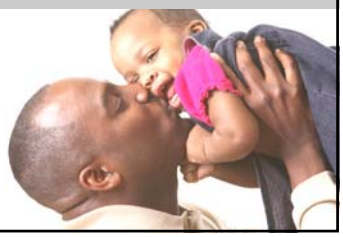
Environmental Health Risks in European Birth Cohorts (ENRIECO)

Maribel Casas

IRAS seminar
4 January 2010



Background

- Foetus and infant are especially vulnerable to the effects of environmental contaminants, and that these effects may manifest themselves throughout the lifetime and even over generations.

Pregnancy and birth cohort studies have played an important role in studying these effects.

In **Europe**, there are many pregnancy and birth cohorts currently collecting a wealth of information on environmental exposure and child outcomes.

Data are often of fragmented nature and there is relatively **little coordination** to structure and consolidate scattered research.

ENRIECO

- SEVENTH FRAMEWORK PROGRAMME THEME 6 - ENVIRONMENT (INCLUDING CLIMATE CHANGE)
- 1 March 2009 - 28 February 2011
- Project co-ordinator: Mark J Nieuwenhuijsen (CREAL, Barcelona)
- Cohorts, Partners:
  - CREAL, Spain
  - INSERM, France
  - IRAS, The Netherlands
  - Helmholtz Zentrum München - Institute of Epidemiology, Germany
  - University of Crete, Greece
  - Karolinska Institutet Stockholm, Sweden
  - Charité University Medical Center Berlin, Germany
  - Aarhus University Hospital, Denmark
- EC project officer: Tuomo Karjalainen
- www.enrieco.org

ENRIECO

Aim:

To coordinate European birth cohort research in the area of environmental exposures.

To advance our knowledge on specific environment and health causal relationships in pregnancy and birth cohorts by providing support to exploitation of past or ongoing studies.

Objectives:

- Make inventories of birth cohorts: health data, environmental exposure data, biological samples, etc
- Evaluate exposure, health and exposure-response data
- Attempt to combine data from various cohorts
- Make recommendations

Work Packages

WP1. Inventory of birth cohorts
WP leader: Martine Vrijheid

WP2. Evaluation of exposures
WP leader: Ulrike Gehring

WP3. Evaluation of health outcomes
WP leader: Remy Slama

WP4. Evaluation of exposure-response relationship
WP leader: Joachim Heinrich

WP5. Database building
WP leader: Thomas Keil

WP6. Dissemination
WP leader: Manolis Kogevinas

WP1 - Inventory

To create an inventory of all existing pregnancy and birth cohorts in Europe with data on environmental exposures and make this publically available as a web-based searchable database.

For use by:

1. Researchers:
- more effective exploitation of existing data
- planning future collaborations

2. Policy Makers and other Stakeholders:
- identification of cohorts with relevant information on specific environmental exposures and outcomes

WP1 - Which cohorts?

The main focus is on cohorts that:

1. Collect data on at least one environmental exposure topic;
2. Start enrolment during pregnancy or at birth (or during first year of life if data on birth outcomes is collected from medical records);
3. Have at least one follow-up point after birth;
4. Include at least 200-300 mother-child pairs.

WP1 - Questionnaire

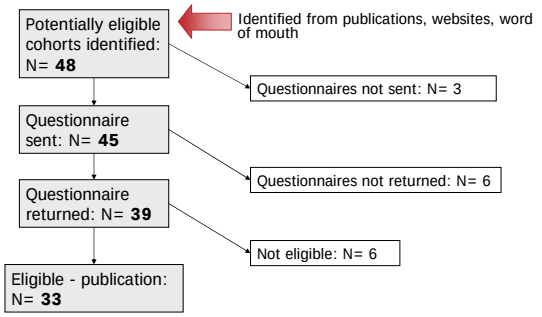
A. Basic protocol details
   - Update of birthcohorts.net
   - Objective, enrolment, N participants, data collection

B. Environmental Exposures
   - Which, when (timing), in who (N participants), how?

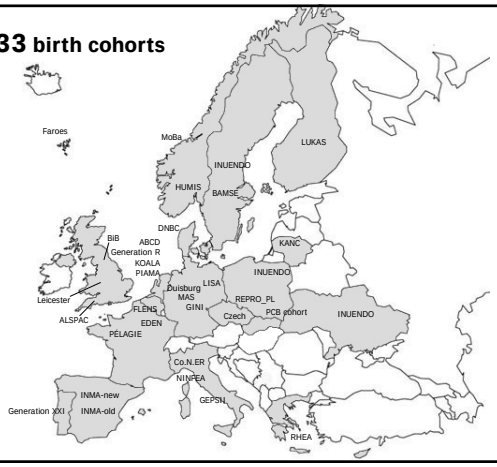
C. Health Outcomes
   - Which, when (timing), in who (N participants), how?

D. Other (diet, SES, genotyping, other important variables)
   - Yes (+timing) / No

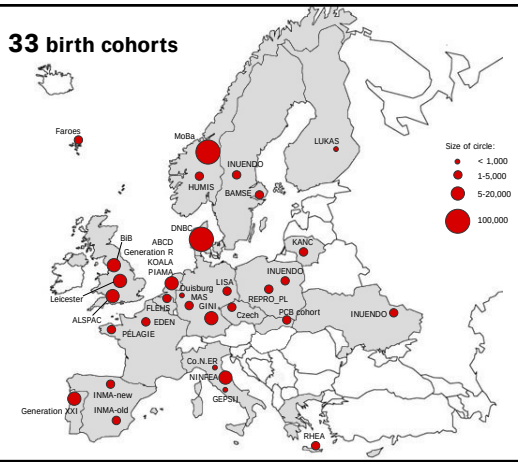
WP1 - Cohorts



33 birth cohorts



33 birth cohorts

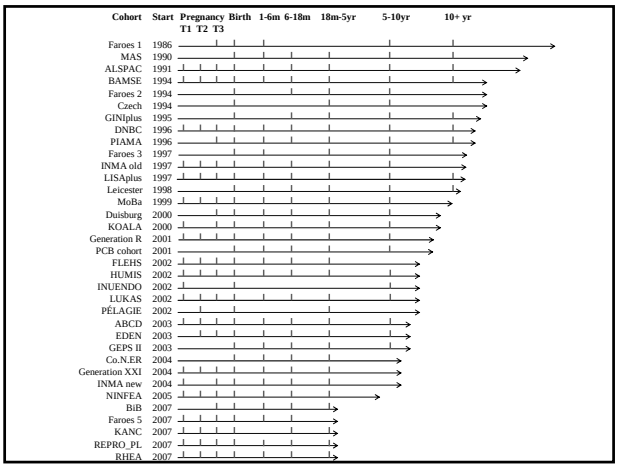


33 Birth Cohorts

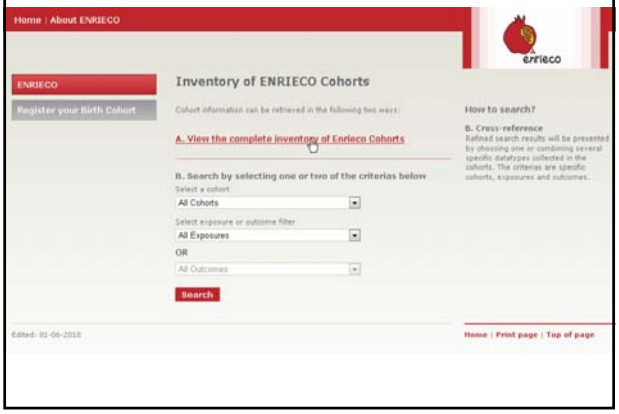
Size (subjects enrolled)	N cohorts
100,000	2
…	…
5-20,000	9
1-5,000	18
<1,000	4

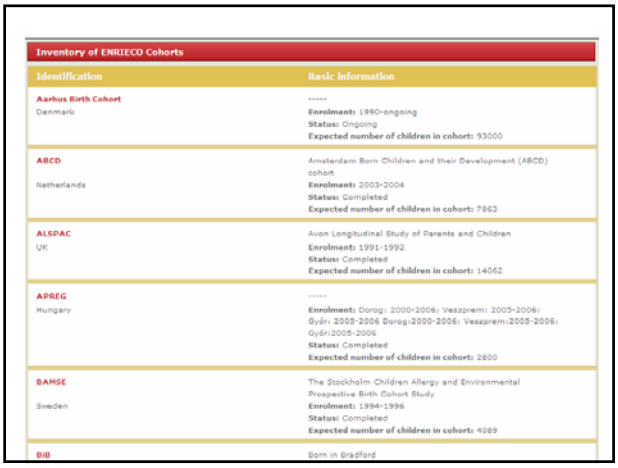
Start years	Current age of children	N cohorts
-1995	>10	11
2000-2005	5-10	16
2005-	< 5 years	6

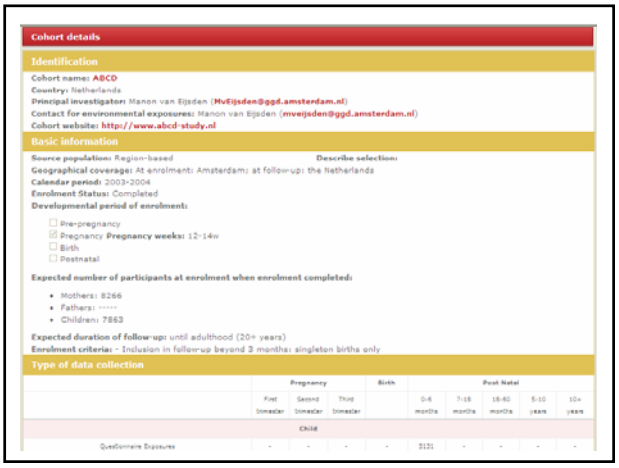
*INMA new and INMA old; INUENDO and Faroes counted as one

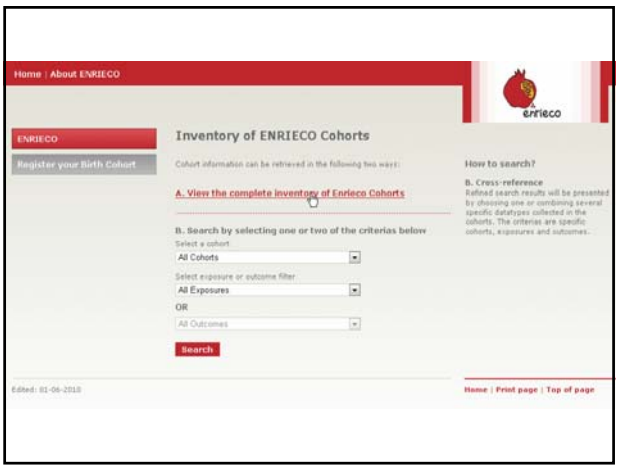


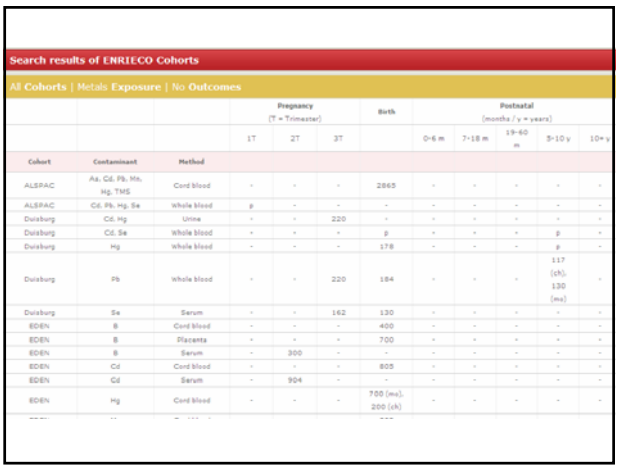
www.birthcohorts.eu











WP2 - Exposure evaluation

To find out whether exposure assessment could be comparable between studies to allow pooled or combined analyses in the future.

Protocol (available in www.enrieco.org):

-To identify cohorts of interest that have assessed each exposure

-To collect the necessary information from the inventory questionnaire

Report (~20 pages):

- Background and context
- Aim
- Current work in the European Birth Cohorts
- Discussion
  - General conclusions
  - Recommendations
- References
- Tables

WP2 - Exposure evaluation

WP leader: Ulrike Gehring

Working Group	Responsible person
Air pollution	Ulrike Gehring
Water Contamination	Mark Nieuwenhuijsen
Allergens/Biological organisms	Joachim Heinrich
Metals	Jordi Sunyer
Pesticides	Sylvaine Cordier
Emerging Exposures (phthalates, BPA, PFCs, BFR)	Martine Vrijheid
Radiations: EMF/UV/ionising	Martine Vrijheid
Second Hand Tobacco Smoke (SHS)	Magnus Wickman
Noise	Thomas Keil
Persistent organic pollutants (POPs)	Jens Peter Bonde

WP2 - Exposures

Cohort	Air pollution - Outdoor	Air pollution-Indoor	Water contamination	Allergens & biological organisms	Metals*	Pesticides*	POPs*	Other chemical exposures*	Radiations	ETS*	Noise	Occupation
ABCD	X*					X			X	X		X*
ALSPAC		X		X	X	X	X*		X	X	X	X
BAMSE	X	X		X						X		X
BiB	X		X									X
Co.N.ER	X*	X		X						X	X	X
Czech	X											X
DNBC	X*	X		X		X	X		X	X		X
Duisburg	X	X	X*	X	X		X	X		X		X
EDEN	X	X	X*		X			X	X	X		X
ELFE	X*	X*	X*	X*	X*	X*	X*	X*	X*	X*		X*
Faroes					X	X*	X	X*				X
FLEHS	X	X		X	X	X	X	X*		X		X
Generation R	X			X		X	X*	X		X	X	X
Generation XXI				X						X		X
GEPS II	X	X		X						X	X	
GINIplus	X			X						X		
HUMIS	X	X		X		X	X	X*	X	X		X
INMA old	X	X	X	X	X*	X	X	X*	X	X	X	X
INMA new	X	X	X	X	X	X	X	X	X	X	X	X
INUENDO					X*	X*	X*	X*				X
KANC	X		X								X*	X
KOALA		X	X	X					X*	X	X	X
Leicester	X	X		X						X		X
LISAplus	X	X		X		X				X	X*	
LUKAS		X		X	X	X	X	X		X		X
MAS		X		X						X	X	X
MoBa	X*	X	X	X	X*	X	X*	X	X	X	X	X
NINFEA	X*	X*		X*		X*		X*	X*	X*	X*	X*
PCB cohort		X			X	X	X	X*		X		X
PELAGIE			X		X*	X	X*	X				X
PIAMA	X	X		X						X		
REPRO_PL	X*			X	X		X*				X	X
RHEA	X	X	X	X	X	X	X*	X*	X	X	X	X

WP2 - Methods

Predominant type of exposure assessment by exposure topic:

Topic	Biomonitoring	Measurements	Modelling	Questionnaire
Outdoor air pollution			■	
Water contamination		■		
Allergens & biological organisms				■
Heavy metals	■			
Pesticides				■
Persistent organic pollutants	■			
Emerging exposures	■			
Radiations				■
Smoking and ETS				■
Noise				■
Occupation				■

WP2 - Recommendations

Main conclusions:

- Little standardization of exposure assessment methods between cohorts,
- Exceptions include studies in which exposure assessment was part of a collaborative effort:
  - TRAPCA and ESCAPE: air pollution
  - HIWATE: water pollution

Recommendations for future collaboration:

- Investigators from each cohort publish the details of their exposure assessment methods in online supplements to journal articles and on their project's websites
- Investigators contact colleagues even before doing a new study to exchange protocols.

WP2 - Recommendations

Example:

Recommendations for analysis of emerging contaminants

Contaminant	Compound analysed	Matrix	N samples	Storage Containers	Storage Temperature	Analytical technique	LOD
Brominated flame retardants	parents	blood, breast milk	one	polyethylene	-20°C (min)	GC-MS	0.001-0.002ng/mL
Perfluorinated compounds	parents	blood	one	polyethylene	-20°C (min)	LC-MS/MS	1.0 ng/mL
Bisphenol A	total (free and conjugated)	urine	multiple	polypropylene	-20°C (min)	LC-MS or GC-MS/MS	0.1ng/mL
Phthalates	metabolites	urine	multiple	polypropylene	-20°C (min)	GC-MS/MS	0.2-1.2ng/mL

LC-MS/MS: liquid chromatography mass spectrometry
GC-MS/MS: gas chromatography mass spectrometry

WP3 - Outcome evaluation

To evaluate the existing health information, the methods and tools that have been applied in the European birth cohorts and make recommendations on how these data can be taken advantage in future analyses.

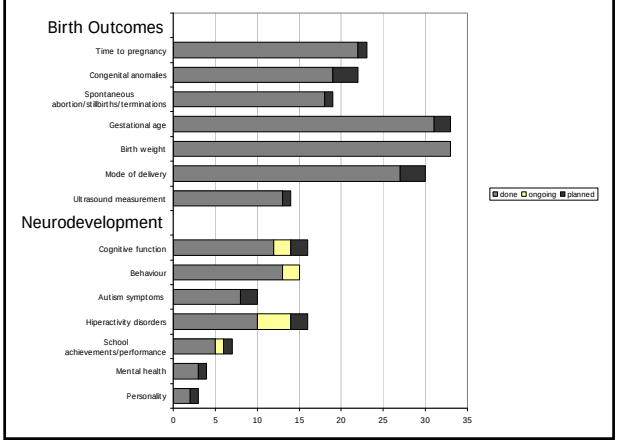
Report (~20 pages):

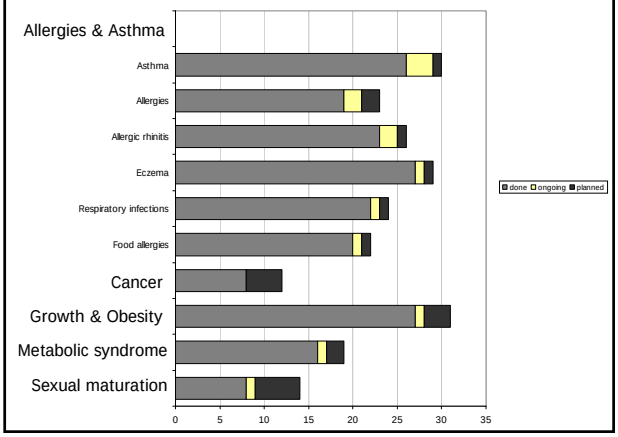
- Background and context
- Aim
- Current work in the European Birth Cohorts
- Discussion
  - General conclusions
  - Recommendations
- References
- Tables

WP3 - Outcome evaluation

WP leader: Remy Slama

Working Group	Responsible person
Birth Outcomes	Remy Slama
Allergies/Asthma/Respiratory Disease (RD)	Thomas Keil
Neurobehaviour	Jordi Sunyer
Cancer	Manolis Kogevinas
Child Growth / Endocrine & Metabolic Disorders	Marie Aline Charles





WP3 - Recommendations

- **Reproductive outcomes**: we encourage cohorts with a prenatal recruitment, to characterize pregnancy-related events, such as specific congenital anomalies, preterm and very preterm birth.
- **Respiratory health**: use of standard questionnaires already used in other large surveys (ISAAC) is strongly advised.
- **Child neurodevelopment**: at least one assessment of all the areas of neurodevelopment (cognition, emotion, behavior).
- **Child growth**: serial measures covering the different periods of interest are needed to allow studying the effect of early exposures on critical periods of growth.
- **Childhood cancer**: continue promoting the initiative of the International Childhood Cancer Cohort Consortium (I4C) in which European cohorts are implied. Development of biomarker-based studies.

WP4: Exposure-Response evaluation

To find out which are the discrepancies of the methodology between the studies (exposures and outcomes) and how they are linked to inconsistent observed exposure-response relationships.

Systematic review (~20 pages):

- Background and context
- Aim
- Methods
- Results
- Discussion
  - General conclusions
  - Recommendations
- References
- Tables

WP4: Exposure-Response evaluation

WP leader: Joachim Heinrich

Working Group	Responsible person
Air pollution and Birth outcomes	Manolis Kogevinas
SHS and Birth outcomes	Constantine Vardavas
Pesticides and Birth outcomes	Sylvaine Cordier
Occupation and Birth outcomes	Martine Vrijheid
POPs and Birth outcomes	Jens Peter Bonde
Metals and Birth outcomes	Jordi Sunyer
Water contaminants and Birth outcomes	Mark Nieuwenhuijsen
Noise and Asthma/Birth outcomes	Thomas Keil
Air pollution and Allergy/Asthma/RD	Bert Brunekreef
Allergens/biological organism and Allergy/Asthma	Joachim Heinrich
Metals and Neurobehaviour	Jordi Sunyer
POPS and Neurobehaviour	Jordi Sunyer

WP4 - Recommendations

- **Occupation & Birth outcomes**: sometimes difficult to detect small differences in pregnancy outcomes between different occupations and job groups. Standardization of occupational questionnaires will facilitate further joint analyses.
- **Air pollution & Allergy and Asthma**: traffic-related air pollution contributes to the development of respiratory illness and allergic sensitization. Growing evidence for an association between traffic-related air pollution exposure and eczema.
- **Metals & Neurodevelopment**: most studies focused on Hg and Pb effects on cognitive function – none studies about Pb effects on early development milestones. Other metals that must be further studied (As, Cd, Al, Tl, etc).
- **POPs & Neurodevelopment**: PCBs followed by DTT/DDE, HCB the most studied compounds. Common expression units should be applied.
- **Noise & Asthma & Birth outcomes**: 30 publications were identified showing some weak effects but the studies are methodologically doubtful.
- **Second Hand Smoke & Birth outcomes**: the majority of studies used self-reported questionnaires – biomarker assessment (cotinine) conducted in few studies.

Case Studies

WP	Case study	Responsible person
WP2	Occupational Exposures during pregnancy	Sylvaine Cordier
WP3	Persistent Organic Pollutants and birth weight	Jens Peter Bonde
WP5	Case study on dampness and the association with asthma and allergy in European birth cohorts	Chen-Chih Mey Joachim Heinrich Christina Tischler
	Case study on foetal tobacco smoke exposure and asthma among 4-6 years old	Magnus Wickmann
	Case study on foetal tobacco smoke exposure and wheezing among 0-2 years old	Constantine Vardavas

Case Studies

WP2: **Occupational Exposures during pregnancy**

- Most cohorts have recorded information on maternal occupation at one point
- 12 cohorts have already translated this information into codes (ISCO-88)
- A protocol has been developed to conduct a meta-analysis of the risk of adverse outcomes in the various cohorts for selected "at risk" occupations (this work will be continued in the CHICOS project)

WP3: Persistent Organic Pollutants and birth weight

- 12 cohorts (7300 mother-child pairs) have already assessed CB-153 and p,p-DDE as markers of POP exposure regardless of matrix (cord blood, maternal serum, breast milk)
- Statistical analysis based upon uniform software code
- Results coming soon

Case Studies

WP5:

WG1: Case study on dampness and the association with asthma and allergy

- 8 cohorts (21559 children) included - parental questionnaires and between birth and 10 years
- Exposure to early visible mould/dampness increases the risk of developing allergic disorders in children up to 10 years of age.

WG2: Case study on foetal tobacco smoke exposure and asthma among 4-6 year olds

- 9 cohorts (35000 children) included
- Preliminary results (not adjusted): association between prenatal SHSE and asthma at age 4-6 years at least in 2 cohorts.

WG3: Case study on foetal tobacco smoke exposure and wheezing among 0-2 year olds

-under development (case study initially not included in the project)

CHICOS - "Developing a Child Cohort Research Strategy for Europe"

- **"FP7 HEALTH-2009-3.3-4:** Birth/Mother-Child Cohorts co-ordination.
- **Project Coordinator:**
  - Martine Vrijheid (CREAL, Barcelona)
- **Cohorts, Partners:**
  - Danish National Birth Cohort
  - RHEA, Greece
  - NINFEA, Italy
  - Generation R, The Netherlands
  - MoBa, Norway
  - ALSPAC, Bristol, UK
  - INMA, Spain
- **Start:** Jan 2010, 3 years
- EC Project Officer: Kevin McCarthy

CHICOS

Aim:

To improve child health across Europe by developing an integrated strategy for mother-child cohort research through the coordination of important European birth cohorts.

Objectives:

- To make an overview of birth and mother-child cohorts in Europe;
- To evaluate existing information on child health outcomes and determinants from cohorts;
- To develop recommendations for research action at European level for the next 15 years, focusing on key areas of policy concern;
- To develop an effective dissemination between research and policy area.

CHICOS

Outcome Themes

- Perinatal outcomes
- Asthma, respiratory health, allergies
- Obesity, vascular and metabolic health
- Neuro-cognitive and behavioural development
- Accidents and injuries
- Infectious diseases
- Childhood cancer

Determinant Themes

- Social/cultural inequalities
- Nutrition and physical activity
- Life-style exposures
- Environmental exposures
- Biobanks and genetics
- Multiple determinants (integrated risk assessment)

CHICOS

- Next meeting: 11-12 April 2011 Barcelona
- www.chicosproject.eu

The CHICOS Project Team