Integrating birth cohorts

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CREAL, 4th March 2016

Birth Cohorts

➢ Many birth cohorts in Europe with shared aim to examine early determinants of health by following participants from the intrauterine period, through childhood and adolescence, into adulthood.

➢ Individual birth cohort studies have contributed importantly to understanding the environmental causes of childhood disease.

➢ Collaboration needed to reach full potential…

Collaboration – Why?

1. Improving causal inference
   - Replication of findings
   - Comparison of results
   - Increased sample size: rare exposures/outcomes, interactions…
   - Exposure diversity (e.g. specific diets)

2. Understanding inequalities
   - Contrast needed in prevalence of disease, risk factors and behaviors, and policies

3. Greater and more efficient use of cohorts
   - Shared expertise, improved methodology, use of data otherwise not used

4. Coordinated (fast) response to important policy questions
   - E.g. New chemicals

Environment

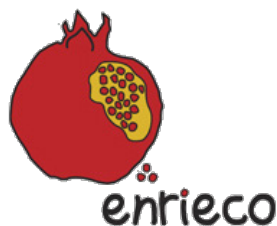**Health**

ENRIECO

CHICOS

ENRIECO

Environmental Health Risks in European Birth Cohorts

- ➢ 2009-2011
- ➢ Focus on environmental contaminants
- ➢ 35+ cohorts
- ➢ Coordinator: Mark Nieuwenhuijsen, CREAL

CHICOS

Developing a Child Cohort Research Strategy for Europe

- ➢ 2010-2013
- ➢ Wider focus
- ➢ 70+ cohorts
- ➢ Coordinator: Martine Vrijheid, CREAL
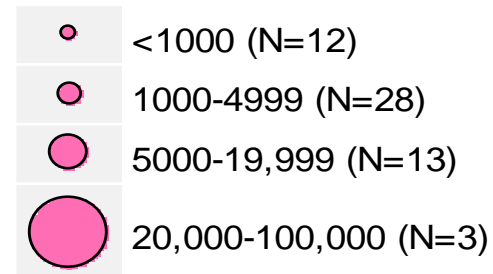
enrieco

chicos

Coordination - How?

1. Inventory and review of birth cohort data in Europe

2. Pooling of cohort data

3. Recommendations for research action

4. Evaluation of contribution to policy

Inventories: www.birthcohorts.net

More than 70 cohorts, following more than 500,000 children and parents
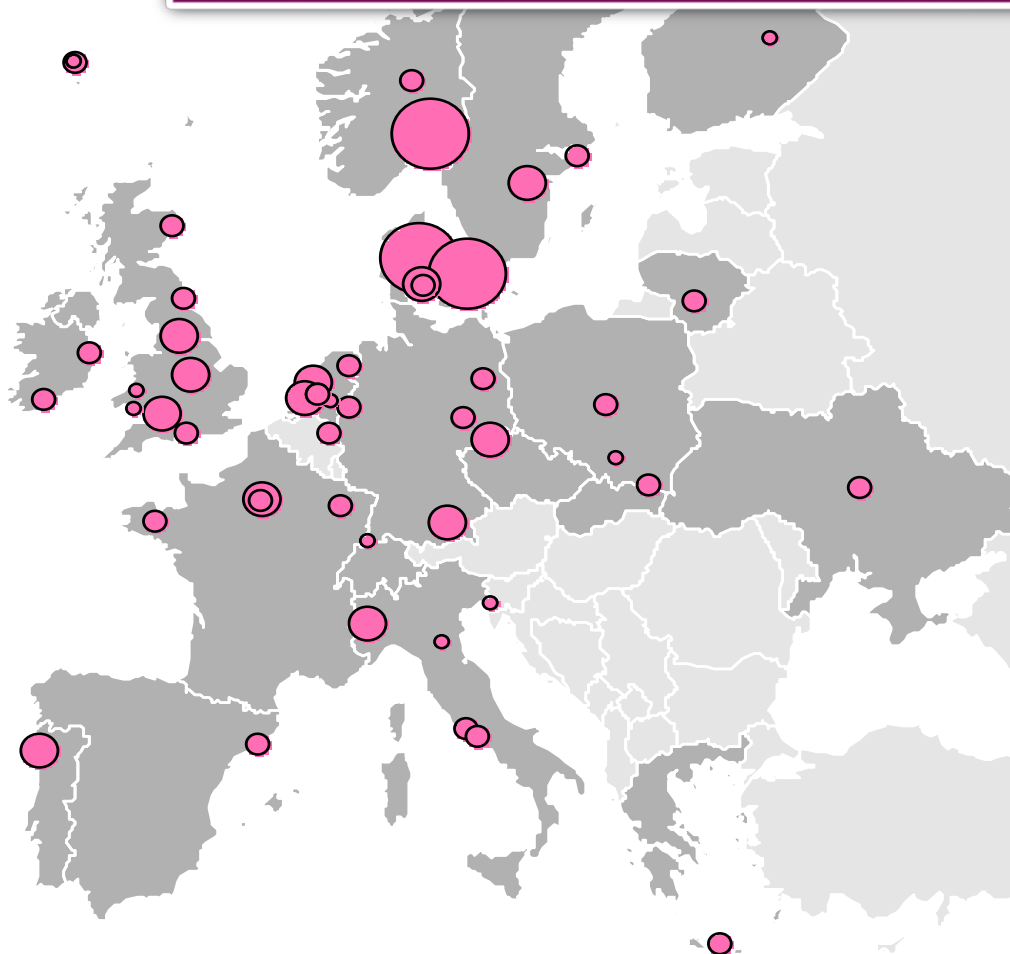
Sample size (N of children)

- <1000 (N=12)
- 1000-4999 (N=28)
- 5000-19,999 (N=13)
- 20,000-100,000 (N=3)

Larsen et al, Paediatr Perinat Epidemiol 2013 (CHICOS)

Vrijheid et al, EHP 2011 (ENRIECO)

European Birth Cohorts

➢ 19 countries represented – majority of cohorts located in Northen and Western Europe

➢ 1 cohort enrolled participants before pregnancy, 34 during pregnancy and 21 at birth

➢ The oldest cohort enrolled participants from in 1982 to 1984

➢ Most cohorts had completed several waves of follow-up of the children at different ages

Inventory: www.birthcohorts.net
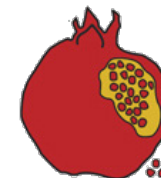
70 birth cohorts

Inventory of Birth Cohorts

Register/edit cohort

Inventory of ENRIECO

European birth cohorts with data on environmental contaminant exposures

Which cohorts are included?

- Cohorts started in pregnancy or at least at birth
- Cohorts with at least one year of follow-up
- Cohorts with at least 300 mother-child pairs

Inventory of Birth Cohorts

Cohort information can be retrieved in the following ways:

A. View the complete inventory of Birth Cohorts
Click here

B. Search by selecting criterias below
(This performs a search for cohorts with information on selected exposures, outcomes, biological samples or health and development)
Please, be aware that this search may take up to a few minutes.

1. Choose group ▼

Search

C. Search by region

Africa ▼

Search

Larsen et al. Paediatr Perinat Epidemiol 2013

⊙ Identification

Cohort, name
Amsterdam Born Children and their Development

Cohort, abbreviation
ABCD

Cohort, country
Netherlands (Nederland)

Cohort, website
http://www.abcd-studie.nl

Cohort, facebook-site

Key reference
van Eijsden M, Vrijkotte TG, Gemke RJ, van der Wal MF. Cohort
profile: the Amsterdam Born Children and their Development
(ABCD) study. Int J Epidemiol. 2011 Oct;40(5):1176-86.

Date of filling in this questionnaire:
2011-10-11

Principal investigator(s)
- name
Manon van Eijsden; Tanja G.M. Vrijkotte

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Municipal Health Service Amsterdam; Academic Medical Centre/
University of Amsterdam

Contact person(s)
- name
Eva M. Loomans

- e-mail address
abcd@ggd.amsterdam.nl

- institution address

⊙ Basic description

Main aim of cohort
Prospective cohort study on the association between lifestyle, psychosocial conditions, and nutritional status during pregnancy, and
the childs health at birth (birth weight, pregnancy duration, perinatal mortality) and in later life (growth, physical development,
behhaviour and cognitive functioning).

Recruited number of:
6161 children / 8266 mothers / 0 fathers / 0 grand parents / 0 other family members

Approximate proportion of source population included
0

Source population
Region-based

Children

Birth outcomes	
Birth weight	X
Birth length	
Gestational age at birth	X
Apgar score	X
Congenital malformations	X
Stillbirth (>= 22 weeks)	X
Child's sex	X

Child exposures	---------- Child age (years) at assessment ----------																		
	<1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Childcare attendance																			
Passive smoking	X					X													
Tobacco smoking																			
Alcohol consumption																			
Substance abuse																			
Breast feeding	X	X	X																
Diet	X					X													
Physical activity						X													
Medicine intake	X					X													
Vaccinations																			

Child development and health	---------- Child age (years) at assessment ----------																		
	<1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Renal ultrasound																			
Brain MRI																			
Congenital anomalies	X					X													

Maternal Exposures	Timing of assessment				
	Pre-pregnancy	First trimester	Second trimester	Third trimester	Post pregnancy
Tobacco smoking	X	X	X	X	X
Passive smoking	X	X	X	X	X
Alcohol consumption	X	X	X	X	X
Binge drinking	X	X	X	X	X
Substance abuse	X	X	X	X	X
Medicine intake	X	X	X	X	X
Diet	X	X	X	X	
Dietary supplements	X	X	X	X	
Coffee drinking	X	X	X	X	
Stress	X	X	X	X	X
Occupational hazards	X	X	X	X	X
Outdoor air pollution					X
Indoor contaminants					X
Physical activity	X	X	X	X	
Heavy lifts	X	X	X	X	
Education	X	X	X	X	X
Income	X	X	X	X	X
Occupation	X	X	X	X	X
Single parenthood	X	X	X	X	X
Weight	X	X	X	X	X
Height	X	X	X	X	X

Maternal health	---------- Timing of assessment ----------				
	Pre-pregnancy	First trimester	Second trimester	Third trimester	Post pregnancy
Preeclampsia	X	X	X	X	
Diabetes	X	X	X	X	X
Mental health	X	X	X	X	X
Cardio-vascular disease	X	X	X	X	X
Cancer	X	X	X	X	X
Autoimmune disease	X	X	X	X	X
Musculo-skeletal disease	X	X	X	X	X
Asthma/allergy	X	X	X	X	X
Infectious disease	X	X	X	X	X
Blood pressure	X	X	X	X	
Low density lipoprotein					
High density lipoprotein					
Total cholesterol					
Insulin					
Glucose					
Triglyceride levels		X	X	X	
Other blood measurements		X	X	X	
Fever					

Inventory: www.birthcohorts.net

Larsen et al. Paediatr Perinat Epidemiol 2013

www.birthcohortsenrieco.net

37 birth cohorts

ENRIECO

Register your Birth Cohort

Inventory of ENRIECO Cohorts

Cohort information can be retrieved in the following two ways:

A. View the complete inventory of Enrieco Cohorts

B. Search by selecting one or two of the criterias below

Select a cohort

All Cohorts

Select exposure or outcome filter

All Exposures

OR

All Outcomes

Search

How to search?

B. Cross-reference
Refined search results will be presented by choosing one or combining several specific datatypes collected in the cohorts. The criterias are specific cohorts, exposures and outcomes.

Edited: 01-06-2010

Vrijheid et al, EHP 2011

Vrijheid et al, EHP 2011

Cohort	Air pollution outdoor	Air pollution indoor	Water contamination	Allergens and biological organisms	Metals[b]	Pesticides[c]	Persistent organic pollutants	Other chemical exposures[d]	Radiations	Passive smoking[e]	Noise	Occupation
ABCD	X					X			X[g]	X		X
ALSPAC		X		X	X	X	X[g]		X	X	X	X
ArcRisk-Norway					X		X	X[g]		X		X
BAMSE	X	X		X						X		X
BiB	X		X									X
Co.N.ER	X[g]	X		X						X	X	X
Czech	X									X		X
DARC	X	X		X						X		X
DNBC	X[g]	X		X		X	X		X	X		X
Duisburg	X	X	X[g]	X	X		X	X		X		X
EDEN	X	X	X[g]		X		X		X	X		X
ELFE	X[g]	X[g]	X[g]	X[g]	X[g]	X[g]	X[g]	X[g]	X[g]	X[g]		X[g]
Faroes					X	X[g]	X	X[g]		X		X
FLEHS I	X	X		X	X	X	X			X		X
GASPII	X	X		X						X	X	
Generation R	X			X		X	X[g]	X		X	X	X
Generation XXI				X						X		X
GINIplus	X	X		X						X		
HUMIS[f]	X	X	X	X	X[g]	X	X	X	X	X		X
INMA old	X	X	X	X	X[g]	X	X	X	X	X	X	X
INMA new	X	X	X	X	X	X	X	X	X	X	X	X
INUENDO					X[g]	X[g]	X[g]	X[g]		X		X
KANC	X		X							X	X[g]	X
KOALA		X	X	X					X[g]	X	X	X
Kraków	X	X		X	X	X	X	X		X		X
Leicester	X	X		X						X		X
LISAplus	X	X		X						X	X[g]	
LUKAS		X		X	X	X	X	X[g]		X		X
MAS		X		X						X	X	X
MoBa	X[g]	X	X	X	X[g]	X	X[g]	X	X	X	X	X
NINFEA	X[g]	X[g]		X[g]		X[g]		X[g]	X[g]	X[g]	X[g]	X[g]
PARIS	X	X	X	X						X		X
PCB cohort		X			X	X	X	X[g]		X		X
PELAGIE		X	X		X	X	X	X		X		X
PIAMA	X	X		X						X		
REPRO_PL	X[g]			X	X		X			X	X	
RHEA	X	X	X	X	X	X	X[g]	X[g]	X	X	X	X

Exposure Biomarkers

Cohort	Metals	Persistent organic pollutants	Other pesticides	Tobacco smoking	Other chemicals
ALSPAC	As, Cd, Hg, Mn, Pb, Se,[b] TMS	PFCs[b]	—	Cotinine	—
ArcRisk-Norway	As, Cd, Co, Hg, Mb, Mn , Pb	Chlordane, DDT/DDE, HCB, PCBs	—	—	Planned
BAMSE	—	—	—	Cotinine	—
Czech	—	—	—	Cotinine	PAHs
DNBC	—	PFCs	—	—	—
Duisburg	Cd, Hg, Pb, Se	DDT/DDE, HCB,[b] HCH, PCBs, PCDDs, PCDFs, PFCs	—	Cotinine[b]	BPA, phthalates
EDEN	B, Cd, Mn, Hg, Pb	—	—	Cotinine	Phthalates, phenols (including BPA)
ELFE	Al,[b] As,[b] Cd,[b] Hg,[b] Pb[b]	BFRs,[b] organochlorines,[b] PFCs,[b] PCBs,[b] PCDDs,[b] PCDFs[b]	Organophosphates,[b] pyrethroids[b]	Cotinine[b]	BPA,[b] phthalates[b]
Faroes	Hg, Pb, Se	BFRs,[b] chlordane, DDT/DDE, dieldrin/ endrin, heptachlor, HCB, β-HCH, mirex, organometallic compounds, PCBs, PFCs,[b] toxaphene	—	—	BPA,[b] phthalates[b]
FLEHS I	Cd, Pb	DDT/DDE, dioxin-like compounds, HCB, PCBs	—	—	—
Generation R	—	Organochlorines[b]	Organophosphates	—	BPA, phthalates
GINIplus	—	—	—	Cotinine	—
HUMIS	Hg,[b] Pb[b]	BFRs, DDT/DDE, HCB, HCH, mirex, PCBs, PCDDs, PCDFs, PFCs, toxaphene	—	—	Phthalates
INMA old	Hg, Pb,[b] TMS[b]	Aldrin/dieldrin/endrin, BFRs, DDT/DDE, endosulfan, lindane, methoxychlor, mirex, HCB, HCH, PCBs	—	Cotinine	Phthalates, phenols (including BPA)
INMA new	Hg, Pb, TMS[b]	BFRs, DDT/DDE, HCB, HCH, PCBs	—	Cotinine	Phthalates, phenols (including BPA)
INUENDO	Cd,[b] Hg,[b] Pb[b]	BFRs,[b] DDT/DDE, HCB,[b] PCBs, PFCs[b]	—	—	BPA,[b] phthalates[b]
Kraków	Cd, Hg, Pb	—	—	Cotinine	Phthalates, PAHs, benzo[a]pyrene-adducts
LISAplus	—	—	—	Cotinine	—
LUKAS	As, Cd, Hg, Pb, Se	BFRs, DDT/DDE, organometallic compounds, PCBs, PCDDs, PCDFs, polychlorinated naphthalene	—	—	Phthalates[b]
MAS	—	—	—	Cotinine	—
MoBa	Planned	BFRs,[b] DDT/DDE,[b] PCBs[b]	Organophosphates	—	BPA, phthalates
NINFEA	—	—	—	—	—
PCB cohort	Hg, Pb	DDT/DDE, HCB, HCH, PCBs, PFCs[b]	—	—	Phthalates[b]
PÉLAGIE	Hg	Aldrin, BFRs, DDT/DDE, dieldrin/endrin, heptachlor, HCB, PCBs	Acetochlor, alachlor, metolachlor, organophosphorus, propoxur, triazines	—	Phthalates
REPRO_PL	Cd, Hg, Pb, Se, Zn, Cu	PCBs, PCDDs, PCDFS	—	Cotinine	PAHs (1-hydroxypyrene)
RHEA	As, Cd, Hg, Mn, Pb	DDT/DDE,[b] HCB,[b] PCBs,[b] PCDDs,[b] PFCs[b]	—	NNAL, cotinine	Phthalates[b]

			Pregnancy (T = Trimester)			Birth	Postnatal (months / y = years)				
			1T	2T	3T		0-6 m	7-18 m	19-60 m	5-10 y	10+ y
Cohort	Contaminant	Method									
ALSPAC	As, Cd, Pb, Mn, Hg, TMS	Cord blood	-	-	-	2865	-	-	-	-	-
ALSPAC	Cd, Pb, Hg, Se	Whole blood	p	-	-	-	-	-	-	-	-
Duisburg	Cd, Hg	Urine	-	-	220	-	-	-	-	-	-
Duisburg	Cd, Se	Whole blood	-	-	-	p	-	-	-	p	-
Duisburg	Hg	Whole blood	-	-	-	178	-	-	-	p	-
Duisburg	Pb	Whole blood	-	-	220	184	-	-	-	117 (ch), 130 (mo)	-
Duisburg	Se	Serum	-	-	162	130	-	-	-	-	-
EDEN	B	Cord blood	-	-	-	400	-	-	-	-	-
EDEN	B	Placenta	-	-	-	700	-	-	-	-	-
EDEN	B	Serum	-	300	-	-	-	-	-	-	-
EDEN	Cd	Cord blood	-	-	-	805	-	-	-	-	-
EDEN	Cd	Serum	-	904	-	-	-	-	-	-	-
EDEN	Hg	Cord blood	-	-	-	700 (mo), 200 (ch)	-	-	-	-	-

Data pooling/combination studies

Evaluation of:

- Usefulness of existing inventories

- Cohort willingness and preparedness

- Ethical issues in data use

- Efforts needed to obtain data

- Comparability of data

Two approaches:

- Local analysis and subsequent meta-analysis

- Central data collection and meta- or pooled- analysis
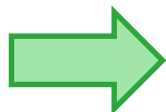
→ **Guidelines and recommendations**

Data pooling/combination studies

YES WE CAN!!

	N Cohorts	N Subjects
Socioeconomic inequalities in preterm delivery	12	>200,000
Maternal occupation and fetal growth	12	>200,000
Fish consumption and fetal growth	20	152,000
Early infant growth and childhood asthma	31	147,000
Maternal complications during pregnancy and childhood wheezing	14	114,000
PCBs and fetal growth	15	9,000
PCBs and respiratory health	9	4,600

11 studies already published and

11 more under development

Research initiatives

Mechanisms of the
Development of ALLergy

European Study of Cohorts for
Air Pollution Effects

Early Genetics Growth/Early Genetics and Lifecourse
Epidemiology

Novel tools for integrating early-life
environmental exposures and child
health across Europe

Enhanced exposure assessment
and omic profiling for high
priority environmental

Our plans for BRIDGE

Main aim: facilitate birth cohort's relationships

➢ **Merge** the ENRIECO inventory with the main birthcohort.net inventory in a unique platform and ask cohorts to update their information:

   ➢ New platform:

      ➢ easy to be completed by cohorts

      ➢ easy to find the information

      ➢ give general information about the cohort

   ➢ Update every year

   ➢ Promote joint analysis (guidelines, previous publications, new methodologies)

   ➢ Create working groups on specific exposures/outcomes

Our plans for BRIDGE

- ➢ **Identify new birth cohorts** in Europe and invite them to join the inventory

- ➢ **Up-date** ENRIECO contact lists

- ➢ **Newsletters** to update cohorts

- ➢ Update publications, reports, recommendations

Main challenge

→**Integration and Harmonization of cohort and registry data**

→ Barriers to cross-cohort analyses:

➢ Burden on collaborators of repeatedly preparing and analysis data

➢ Collaborators fear loss of ownership of the data

➢ Complex data-sharing or deposition agreements are needed

Main challenges

InterConnect: a global initiative on diabetes gene-environment interaction
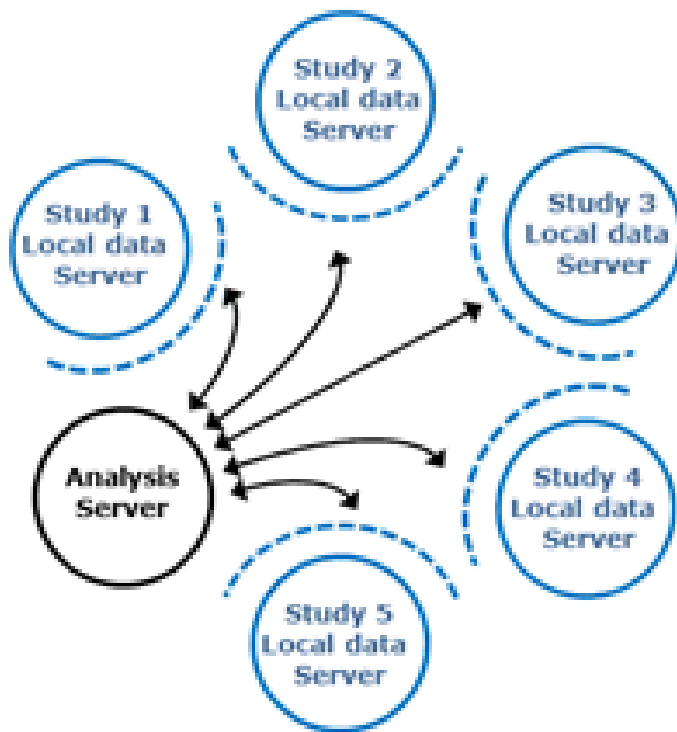
- Take the analysis to the data - federated analysis.
- Data stay within the governance structure of the cohort
- Analytical instructions and non-identifying summary parameters allowed to pass between computers
- Any user with appropriate log in credentials can remotely access the analysis server to run analysis code

InterConnect: a global initiative on diabetes gene-environment interaction

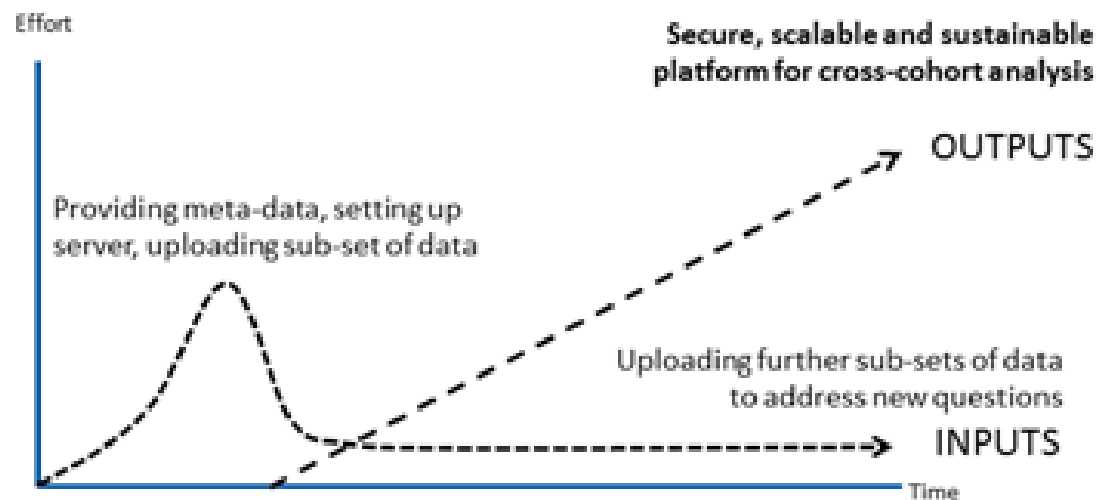You don't lose the controls of the data because the data is behind your local server firewall

You control the access and the analyses undertaken
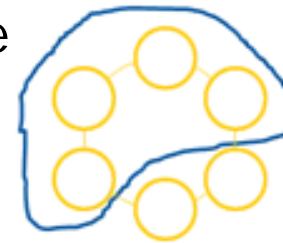
Consortium 1
Question A

Consortium 2
Question B

Effort

Secure, scalable and sustainable platform for cross-cohort analysis

OUTPUTS

Providing meta-data, setting up server, uploading sub-set of data

Uploading further sub-sets of data to address new questions

INPUTS

Time
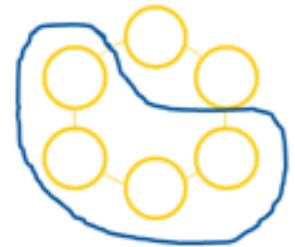
Main challenges

→ **Integration and Harmonization of cohort and registry data**

1. Already barriers to cross-cohort analyses

2. Consent forms - anonymization

3. Differences in linking routine and research data in Northern/Central vs Southern/Eastern European countries

4. Linkage with registries will facilitate data collection in birth cohorts (and collection of more data)

Contributors

Martine Vrijheid , CREAL
Mark Nieuwenhuijsen, CREAL
Anne-Marie Nybo Andersen

ENRIECO, CHICOS partners
And all birth cohorts participants!

ENRIECO

- Website: www.enrieco.org (reports publically available)
- Inventory: www.birthcohortsenrieco.net

CHICOS

- Website: www.chicosproject.eu (reports publically available)
- Inventory: www.birthcohorts.net