International Childhood Cancer Cohort Consortium Initiative

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Over the last 30 years there have been great improvements in the treatment of childhood cancer, but treatment is unpleasant for children. and their families, and costly.

There has been little progress In finding out how to prevent childhood cancer!

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Incidence of childhood leukemia /100,000

	Zimbabwe	USA		*India*	Japan	Australia
		B	*W*			
ALL	11.6	20.8	38.0	16.0	28.4	49.9

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Prospective Cohort studies

Healthy subjects some exposed some not

cases

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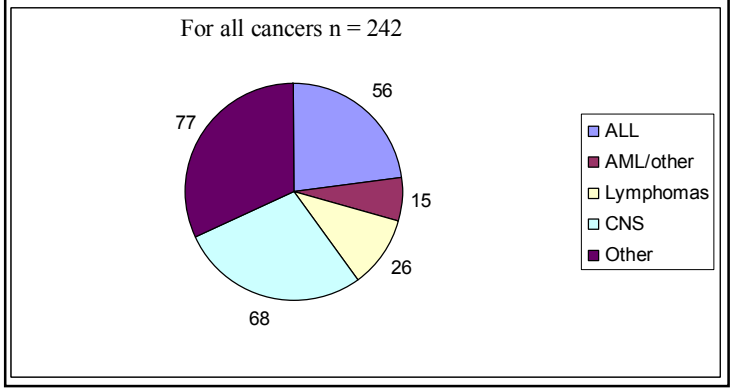
In epidemiological studies of most diseases cohort studies are desirable

- to collect the most valid data from questionnaire
- to permit collection of biological specimens prior to disease onset

In childhood cancer, cohort studies have been difficult to develop

because they need to be very large as childhood cancer is rare

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



How large a cohort would be needed to detect effects of exposures on childhood cancer?

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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Total number of subjects = >500,000

>300 cases of childhood leukemia

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No study of children in the world involves the necessary 0.5 – 1 million subjects.

However, since 1990 a number of countries have commenced large infant/child cohort studies

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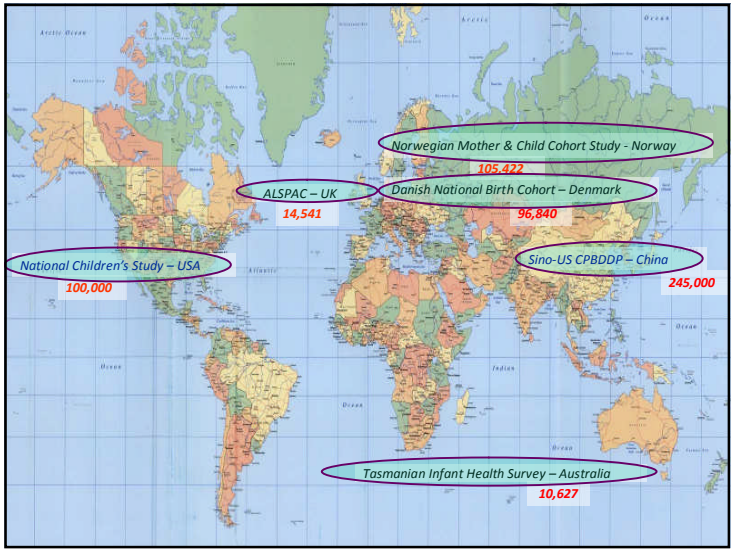

These cohorts have been termed
"Foundation cohorts"

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Recently, several other cohorts or planned cohorts have joined or are discussing joining the 14C

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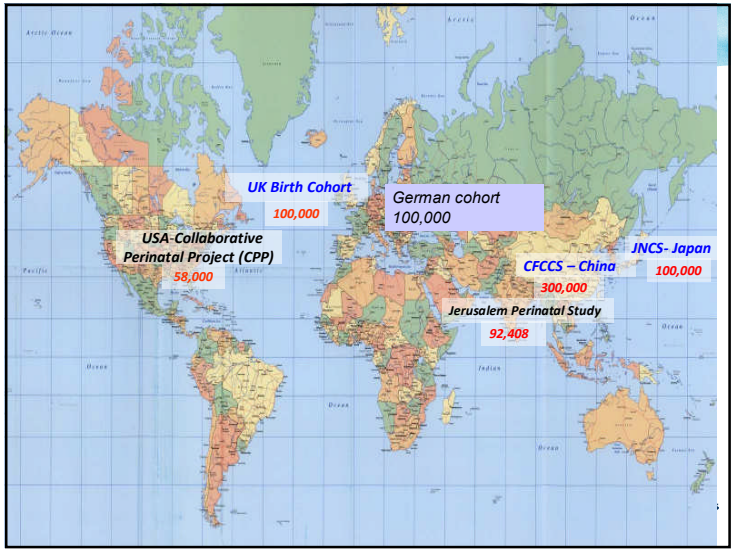

	Biological samples for genotyping etc	Birth weight and birth order	Folate	Environ/chemicals	Childhood infections
National Children's Study	√	√	√	√	√
Norwegian Mother and Child Study	√	√	√	√	√
Danish National Birth Cohort	√	√	√	√	√
Avon Longitudinal Study of Parents and Children	√	√	√	√	√
Tasmanian Infant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

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Comparability of data and the standardization process

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NCPS Package

International Childhood Cancer Cohort Consortium (I4C)

New Cohort Protocol Support Package (NCPS)

Developed by:
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- The NCPS package comprises of 2 main parts:

1) An Excel Workbook

2) A Word document.

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Example of how to use the NCPS :
Maternal prenatal maternal folic acid supplementation

Excel workbook

CORE FROM FOUNDATION COHORTS
1) Intake of folic acid supplementation during pregnancy by trimester (or weeks gestation when used)
2) Supplementation source: Folic acid on its own, with iron Or in a multi-vitamin
3) Other vitamins include: Calcium, Iron, Zinc, Multivitamins

ADDITIONAL COMPLEMENTARY DATA (includes source/cohort)
Obtain information from packaging/bottle brought into interview (OR collect information from manufacturers, supermarkets and pharmacies)
1) Include 3 months prior to finding out about pregnancy (ALSPAC, NCS)
2) Frequency of intake during each trimester- need to establish definition of 'regular' use ??
3) Total micrograms of folic acid taken during pregnancy
4) FFQ that calculates amount of folate obtained from diet (currently computed for ALSPAC, MoBa
5) Other vitamins : Vits B1,2, 6,12; Vits A,C, D, E etc (collected in ALSPAC ,MoBa, DNBC and NCS

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Results from I4C to date

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Exposure prevalence comparison across I4C cohorts: Maternal factors cont.

	TIHS	ALSPAC	BDSS- CHINA	MoBa	DNBC
Total live births at baseline	10, 628	14, 062	245, 336	108, 407	96, 841
Maternal prenatal alcohol					
- Alcohol consumption during pregnancy % (n)	34 (3,591)	67 (9,135)	2	9 (6934)	55 (51,977)
- Alcohol consumed during trimester 1	29 (3,075)	55 (7,167)	?	28 (19,274)	na
trimester 2	27 (2,853)	49 (6,356)	?	12 (7,913)	na
trimester 3	26 (2,786)	50 (5,923)	?	12 (7,978)	na
Maternal prenatal smoking					
- Smoked during any stage of pregnancy % (n)	51 (5,433)	27 (3,664)	2	9	25 (24,712)
- Smoked during trimester 1	49 (5,246)	25 (3,281)	?	10 (7864)	23 (23,460)
trimester 2	46 (4,906)	20 (2,605)	?		16 (15, 690)
trimester 3	45 (4,815)	20 (2,314)	?	8 (6,003)	na
Maternal prenatal insecticide exposure					
- Exposed to any type of insecticide during pregnancy % (n)	n/a	22 (2,410)	n/a	4 (3878)	?

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Exposure prevalence comparison across I4C cohorts: Child and Paternal factors

	TIHS	ALSPAC	BDSS-CHINA	MoBa	DNBC
Total live births at baseline	10, 628	14, 062	245, 336	108, 407	96,841
Child Measures					
- Male gender % (n)	69 (7309)	52 (7319)	?	?	?
- Gestation age, (weeks) mean ± sd	38.47±2.73	38.37±5.50	39.82±1.81	39.28 ± 2.29	39.9 ± 2.0
- Birth weight, (grams) mean ± sd	3108.14±768.9	3381±.580.84	3295.22±426.59	3563.43 ± 630	3536 ± 619
- Body length at birth, (cm) mean ± sd	48.46±3.56	?	49.46±2.26	50.21 ± 2.95	51.4 ± 6.7
- Head circumference at birth, (cm) mean ± sd	33.80±2.29	?	33.53±1.80	35.23 ± 1.85	34.3 ± 6.0
Breastfeeding					
- Child breastfed during first six months % (n)	63 (6236)	75 (8387)	?	?	?
Paternal demographics					
- Age at time of birth (years): mean ± sd	27.11±5.88	30.72±5.74	?	32.64 ± 5.4	?
- Completed university degree % (n)	7 (702)	18 (2181)	?	24	?

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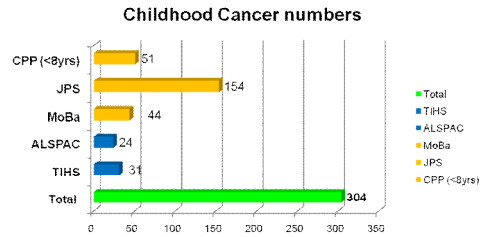
Childhood Cancer Cases: Updated numbers



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I4C Organizational Structure

Steering Committee

T Dwyer (TIHS.MCRI); M Linet (NCI-US), L Zhu (China); A Chao (China); J Golding(UK); J Olsen (Denmark); C Stoltenberg (Norway) ; O Paltiel (Israel); G Tikellis (MCRI-Australia); K Schoendorf (NCS-USA); M Vrijheid (Spain); Z Herceg (IARC-France)

Epigenetic Working Group

Led by Z Herceg and H Vargas

Examining the correlation between **birthweight** and epigenomic profiling at birth studying micro RNA expression and DNA methylation derived from cord blood samples.

Contact: herceg@iarc.fr
vargash@fellows.arc.fr

Environmental Working group

Pesticide exposure

Led by M Linet and M Vrijheid

Examining the association between prenatal pesticide exposure and subsequent risk of childhood leukemia

Contact: linetm@mail.nih.gov
mvrijheid@creal.cat

Determinants of birth weight

Led by M Kogevinas and O Paltiel

Examining the determinants of birth weight associated with childhood leukemia

Contact : kogevinas@creal.cat
ora@ums.huji.ac.il

International Data Coordinating Centre

Murdoch Childrens Research Institute (MCRI)

Director: T Dwyer
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Data Coordinator: G Tikellis
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Data Management Coordinator: L Stevens, AL Ponsonby
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I4C Web Portal: Content Ideas

- Publicly Accessible Information
  - General information: organisation, research aims
  - Consortium members: foundation, current and prospective
  - Links to publications
  - Acknowledgements: funding, collaboration efforts
- Consortium Member Access
  - Secure file exchange
  - Policies and procedures
  - Contacts: consortium members
  - Progress reports: current research activity
  - Future research: areas of prospective future analyses
  - Summary data: contributed datasets, pooled data
- https://communities.nci.nih.gov/i4c/default.aspx

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International Meetings

- International Childhood Cancer Cohort Consortium Workshops:
  - Sept 28-29 2005 Rockville, USA
  - Aug 29-30 2007 Copenhagen, Denmark
  - Nov 16-17 2009 Lyon, France
- Next workshop being planned for Sept 19-20 2011 Barcelona, Spain

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