International Childhood Cancer Cohort Consortium (14C)

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Healthier Kids. Healthier Future.

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Data on human subjects is essential for gaining an understanding of the environmental causes of childhood cancer and adds great value to the genetic research

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Case-control studies of the kind involved in the CLIC consortium are a central component of this work

because they allow us to conduct studies with substantial power and focused measurement of exposures – cost-effectively

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However in research on childhood cancer additional evidence from prospective cohort studies is highly desirable

– to address concerns regarding recall bias and

– to permit collection of biological specimens prior to disease onset
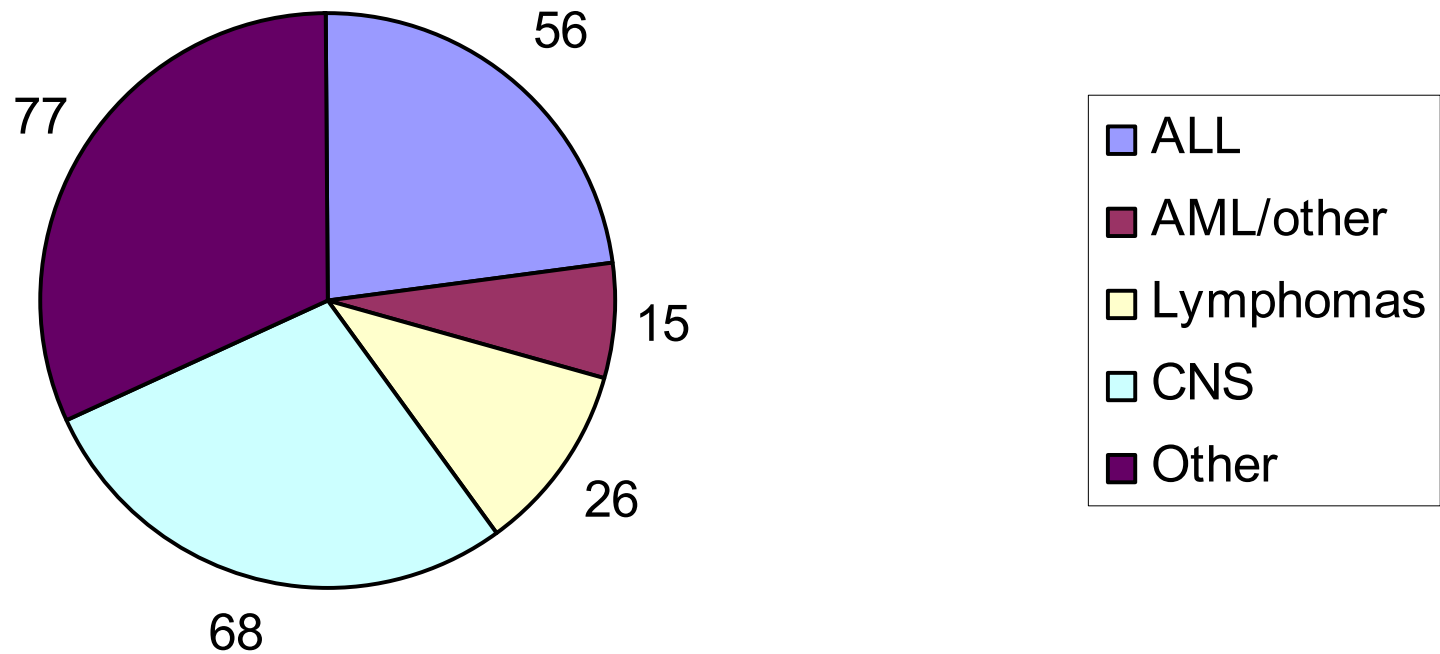
Environmental chemicals   Infections in childhood

Birth weight

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In childhood cancer, cohort studies have been difficult to mount

because they need to be very large

Number of cases of cancer occurring in a cohort of 100,000 children followed from 0-14

For all cancers n = 242

Number needed to study leukemia (Acute Lymphoblastic Leukemia & Acute Myeloid Leukemia)

Percentage of subjects exposed	Minimum risk detectable	Power %	Number Required
5	1.5	80	1180059
15	**1.5**	**80**	**446633**
30	1.5	80	277781

Garcia-Closas M, Lubin JH. *Am J Epidemiol.* 1999

Age-adjusted SEER cancer incidence rates USA 1975-2002

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No study of children in the world involves the necessary 1 million subjects.

However, since 1990 a number of countries have commenced large infant/child cohort studies
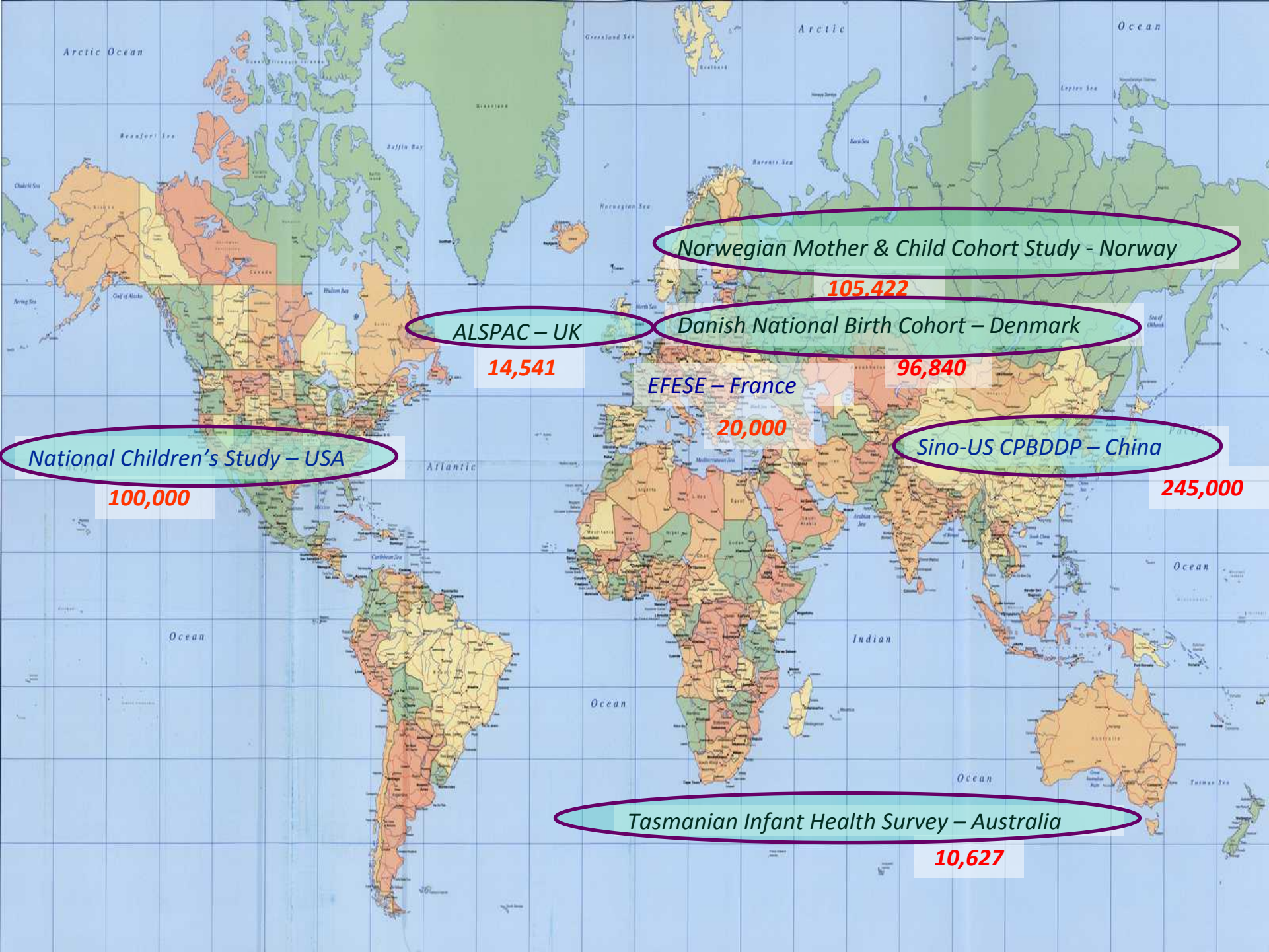
Norwegian Mother & Child Cohort Study - Norway
105.422

ALSPAC – UK
14,541

Danish National Birth Cohort – Denmark
96,840

EFESE – France
20,000

National Children's Study – USA
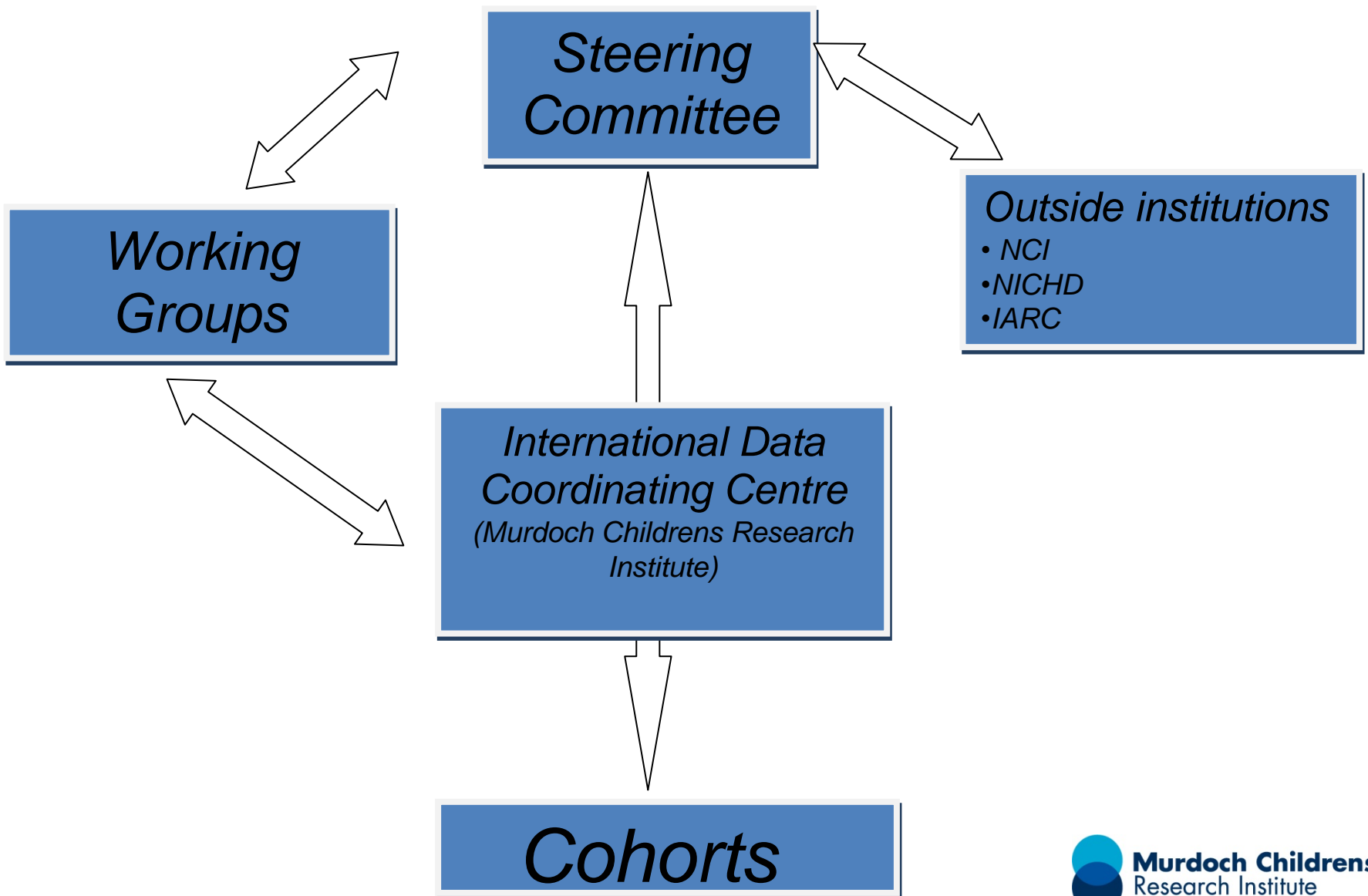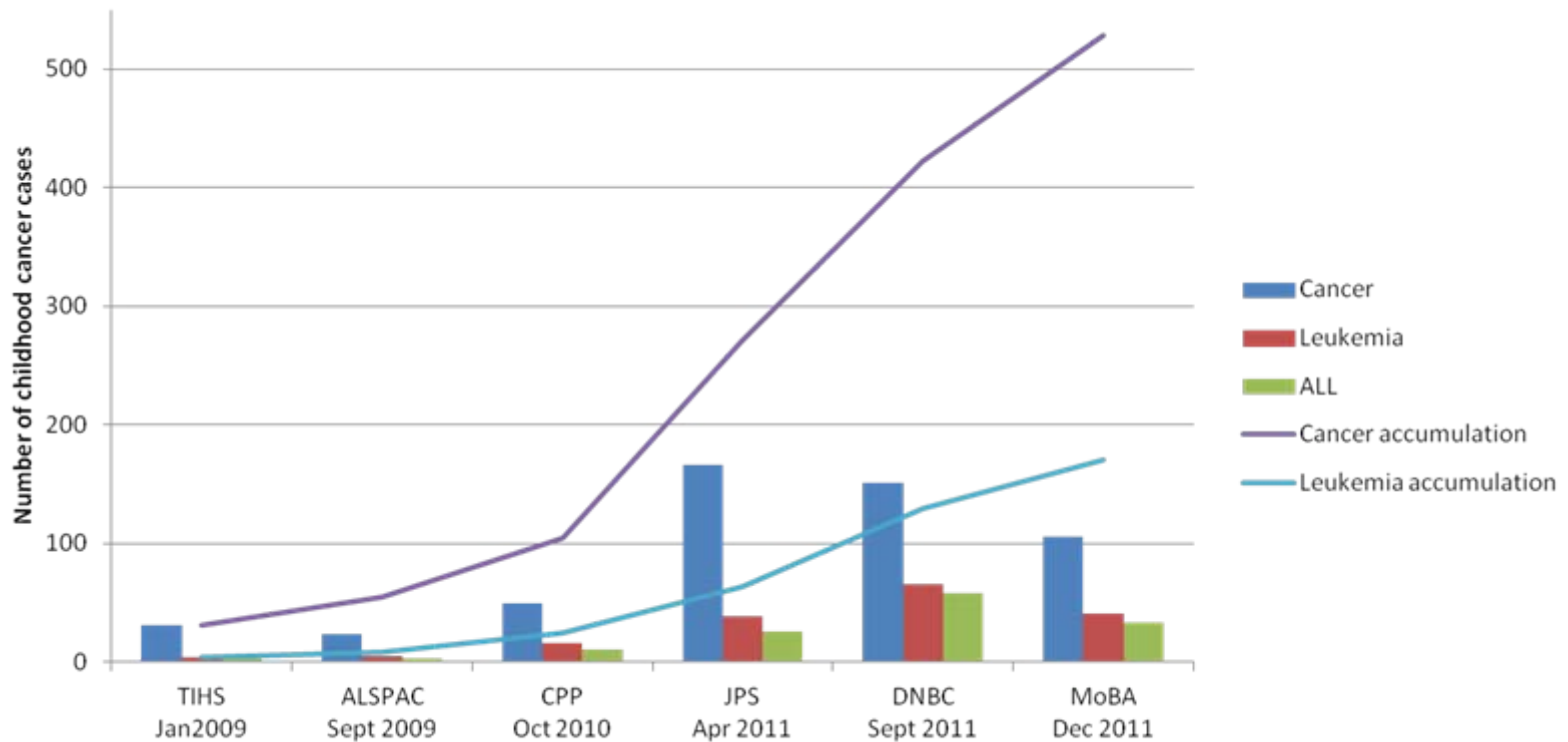100,000

Sino-US CPBDDP – China
245,000

Tasmanian Infant Health Survey – Australia
10,627

	Biological samples for genotyping etc	Birth weight and birth order	Folate	Environmental exposures	Childhood infections
National Children's Study	√	√	√	√	√
Norwegian Mother and Child Study	√	√	√	√	√
Danish National Birth Cohort	√	√	√	√	√
Avon Longitudinal Study of Parents and Children	√	√	√	√	√
Tasmanian Infant Health Survey	√	√	√	√	√
Jerusalem Perinatal Study	X	√	X	√	√
Collaborative Perinatal Project	√	√	?	√	√

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Data on 380,000 subjects has now been received at the IDCC.

Pooled analysis on 190,000 subjects: birth weight and child cancer

POOLED DATA FROM TIHS, ALSPAC, CPP AND JPS 2: Case-cohort analysis (Sept 8th 2011)

Subcohort = 2323	ALL CHILDHOOD CANCER (N=130) and Birth weight (groups) HR (95%CI)	ANY LEUKEMIA (N=33) and Birth weight (groups) HR (95%CI)	ALL (N=25) and Birth weight (groups) HR (95%CI)
UNADJUSTED			
<2500g	1.22 (0.67-2.22)	0.82 (0.19-3.44)	0.50 (0.07-3.75)
2500-3999	Ref	Ref	Ref
4000+	1.63 (0.92-2.91)	2.50 (0.96-6.50) p=0.06	1.85 (0.55-6.19)
ADJ for GEST AGE			
<2500g	0.72(0.35-1.48)	0.72 (0.12-4.25)	0.39 (0.05-2.98)
2500-3999	Ref	Ref	Ref
4000+	1.70 (0.90-3.20)	**3.16 (1.16-8.63) p=0.025**	2.33 (0.68-7.99)
ADJ for GEST AGE, SEX			
<2500g	0.74 (0.36-1.52)	0.72 (0.12-4.33)	0.41 (0.05-3.12)
2500-3999	Ref	Ref	Ref
4000+	1.61 (0.85-3.06)	**3.04 (1.10-8.38) p=0.03**	2.12 (0.64-7.06)
ADJ for GEST AGE, MAT Diabetes*			
<2500g	0.62 (0.20-1.92)	0.59 (0.05-6.95)	too small numbers
2500-3999	Ref	Ref	Ref
4000+	**2.25 (1.10-4.61) p=0.026**	**3.42 (1.12-10.45) p=0.03**	**3.37 (1.03-10.97) p=0.04**
*n=6			
ADJ for GEST AGE, MAT AGE			
<2500g	1.18 (0.57-2.42)	0.73 (0.11-4.76)	0.39 (0.05-3.21)
2500-3999	Ref	Ref	Ref
4000+	1.91 (0.98-3.73) p=0.057	2.86 (0.99-8.28) p=0.052	2.02 (0.55-7.43)
ADJ for GEST AGE, PAT AGE			
<2500g	0.63 (0.27-1.46)	0.64 (0.05-7.50)	too small numbers
2500-3999	Ref	Ref	Ref
4000+	1.40 (0.70-2.77)	**2.89 (1.01-8.25) p=0.048**	2.10 (0.59-7.48)

Maternal prenatal smoking

TIHS

- **One month postnatal**

Q31: How much did you smoke during your pregnancy?

Cigarettes Smoked	A 1st Trimester (0-13 weeks)	B 2nd Trimester (14-27 weeks)	C 3rd Trimester (28-40 weeks)
Nil			
1-10/day			
11-20/day			
21-40/day			
41+/day			

Old_T		New	
Category score	Meaning	Category score	Meaning
0	None	0	None
1	1-10	1	1-10
2	11-20	2	11-20
3	21-40	3	21+
4	41+	3	

ALSPAC

- **18 weeks gestation**

G3. f) Did you smoke regularly at any of the following times in the last 9 months?

First 3 months of pregnancy last 2 weeks.
- No   Yes, cigarettes   Yes, other

- **32 weeks gestation**

E3 How many cigarettes per day are you yourself smoking at the moment?.........................cigarettes

Old_A		New	
Category score	Meaning	Category score*	Meaning
0	None	0	None
1	1-4	1	1-10
2	5-9	1	
3	10-14	2	11-20
4	15-19	2	
5	20-24	3	21+
6	25-20	3	
7	30+	3	

*New score=0 if type of smoking **not** cigarettes*

I4C cohorts:Biospecimens

	TIHS	ALSPAC	BDSS-China	DNBC	MoBa	CPP
Biospecimens – Mother Blood	√	√	X	√	√	X
Biospecimens - Child Cord blood Guthrie cards	(1,000) Guthrie (n~520)	√	X x	√ X	√ PKU	√ X

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NCPS Package

International Childhood
Cancer Cohort Consortium
(I4C)

New Cohort Protocol
Support Package (NCPS)

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- The NCPS package comprises of 2 main parts:

1) An Excel Workbook

2) A Word document.

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