

MaMo Germany to I4C n≈120

A Wiesel

Birth Registry Mainz Model, University Children's Hospital Mainz, Germany

8th I4C International meeting, Oxford, November 2015

Aims of the Cooperation

- To incorporate the Mainz Cancer Cases to the check all collected items harmonizability with I4C
- Provide data on controls (no cancer, same MaMo data) if needed

Birth Registry Mainz Model (MaMo)

Initiated in 1990 after “Chernobyl” to

- detect congenital anomalies (CA), combinations and patterns
- define prevalence rates for CA
- causal relations to potential risk factors (known & unknown)

≈ 100,000 infants underwent standardized examination to date

Major research includes

- low dose ionizing radiation
- maternal drug intake
- artificial reproductive techniques

All of which might be relevant for the later development of cancer

MaMo

- Population based birth cohort (\approx 95% of all regional births)
- Livebirths, stillbirths, and abortions
- Standardized procedures, definitions, examination, coding
- Trained investigators (paediatricians; obstetric dept./ward)
- Anamnestic data taken before birth
- Prospective study design
 - *Anamnestic findings: family history, social state, pregnancy, environment*
 - *Clinical findings*
 - *Sonographic findings*
 - *Findings of the pathology*

MaMo monitored region

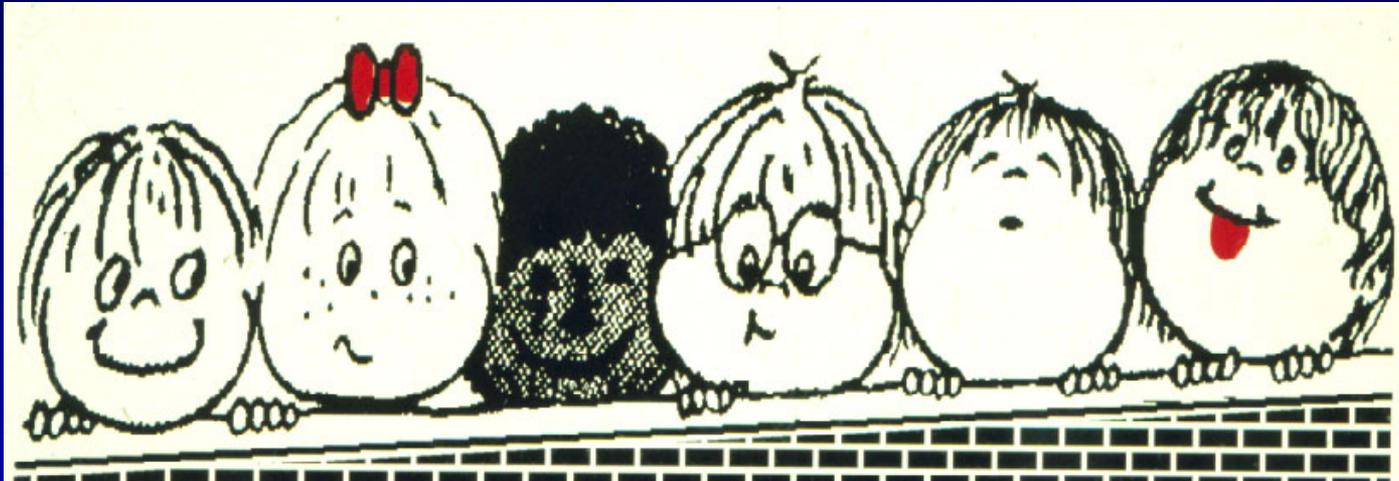
Germany



≈ 370,000 inhabitants and 3,600 births / year



Covering ≈ 95 % of all births in this region



Definition of CCC :

Children <15 years of age

- > Followed in the pediatric oncologic department
- > Re-identified by the place and date of birth

Outcome Childhood Cancer

Mainz Department of Pediatric Oncology

is the only regional center. 1,157 Children were diagnosed/treated between 1990 and 2012. Validated diagnoses by German reference centers (GPOH) and categorization by SIOP.

We have identified >120 infants in MaMo.

German Childhood Cancer Registry (GCCR)

- Founded in 1980, basic data collection on CCC since 1992
- Mandatory by law since 2007 (coverage >95%)
- >45,000 pseudonym cases up to date
- Data include: date & place of birth, and 1st diagnosis, type of cancer

> For further evaluation a cooperation is possible

MaMo goes I4C currently available

- > MaMo collects data on 64 items incl. renal ultrasound
- > I4C collects data on 36 items
- > After cross-checking and modifications
we identified **25 items** - including all core variables -
5 of which need a small adaptations

MaMo goes I4C add ons

➤ GIS data could be done on location at diagnosis, home history?

1) No biospecimens currently available

- accesable via studies/projects – hard to get

2) No DNA / Genotyping currently available

- could be recontacted and requested

need Ethics / data protection / GCCR approval

MaMo available (incl minor calculations)

VARIABLE	CORE POOLED DATASET	MoMa DAT
Maternal age	Age at delivery in years	
Paternal age, years	Continuous	
Marital status	Married	Living with partner
Maternal occupation	Focus of working group	Job title / Occup. risk - diff. CODE
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Prenatal folic acid supplementation	Dichotomous	
folate during pregnancy	Continuous	
Multivitamin use during pregnancy	Dichotomous	
Maternal, prenatal smoking	Any smoking during pregnancy	
Passive smoking, prenatal	Live with a smoker, exposed	paternal smoking / not obligatory
Maternal, prenatal alcohol consumption	maternal alcohol consumption	Alcohol abuse in pregnancy
Maternal prepregnancy BMI, kg/m2	categorized normal, overweight, obese	only obese (BMI >= 30kg/m2) Y/N
Maternal DM	Any type of DM	
Paternal DM	Any type of DM	
Parity (number of prior live births)	Parity grouped	
Gestation age, weeks	Continuous	
Birth weight, grams	Continuous	
Gender of index child	Male, Female	
Caeserean section delivery	Dichotomous	
Length at birth, cm	Continuous	
Head circumference at birth, cm	Continuous	
Congenital abnormality	Down Syndrome	ICD 9 codes
First born	Dichotomous	
Multiple births	Singleton, twin, triplet...	
Previous miscarriages	Dichotomous	
Medications during pregnancy		ATC codes

MaMo limits

VARIABLE	CORE POOLED DATASET	MaMo
Maternal education, years	Completed 12+ years of education	NO (could only be estimated for approx. 60% on valid grounds)
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Maternal pregnancy weight gain, kg	categorized into >16kg, ≤16kg based on IOM	NO
Maternal height, cm	Continuous	NO
Radiations exposure, prenatal	Any exposure to radiation during pregnancy	NO; only on population level by subgroup analysis of 1000 birth
Placental weight, grams	Continuous	NO
Breastfeeding	breastfeeding during first six months	NO
Pesticide exposure	Dichotomous	NO; only on population level by subgroup analysis of 1000 birth
Daycare attendance	Dichotomous	NO



Final Case Data Set & Controls

100 – 150 Childhood Cancer Cases

- All cases with cancer in the given time /region
- Data of the conducted therapy
- Follow up e.g. time of survival
 death
 development of secondary tumors

Estimates:

ALL / AML / anaplastic /	30%
CNS	20%
(Non-) Hodgking /	20%
Neuroblastoma	10%
Others	20%

Controls

Controls drawn from non-cancer infants of the MaMo
(identical ascertainment).

i.e.: 100 cases = 10,000 out of >75,000 eligible controls

Either selected randomly and/or matched

i.e. + sex (m/f)

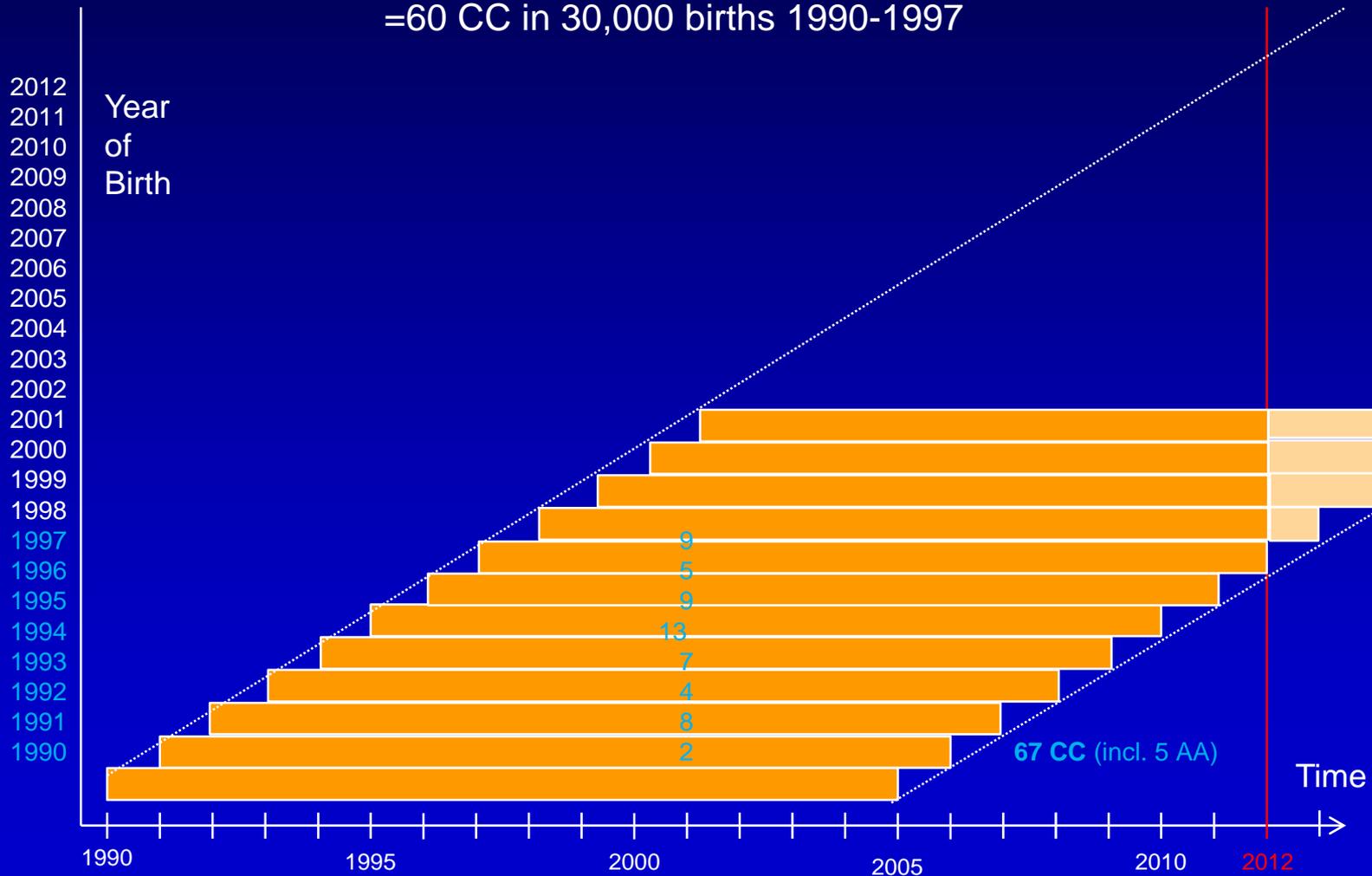
+ gestational month (+/- 2 month)

+ region (urban 2,000 inhabitants vs. rural 330 /square km)

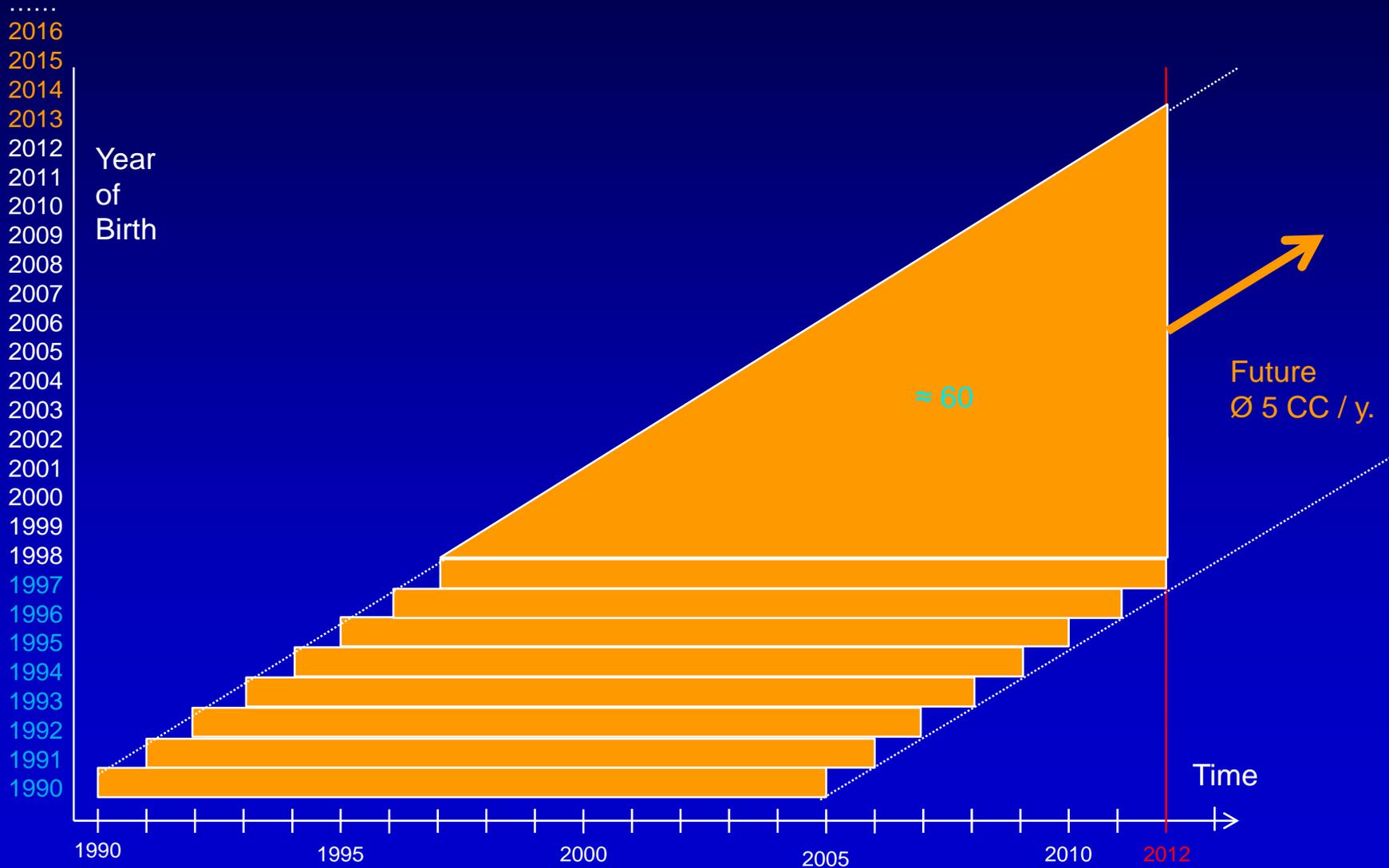
+ maternal age (+/- 3 years)

Completeness

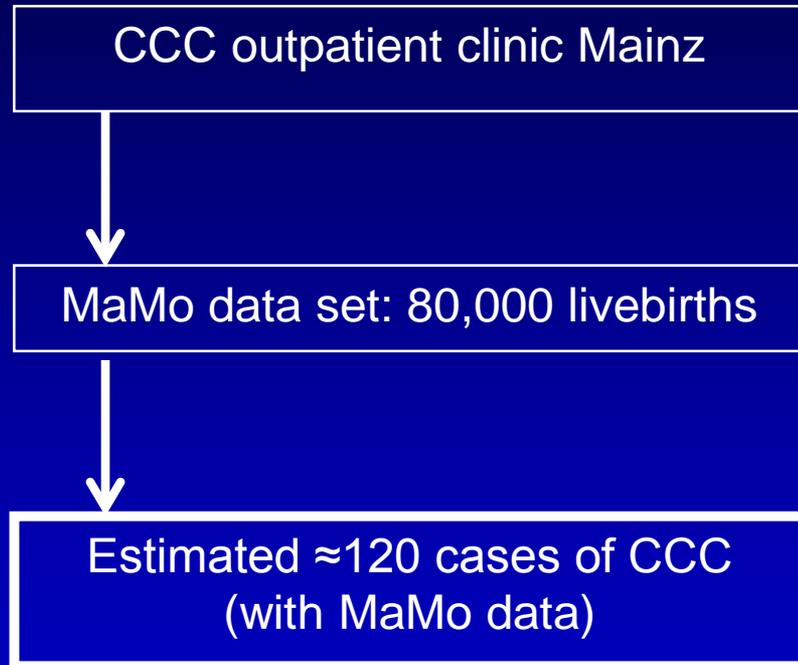
Estimate CC Incidence by GCCR 1 in 500
=60 CC in 30,000 births 1990-1997



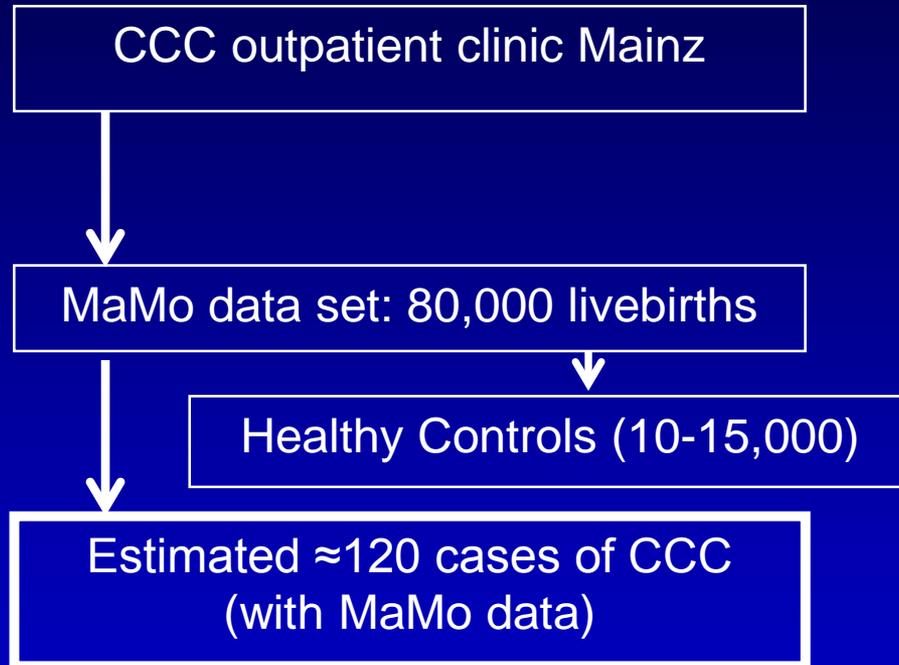
Estimate and Outlook



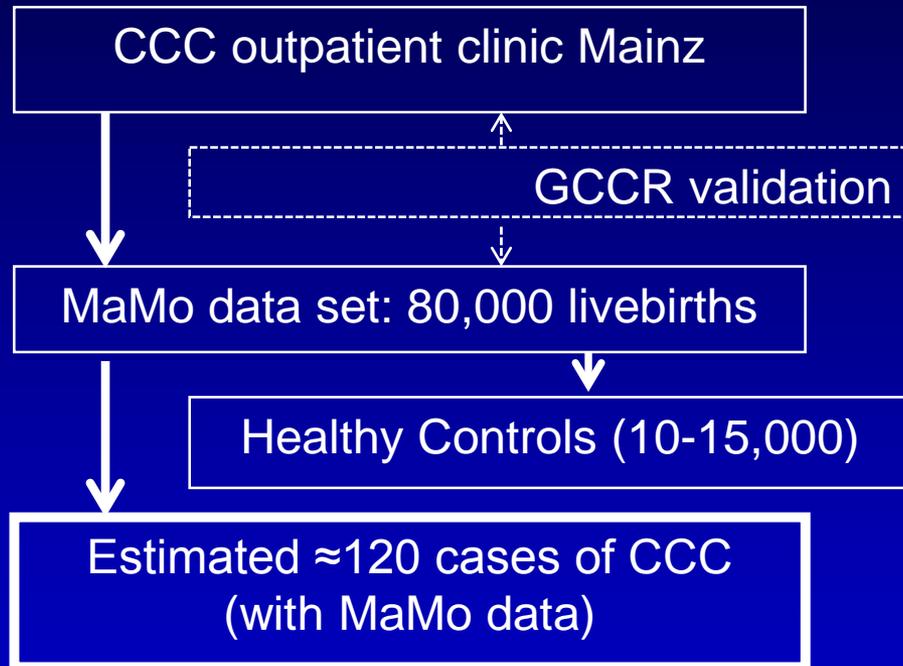
Chart



Chart



Chart



Thank you for the attention
Further questions ?



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Birth Registry Mainz Model

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Children's Hospital

UNIVERSITY MEDICAL CENTER

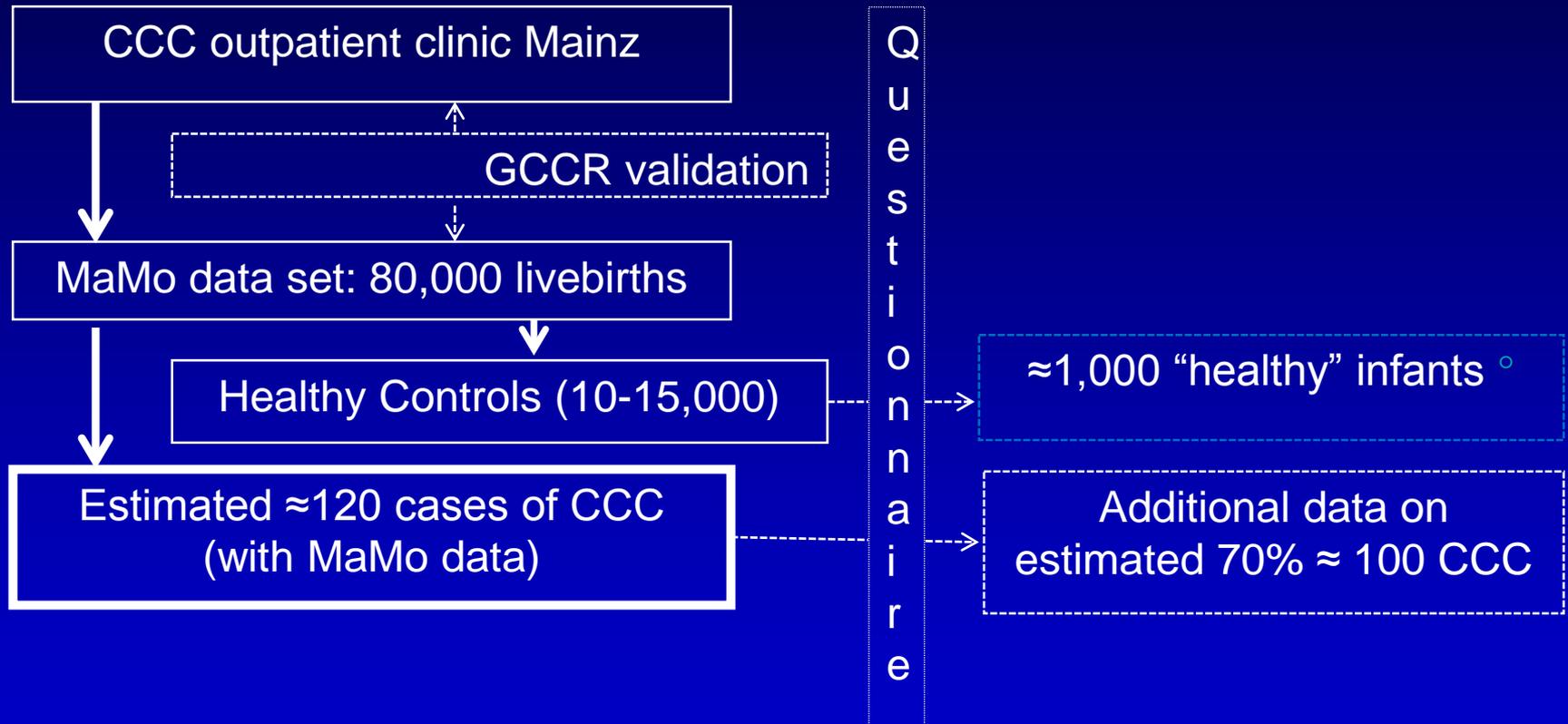
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Chart



◦ 10% participation rate estimated.
Potential recipients have to be selected (unlocking the pseudonym).

Time schedule / benchmarks

Approval for step1 March2015

Deliverable within 2 month after agreement

- CCC ≈100-120 and MaMo data	(210€/case)	25,000
- 10,000 healthy controls	(1€/control)	10,000

Optional (GCCR) validation of CCC by 10/2015		5,000

- Additional questionnaire to alive CCC by 10/2015		20,000*
+ <i>questionnaire to controls by 10/2015</i> †		
(estimated response rate 10%)		

* Incl. Q development, postal expenses (>10,000 letters), men power, computing, office prerequisites.