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## Unique registers and advanced family designs to address causes and consequences of common childhood disorders

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## Unique registers and advanced family designs ...

- Swedish Initiative for Research on Microdata in the Social And Medical Sciences (SIMSAM)
- Swedish Medical Research Council (Vetenskapsrådet)
- 1 January 2014 – 31 December 2018

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## Co-investigators

- Anastasia Iladou Nyman, MEB 
- Arvid Sjölander, MEB 
- Brian D'Onofrio, University of Indiana USA 
- Henrik Larsson, MEB 
- Paul Lichtenstein, MEB 
- Sara Öberg, MEB and Harvard School of Public Health 
- Tove Fall, Uppsala University 
- Yudi Pawitan, MEB 
- Catarina Almqvist Malmros, MEB and Astrid Lindgren Children's Hospital 

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## Aims

1. Causes and ...
2. ... consequences of common childhood disorders ...
3. ... to be addressed using unique registers and advanced family designs

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## Introduction

- most childhood disorders influenced by genetic and early environmental factors
- the effect of childhood disorders on subsequent development may be confounded by genetic and early environmental factors
- innovation – to apply advanced family (twin, sibling, and cousin-comparisons i.e. within twin/sibling/cousin) designs to account for confounding
- unique new and established health registers

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## Registers

<p><b>National Board of Health and Welfare</b></p> <ul style="list-style-type: none"> <li>▪ Medical Birth Register</li> <li>▪ National Patient Register</li> <li>▪ Prescribed Drug Register</li> </ul> <p><b>Statistics Sweden</b></p> <ul style="list-style-type: none"> <li>▪ Multi-Generation Register, Migration</li> <li>▪ LISA, Education, School registers</li> </ul> <p><b>Others</b></p> <ul style="list-style-type: none"> <li>▪ Conscript and Crime registers</li> <li>▪ Swedish Twin Registry</li> </ul>	<p><b>Quality health registers</b></p> <ul style="list-style-type: none"> <li>▪ PASTILL, Hab, Bipolär</li> <li>▪ RIKSÅT</li> <li>▪ Q-IVF</li> <li>▪ National Diabetes Register</li> </ul>
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## Family design

Figure 2. A traditional between-family analysis (upper panel) compares individuals from different families. A within-family analysis (lower panel) compares individuals within the same family (siblings or twins), thus adjusting for all potential confounders that are constant within the family

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## 1. To determine early risk factors for childhood disorders

**Aim 1a**

- infertility and the use of assisted reproductive techniques (ART)

**Aim 1b**

- pre- and perinatal factors, including medication use during pregnancy

**Aim 1c**

- early life exposure such as pets, antibiotics and socioeconomic factors

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## 2. To assess consequences of childhood disorders

**Aim 2a**

- the effect of early childhood disorders on *subsequent* somatic and psychiatric disorders, and social factors (socioeconomic status and mobility)

**Aim 2b**

- consequences of pharmacological treatment for common childhood disorders

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## 3. To develop statistical methods to address causal effects using genetically informed population based data

**Aim 3**

- have developed and will use family designs (within twin/sibling/individual designs) to rigorously test causal hypotheses
- identified a need for further methodological development
- to develop new models for estimating within and between-within effects

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## Cohorts

- CATSS** – Child and Adolescent Twin Study in Sweden; all 9-12 year old twins, N=24,000
- STOPPA** – Swedish Twin study On Perinatal characteristics to Prevent Asthma <http://ki.se/meb/stoppa>
  - MZ and DZ twins 9-14 years, discordant, concordant for asthma. Clinical examination for lung function, blood (DNA, serology), saliva (cortisol), fecal (µbiota) urine (metabolites)
- UppStART** – Uppsala-Stockholm Assisted Reproductive Techniques study PI Anastasia Iliadou Nyman <http://ki.se/meb/uppstart>
  - Couples followed; risk factors for unsuccessful treatment and short term health effects, growth and epigenetics in offspring
- Born into Life**
  - Women recruited from LifeGene, followed through pregnancy, delivery and children 6, 12 and 24 months
- MAESTRO** – Maternal Asthma Events, STress and Offspring <http://ki.se/meb/maestro>
  - Pregnant women recruited from antenatal clinics, followed through pregnancy and post-delivery

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## Budget

**Total**

- 19,660,000 SEK = 3,932,000 SEK/year

**Personnel**

- PhD students and Post-docs
  - cost equal to 50% FTE for four years per co-PI
- Research administrator, biostatistician, and database manager
- Guest researcher
- National coordination

**Other project-related costs**

- Register-based linkages
- Publication costs, travel to attend national and international meetings

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**Objectives of the national SIMSAM network**

**Create internationally leading research community for register-based research**

- conduct, support, initiate interdisciplinary research
- improve the quality of data
- enlarge pool of scientific knowledge produced
- support, share methodological developments to maximize the possibilities for the use of Swedish register data for research purposes
- encourage, take part in international research collaborations

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**Organization of the national SIMSAM network**

**Nodes and graduate school 2014-2018**

- Karolinska Institutet (KI) UGIR  
MEB family design  
SINGS
- Stockholm University (SU) SUNDEM
- Lund University (LU) SIMSAM Lund
- University of Gothenburg (GU) GOCARTs
- Institute for Future Studies (IF) SIMSEG

- Steering group
- National coordinator 50%
- [www.simsam.nu](http://www.simsam.nu)
- Scientific Advisory board (SAB)

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**SIMSAM**

Start Events About us Network nodes SINGS graduate school SIMSAM INFRA News archive Contact Links Svenska

**Start**

**News posts**

Statistics seminar at the University of Gothenburg May 21 20140506

Biobank WEBINAR May 23 Medical studies in the Multi-Generation Register 20140506

Biobanking news 20140423

Nordforsk funding opportunities focusing on "Health and Welfare" and "Nordic data resources" 20140408

Meeting on Big Data and e-Science in Medical Science at

SIMSAM is short for "Swedish Initiative for Research on Microdata in the Social And Medical Sciences", an initiative supported by the Swedish Research Council. By giving priority to interdisciplinary, innovative register-based research, SIMSAM will contribute to better public health and increased knowledge of social issues. For instance which factors in childhood that result in increased risk for obesity or cancer later in life. The initiative is also intended to promote improved and expanded use of registers in research and to increase the knowledge of how registry research is organized in Sweden and internationally. Six research nodes and one graduate school were granted funding for five years from December 2009 until November 2013. Principal investigators of nodes and a graduate school of a new SIMSAM five year period (2014-2018) were announced by the Swedish Research Council 4 November 2013.

UPCOMING EVENTS

21 SIMSAM steering group meeting @ Institute for Future Studies

18 Open national SIMSAM meeting on @ Karolinska Institutet

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**Focus of SIMSAM nodes**

- GOCARTs** Gothenburg Cardiovascular RegisTry Studies
- SIMSAM Lund** Interdisciplinary research on early life exposures in a life course perspective
- SIMSAM UGIR** Registry-based research of three associated public health concerns: upper gastrointestinal cancer, reflux and obesity
- SIMSEG** Dynamics of school segregation
- SUNDEM** Stockholm University SIMSAM Node for Demographic Research
- SIMSAM MEB Family Design** Unique registers and advanced family designs to address causes and consequences of common childhood disorders

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**Swedish INTERdisciplinary Graduate School in register-based research (SINGS)**

- Institute of Environmental Medicine (IMM) at KI
- Steering group: SIMSAM nodes + other research groups
- Interdisciplinary profile - quantitative research disciplines; epidemiology, public health, sociology, demography, psychology, statistics, health economics
- Objectives:
  - thorough knowledge of existing registers
  - ability to identify + formulate problems, use appropriate methods to perform register-based research
  - capacity to perform and assess register-based research, following laws and research ethical principles
  - methodological + practical skills when undertaking register-based research
  - insight into the possibilities and limitations of register-based research
- Cross-fertilisation between disciplines, communication within/outside SIMSAM
- First new cohort - fall semester 2014

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**Questions and answers on SINGS**

**How do you plan to organise the "new" SINGS?**

- A cohort of students for 2 years + a few positions per course/workshop for other doctoral students and post-docs – advertised broadly via [simsam.nu](http://simsam.nu) and nodes

**How many students are admitted per cohort?**

- 25-30

**What type of courses will be given?**

- core courses to be taken by all students and some elective courses given by 1) SINGS and 2) elsewhere.
- more advanced courses and in collaboration with KI epi-program and others, seminars online
- course givers get support on course design and intended learning outcomes

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## Questions and answers on SINGS, cont'd

**How many ECTS (högskolepoäng) in total for a full cohort curriculum?**

- 12 minimum, depending on number of courses taken

**Who sits on the SINGS steering committee?**

- Olof Akre, Coordinator SINGS (2014), Anita Berglund Director/Coordinator SINGS, Erik Bihagen, SUNSTRAT SU, Ilona Koupiol, CHES, Gunnar Andersson, SUNDEM SU, Xavier de Luna, Umeå SIMSAM, Kirk Scott, Early Life and SIMSEG Lund, Arvid Sjölander, SIMSAM MEB-family design, Anna Lindam, SIMSAM UGIR, PhD student reps + representatives SIMSAM UGIR and GOCARTs
- Eva Willis, Education and Economy Administrator SINGS (Cattis Bollö, IMM in new SINGS)

**When will the first SINGS course and cohort be announced?**

- positions will be announced end of May, courses to start end of fall, each cohort 2 years

<http://simsam.nu/sings-graduate-school/>

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## Scheduled meetings

- Big Data Stockholm 18 December
- GOCARTs Göteborg 4 mars 2015
- SIMSEG fall 2015

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## More information

- SIMSAM home page <http://simsam.nu/network-nodes/simsam-meb-family-design/>
- KI new home page <http://ki.se/en/meb/simsam-meb-family-design>
- Webb profile <http://ki.se/en/people/catalm>
- Barnläkaren (Journal of Swedish Pediatric Association) [www.barnlakaren.se](http://www.barnlakaren.se)
- SVEPET (Journal of Swedish Medical Society Section for Epidemiology) [www.svepet.se](http://www.svepet.se)

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## Thank you!

- The Swedish Research Council, VR
- MEB faculty collaborators
- SIMSAM-MEB PI Weimin Ye
- SFO-epi PI Nancy Pedersen
- Head(s) of Department Henrik Grönberg, Paul Lichtenstein
- Doctoral students
- Post-docs
- Database managers, biostatisticians, data collectors
- HR support and MEB economy

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