of Wilms tumour from the GCCR were eligible, if they were diagnosed between July 1988 and June 1993 and if at date of diagnosis they were less than 15 years old and lived within the boundaries of Lower Saxony. The second study was also based on the GCCR [12]. Cases of Wilms tumour were included if they were diagnosed between October 1992 and September 1994 and if at date of diagnosis they were less than 15 years old and lived in the former Federal Republic of Germany (nationwide study; NWS). Patients, who lived in Lower Saxony and were diagnosed between October 1992 and June 1993, were eligible for both studies; therefore they were used twice in study-specific analyses but only once in the pooled analyses.

For both studies, control children were selected from complete files of local offices for registration of residents. We requested a list of four potential controls and drew one family at random. If the selected family did not want to participate, we contacted another family from the remaining names on the list. This procedure of control selection was repeated until a selected family agreed to participate or until no more potential controls remained. While the sampling procedure was identical for both studies, it differed regarding the matching criteria. In the LSS, we sampled two controls for each child with leukaemia. The first control was sampled from the community (smallest administrative unit in Germany) where the diseased child lived, the second control was sampled from a randomly selected community in Lower Saxony using a population-weighted sampling procedure. Further matching criteria were gender and date of birth within 1 year. No controls were drawn for the group of cases with a solid tumour (including Wilms tumour). In the NWS, for each case, one control matched for gender, date of birth within 1 year, and community was selected. Consequently, 1:1 matched controls for cases of Wilms tumour were available only for the NWS.

We collected information on potential risk factors both by self-administered questionnaires and subsequent telephone interviews. The questions were based on a structured questionnaire developed by the United States Children's Cancer Group [5] but modified to assess country-specific issues. In addition, we performed telephone interviews for validation and completion of the questionnaire. The interviews were done by trained personnel. Questionnaire, interview procedure and interviewers were the same for both studies. If

possible, both parents were interviewed. We checked for discrepancies between the questionnaire and the telephone interview to ensure a high data quality. Therefore, some parents were asked a few questions twice. If the participating family had no telephone, we had to rely solely on the information from the questionnaire. For each control, the date of diagnosis of the corresponding case was defined as a reference date (hereafter the date of diagnosis will also be called reference date). Assessment of exposures was done only for exposures that occurred before the reference date. Questions covered sociodemographic factors, pregnancy history, birth characteristics, parental smoking habits, parental occupational history, residential history, and potential exposure to ionising radiation and pesticides.

Two models were used for calculating the maximum likelihood estimate of the odds ratio (OR) and respective 95% confidence intervals (CI). ORs for the pooled analyses of the two studies derived from a conditional logistic regression model using frequency matching (m:n matching, cases:controls) were of primary interest [4, 20]. This model involved a posterior stratification for gender, age (age groups of 1 year), and year of birth with additional adjustments for degree of urbanisation (rural, mixed, urban) and socioeconomic status (high, other). Socioeconomic status was estimated by monthly family net income and parental educational level. In this first model, all controls were included even if they were selected as individual controls for other diagnoses or if the individual match partner had not participated. In addition to the pooled analyses, we carried out analysis separately for both study components and analysis based on the original 1:1 matching status. Since differences among risk estimates derived from the different analytical approaches could all be explained by random variability, we chose to present the results from the pooled analyses because from these we obtained the most stable risk estimates. The regression models were calculated using Proc Phreg, SAS Software Release 6.12 [26].

Only four children with Wilms tumour were older than 9 years of age at date of diagnosis, hence, there were too few cases to consider the higher age groups in our age-stratified analysis. Consequently, only children aged 9 years or less at date of diagnosis were included in the calculation of the risk estimates.

Results

Of 235 eligible families of Wilms tumour cases, 13 (5.5%) were not contacted. The physician responsible for treating the child recommended that the parents should not be interviewed because they were too severely affected by their child's disease. Response rates were 85.1% among cases (189 of 222) and 71.0% among controls (2,537 of 3,575), respectively. More than 66% of all non-participants were refusals. Other reasons for non-participation were loss to follow-up and insufficient knowledge of the German language. Eight case families as well as 79 control families responded but were not included in the analyses because of violations of the study inclusion criteria. After excluding children aged 10 years or older, 177 cases and 2,006 controls were available for analysis.

Demographic characteristics of cases and controls are shown in Table 1. The distributions of gender and age in the Wilms tumour group differed from those in the control group because the majority of controls was selected as match partners for children with leukaemia or other solid tumours. These differences were considered when applying logistic regression models that were stratified by gender and age groups of 1 year. More parents of controls had a high socioeconomic status

Table 1 Distributions of age, gender, degree of urbanisation, and socioeconomic status

	Wilms tumour cases		Controls	
	N	Percentage	N	Percentage
Age (years)				
0	39	22.0	229	11.4
1–4	101	57.1	1030	51.3
5–9 ^a	37	20.9	747	37.2
Gender				
Male	83	46.9	1118	55.7
Female	94	53.1	888	44.3
Socioeconomic status				
Other	132	74.6	1419	70.7
High	45	25.4	587	29.3
Degree of urbanisation				
Urban	67	37.9	758	37.8
Mixed	66	37.3	682	34.0
Rural	44	24.9	566	28.2
Study population ^b				
NWS	135	76.3	1634	81.5
LSS	33	18.6	346	17.2
Both	9	5.1	26	1.3
Total	177		2006	

^a Only children aged 9 years or less were included in the analyses

^b Due to partially overlapping study regions and diagnostic periods, some participants were eligible for both studies (but were counted only once in the pooled analysis)

Table 2 Parental smoking and maternal exposure during pregnancy to alcohol, coffee, or tea

	Cases (n)	Controls (n)	OR ^a	95% CI
Maternal smoking (cigarettes/day)				
None (reference)	138	1574	1.00	–
1–10	26	347	0.86	0.55–1.36
11+	9	69	1.19	0.54–2.62
Paternal smoking (cigarettes/day)				
None (reference)	94	1061	1.00	–
1–10	18	225	0.99	0.57–1.70
11+	60	670	0.97	0.67–1.39
Maternal alcohol consumption (glasses/week)				
None (reference)	142	1495	1.00	–
1–7	31	469	0.76	0.50–1.15
8+	0	17	–	–
Maternal consumption of coffee or tea (cups/day)				
None (reference)	43	471	1.00	–
1–3	95	1090	0.94	0.64–1.38
4+	38	430	1.02	0.64–1.64
Maternal consumption of decaffeinated coffee (cups/day)				
None (reference)	139	1593	1.00	–
1–3	28	307	1.12	0.72–1.74
4+	6	65	1.20	0.50–2.90

^a OR from logistic regression analysis stratified by age, gender and year of birth, and adjusted for socioeconomic status and degree of urbanisation

than did parents of diseased children. Hence, all logistic regression analysis were adjusted for that factor. Table 2 presents the analysis of parental smoking history and

Table 3 Parental age, maternal reproductive history and other selected factors related to pregnancy and birth

	Cases (n)	Controls (n)	OR ^a	95% CI
Maternal age (years)				
< 20	7	34	2.47	1.02–5.96
20–34 (reference)	154	1800	1.00	–
≥35	14	169	0.95	0.52–1.71
Paternal age (years)				
≤20	3	15	3.62	0.94–13.9
21–30 (reference)	85	1008	1.00	–
31–40	76	865	1.20	0.86–1.69
> 40	11	100	1.52	0.76–3.03
First-born child				
No (reference)	80	1041	1.00	–
Yes	93	957	1.26	0.91–1.76
Previous fetal loss				
No (reference)	136	1541	1.00	–
Yes	41	461	1.01	0.69–1.48
Maternal use of oral contraceptives during pregnancy				
No (reference)	171	1957	1.00	–
Yes	2	32	0.69	0.16–3.03
High blood pressure during pregnancy				
No (reference)	162	1854	1.00	–
Yes	12	129	0.99	0.52–1.86
Birth weight (g)				
< 2,500	6	69	1.05	0.44–2.52
2,500–4,000 (reference)	142	1714	1.00	–
> 4,000	28	217	1.58	1.01–2.48

^a OR from logistic regression analysis stratified by age, gender and year of birth, and adjusted for socioeconomic status and degree of urbanisation

maternal alcohol and coffee or tea consumption during pregnancy. Neither maternal nor paternal smoking during pregnancy was found to be associated with Wilms tumour (Table 2). A comparison of the two extreme groups that both father and mother smoked more than ten cigarettes daily compared to both father and mother were non-smokers, also revealed an only slightly elevated OR of 1.19 (95% CI 0.48–2.98). Mother's consumption of alcohol and consumption of regular coffee or tea and decaffeinated coffee were not associated with the disease (Table 2).

Table 3 presents the results for other factors related to pregnancy and birth. Maternal age at birth of 19 years or younger was associated with a nearly 2.5-fold increased OR, but no association was seen for mothers aged 36 years or older. Young paternal age at birth (≤20 years) was also found to be related to Wilms tumour, but the numbers were small and the risk increase was not statistically significant (Table 3). A 1.5-fold increased OR was observed for paternal age at birth of 41 years or older; analysis by age of the child showed that this increase was completely attributable to children aged 6 years or older (data not shown). Other evaluated factors with an OR < 1.5 included the following: the index child was the first-born child; the mother had at least one fetal loss before the index child's birth; the

mother had conditions of high blood pressure during pregnancy; and the mother used oral contraceptives during pregnancy (Table 3). Of cases, 16% had a birth weight >4000 g compared to only 11% of controls, leading to a statistically significantly increased OR of 1.58 (95% CI 1.01–2.48, Table 3), which was higher for children aged 2 years or older (OR 2.03; 95% CI 1.21–3.40) and lower for children less than 2 years of age (OR, 0.78, 95%-CI, 0.30–2.08). This association was seen for both LSS and NWS and was also confirmed by the 1:1 matched analysis (data not shown). The duration of gestation for most Wilms tumour cases with a higher birth weight was between 39 and 41 weeks; except for two cases of 37 and 38 weeks, respectively, and three cases of 42 weeks.

The results for the analysis of different exposures to pesticides are shown in Table 4. No association was seen between Wilms tumour and the child's exposure to pesticides in gardens and on farms (there were a few families who reported pesticide use in gardens as well as on farms; they were included in the "on farms" category). Regarding indoor extermination of insects by parents, we found an only slightly increased OR by comparing category "once or more per year" to "less than once per year". Parents that reported a indoor extermination of insects by a professional pest controller (four cases, 1.8%; 28 controls, 1.6%) were included in the higher exposure category. No trend with increasing exposure was observed after subdividing the category "once or more per year" into four levels (1, 2–5, 6–10, >10 per year), but data were sparse (data not shown). Only six fathers of cases reported an occupational exposure to pesticides after the index child's birth (Table 4). Even less mothers were occupationally exposed to pesticides; only two mothers of cases were ever exposed to pesticides at work (which means in the year

before conception, during pregnancy and after birth), that yielded an OR of 2.52 (Table 4), and only one mother reported an occupationally related exposure to pesticides during pregnancy (the respective OR was 2.18; 95% CI 0.23–20.3). Other parental occupational exposures evaluated in our study included solvents; paints or lacquers; oil products; plastic or resin fumes; industrial dusts; and metal melting [28]. No association occurred with any specific item except for paternal occupational exposure to industrial dusts before conception (OR 1.54, 95%CI 1.00–2.38; 18.3% among cases and 11.6% among controls) and maternal occupational exposure to solvents before conception (OR 2.07, 95% CI 1.13–3.78; 8.6% among cases and 4.7% among controls); ORs for the different types of occupational exposure were mostly in the range between 0.95 and 1.50 (data not shown).

Except for one study [2], no previous study observed an association between Wilms tumour and ionising radiation. This was confirmed by our study; for maternal X-ray examinations during pregnancy as well as for the index child's diagnostic X-ray examinations, ORs were close to unity (data not shown).

Discussion

Despite the known genetic aetiology for a subset of cases, little is known about risk factors for Wilms tumour. One reason is that many of earlier epidemiological studies on childhood renal tumours were either small with a low statistical power to detect moderate associations, based on indirect exposure information, e.g. from birth files or death certificates, or focused on only one specific potential risk factor [18]. Here, we present data from a large-scale population-based case-control study in Germany, providing the second largest case group studied in a comprehensive study to date (the largest comprised 200 cases [24]).

One advantage of this study is the statistical power. For proportions of exposed in the range of 10% to 25% of the study population, the statistical power was >80% to detect associations with ORs between 1.75 and 1.62. Another strength is the population basis. But there are also some limitations. Firstly, selection bias introduced by non-participation cannot be ruled out. There is some evidence that control families of higher socioeconomic status were more likely to participate than those of average socioeconomic status, and there are also some risk factors which are related to social factors. We adjusted for socioeconomic status in all analyses, however, residual confounding by this factor cannot be excluded. Secondly, recall bias is a problem in studies relying on information from self-administered questionnaires and interviews, particularly for exposures which are not easy to remember. For the NWS, however, the time period between the date of diagnosis and the interview date was very short. Looking at the patterns of risk estimates derived for different diagnostic groups gives us the opportunity to evaluate effects of recall bias, but never-

Table 4 Environmental and paternal occupational exposure to pesticides

	Cases (n)	Controls (n)	OR ^a	95% CI
Child's exposure to pesticides				
No (reference)	144	1538	1.00	–
In garden	13	210	0.80	0.44–1.47
On farms ^b	5	64	0.84	0.32–2.25
In-house use of insecticides (per year)				
<1 (reference)	145	1686	1.00	–
≥1 ^c	23	230	1.27	0.78–2.08
Maternal occupational exposure to pesticides ever				
No (reference)	173	1984	1.00	–
Yes	2	14	2.52	0.50–12.6
Paternal occupational exposure to pesticides after birth				
No (reference)	167	1892	1.00	–
Yes	6	66	0.97	0.39–2.37

^aOR from logistic regression analysis stratified by age, gender and year of birth, and adjusted for socioeconomic status and degree of urbanisation

^bIncluding exposure to pesticides on farms as well as in gardens

^cIncluding extermination of insects by professional pest controller

theless, recall bias could have had some impact on some of our results. This is particularly the case for occupational exposures, which might have been overreported for case families if the perception of exposure was more sensitive among parents of children with cancer. Thirdly, we had no information which Wilms tumour cases were of hereditary origin, while there may be differences of the influence of the factors studied in the hereditary cases compared to the non-hereditary cases.

In our study, only few factors were found to be related to Wilms tumour. The association with maternal age < 20 years, which we also observed for other diagnostic groups [27], might partially be explained by non-participation bias. According to demographic data from the whole of Germany [36], 2.8% of all mothers giving birth to children in 1993 were aged less than 20 years. This was true for only 1.7% of control mothers, indicating that among controls young mothers might have been less likely to participate. However, the fraction of younger mothers among Wilms tumour cases was 4.0%. A previously unreported association was found with paternal occupational exposure to industrial dusts and maternal exposure to solvents [3,18]. These findings might be due to chance or recall bias because assessing past parental occupational exposures by a self-administered questionnaire has its limitations [7].

We found an association between Wilms tumour and high birth weight which was strongest for children aged 2 years or older. This confirms associations reported by other recent studies. Yeazel et al. [40] found a two-fold increased OR with birth weights above 3859 g and an OR of 2.4 (95% CI 1.4–4.1) for children aged 2 years or older with a birth weight of more than 4000 g. Smulevich et al. [12] observed an OR of 5.1 (95% CI 1.6–16.4, ≥ 4000 g) in a Russian case-control study. In contrast to this, a statistically significantly increased OR of about 2 for birth weights > 4000 g was observed only for Wilms tumour cases younger than 2 years of age in a Norwegian study, where information from the Medical Birth Register was linked with the Cancer Registry data [10]. No association was seen for all age groups combined. In 1984, Daling et al. [8] reported four cases of Wilms tumour > 4000 g compared to 1.2 expected when they linked birth certificates from Washington State with the Cancer Registry data. Leisenring et al. [16] compared the data from the United States National Wilms Tumour Study with the general population and observed that 59% of cases had a birth weight above the United States median birth weight. No association with high birth weight was found in a large United States case-control study [24], a Swedish case-control study [17], and earlier studies in the United States or Canada [6, 19, 39].

Olshan [22] suggested that the association between high birth weight, overgrowth associated with Beckwith-Wiedemann syndrome and hemihypertrophy, and Wilms tumour may be due to the action of loci in addition to the putative Wilms tumour locus on the short arm of chromosome 11; these genes include insulin-like growth fac-

tor 2, insulin and the Harvey ras protooncogene. Both insulin and insulin-like growth factor 2 are postulated to be important in the regulation of cell proliferation during fetal development. Fetal overgrowth and undergrowth, as found in a subgroup of Wilms tumour patients with certain congenital malformations, may therefore be linked to the actions of insulin-like growth factor 2, insulin, and possibly other growth factors. Epidemiological support of this hypothesis comes especially from the study by Leisenring et al. [16]. In this study, birth weights were particularly elevated for Wilms tumour patients with Beckwith-Wiedemann syndrome, hemihypertrophy, or perilobular nephrogenic rests, but their findings also suggest that the growth factor excess postulated to contribute to the aetiology of Wilms tumour may not be limited to those with specific overgrowth syndromes. In our study, no data were available on how many of the 28 Wilms tumour patients with a birth weight > 4,000 g had one of those overgrowth syndromes.

As opposed to some previous studies, we found no association with exposure to pesticides. An almost four-fold increased OR for children whose fathers had been exposed to pesticides during employment in agriculture was reported from Brazil [30]. In the United Kingdom, a 1.6-fold excess of kidney cancer was observed for paternal employment in agriculture [9], but no data on pesticide use were available. In Norway, Wilms tumour was related to living on a farm with orchards and greenhouses or on a farm with pesticide spraying equipment; the respective ORs were 4.8 (95% CI 1.6–14.7) and 2.5 (95% CI 1.0–6.6) [15]. Olshan et al. [24] found an association for a history of household insect and pest extermination, but no dose-response relationship with the number of exterminations was evident. In other studies, paternal employment in agriculture has not been associated with Wilms tumour [14, 21, 23, 39].

Previous studies have reported other associations that conflict with our results. We did not observe an association with high parental age at birth. This is in contrast to one study from Brazil [31] and to one study from the United States [25], however, as reviewed by Little [18], a couple of other studies found no association between parental age and Wilms tumour. We did not find an association between Wilms tumour and maternal consumption of tea or coffee during pregnancy. This contradicts findings by Bunin et al. [6], but confirms findings by Olshan et al. [24]. Bunin et al. [6] detected a five-fold increased OR for mother's high blood pressure during pregnancy and a Wilms tumour excess due to maternal use of oral contraceptives during pregnancy, but these findings were neither found in our nor in another study [24].

This large-scale population-based study has failed to confirm previously reported associations with high parental age at birth, maternal coffee and tea consumption during pregnancy and exposure to pesticides. Other factors that were not associated with Wilms tumour in our study were birth order, X-ray examinations of the child, and exposure during pregnancy including parental smoking; maternal alcohol consumption; maternal high

blood pressure; maternal use of oral contraceptives or maternal X-ray examinations. We found some evidence that high birth weight may play a role in the aetiology of Wilms tumour. Our findings for young maternal age at birth and certain parental occupationally-related exposures may be chance findings.

References

- Beckwith JB, Kiviat NB, Bonadio JF (1990) Nephrogenic rests, nephroblastomatosis, and the pathogenesis of Wilms tumor. *Pediatr Pathol* 10: 1–36
- Bithell JF, Stewart AM (1975) Pre-natal irradiation and childhood malignancy: a review of British data from the Oxford survey. *Br J Cancer* 31: 271–287
- Breslow N, Olshan A, Beckwith JB, Green DM (1993) Epidemiology of Wilms tumor. *Med Pediatr Oncol* 21: 172–181
- Brookmeyer R, Liang KY, Linet M (1986) Matched case-control designs and overmatched analyses. *Am J Epidemiol* 124: 693–701
- Buckley JD, Buckley CM, Ruccione K, Sather HN, Waskerwitz MJ, Woods WG, Robison LL (1994) Epidemiological characteristics of childhood acute lymphocytic leukemia. Analysis by immunophenotype. The Children's Cancer Group. *Leukemia* 8: 856–864
- Bunin GR, Kramer S, Marrero O, Meadows AT, Annegers JF, Kurland LT, Hauser WA (1987) Gestational risk factors for Wilms tumor: results of a case-control study. *Cancer Res* 47: 2972–2977
- Colt JS, Blair A (1998) Parental occupational exposures and risk of childhood cancer. *Environ Health Perspect* 106[Suppl 3]: 909–925
- Daling JR, Starzyk P, Olshan AF, Weiss NS (1984) Birth weight and the incidence of childhood cancer. *J Natl Cancer Inst* 72: 1039–1041
- Fear NT, Roman E, Reeves G, Pannett B (1998) Childhood cancer and paternal employment in agriculture: the role of pesticides. *Br J Cancer* 77: 825–829
- Heuch JM, Heuch I, Kvale G (1996) Birth characteristics and risk of Wilms tumour: a nationwide prospective study in Norway. *Br J Cancer* 74: 1148–1151
- Kaatsch P, Kaletsch U, Krummenauer F, Meinert R, Miesner A, Haaf HG, Michaelis J (1996) Case-control study on childhood leukemia in Lower Saxony, Germany. *Klin Padiatr* 208: 179–185
- Kaatsch P, Kaletsch U, Meinert R, Miesner A, Hoisl M, Schüz J, Michaelis J (1998) German case control study on childhood leukemia: basic considerations, methodology and summary of the results. *Klin Padiatr* 210: 185–191
- Kaatsch P, Kaletsch U, Spix C, Michaelis J (1999) German Childhood Cancer Registry: annual report 1998. Technical Report [http://info.imsd.uni-mainz.de/K_Krebsregister]
- Kantor AF, Curnen MG, Meigs JW, Flannery JT (1979) Occupations of fathers of patients with Wilms tumour. *J Epidemiol Community Health* 33: 253–256
- Kristensen P, Andersen A, Irgens LM, Bye AS, Sundheim L (1996) Cancer in offspring of parents engaged in agricultural activities in Norway: incidence and risk factors in the farm environment. *Int J Cancer* 65: 39–50
- Leisenring WM, Breslow NE, Evans IE, Beckwith JB, Coppes MJ, Grundy P (1994) Increased birth weights of National Wilms Tumor Study patients suggest a growth factor excess. *Cancer Res* 54: 4680–4683
- Lindblad P, Zack M, Adami HO, Ericson A (1992) Maternal and perinatal risk factors for Wilms tumor: a nationwide nested case-control study in Sweden. *Int J Cancer* 51: 38–41
- Little J (1999) *Epidemiology of childhood cancer*. IARC Scientific Publications, Lyon
- MacMahon B, Newill VA (1962) Birth characteristics of children dying of malignant neoplasms. *J Natl Cancer Inst* 28: 231–244
- Neuhäuser M, Becher H (1997) Improved odds ratio estimation by post hoc stratification of case-control data. *Stat Med* 16: 993–1004
- Pearce MS, Parker L (2000) Paternal employment in agriculture and childhood kidney cancer. *Pediatr Hematol Oncol* 17: 223–230
- Olshan AF (1986) Wilms tumor, overgrowth, and fetal growth factors: a hypothesis. *Cancer Genet Cytogenet* 21: 303–307
- Olshan AF, Breslow NE, Daling JR, Falletta JM, Grufferman S, Robison LL, Waskerwitz M, Hammond GD (1990) Wilms tumor and paternal occupation. *Cancer Res* 50: 3212–3217
- Olshan AF, Breslow NE, Falletta JM, Grufferman S, Pendergrass T, Robison LL, Waskerwitz M, Woods WG, Vietti TJ, Hammond GD (1993a) Risk factors for Wilms tumor. Report from the National Wilms Tumor Study. *Cancer* 72: 938–944
- Olson JM, Breslow NE, Beckwith JB (1993b) Wilms tumour and parental age: a report from the National Wilms Tumour Study. *Br J Cancer* 67: 813–818
- SAS Institute (1994) *SAS/STAT User's Guide*. Vol 1, 4th edn. Cary
- Schüz J, Kaatsch P, Kaletsch U, Meinert R, Michaelis J (1999) Association of childhood cancer with factors related to pregnancy and birth. *Int J Epidemiol* 28: 631–639
- Schüz J, Kaatsch U, Meinert R, Kaatsch P, Michaelis J (2000) Risk of childhood leukemia and parental self-reported occupational exposure to chemicals, dusts, and fumes: results from pooled analyses of German population-based case-control studies. *Cancer Epidemiol Biomark Prev* 9: 835–838
- Sharpe CR, Franco EL (1995) Etiology of Wilms tumor. *Epidemiol Rev* 17: 415–432
- Sharpe CR, Franco EL, de Camargo B, Lopes LF, Barreto JH, Johnsson RR, Mauad MA (1995) Parental exposures to pesticides and risk of Wilms tumor in Brazil. *Am J Epidemiol* 141: 210–217
- Sharpe CR, Franco EL, de Camargo B, Lopes LF, Barreto J, Johnsson R, Mauad M (1999) The influence of parental age on the risk of Wilms tumour. *Paediatr Perinat Epidemiol* 13: 138–143
- Smulevich VB, Solionova LG, Belyakova SV (1999a) Parental occupation and other factors and cancer risk in children: I. Study methodology and non-occupational factors. *Int J Cancer* 83: 712–717
- Smulevich VB, Solionova LG, Belyakova SV (1999b) Parental occupation and other factors and cancer risk in children: II. Occupational factors. *Int J Cancer* 83: 718–722
- Sorahan T, Lancashire RJ, Hulten MA, Peck I, Stewart AM (1997a) Childhood cancer and parental use of tobacco: deaths from 1953 to 1955. *Br J Cancer* 75: 134–138
- Sorahan T, Prior P, Lancashire RJ, Faux SP, Hulten MA, Peck IM, Stewart AM (1997b) Childhood cancer and parental use of tobacco: deaths from 1971 to 1976. *Br J Cancer* 76: 1525–1531
- Statistisches Bundesamt (1995). *Statistisches Jahrbuch der Bundesrepublik Deutschland* (in German). Berichte des Statistischen Bundesamtes, Wiesbaden
- Stiller CA, Parkin DM (1990) International variations in the incidence of childhood renal tumours. *Br J Cancer* 62: 1026–1030
- Stiller CA, McKinney PA, Bunch KJ, Bailey CC, Lewis IJ (1991) Childhood cancer and ethnic group in Britain: a UKCCSG study. *Br J Cancer* 64: 543–548
- Wilkins JR, Sinks TH (1984) Paternal occupation and Wilms tumour in offspring. *J Epidemiol Community Health* 38: 7–11
- Yeazel MW, Ross JA, Buckley JD, Woods WG, Ruccione K, Robison LL (1997) High birth weight and risk of specific childhood cancers: a report from the Children's Cancer Group. *J Pediatr* 131: 671–677
- Yokomori K (1999) Wilms tumor (nephroblastoma). *Contrib Nephrol* 128: 82–98